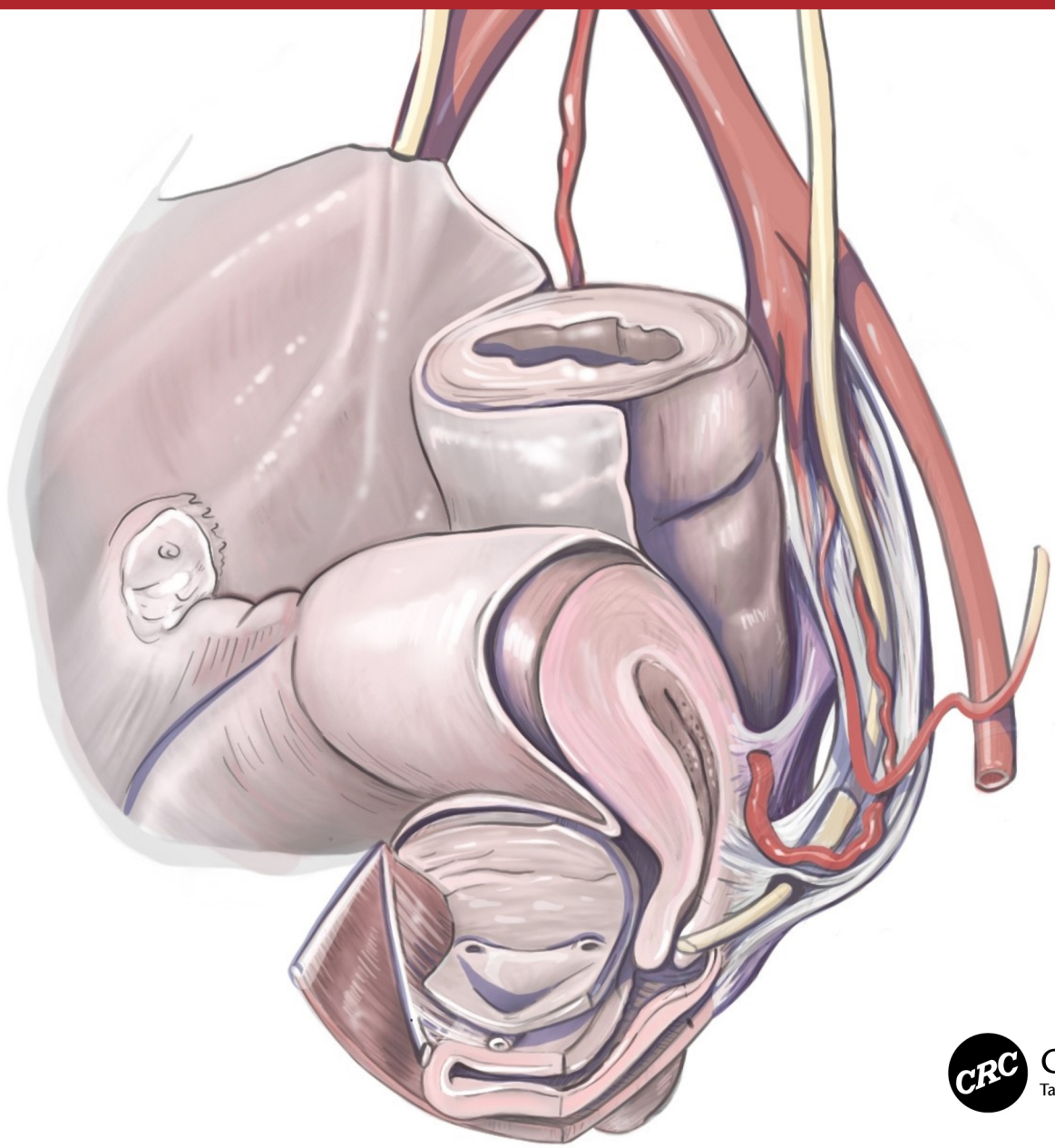
SUPPORT MATERIAL

TEXTBOOK OF MINIMALLY INVASIVE GYNECOLOGIC SURGERY

EDITED BY

ALI AZADI • JUBILEE BROWN
NASH S. MOAWAD • RESAD PAYA PASIC
MEGAN WASSON



CRC Press
Taylor & Francis Group

Textbook of Minimally Invasive Gynecologic Surgery

This comprehensive review of the field of gynecology with emphasis on minimally invasive approaches, with contributions from more than 100 experts in the field, presents a great resource for fellows and residents seeking to master complex gynecology and minimally invasive gynecologic skills.

Features

- Epidemiology, relevant anatomy, pathology, and diagnosis of common gynecological conditions
- Presents state-of-the-art hysteroscopic management of gynecological conditions
- Chapters dedicated to endometriosis, including diagnostic tools and imaging, treatment strategies, medical management, and complex surgical treatment approaches
- Overview of urogynecology and gynecologic oncology relevant to minimally invasive surgeons
- A comprehensive review of minimally invasive gynecology, including laparoscopic, robotic, hysteroscopic, and vaginal surgery, including vNOTES

Taylor & Francis
Taylor & Francis Group
http://taylorandfrancis.com

Textbook of Minimally Invasive Gynecologic Surgery

Edited by

Ali Azadi, MD, MSc
Associate Professor, Urogynecology & Minimally Invasive Gynecologic Surgery
University of Arizona & Creighton University School of Medicine, Phoenix, Arizona

Jubilee Brown, MD
Professor, Gynecology Oncology & Minimally Invasive Gynecologic Surgery
Wake Forest University, Charlotte, North Carolina

Nash S. Moawad, MD, MS
Professor, Minimally Invasive Gynecologic Surgery
University of Florida College of Medicine, Gainesville, Florida

Resad Paya Pasic, MD, PhD
Professor, Minimally Invasive Gynecologic Surgery
University of Louisville School of Medicine, Louisville, Kentucky

Megan Wasson, DO
Professor, Minimally Invasive Gynecologic Surgery
Mayo Clinic, Phoenix, Arizona

CRC Press
Taylor & Francis Group
Boca Raton London New York

CRC Press is an imprint of the
Taylor & Francis Group, an **informa** business

Designed cover image: Dr Polina Sawyer

First edition published 2026
by CRC Press
2385 NW Executive Center Drive, Suite 320, Boca Raton, FL 33431

and by CRC Press
4 Park Square, Milton Park, Abingdon, Oxon, OX14 4RN

CRC Press is an imprint of Taylor & Francis Group, LLC

© 2026 selection and editorial matter, Ali Azadi, Jubilee Brown, Nash S. Moawad, Resad Paya Pasic, and Megan Wasson; individual chapters, the contributors

This book contains information obtained from authentic and highly regarded sources. While all reasonable efforts have been made to publish reliable data and information, neither the authors nor the publisher can accept any legal responsibility or liability for any errors or omissions that may be made. The publishers wish to make clear that any views or opinions expressed in this book by individual editors, authors or contributors are personal to them and do not necessarily reflect the views/opinions of the publishers. The information or guidance contained in this book is intended for use by medical, scientific or health-care professionals and is provided strictly as a supplement to the medical or other professional's own judgement, their knowledge of the patient's medical history, relevant manufacturer's instructions and the appropriate best practice guidelines. Because of the rapid advances in medical science, any information or advice on dosages, procedures or diagnoses should be independently verified. The reader is strongly urged to consult the relevant national drug formulary and the drug companies' and device or material manufacturers' printed instructions, and their websites, before administering or utilizing any of the drugs, devices or materials mentioned in this book. This book does not indicate whether a particular treatment is appropriate or suitable for a particular individual. Ultimately it is the sole responsibility of the medical professional to make his or her own professional judgements, so as to advise and treat patients appropriately. The authors and publishers have also attempted to trace the copyright holders of all material reproduced in this publication and apologize to copyright holders if permission to publish in this form has not been obtained. If any copyright material has not been acknowledged please write and let us know so we may rectify in any future reprint.

Except as permitted under U.S. Copyright Law, no part of this book may be reprinted, reproduced, transmitted, or utilized in any form by any electronic, mechanical, or other means, now known or hereafter invented, including photocopying, microfilming, and recording, or in any information storage or retrieval system, without written permission from the publishers.

For permission to photocopy or use material electronically from this work, access www.copyright.com or contact the Copyright Clearance Center, Inc. (CCC), 222 Rosewood Drive, Danvers, MA 01923, 978-750-8400. For works that are not available on CCC please contact mpkbookspermissions@tandf.co.uk

Trademark notice: Product or corporate names may be trademarks or registered trademarks and are used only for identification and explanation without intent to infringe.

ISBN: 978-1-032-31939-1 (hbk)
ISBN: 978-1-032-31940-7 (pbk)
ISBN: 978-1-003-31210-9 (ebk)

DOI: 10.1201/9781003312109

Typeset in Warnock Pro
by Apex CoVantage, LLC

Access the Support Material: www.routledge.com/9781032319407

CONTENTS

Editors viii
Contributors ix

1 Laparoscopy through a Historical Lens 1
Rebecca Barbaresso, Jerar Palian, Zoë Pennington, Rana Khaloghi, Roya Taghavi, Elif Polat, and Resad Paya Pasic

2 Pelvic Anatomy and the Art of Surgical Dissection 8
Polina Sawyer and Robert Rogers

3 Physiology of the Female Reproductive Tract 16
Archana Ayyar, Emily Marra, Lauren Griebel, and Rebecca Flyckt

4 Epidemiology, Research Methods, Statistics, and Outcome Measurements 22
Ritchie Delara and James Symanowski

5 Perioperative Considerations and Enhanced Recovery After Surgery (ERAS) 28
Gregg Nelson, Jennifer Mateshaytis, Simrit K. Warring, and Sean C. Dowdy

6 Principles of Laparoscopic and Robotic Surgery 34
Megan Cesta and Natalie Wallace

7 Principles of Vaginal Surgery and vNOTES 47
Ali Azadi, Jan Baekelandt, and Greg Marchand

8 Energy Systems in Laparoscopy 55
Andrew I. Brill

9 Imaging and Imaging-Guided Interventions in Minimally Invasive Gynecologic Surgery 66
Scott W. Young

10 Suture, Mesh, and Grafts 72
Meghan Hagedorn and Amy Park

11 Medical and Surgical Management of Ectopic Pregnancy 79
Raanan Meyer, Kacey Hamilton, Mireille Truong, Matthew Siedhoff, and Kelly Wright

12 Evaluation of Women and Adolescent Girls with Abnormal Uterine Bleeding (AUB) in the Reproductive Years 94
Malcolm G. Munro

13 Uterine Leiomyoma: Pathophysiology, Symptomatology, and Evaluation 108
Radmila Sparić, Mladen Anđić, and Andrea Tinelli

14 Adenomyosis: From Pathophysiology to Symptomatology and Evaluation 117
Giovanni Pecorella, Roberta Montefrancesco, and Andrea Tinelli

15 Laparoscopic and Robotic Myomectomy 133
Shan Biscette and Nita Desai

16 Laparoscopic and Robotic-Assisted Hysterectomy 139
Olanrewaju Dawodu, Briana Baxter, Natalia Parra, and Jin Hee Kim

17 Alternative Management of Leiomyoma (Including RF and UAE) 150
Sarah Allen and Richard Guido

18 Evaluation and Management of Chronic Pelvic Pain 156
Erin T. Carey and Asha McClurg

19 Principles of Neuropelveology 166
Marc Possover, Varnita Vishwanath, and Ali Azadi

20 Endometriosis: Diagnosis and Pathophysiology 175
Guilherme Henrique Zanluchi, Marina Paula Andres, and Mauricio S. Abrão

21 Medical Management of Endometriosis 179
Papri Sarkar, Devon Marks, Maha Al Jumaily, and Emad Mikhail

22 Surgical Management of Pelvic Endometriosis and Endometrioma 187
Mario Malzoni, Megan Wasson, Luca Nardone, Giorgia Poppi, Maria Cristina Solazzo, Alessia Oliviero, and Francesca Falcone

23 Extrapelvic Endometriosis 192
Ricardo M.A. Pereira

24 Surgical Management of Gastrointestinal and Genitourinary Endometriosis 204
Eung-Mi Lee and Ted Lee

25 Fertility Considerations in Management of Endometriosis 216
Jack Przebienda, Elliott G. Richards, and Tommaso Falcone

26 Office Hysteroscopy 222
Aparna Ramanathan, Mariam Barseghyan, and James K. Robinson

27 Hysteroscopy for Abnormal Uterine Bleeding (Diagnostic, Polyps, Visually Guided Biopsy, Myomectomy) 232
Salvatore Giovanni Vitale, Gilda Sicilia, Antonio Succu, Stefano Angioni, and Jose Carugno

28 Hysteroscopy and Müllerian Anomalies 242
Maria Chiara De Angelis, Virginia Foreste, Alfonso Manzi, Alessandra Gallo, Serena Guerra, Brunella Zizolfi, and Attilio Di Spiezio Sardo

29 Hysteroscopy and Early Pregnancy Loss (Missed AB, RPOC, Tissue Removal Systems) 252
Salvatore Giovanni Vitale, Gilda Sicilia, Stefania Saponara, Jose Carugno, and Stefano Angioni

30 Asherman Syndrome; Hysteroscopically Diagnosed Intrauterine Adhesions 260
Miriam M.F. Hanstede and Esther A.M. Kuijper

31 Cesarean Scar Defect (Isthmocele) 268
Sergio Haimovich and Noam Smorgick

32 Tubal Sterilization 274
Nicole Afuape and Danielle Dukes

33 Tuboplasty 280
William Nolan and Naomi Whittaker

34 Pediatric and Adolescent Gynecology: MIGS Considerations for Our Youngest Patients 287
Lissa Yu and Kate McCracken

35 Surgical Management of Female Reproductive Anomalies 293
Leila V. Adamyan and Assia A. Stepanian

36 Genitourinary Syndrome of Menopause and Energy-Based Therapies 304
Johnathan Pai and Bobby Garcia

37 Hereditary Malignancies, Genetic Testing, and Risk-Reducing Surgeries 308
Yovanni Casablanca

38 Adnexal Masses 314
Tullia Rushton, Rebecca L. Stone, and Amanda N. Fader

39 Minimally Invasive Surgery Applications for the Care of Women with Epithelial Ovarian Cancer 321
Roni Nitecki and J. Alejandro Rauh-Hain

40 Uterine Cancer 327
Emma Rossi

41 Cervical Cancer 342
R. Wendel Naumann

42 The Role of Minimally Invasive Surgery in the Management of Gestational Trophoblastic Disease 355
Neil Horowitz

43 Laparoscopic Colostomy 359
Vance Broach

44 Pelvic Organ Prolapse and Stress Urinary Incontinence 362
Kate V. Meriwether

45 Pelvic Floor Dysfunction 379
Rodger Rothenberger, Sean Francis, and Ankita Gupta

46 Fistulas and Repair of Obstetric Lacerations 392
Emily E. Weber LeBrun and Veronica O. Demtchouk

47 Urethral Diverticula and Vaginal Cysts 403
K. Marie Douglass and Tajnoos Yazdany

48 Cystoscopy, Urinary Stents, and Suprapubic Tubes to Assist with Pelvic Surgery 409
Paige K. Kuhlmann, Kris E. Gaston, and Philippe Zimmern

49 Cosmetic Gynecology 415
Bayley Clarke, Cheryl Iglesia, and Wakako Horiuchi

50 Avoidance and Management of Laparoscopic Complications 421
Shivani Parikh, Hosam Hanna, and Resad Paya Pasic

51 Hemostatic Agents in Gynecologic Surgery 429
Traci Ito

52 Anesthesia in Laparoscopy 433
Daisy Sangroula, Jeremy Haysley, Alexander Bautista, and Laura Clark

53 Transabdominal Cerclage 439
Jamal Mourad

54 Principles of Fetal Surgery 445
Eyal Krispin and Alireza A. Shamshirsaz

55 Obesity and Minimally Invasive Gynecology 452
Jordann-Mishael Duncan, Gina Ranieri, and Michelle Louie

56 Innovations and Medical Devices 457
S. Abbas Shobeiri

57 Informed Consent in Minimally Invasive Gynecologic Surgery 464
Isabelle C. Band and Louise P. King

Index 469

EDITORS

Ali Azadi is Associate Professor of Obstetrics and Gynecology at the University of Arizona and Creighton University, Phoenix campus. He is a fellowship trained urogynecologist and is double board certified in gynecology and urogynecology. Dr. Azadi is also certified in minimally invasive gynecology surgery (MIGS Practice Focus). He has over 50 peer-reviewed publications and authored book chapters and has served as editor of textbooks. He has a master's degree in clinical research in addition to a master's degree in business administration in healthcare management.

Jubilee Brown is Professor of Obstetrics and Gynecology at Wake Forest University and Division Director of Gynecologic Oncology at Atrium Health Wake Forest University in Charlotte, North Carolina. She is the past President of the AAGL and the President Elect II of the Society of Gynecologic Oncology. She is the Experiential Lead in Gynecologic Oncology of IRCAD North America and the Co-Chair of the NRG Oncology Rare Tumor Committee. She has over 150 peer-reviewed publications, has edited three textbooks, and has lectured on five continents. Her research focuses on minimally invasive surgery and rare ovarian cancer, and she has dedicated decades to the mentorship of fellows, residents, and students.

Nash S. Moawad is Professor, Division Chief, and the Program Director of the Center of Excellence in Minimally Invasive Gynecologic Surgery (COEMIG) and the Center of Excellence in Complex Endometriosis Care (COECEC) at the University of Florida College of Medicine. He serves as the Secretary-Treasurer on the board of directors of the AAGL and chairs the steering committee of EMIGS. He completed his fellowship training in MIGS at Magee–Womens Hospital of the University of Pittsburgh Medical Center and has built a successful practice at UF Health that is dedicated to laparoscopic and robotic surgery for complex endometriosis, pelvic pain, fibroids, abnormal uterine bleeding, and Müllerian anomalies, with a special interest in fertility-sparing surgery. In addition, he has developed a successful program of office and operative intrauterine surgery. The author of numerous scientific articles, book chapters, and a clinical case book on fibroids, he is also an international speaker and a subject matter expert on advanced laparoscopic, robotic, and hysteroscopic surgery.

Resad Paya Pasic is Professor of Obstetrics and Gynecology and Director of the Fellowship in Minimally Invasive Gynecologic Surgery at the Department of Obstetrics and Gynecology and Women's Health at the University of Louisville. Dr. Pasic is internationally recognized as a leader in MIGS: he has published 6 textbooks, 62 peer-reviewed articles, 77 abstracts, 42 book chapters, and 61 educational videos. Dr. Pasic has been a speaker at conferences and courses and he has performed numerous live tele-surgeries worldwide. He has educated 24 MIGS AAGL fellows and 35 generations of OB/GYN residents. Dr. Pasic has served as a member of the board of trustees of AAGL and in 2009 he served as its president. He has also served as the fellowship Board Director for Minimally Invasive Gynecology in 2011 and as President of the International Society of Gynecologic Endoscopy ISGE 2018–2020. For more information about Dr. Pasic's professional accomplishments, please visit his personal website: www.gynlaparoscopy.com.

Megan Wasson is the Chair of the Department of Medical and Surgical Gynecology at Mayo Clinic in Arizona. She is Professor of Obstetrics and Gynecology at the Mayo Clinic College of Medicine and Science and was awarded the Outstanding Emerging Educator Award in 2020. She completed her fellowship in minimally invasive gynecologic surgery at the Mayo Clinic in Arizona. She is a fellow of the American College of Obstetricians and Gynecologists (FACOG) and of the American College of Surgeons (FACS). Dr. Wasson is actively involved in multiple national and international medical societies and committees, including Immediate Past Chair of the International Federation of Gynecology and Obstetrics (FIGO) Minimal Access Surgery Committee, Director of AAGL Essentials in Minimally Invasive Gynecologic Surgery (EMIGS) Curriculum, former member of the Fellowship in Minimally Invasive Gynecologic Surgery (FMIGS) Board of Directors, Co-Founder of the FMIGS Young Alumni Network, and former member of the Surgery Board of Directors. She is the incoming Division Director for FIGO's Division of Benign Surgery. Her clinical interests include endometriosis, chronic pelvic pain, and robotic and minimally invasive gynecologic surgery.

CONTRIBUTORS

Mauricio S. Abrão
Gynecology Department, FMIGS – BP – A Beneficência Portuguesa de São Paulo
Department of Obstetrics and Gynecology, Faculdade de Medicina FMUSP
Universidade de São Paulo
São Paulo, SP, Brazil

Leila V. Adamyan
Department of Reproductive Medicine and Surgery
A.I. Evdokimov Moscow State University of Medicine and Dentistry
Moscow, Russia

Nicole Afuape
Advanced Gynecologic Surgery and Pelvic Pain
Creighton University
Phoenix, AZ, USA

Stefano Angioni
Division of Gynecology and Obstetrics
Department of Surgical Sciences
University of Cagliari
Cagliari, Italy

Sarah Allen
UPMC Magee–Womens Hospital
Pittsburgh, PA, USA

Mladen Anđić
Clinic for Gynecology and Obstetrics
Clinical Centre of Serbia
Belgrade, Serbia

Marina Paula Andres
Gynecology Department, FMIGS – BP – A Beneficência Portuguesa de São Paulo
Department of Obstetrics and Gynecology, Faculdade de Medicina FMUSP
Universidade de São Paulo
São Paulo, SP, Brazil

Archana Ayyar
Department of OB/GYN
University Hospitals Cleveland Medical Center
Case Western Reserve University
Cleveland, OH, USA

Jan Baekelandt
Imelda Hospital
Bonheiden, Belgium

Isabelle C. Band
Icahn School of Medicine at Mount Sinai
New York City, NY, USA

Rebecca Barbaresso
Advanced Gynecologic Endoscopic Surgery
University in Louisville
Louisville, KY, USA

Mariam Barseghyan
Reproductive Endocrinology and Infertility
Augusta University Health
Augusta, GA, USA

Alexander Bautista
Department of Anesthesiology and Perioperative Medicine
University of Louisville
Louisville, KY, USA

Briana Baxter
Department of Obstetrics and Gynecology
Columbia University Irving Medical Center
New York City, NY, USA

Shan Biscette
Atrium Health Women's Care
Urogynecology and Pelvic Surgery
Charlotte, NC, USA

Andrew I. Brill
Minimally Invasive Gynecology
California Pacific Medical Center
San Francisco, CA, USA

Vance Broach
Memorial Sloan Kettering Cancer Center
New York City, NY, USA

Erin T. Carey
Department of Obstetrics and Gynecology
Division of Minimally Invasive Gynecologic Surgery
University of North Carolina
Chapel Hill, NC, USA

Jose Carugno
Minimally Invasive Gynecology Division
Obstetrics, Gynecology, and Reproductive Sciences Department
Miller School of Medicine
University of Miami
Miami, FL, USA

Yovanni Casablanca
Division of Gynecologic Oncology
Levine Cancer Institute at Atrium Health
Wake Forest University
Charlotte, NC, USA

Megan Cesta
Obstetrics and Gynecology
Summa Health Pelvic Health
Akron, OH, USA

Laura Clark
Department of Anesthesiology and Perioperative Medicine
University of Louisville
Louisville, KY, USA

Bayley Clarke
MedStar Washington Hospital Center
Washington, DC, USA

Olanrewaju Dawodu
Department of Obstetrics and Gynecology
Columbia University Irving Medical Center
New York City, NY, USA

Maria Chiara De Angelis
Department of Public Health
University of Naples "Federico II"
Napoli, Italy

Ritchie Delara
Division of Gynecologic Oncology
Levine Cancer Institute at Atrium Health
Wake Forest University
Charlotte, NC, USA

Veronica O. Demtchouk
Division of Female Pelvic Medicine and Reconstructive Surgery
University of Florida
Gainesville, FL, USA

Nita Desai
Atrium Health Women's Care
Urogynecology and Pelvic Surgery
Charlotte, NC, USA

K. Marie Douglass
Harbor–UCLA Department of OB/GYN
Division of Urogynecology
West Carson, CA, USA

Sean C. Dowdy
Department of Obstetrics and Gynecology
Mayo Clinic
Rochester, MN, USA

Danielle Dukes
Department of Obstetrics and Gynecology
Creighton University
Phoenix, AZ, USA

Jordann-Mishael Duncan
Department of Medical and Surgical Gynecology
Mayo Clinic in Arizona
Phoenix, AZ, USA

Amanda N. Fader
Kelly Gynecologic Oncology Service
Department of Gynecology and Obstetrics
Johns Hopkins School of Medicine
Baltimore, MD, USA

Francesca Falcone
Department of Medical and Surgical Gynecology
Mayo Clinic in Arizona
Phoenix, AZ, USA

Tommaso Falcone
Cleveland Clinic
Cleveland, OH, USA

Rebecca Flyckt
Department of OB/GYN
University Hospitals Cleveland Medical Center
Case Western Reserve University
Cleveland Clinic
Cleveland, OH, USA

Virginia Foreste
Department of Public Health
University of Naples "Federico II"
Napoli, Italy

Sean Francis
Division of Female Pelvic Medicine and Reconstructive Surgery
University of Louisville
Louisville, KY, USA

Alessandra Gallo
Department of Public Health
University of Naples "Federico II"
Napoli, Italy

Bobby Garcia
Female Pelvic Medicine and Reconstructive Surgery
University of California Riverside
Riverside, CA, USA

Kris E. Gaston
Department of Urology
University of Texas Southwestern Medical Center
Dallas, TX, USA

Lauren Griebel
Department of OB/GYN
University Hospitals Cleveland Medical Center
Case Western Reserve University
Cleveland, OH, USA

Serena Guerra
Department of Public Health
University of Naples "Federico II"
Napoli, Italy

Richard Guido
UPMC Magee–Womens Hospital
Pittsburgh, PA, USA

Ankita Gupta
Division of Female Pelvic Medicine and Reconstructive Surgery
University of Louisville
Louisville, KY, USA

Meghan Hagedorn
Cleveland Clinic
Cleveland, OH, USA

Sergio Haimovich
Endometrial Pathology Hysteroscopy Unit
Gynecology and Obstetrics Department
Del Mar University Hospital
Barcelona, Spain

Kacey Hamilton
Division of Minimally Invasive Gynecologic Surgery
Department of Obstetrics and Gynecology
Cedars-Sinai Medical Center
Los Angeles, CA, USA

Hosam Hanna
Minimally Invasive Gynecologic Surgery
University of Louisville School of Medicine
Louisville, KY, USA

Miriam M.F. Hanstede
Academisch Medisch Centrum
Universiteit van Amsterdam
Amsterdam, Netherlands

Jeremy Haysley
Department of Anesthesiology and Perioperative Medicine
University of Louisville
Louisville, KY, USA

Wakako Horiuchi
Obstetrics and Gynecology
MedStar Washington Hospital Center
Washington, DC, USA

Neil Horowitz
Obstetrics, Gynecology, and Reproductive Biology
Harvard Medical School and Dana-Farber Cancer Institute
Brigham and Women's Hospital
Boston, MA, USA

Cheryl Iglesia
Obstetrics and Gynecology
MedStar Washington Hospital Center
Washington, DC, USA

Traci Ito
Minimally Invasive Gynecology Surgery
University of California
San Francisco, CA, USA

Maha Al Jumaily
Department of Obstetrics and Gynecology
University of South Florida
Tampa, FL, USA

Rana Khaloghi
Camran Nezhat Institute
Woodside, CA, USA

Jin Hee Kim
Department of Obstetrics and Gynecology
Columbia University Irving Medical Center
New York City, NY, USA

Louise P. King
Obstetrics, Gynecology, and Reproductive Biology
Harvard Medical School
Boston, MA, USA

Eyal Krispin
Maternal Fetal Care Center
Boston Children's Hospital
Boston, MA, USA

Paige K. Kuhlmann
Department of Urology
University of Texas Southwestern Medical Center
Dallas, TX, USA

Esther A.M. Kuijper
Center for Reproductive Medicine
Amsterdam UMC
Amsterdam, Netherlands

Emily E. Weber LeBrun
Urogynecology and Reconstructive Pelvic Surgery
University of Florida
Gainesville, FL, USA

Eung-Mi Lee
Obstetrics and Gynecology
Weill Cornell Medical College
New York City, NY, USA

Ted Lee
Minimally Invasive Gynecologic Surgery
NYU Langone
New York City, NY, USA

Michelle Louie
Department of Medical and Surgical Gynecology
Mayo Clinic in Arizona
Phoenix, AZ, USA

Mario Malzoni
Endoscopica Malzoni
Center for Advanced Endoscopic Gynecologic Surgery
Avellino, Italy

Alfonso Manzi
Department of Public Health
University of Naples "Federico II"
Napoli, Italy

Greg Marchand
Minimally Invasive Gynecologic Surgery
Marchand Institute for Minimally Invasive Surgery
Mesa, AZ, USA

Devon Marks
University of South Florida Morsani College of Medicine
Tampa, FL, USA

Emily Marra
Department of OB/GYN
University Hospitals Cleveland Medical Center
Case Western Reserve University
Cleveland, OH, USA

Jennifer Mateshaytis
Department of Obstetrics and Gynecology
University of Calgary
Calgary, Alberta, Canada

Asha McClurg
Department of Obstetrics and Gynecology
Division of Minimally Invasive Gynecologic Surgery
University of North Carolina
Chapel Hill, NC, USA

Kate McCracken
Department of Obstetrics and Gynecology
University of Michigan and Von Voigtlander Women's Hospital
Ann Arbor, MI, USA

Kate V. Meriwether
Obstetrics and Gynecology
University of New Mexico
Albuquerque, NM, USA

Raanan Meyer
Division of Minimally Invasive Gynecologic Surgery
Department of Obstetrics and Gynecology
Cedars-Sinai Medical Center
Los Angeles, CA, USA

Emad Mikhail
Division of Gynecologic Subspecialties
Department of Obstetrics and Gynecology
University of South Florida
Tampa, FL, USA

Roberta Montefrancesco
Department of Obstetrics and Gynecology and CERICSAL (CEntro di RIcerca Clinico SALentino)
"Verisdelli Ponti Hospital," Scorrano
Lecce, Italy

Jamal Mourad
Obstetrics and Gynecology
Mayo Clinic in Arizona
Phoenix, AZ, USA

Malcolm G. Munro
Department of Obstetrics and Gynecology
David Geffen School of Medicine at UCLA
Los Angeles, CA, USA

Luca Nardone
Endoscopica Malzoni
Center for Advanced Endoscopic Gynecologic Surgery
Avellino, Italy

R. Wendel Naumann
Levine Cancer Institute at Atrium Health Wake Forest University
Charlotte, NC, USA

Gregg Nelson
Department of Obstetrics and Gynecology
University of Calgary
Calgary, Alberta, Canada

Roni Nitecki
Department of Gynecologic Oncology and Reproductive Medicine
The University of Texas MD Anderson Cancer Center
Houston, TX, USA

William Nolan
Department of Obstetrics and Gynecology
University of Louisville
Louisville, KY, USA

Alessia Oliviero
Endoscopica Malzoni
Center for Advanced Endoscopic Gynecologic Surgery
Avellino, Italy

Johnathan Pai
Hematology/Oncology
University of California at San Francisco
San Francisco, CA, USA

Jerar Palian
Public Health Services
University of California Irvine
Irvine, CA, USA

Shivani Parikh
Department of Obstetrics, Gynecology, and Women's Health
University of Louisville
Louisville, KY, USA

Amy Park
Obstetrics & Gynecology and Women's Health Institute
Cleveland Clinic
Cleveland, OH, USA

Natalia Parra
Department of Obstetrics and Gynecology
Columbia University Irving Medical Center
New York City, NY, USA

Giovanni Pecorella
Department of Obstetrics and Gynecology
CERICSAL (CEntro di RIcerca Clinico SALentino)
"Verisdelli Ponti Hospital," Scorrano
Lecce, Italy

Zoë Pennington
Center for Special Minimally Invasive and Robotic Surgery
Redwood City, CA, USA

Ricardo M.A. Pereira
Center of Endometriosis and Minimally Invasive Gynecologic Surgery
Santa Joana Hospital
São Paulo, Brazil

Elif Polat
Camran Nezhat Institute
Palo Alto, CA, USA

Giorgia Poppi
Endoscopica Malzoni
Center for Advanced Endoscopic Gynecologic Surgery
Avellino, Italy

Marc Possover
Possover International Medical Center
Zurich, Switzerland

Jack Przebienda
Northeast Ohio Medical University
Rootstown, OH, USA

Aparna Ramanathan
OB/GYN and Primary Care
UW Medical Center Roosevelt
Seattle, WA, USA

Gina Ranieri
Department of Medical and Surgical Gynecology
Mayo Clinic in Arizona
Phoenix, AZ, USA

J. Alejandro Rauh-Hain
Department of Gynecologic Oncology and Reproductive Medicine
The University of Texas MD Anderson Cancer Center
Houston, TX, USA

Elliott G. Richards
Cleveland Clinic
Cleveland, OH, USA

James K. Robinson
MedStar Washington Hospital Center
Washington, DC, USA

Robert Rogers
Urogynecology
Logan Health
Kalispell, MT, USA

Emma Rossi
Department of Obstetrics and Gynecology
Duke University
Durham, NC, USA

Rodger Rothenberger
Division of Female Pelvic Medicine and Reconstructive Surgery
University of Louisville
Louisville, KY, USA

Tullia Rushton
Kelly Gynecologic Oncology Service
Department of Gynecology and Obstetrics
Johns Hopkins School of Medicine
Baltimore, MD, USA

Daisy Sangroula
Department of Anesthesiology and Perioperative Medicine
University of Louisville
Louisville, KY, USA

Stefania Saponara
Division of Gynecology and Obstetrics
Department of Surgical Sciences
University of Cagliari
Cagliari, Italy

Attilio Di Spiezio Sardo
Department of Public Health
University of Naples "Federico II"
Napoli, Italy

Papri Sarkar
Department of Obstetrics and Gynecology
University of South Florida
Tampa, FL, USA

Polina Sawyer
Star Urogynecology
Peoria, AZ, USA

Alireza A. Shamshirsaz
Obstetrics and Gynecology
Boston Children's Hospital
Boston, MA, USA

S. Abbas Shobeiri
Inova Health System
Fairfax, VA
and
Bioengineering, Department of Obstetrics and Gynecology
George Mason University
Falls Church, VA, USA

Gilda Sicilia
Division of Gynecology and Obstetrics
Department of Surgical Sciences
University of Cagliari
Cagliari, Italy

Matthew Siedhoff
Division of Minimally Invasive Gynecologic Surgery
Department of Obstetrics and Gynecology
Cedars-Sinai Medical Center
Los Angeles, CA, USA

Noam Smorgick
Department of Obstetrics and Gynecology
Shamir (Assaf Harofe) Medical Center
and
Tel Aviv University School of Medicine
Tel Aviv, Israel

Maria Cristina Solazzo
Endoscopica Malzoni
Center for Advanced Endoscopic Gynecologic Surgery
Avellino, Italy

Radmila Sparić
Clinic for Gynecology and Obstetrics
Clinical Centre of Serbia
and
Medical Faculty
University of Belgrade
Belgrade, Serbia

Assia A. Stepanian
Academia of Women's Health and Endoscopic Surgery
Atlanta, GA, USA

Rebecca L. Stone
Kelly Gynecologic Oncology Service
Department of Gynecology and Obstetrics
Johns Hopkins School of Medicine
Baltimore, MD, USA

Antonio Succu
Division of Gynecology and Obstetrics
Department of Surgical Sciences
University of Cagliari
Cagliari, Italy

James Symanowski
Department of Biostatistics and Data Sciences
Levine Cancer Institute at Atrium Health
Wake Forest University
Charlotte, NC, USA

Roya Taghavi
Obstetrics and Gynecology
University of California Davis
Davis, CA, USA

Andrea Tinelli
Department of Obstetrics and Gynecology
CERICSAL (CEntro di RIcerca Clinico SALentino)
"Verisdelli Ponti Hospital," Scorrano
Lecce, Italy

Mireille Truong
Division of Minimally Invasive Gynecologic Surgery
Department of Obstetrics and Gynecology
Cedars-Sinai Medical Center
Los Angeles, CA, USA

Varnita Vishwanath
Arizona College of Osteopathic Medicine
Midwestern University
Glendale, AZ, USA

Salvatore Giovanni Vitale
Obstetrics and Gynecology Unit
"Gaspare Rodolico" University Hospital
Department of General Surgery and Medical Surgical Specialties
University of Catania
Catania, Italy

Natalie Wallace
Private Practice
Salem, OR, USA

Simrit K. Warring
Department of Obstetrics and Gynecology
Mayo Clinic
Rochester, MN, USA

Naomi Whittaker
University of Pittsburgh Medical Center of Central Pennsylvania
Pittsburgh, PA, USA

Kelly Wright
Division of Minimally Invasive Gynecologic Surgery
Department of Obstetrics and Gynecology
Cedars-Sinai Medical Center
Los Angeles, CA, USA

Tajnoos Yazdany
Harbor–UCLA Department of OB/GYN
Division of Urogynecology
West Carson, CA, USA

Scott W. Young
Mayo Clinic in Arizona
Phoenix, AZ, USA

Lissa Yu
Obstetrics and Gynecology
Division of Pediatric and Adolescent Gynecology
University of Washington School of Medicine
Seattle, WA, USA

Guilherme Henrique Zanluchi
Gynecology Department
FMIGS – BP – A Beneficência Portuguesa de São Paulo
São Paulo, SP, Brazil

Philippe Zimmern
Department of Urology
University of Texas Southwestern Medical Center
Dallas, TX, USA

Brunella Zizolfi
Department of Public Health
University of Naples "Federico II"
Napoli, Italy

Taylor & Francis
Taylor & Francis Group
http://taylorandfrancis.com

1 LAPAROSCOPY THROUGH A HISTORICAL LENS

Rebecca Barbaresso, Jerar Palian, Zoë Pennington, Rana Khaloghi, Roya Taghavi, Elif Polat, and Resad Paya Pasic

1.1 Lineage of Laparoscopy

As Marcus Tullius Cicero stated, "We study history not to be clever in another time, but to be wise always." As such, knowing the foundation of laparoscopy can help us understand the future directions of this surgical artform. The art of laparoscopy has a rich and extensive history, with its origins over 200 years ago. It is important to note that the roots of laparoscopy were established and expanded within the field of obstetrics and gynecology. In this review of the history of laparoscopy, the reader will note that gynecologists were the ones who embraced the concept of endoscopy, harnessed its aptitude, and helped advance minimally invasive surgery to become what it is today, a revolutionary surgical realm.

1.2 Early Endoscopy Enthusiasts

The initial pioneer of early endoscopy was Phillip Bozzini who in 1806 invented the "Lichtleiter," a unique device that evaluated the bladder (1, 2). With this invention and utilization of a complex system of mirrors and candles, Bozzini was able to reflect images back to the operator's eye, allowing for the operator to visualize what laid within the depths of the body's cavities. Bozzini's invention and creativity influenced many successors. Maximilian Nitze and Josef Leiter shortly thereafter developed the first rigid endoscope with a built-in light source which was utilized for the first documented laparoscopies (1). Antonin Desormeaux, a French urologist, followed in Bozzini's footsteps in 1853 by performing numerous cystoscopic procedures by the aid of endoscopic visualization and coined the term "endoscope," making its first appearance in literature in 1878 (2–4).

The first documented live use of laparoscopy to visualize the abdominopelvic cavity was performed in 1901 by Georg Kelling (Figure 1.1) (1, 2, 5). At the 73rd meeting of the Society of German Natural Scientists and Physicians in Hamburg, Kelling demonstrated a procedure he called "coelioscopy" where he examined the abdominal cavity of a dog by insufflating the cavity with air and introducing the aforementioned Nitze cystoscope through a Fiedler trocar (1, 5). Kelling was the first to compile these laparoscopic techniques with the aid of insufflation and he later transitioned this use to human subjects in 1910, performing 45 cases (1, 2).

While Kelling was the first to perform coelioscopy, Hans Christian Jacobaeus is known to have created the actual term of laparoscopy (known as "laparothorakoskopie") in 1910 when he used it to explore the pleural cavity (4). He went on to perform operative laparoscopy of the abdominal cavity by performing adhesiolysis on 17 patients successfully (4). Shortly thereafter, Bertram Bernheim performed the first laparoscopic procedure in the United States at Johns Hopkins in 1911, which he titled "organoscopy," by using a protoscope to inspect the peritoneal cavity in a jaundiced patient (2, 4, 6).

Laparoscopic advancements continued into the 1920s. Richard Zollikofer, a Swiss gynecologist, introduced the use of carbon dioxide to create pneumoperitoneum in 1924, which was a major improvement from using filtered air or oxygen given the elevated risk associated with these gases (2, 4, 7). In 1929, the German surgeon Heinz Kalk developed a forward-viewing 135-degree laparoscope and helped pioneer diagnostic techniques like liver biopsies (4, 8). In the United States, John C. Ruddock helped popularize laparoscopy by using a scope similar to Kalk's in 1930 and incorporated biopsy instruments into laparoscopic procedures to obtain specimens from the liver, spleen, stomach, omentum, and peritoneum (1, 3). These strides in laparoscopy set the tone for its place in diagnostic medicine. However, it was not until several years later that laparoscopy was fully embraced for its operative potential.

1.3 Journey from Diagnostic to Therapeutic

The 1930s was a revolutionary time, as the first reported cases of using laparoscopy for therapeutic purposes were published. Such operative laparoscopy started in 1933 with Fervers with the performance of adhesiolysis with electrocautery (4, 6, 8). In the several years after Fervers, many other firsts followed for the field of operative laparoscopy. Ruddock published over 2500 cases of his laparoscopy performed with room air for pneumoperitoneum and under local anesthesia, 500 of which were performed by 1937 (2, 4). In 1936, Boesch performed the first laparoscopic tubal ligation in Switzerland, while Power and Varnes performed the first in the United States in 1941 in Ann Arbor, MI (6). Over 1937–1938, Hope used laparoscopy to differentiate between tubal pregnancies and ruptured ovarian cysts while Benedict described ovarian cyst aspiration under laparoscopic view (1, 9).

Then came Raoul Palmer, a French gynecologist, who experimented with laparoscopy during World War II (3, 10). Palmer had groundbreaking contributions to the field and published his contributions shortly after the war ended. In 1944, he performed laparoscopy for the first time in Trendelenburg positioning (4). Palmer's first publication described 250 of his procedures including the use of the Veress needle for establishing pneumoperitoneum with emphasis of limiting intra-abdominal pressure below 25 mmHg, optimizing patient positioning through the use of Trendelenburg, and introducing the first tool to manipulate the uterus (2, 3, 10, 11). Palmer was a stellar advocate for the field and had many predecessors who learned from visiting him in Paris, including Kurt Semm who reported, "It was customary then for university-based gynecologists to visit the Palmers in Paris" (10). In 1955, Hans Frangenheim, a German gynecologist, visited Palmer to learn his techniques (12). Frangenheim contributed to the field by developing an improved insufflator for pneumoperitoneum, teaching laparoscopy to others at Wuppertal Hospital and publishing a book about laparoscopy in gynecology in 1959 (4, 12). Frangenheim emphasized the importance of good technique as he taught of the complications of laparoscopy and advocated for general anesthesia use (2).

The 1960s was the turning point for Palmer's contributions to laparoscopy. In 1961, Palmer discussed how he retrieved the first human oocyte via laparoscopy during a speech at the

DOI: 10.1201/9781003312109-1

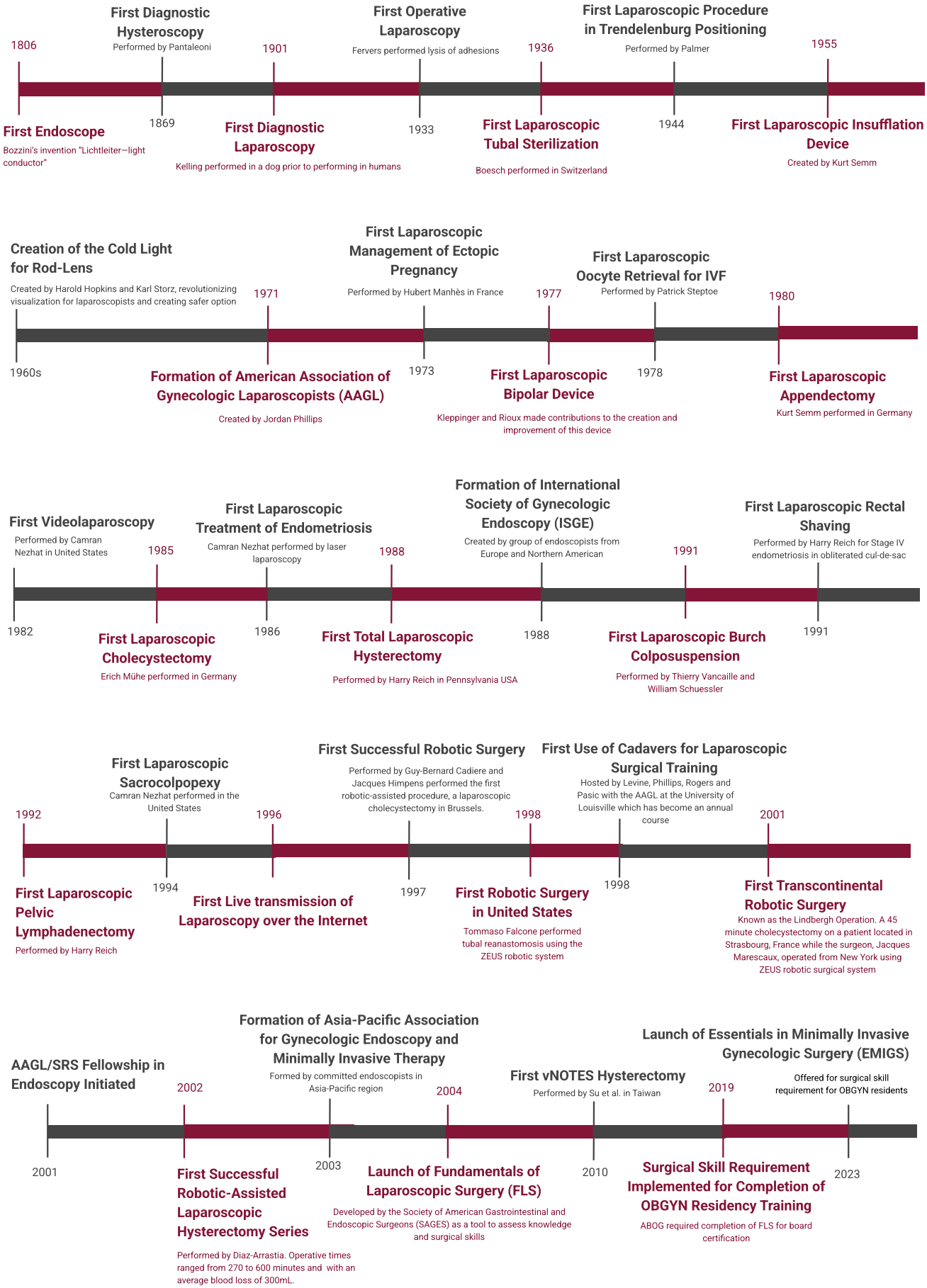


FIGURE 1.1 Timeline of major events.

"Societe de Biologie" (3, 10). During this speech, he stated, "This technique should be of great interest for the study of the physiology of ovulation and should lead to a new way of treating sterility due to tubal occlusion" (10). The following year in 1962, Palmer started performing laparoscopic sterilization with Frangenheim (3, 10). Palmer also influenced Patrick Steptoen who utilized laparoscopic surgery to retrieve oocytes for the first successful in vitro fertilization (IVF) in 1978 (13).

The late 1960s also was the time when Harold Hopkins and Karl Storz joined forces to create the cold light using Hopkins' patent for a rod-lens system, revolutionizing visualization for laparoscopists as well as offering a safer option (4, 11). Such an invention allowed laparoscopists to thrive in their ingenuity into the 1970s.

1.4 The 1970s and the Sapience of Semm

Despite the advancements from Palmer, Frangenheim, and Steptoe, laparoscopy plateaued in the mid-20th century. This was thought to be secondary to reported complications due to laparoscopic technique. However, the 1950s noted improvements in medications that could be utilized intraoperatively such as anesthetic and antibiotic agents. Such welcomed advancements created an operative shift; most surgeons performed laparotomy even for diagnostic purposes. Laparoscopy was deemed as an inferior alternative and any improvements in this field were met with contempt. But nevertheless, laparoscopists persisted and this persistence penetrated the 1970s. Over 35,000 laparoscopic cases were published in literature by 1972 (1). Despite this, in the early 1970s only 1% of sterilizations performed in the United States were done laparoscopically (8). Hubert Manhès in 1973 treated the first ectopic pregnancy laparoscopically (14, 15). A switch was then flipped for the majority of surgeons and by 1976 60% of tubal ligations were laparoscopic (6, 8). Much of this was due to the creations and advancements of Kurt Semm.

Dr. Kurt Semm, a toolmaker and gynecologist, utilized his genius to revolutionize the field of operative laparoscopy. Semm's contributions actually started in 1955, when he created an insufflation device specifically designed for laparoscopy (4, 16). In order to have his device gain traction, Semm reached out to a laparoscopist in Munich who agreed to trial his device (16, 17). Semm reflected on this time,

> I had a constant feeling of fear. You have to remember, I had clinical experience with tubal insufflation, and at that time deaths due to gas insufflation into tubes had been reported – air emboli. I was afraid that a patient . . . would die of air embolism and my apparatus would be blamed.
>
> **(16, 17)**

Semm did not let his fear halt, as his motivation to create safe equipment and instruments outweighed his fear. The prolific inventor headed the Kiel School's development of operative laparoscopy instruments and helped develop a medical instrument company, WISAP, in Germany which still produces endoscopic instruments (18, 19). Semm later became known as the father of modern laparoscopy based on his innumerable contributions to the field (20). Another vital creation in the 1970s was the bipolar cautery device. Initially introduced by Frangenheim in Germany and Rioux and Cloutier in the United States, Kleppinger used these stepping stones to make an improved device in 1977 (21, 22).

In the 1970s, Semm went on to develop tissue morcellator, electronic insufflator, safe electrocoagulation instruments, as well as extra and intracorporeal endoscopic knot tying (6, 8, 16, 17). Semm's inventions created a new age of gynecologic surgery as he pioneered many gynecologic laparoscopic operations including myomectomies, oophorectomies, ovarian cyst resections, treatment of ectopic pregnancies, laparoscopic appendectomy, and the laparoscopic-assisted vaginal hysterectomy (6, 8, 17, 19, 23, 24). Semm went on to publish over 1000 papers in various journals and promoted his work as the chairman of the department of Obstetrics and Gynecology at the University Clinics in Kiel, Germany, from 1970 to 1995 (19, 25).

While Semm created several crucial laparoscopic instruments and developed essential techniques and procedures and Kleppinger, Frangenheim, and Rioux and Cloutier helped improve devices, many of their efforts would not have come to fruition without the advancements of videolaparoscopy.

1.5 Lights, Camera, Action

Developed in the 1960s, video technology was improving through numerous developments: smaller cameras, lighter equipment, enhanced resolutions, better light sources. All of this technology was intriguing for laparoscopists as there were several perks for utilizing this science in surgery, such as magnifying the intraperitoneal image and projecting onto a screen outside of the body that is easily visualized not only by the operator but by all who occupy the operating room (3, 26). However, the development of videolaparoscopy posed significant challenges, primarily because the cameras available were not originally designed for videoendoscopy. This revolutionary idea was worked on throughout the late 1970s into the early 1980s by Dr. Camran Nezhat, a gynecology resident in Buffalo, New York, who combined these concepts into a video-assisted endoscopic surgery system that allowed for improved ergonomics, visualization, operation, and real-time teaching (6, 8, 18, 27). Nezhat's conception of videolaparoscopy was a vital development for laparoscopic advancements. In November 1986 at the combined meeting of the American Fertility Society and the Canadian Fertility and Andrology Society, Dr. Nezhat presented results of over 600 endometriosis surgeries performed by videolaparoscopy (18). In 2000, Kurt Semm discussed the creations of Camron Nezhat, stating, "With his genius, he widened the operative field, creating new techniques and employing new instruments and apparatuses. In my opinion, with the cooperation of his two brothers, Camran enriched the entire field of surgical laparoscopy" (28). This technique not only supported the growth of minimally invasive surgery, but also allowed for permanent recording with numerous opportunities such as in surgical education, patient education, and research. Videolaparoscopy opened many doors for laparoscopists, many that will be utilized for the remainder of time.

1.6 Elevation through the American Association of Gynecologic Laparoscopists (AAGL)

Another important development for laparoscopy in the 1970s was the American Association of Gynecologic Laparoscopists (AAGL). The AAGL was created by four founding fathers in

1971, spearheaded by Dr. Jordan M. Phillips as the president (25, 29). Dr. Phillips founded this society to not only create an organization of laparoscopists but to elevate the surgical standards and bring about forward thinkers and surgeons (29, 30). The remainder of the first members included Richard M. Soderstrom as the vice president, Jacques E. Rioux as the secretary, and Louis G. Keith as the treasurer (29). The membership quickly grew to ten members in that same founding year (29). Dr. Phillips served as the chairman of AAGL for 29 years, during which time he helped build a society that would become internationally renowned for elevating gynecologic surgery (29). He did so by prioritizing research, championing the use of laparoscopy, and advocating for international relationships. In 1972, just one year after the foundation of the AAGL, Dr. Phillips hosted the first International Congress on Gynecologic Laparoscopy, which has transformed into an annual global conference attended by thousands of members representing over 100 countries (29). Phillips also organized more than 80 laparoscopic training courses for Semm and his team from 1980 through 1996 throughout the United States (19, 25). The founding of the AAGL inspired other surgeons to collaborate, demonstrated by the creation of the Germany-based group Surgical Task Group for Endoscopy and Ultrasonography in 1976 and followed by the Society of American Gastrointestinal Endoscopic Surgeons (SAGES) in the United States in 1981 (4). The notoriety and growth of the AAGL continues to this day. In 2023, the AAGL reported to have over 7500 members over 110 countries (29, 30).

1.7 Evolution through the 1980s and 1990s

The synergy between Nezhat's videolaparoscopy and Semm's traditional laparoscopy, involving peering through the eyepiece of the laparoscope, marked a transformative era for laparoscopy in the late 20th century. In 1984, Semm described the technique for laparoscopic-assisted vaginal hysterectomy, streamlining the vaginal portion of the surgery by separating the adnexa (31, 32). Building on this innovation, German surgeon Erich Mühe performed the first laparoscopic cholecystectomy using Semm's instruments, successfully completing 97 procedures by 1987 (4, 17). Semm's and Mühe's accomplishments were notable for their execution of these procedures in the traditional manner, peering through the scope without video assistance. Initially hesitant to adopt videolaparoscopy, Semm's perspective shifted in 1988 when he and Nezhat were invited to debate traditional laparoscopy (referred to as pelviscopy) versus videolaparoscopy at the Third European Congress on Hysteroscopy and Endoscopic Surgery in Amsterdam, the Netherlands. This event marked a pivotal shift from analog methods to modern digital minimally invasive surgery, representing a significant milestone in the field.

Meanwhile, Harry Reich followed Semm's pioneering steps, performing the first total laparoscopic hysterectomy in 1988 in Pennsylvania, USA, with an impressive operating time of 180 minutes (32, 33). Reich championed this technique, presenting it at the AAGL Conference in 1988. His groundbreaking work extended to achieving several laparoscopic milestones, including the first pelvic lymphadenectomy for cancer and excision of deep infiltrating endometriosis in the cul-de-sac that required rectal shaving (34, 35). In 1985, Nezhat reported the laparoscopic excision of stage IV endometriosis involving multiple organs, extragenital endometriosis, and ovarian endometriomas and presented his work at the American Fertility Society conference (36, 37). Nezhat went on to perform the first laparoscopic bowel, bladder, ureter, diaphragm resection and reanastomosis, along with laparoscopic sacrocolpopexy, vesicovaginal fistula repair, and excision of liver endometriosis, expanding the scope of minimally invasive procedures (36–38). He further refined techniques such as safe laser excision and vaporization of endometriosis, addressing complex cases, including extragenital and deep infiltrating endometriosis of the rectovaginal septum (39).

In the early 1990s, endoscopic surgery had a surge secondary to media interest and patient demand (4, 40). Patients, influenced by these mainstream news articles, began demanding these innovative "band-aid" surgeries. This surge in patient-driven demand marked a profound departure from centuries of traditional paternalistic medicine, where doctors had near unquestioned authority over patients' lives. The widespread media coverage and patient enthusiasm paved the way for the acceptance and integration of these advanced surgical techniques into mainstream medical practice.

However, there was concern with this rapidly growing interest, as many surgeons were still not trained in these techniques (4, 40). This dilemma with training was concerning, that is until the advent of Semm's pelvic trainer in 1985 (4, 19, 41). His practical surgical model allowed learners and surgeons to practice laparoscopic techniques (4, 19, 41). AAGL also helped teach by hosting the many laparoscopic training courses. While Kelling recommended practicing endoscopic methods on corpses in the early 20th century, this was not implemented until cadavers were being utilized for laparoscopic training for the first time in 1998 (4, 42). Under the collaboration of Ronald Levine, Jordan Phillips, Robert Rogers Jr., and Resad Paya Pasic with the aid of the AAGL, the first annual Advanced Workshop in Gynecologic Laparoscopic Anatomy and Surgery on Unembalmed Cadavers took place in September 1998 at the University of Louisville (42). This course allowed attendees to master pelvic anatomy that no model could replace. The cadaver course exploded in popularity, and the cadaver courses were then implemented into resident teaching, in which a study by Levine demonstrated that cadaver surgical training significantly improves laparoscopic surgical techniques in residents (43).

With the pelvic trainer and laparoscopic training courses including cadaver courses, surgeons finally had more exposure to learn and practice such skills to keep up with the surgical shift. This not only allowed for proficiency but also aided in standardizing and replicating techniques to help improve patient outcomes as well as provide data for surgical research.

1.8 Furthering Laparoscopy through Fellowship

Clearly throughout the developments of laparoscopy, the common theme of teaching and spreading the knowledge of laparoscopy is apparent. Many of the pioneers of laparoscopy advocated for teaching, watching, and recording for the purpose of spreading the concept of laparoscopy and improving surgical techniques. The idea of a fellowship in advanced laparoscopy was initially started in the 1980s by Dr. Veasy Buttram, who advocated for a one-year fellowship in reproductive surgery (44, 45). This fellowship was initially called the Society of Reproductive Surgeons (SRS) Fellowship. Throughout the 1990s similar fellowships were established with the same vision

as the SRS. In 2001, the AAGL and SRS collaborated to create the AAGL/SRS Fellowship in Endoscopy (44, 45). They formulated a standardized curriculum and a research requirement that upheld the standards of a formal fellowship education. The first fellowships were granted to seven preceptors at seven sites in the US. Eventually the AAGL and SRS parted ways and the Board decided to change the fellowship name to "Fellowship in Minimally Invasive Gynecologic Surgery" (FMIGS) in order to "accurately reflect its content and educational mission" (44–46). The fellowship has expanded immensely, now offered through over 60 hospital sites across the United States, as well as internationally in Canada, Brazil, Columbia, Mexico, and Ireland. To date, FMIGS has graduated over 500 fellows (44).

1.9 Robots, vNOTES, and Modernization

The nineties was a thriving time for laparoscopy. The internet gained traction as new technology in the nineties, and laparoscopists used this for the first time to transmit a live broadcast of laparoscopic surgery over the internet in 1996 (47). Laparoscopy further blossomed with the creation of the first robotic laparoscopic surgery system in 1994, Aesop. (23). ZEUS shortly followed in the United States in 1996, allowing for the inception of the first robotic gynecologic procedure, a tubal reanastomosis, in 1998 by Tommaso Falcone (8, 48). The da Vinci robotic surgical system then followed suit in Europe in 1997 and the United States in 2000 (8, 49). Using the da Vinci surgical system in 1997, Guy-Bernard Cadiere and Jacques Himpens performed the first robotic-assisted procedure, a laparoscopic cholecystectomy in Brussels (8, 50). Kelley and Owens followed in 2000 in the United States, performing a cholecystectomy as the first robotic surgery on the da Vinci in the United States (8). It was in 2001 when robotic surgery really pushed the envelope with the Lindbergh Operation (51, 52). This operation was the first transcontinental robotic surgery performed by Jacques Marescaux who was located in New York performing a cholecystectomy on a patient located in Strasbourg, France (51, 52). The surgery was completed in 54 minutes and there were no postoperative complications (51, 52). The very next year, Concepcion Diaz-Arrastia performed the first series of successful robotic-assisted laparoscopic hysterectomies (53). This series included 16 patients with operative times ranging from 270 to 600 minutes and an average blood loss of 300 mL (53).

Robotic technology was seen for its endless capabilities within the realm of surgery. This technology allowed for completion of incredibly complex tasks that would otherwise exceed a surgeon's specific surgical skill or cause extreme fatigue if performed through traditional laparoscopy techniques. The addition of multiple arms under the control of one surgeon has made surgery more practical for a single surgeon to operate without even requiring an assistant. Robotics have been noted to have a short learning curve as well, making it easily applicable to surgeons of various learning levels and surgical skill sets (4). Robotic consoles are now widely available with training access at the tip of a surgeon's fingers.

In addition to advances in robotics, there has been impressive improvements in natural orifice transluminal endoscopic surgery (NOTES) and surgery via single trocar, known as single port technique (4). Vaginal natural orifice transluminal endoscopic surgery (vNOTES) has specifically taken off in the last several years. In 2010, Su et al. performed the first series of vNOTES hysterectomy (54). The mean operative time was 123 minutes with an average blood loss of 379 mL and no complications noted, including conversion to conventional laparoscopy (54).

While there have been many advances through new avenues to perform hysterectomy including robotics and vNOTES, there still continues to be improvements in conventional laparoscopy allowing for impressive surgical achievements. This was demonstrated perfectly in 2020 when Pasic and Cesta performed a total laparoscopic hysterectomy on the world's largest uterus, weighing 7.4 kg secondary to multiple fibroids (55). By utilizing a four centimeter minilaparotomy at the umbilical port site, the procedure was performed in 4 hours and 12 minutes with less than 700 mL of blood loss and no complications (55). Such notable accomplishments highlight that traditional laparoscopy can be performed in higher risk individuals with good outcomes by skilled and appropriately trained surgeons.

Minimally invasive surgery and laparoscopy has been undergoing a major transformation over the last several years with new technology allowing for even more advancements. Innovations include, but are not limited to, high-intensity focused ultrasound, 3D printing and engineered prosthetics, fluorescence-enhanced procedures, and the integration of artificial intelligence and augmented reality (4). Such ingenious concepts have pushed minimally invasive surgery into a new area of limitless opportunities, which is welcomed with open arms by the medical and technological communities globally.

1.10 Apprehension of MIS Advancements

While advancements in minimally invasive surgery are now enthusiastically embraced, many of the early advances in endoscopy and laparoscopy were met with skepticism. Many surgeons thought it was illogical to change a well-established technique into a complex procedure with an unfamiliar approach. This started with Bozzini, who was censored by the Medical Faculty of Vienna for "undue curiosity" (11). Palmer was met with contempt by surgeons of the time as well, getting asked questions such as "why these acrobats when it is so easy to open a stomach?" (3). Early laparoscopists were continuously repressed by the resistance to change from traditional surgery. Germany even banned laparoscopic surgery from 1956 to 1961 (6, 8).

The theme of skepticism continued from our founding fathers 200 years ago through the latter part of the 20th century. Steptoe butted heads with the Medical Research Council in 1971 after rejecting his application for his research program (13, 56). The Council wrote in response, "Reservations were also expressed about the justifiability of employing the procedure of laparoscopy for purely experimental purposes," and then cited ethical and dangerous concerns they had regarding his work (13, 56).

The pioneer Kurt Semm was met with the most contempt during his lifelong career of innovative laparoscopic techniques and creations. When Semm was the chairman of Obstetrics and Gynecology at the University of Kiel, his colleagues pulled him from the operating room to image his brain in the 1970s (19, 25). Their reasoning was, "only a person with brain damage would perform laparoscopic surgery" (4, 19). Semm was constantly shunned by surgeons and gynecologists alike, calling his presentations "non-sense" and rejecting his initial ideas to perform a laparoscopic cholecystectomy (19). When Semm performed the first laparoscopic appendectomy in 1980, the president of the German Surgical Society wrote

to the board of directors of the German Gynecological Society recommending Semm's suspension from practicing medicine (19). Semm reports that the reaction to his laparoscopic appendectomy was the "worst criticism" he experienced in his career, stating, "Both surgeons and gynecologists were angry with me, they were throwing stones at me. All my initial attempts to publish on laparoscopic appendectomy were refused, with the comment that such nonsense does not and will never belong to general surgery" (17). This was one reason why his report on laparoscopic appendectomy was not published until 1983, several years after it was actually performed (4, 24). Semm also faced resistance when his paper on this surgery was rejected by the *American Journal of Obstetrics and Gynecology* (*AJOG*), as it was deemed unethical (17, 19). Despite all these actions against Semm, he was driven by his determination, as he saw the true potential in laparoscopy and that it would be applicable to all surgical fields once fully embraced.

Another innovative laparoscopist who was dismissed was Carman Nezhat. In the 1980s when Nezhat was presenting his laparoscopic endometriosis procedures at the American Fertility Society's annual meeting, many were in disbelief of his work (27). Nezhat recalls they were "ready to throw tomatoes" given their displeasure with his progressive techniques (27). Prominent figures in the field of laparoscopy initially opposed videolaparoscopy. They continued their laparoscopic procedures by looking through an eyepiece, resisting the shift to video-based techniques. Initially met with skepticism, the success of these techniques was eventually showcased in prominent media outlets like *Time* and *Newsweek*, leading to broader acceptance within medical establishments. Nezhat and his brothers received legal threats as well: not only were they sued, but one lawyer dissuaded medical journals from publishing the Nezhats' work, causing one journal to retract two published articles previously published by the Nezhats (27, 36).

Attacks were not just aimed at individual laparoscopists but rather at laparoscopy as a whole. One such onslaught against laparoscopy was explicitly noted in one detrimental editorial in *Obstetrics and Gynecology* published by Pitkin in 1992 titled, "Operative Laparoscopy: Surgical Advance or Technical Gimmick?" (57). In the article Pitkin wrote, "the evidence concerning other laparoscopic procedures was felt to be inadequate to support use in clinical practice" (57). While tireless criticism of the field could have been unmotivating, the minimally invasive surgery community took this opportunity to create their own publication, then titled the *Journal of the American Association of Gynecologic Laparoscopists* in 1993, eventually changing the name to the *Journal of Minimally Invasive Gynecology* (JMIG) in 2005 (58, 59). Eighteen years later, Pitkin sought to make amends and wrote another paper titled "Operative Laparoscopy: A Second Look after 18 Years" and wrote, "substantial body of evidence that laparoscopy can be used" and "it is now clear that many procedures can be performed laparoscopically" (60). Despite the consistent disbelief and criticism of laparoscopy, the pioneers never faltered in their passionate drive to disseminate the knowledge of this essential surgical technique. Laparoscopists as a whole owe a great debt to those who bore such grief, as minimally invasive surgery would not exist today without such heroes.

1.11 Closing Remarks

Over the last 200 years, minimally invasive surgery has grown to become the standard of surgical care through numerous advancements and continues to exponentially progress with the assistance of improved technology. Minimally invasive surgery with the aid of the laparoscopic pioneers and the AAGL has opened up opportunities globally for education, research, and patient advocacy. The next 200 years is bound to have an even bigger and brighter future for laparoscopy and minimally invasive surgery as a whole.

References

1. Horwitz ST. Laparoscopy in gynecology. *Obstet Gynecol Surv*. 1972;27(1):1–13.
2. Marlow J. History of laparoscopy, optics, fibreoptics, and instrumentation. *Clin Obstet Gynecol*. 1976;19(2):261–275.
3. Schlogel G. Raoul palmer and the coelio-surgical adventure from 1940 to 1995. *Hist Sci Médicales*. 1996;30:281–287.
4. Alkatout I et al. The development of laparoscopy – a historical overview. *Front Surg*. 2021;8:799442.
5. Hatzinger M et al. The seminal contribution of Georg Kelling to laparoscopy. *J Endourol*. 2005;19(10):1154–1156.
6. Nezhat C et al. *Let there be light: an historical analysis of endoscopy's ascension since antiquity* [Internet]. 2023. Available at: http://laparoscopy.blogs.com/endoscopyhistory.
7. Hatzinger M et al. Georg Kelling (1866–1945): Der Erfinder der modernen Laparoskopie. *Urologe A*. 2006;45(7):868–871.
8. Kelley WE. The evolution of laparoscopy and the revolution in surgery in the decade of the 1990s. *JSLS*. 2008;12(4):351–357.
9. Hope RB. The differential diagnosis of ectopic gestation by peritoneoscopy. *Surg Gyne Obstet*. 1937;64:229–234.
10. Litynski GS. Raoul Palmer, World War II, and transabdominal coelioscopy. Laparoscopy extends into gynecology. *JSLS*. 1997;1(3):289–292.
11. Nezhat F. Triumphs and controversies in laparoscopy: the past, the present, and the future. *JSLS*. 2003;7(1):1–5.
12. Litynski GS. Hans Frangenheim – culdoscopy vs. laparoscopy, the first book on gynecological endoscopy, and "cold light." *JSLS*. 1997;1(4):357–361.
13. Litynski GS. Patrick C. Steptoe: laparoscopy, sterilization, the test-tube baby, and mass media. *JSLS*. 1998;2(1):99–101.
14. Bruhat MA et al. Treatment of ectopic pregnancy by means of laparoscopy. *Fertil Steril*. 1980;33(4):411–414.
15. Bruhat MA et al. Endoscopic treatment of ectopic pregnancies. *Curr Opin Obstet Gynecol*. 1993;5(2):260–266.
16. Litynski GS. Kurt Semm and an automatic insufflator. *JSLS*. 1998;2(2):197–200.
17. Litynski GS. Kurt Semm and the fight against skepticism: endoscopic hemostasis, laparoscopic appendectomy, and Semm's impact on the "laparoscopic revolution." *JSLS*. 1998;2(3):309–313.
18. Nezhat C et al. Operative laparoscopy: videolaparoscopy and videolaseroscopy. *Ann N Y Acad Sci*. 1994;734(1):433–444.
19. Bhattacharya K. Kurt Semm: a laparoscopic crusader. *J Minimal Access Surg*. 2007;3(1):35.
20. Moll FH et al. A pioneer in laparoscopy and pelviscopy: Kurt Semm (1927–2003). *J Endourol*. 2005;19(3):269–271.
21. Jaiswal A et al. Energy devices in gynecological laparoscopy – archaic to modern era. *Gynecol Minim Invasive Ther*. 2017;6(4):147–151.
22. Kleppinger RK. Female outpatient sterilization using bipolar coagulation. *Bull Post-Grad Comm Med Univ Syd*. 1977;33(8):144–154.
23. Semm K et al. Technical progress in pelvic surgery via operative laparoscopy. *Am J Obstet Gynecol*. 1980;138:121–127.
24. Semm K. Endoscopic appendectomy. *Endoscopy*. 1983;15:59–64.
25. Mettler L. The evolution of gynecologic endoscopic surgery over 50 years – a pleasant adventure. *Med Res Arch*. 2017;5(6):1–18.
26. Spaner SJ et al. A brief history of endoscopy, laparoscopy, and laparoscopic surgery. *J Laparoendosc Adv Surg Tech*. 1997;7(6):369–373.
27. Carter JE. Biography of Camran Nezhat, MD, FACOG, FACS. *JSLS*. 2006;10(2):275–280.

28. Nezhat C et al. Complications. In: Nezhat C et al., eds. *Operative Gynecologic Laparoscopy Principles and Techniques*, 2nd edn. New York: McGraw-Hill; 2000:365–390.
29. *AAGL history* [Internet]. 2023. Available at: https://aagl.org/aagl-history/
30. AAGL to pay tribute to founder Dr. Jordan M. Phillips. *NewsScope*. 2008;22(3).
31. Munro MG et al. Laparoscopic hysterectomy: does it work? A bicontinental review of the literature and clinical commentary. *Clin Obstet Gynecol*. 1995;38(2):401–425.
32. Härkki P et al. Safety aspects of laparoscopic hysterectomy. *Acta Obstet Gynecol Scand*. 2001;80:383–391.
33. Reich H et al. Laparoscopic hysterectomy. *J Gynecol Surg*. 1989 Jan;5(2):213–216.
34. Reich H et al. Laparoscopic treatment of cul-de-sac obliteration secondary to retrocervical deep fibrotic endometriosis. *J Reprod Med*. 1991;36(7):516–522.
35. Reich H. Laparoscopic lymphadenectomy. *Surg Laparosc Endosc*. 1992;2(1):61–63.
36. Nezhat FR et al. Forward we go! *JSLS*. 2023;27(1):e2022.00073.
37. Nezhat C et al. Laparoscopically assisted anterior rectal wall resection and reanastomosis for deeply infiltrating endometriosis. *Surg Laparosc Endosc*. 1991;1(2):106–108.
38. Nezhat CH et al. Laparoscopic sacral colpopexy for vaginal vault prolapse. *Obstet Gynecol*. 1994;84(5):885–888.
39. Nezhat C et al. Safe laser endoscopic excision or vaporization of peritoneal endometriosis. *Fertil Steril*. 1989;52(1):149–151.
40. Schlich T et al. Patient choice and the history of minimally invasive surgery. *The Lancet*. 2016;388(10052):1369–1370.
41. Morgenstern L. Against the tide: Kurt Karl Stephan Semm (1927–2003). *Surg Innov*. 2005;12(1):5–6.
42. Levine RL. Cadaver workshop: the ultimate learning experience. *NewsScope*. 1998;3(4).
43. Levine RL et al. The use of lightly embalmed (fresh tissue) cadavers for resident laparoscopic training. *J Minim Invasive Gynecol*. 2006;13(5):451–456.
44. *FMIGS* [Internet]. [cited 2023 Oct 2]. Available at: https://aagl.org/fmigs/
45. Loffer FD. Fellowship in gynecologic endoscopy: training our future leaders. *NewsScope*. 2008;22(2).
46. Brill A. Fellowship changes name to reflect its focus. *NewsScope*. 2009;23(2).
47. Gandsas A et al. Live interactive broadcast of laparoscopic surgery via the Internet. *Surg Endosc*. 1998;12(3):252–255.
48. Advincula AP et al. Laparoscopic robotic gynecologic surgery. *Obstet Gynecol Clin North Am*. 2004;31(3):599–609.
49. Ballantyne GH et al. The da Vinci telerobotic surgical system: the virtual operative field and telepresence surgery. *Surg Clin North Am*. 2003;83(6):1293–1304.
50. Hargest R. Five thousand years of minimal access surgery: 1990–present: organisational issues and the rise of the robots. *J R Soc Med*. 2021;114(2):69–76.
51. Mohan A et al. Telesurgery and robotics: an improved and efficient era. *Cureus* [Internet], 2021 [cited Oct 2023]. Available at: www.cureus.com/articles/54068-telesurgery-and-robotics-an-improved-and-efficient-era.
52. Marescaux J. Nom de code : " Opération Lindbergh ." *Ann Chir*. 2002;127(1):2–4.
53. Diaz-Arrastia C et al. Laparoscopic hysterectomy using a computer-enhanced surgical robot. *Surg Endosc*. 2002;16(9):1271–1273.
54. Su H et al. Hysterectomy via transvaginal natural orifice transluminal endoscopic surgery (NOTES): feasibility of an innovative approach. *Taiwan J Obstet Gynecol*. 2012;51(2):217–221.
55. Cesta M et al. Total laparoscopic hysterectomy of a 7400 g uterus. *J Minim Invasive Gynecol*. 2021;28(4):748–749.
56. Edwards R et al. *A Matter of Life. The Story of a Medical Breakthrough*. London: Hutchinson Publishers; 1980.
57. Pitkin RM. Operative laparoscopy: surgical advance or technical gimmick? *Obstet Gynecol*. 1992;79(3):441–442.
58. Corson SL. Editorial report. *J Minim Invasive Gynecol*. 2005;12(1):4–5.
59. Eldredge JD. Journal of the American Association of gynecologic laparoscopists. *JAMA J Am Med Assoc*. 1995;274(6):509.
60. Pitkin RM et al. Operative laparoscopy: a second look after 18 years. *Obstet Gynecol*. 2010;115(5):890–891.

2 PELVIC ANATOMY AND THE ART OF SURGICAL DISSECTION

Polina Sawyer and Robert Rogers

Mastery of surgical technique in minimally invasive gynecologic surgery is undoubtedly essential for achieving successful outcomes and minimizing complications. However, it is crucial to emphasize that surgical technique alone is not sufficient to become an expert surgeon. Excellent knowledge of the anatomical spaces within the pelvis is equally imperative. By combining meticulous and controlled dissection techniques with a comprehensive understanding of pelvic anatomy, surgeons can optimize their surgical approach. This integration allows for accurate orientation, step-by-step control, safe exposure, and minimal blood loss, enhancing surgical efficiency and visualization of the operative field. Laparoscopic techniques, with their superior visualization and recognition of tissue planes, provide an advantageous platform for executing these surgical maneuvers. Therefore, an integrated approach that combines surgical skill and anatomical knowledge is paramount to becoming a proficient minimally invasive gynecologic surgeon.

2.1 Surgical Anatomy of the Female Pelvis

Good comprehensive knowledge of the surgical anatomy of the female pelvis is of utmost importance for laparoscopists, as it helps them identify and navigate relevant anatomic structures safely during surgery.

Visualizing the three dimensions of pelvic anatomy through the two-dimensional plane of the laparoscope can be challenging. Therefore, laparoscopic gynecologists need to study and observe carefully to develop a working knowledge of pelvic anatomy. Continuous practice and experience can help improve both technical skills and understanding of gynecologic surgical pelvic anatomy.

In this chapter, the following anatomic areas are discussed:

1. Anterior Abdominal Wall
2. Superficial Peritoneal Anatomy
3. Presacral Space
4. Pelvic Brim
5. Pelvic Sidewall
6. Base of the Broad Ligament
7. Extraperitoneal Surgical Spaces
8. Pelvic Blood Supply
9. Pelvic Innervation

2.1.1 Anterior Abdominal Wall

Knowledge of the anatomy of the anterior abdominal wall is crucial to avoid complications during laparoscopic surgery. Key landmarks such as the umbilicus, anterior superior iliac spines, and pubic symphysis guide the safe placement of trocars, preventing injury to vital structures including arteries and veins. The cephalocaudal relationship between the aortic bifurcation and umbilicus varies widely and is not related to body mass index in anesthetized patients (1). Regardless of body mass index, the aortic bifurcation is more likely to be located caudal to the umbilicus in Trendelenburg compared with the supine position. The position of the umbilicus in relation to the bifurcation of the aorta may vary, depending on the patient's habitus and weight, and in obese patients, the umbilicus can be located several centimeters below the aortic bifurcation. Additional considerations for laparoscopic entry are in the positions of the inferior and superficial epigastric arteries and veins, which travel on the posterior surface of the rectus abdominis muscle and within the subcutaneous tissue of the anterior abdominal wall, respectively (Figure 2.1). Transillumination can help visualize the superficial vessels, while identification of the inferior epigastric vessels requires direct visualization through the laparoscope. Placing lateral ports approximately 8 cm from the midline and 8 cm superior to the pubic symphysis reduces the risk of injury to these vessels.

2.1.2 Superficial Peritoneal Anatomy

A systematic inspection of both the pelvis and upper abdomen is crucial at the beginning of any laparoscopic procedure. This examination involves visually assessing the condition of pelvic viscera, pelvic surfaces, and various abdominal structures including the appendix, ascending colon, falciform ligament, liver and gallbladder, omentum, transverse colon, stomach, right and left hemidiaphragms, and descending colon. The laparoscopist should carefully look for signs of adhesions, inflammation, endometriosis, fluid in the cul-de-sac, peritoneal studding, tumors, and any distortion of pelvic or abdominal anatomy. The laparoscope provides a unique view of the structures on the undersurface of the anterior abdominal wall. Notably, the median umbilical fold

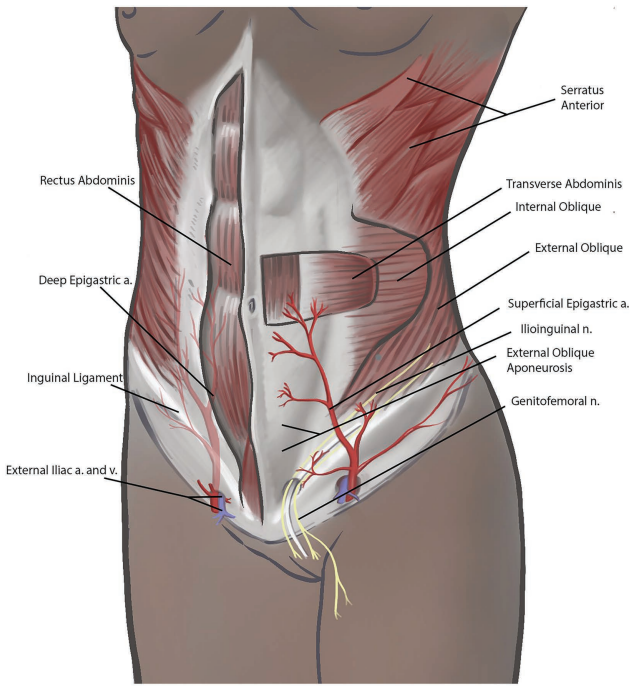


FIGURE 2.1 Anterior abdominal wall with emphasis on vascular anatomy and neuroanatomy.

DOI: 10.1201/9781003312109-2

represents the obliterated urachus, running from the bladder dome underneath a peritoneal fold. Adjacent to it are the medial umbilical folds, formed by peritoneum covering the obliterated umbilical arteries (Figure 2.2). Following these arteries underneath the round ligament into the broad ligament leads to the superior vesical artery and ultimately to the termination of the internal iliac artery. The lateral umbilical fold, formed by tenting of the peritoneum over the inferior epigastric artery and vein, lies lateral to the medial umbilical fold. Identifying these structures through the laparoscope allows the surgeon to place lateral trocars safely, away from the epigastric vessels. Applying anterior traction on the uterus reveals the uterosacral ligaments and facilitates visualization of the ureters in the pelvic sidewall. The dome of the bladder can be identified as a semilunar outline overlying the pubic symphysis (Figure 2.3).

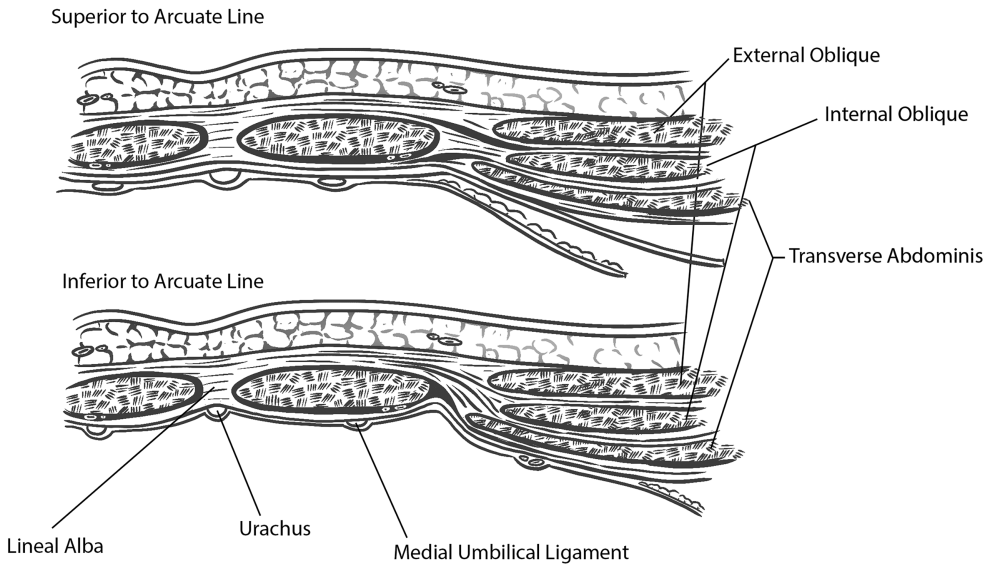


FIGURE 2.2A Cross sections of the anterior abdominal wall superior and inferior to the arcuate line.

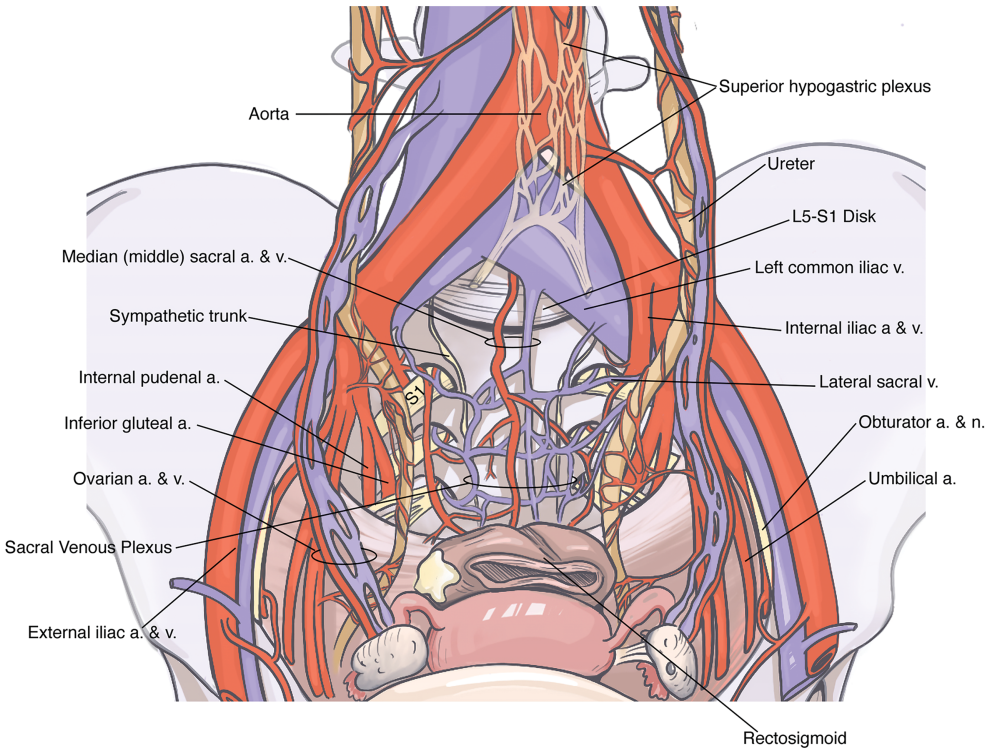


FIGURE 2.2B Pelvic retroperitoneal structures: posterior and lateral.

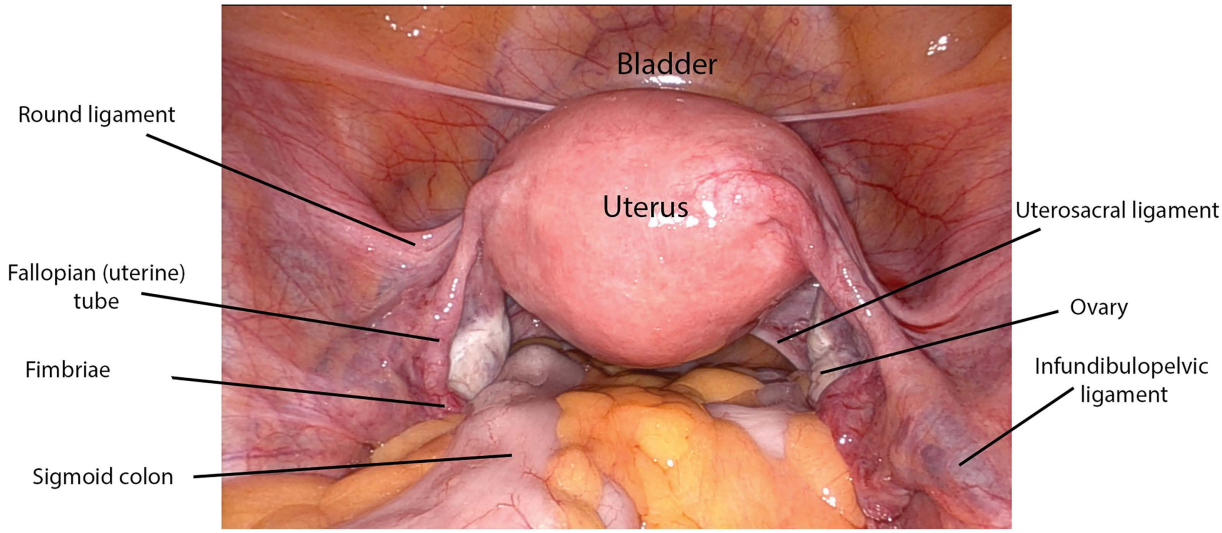


FIGURE 2.3 Laparoscopic view of normal female pelvic anatomy.

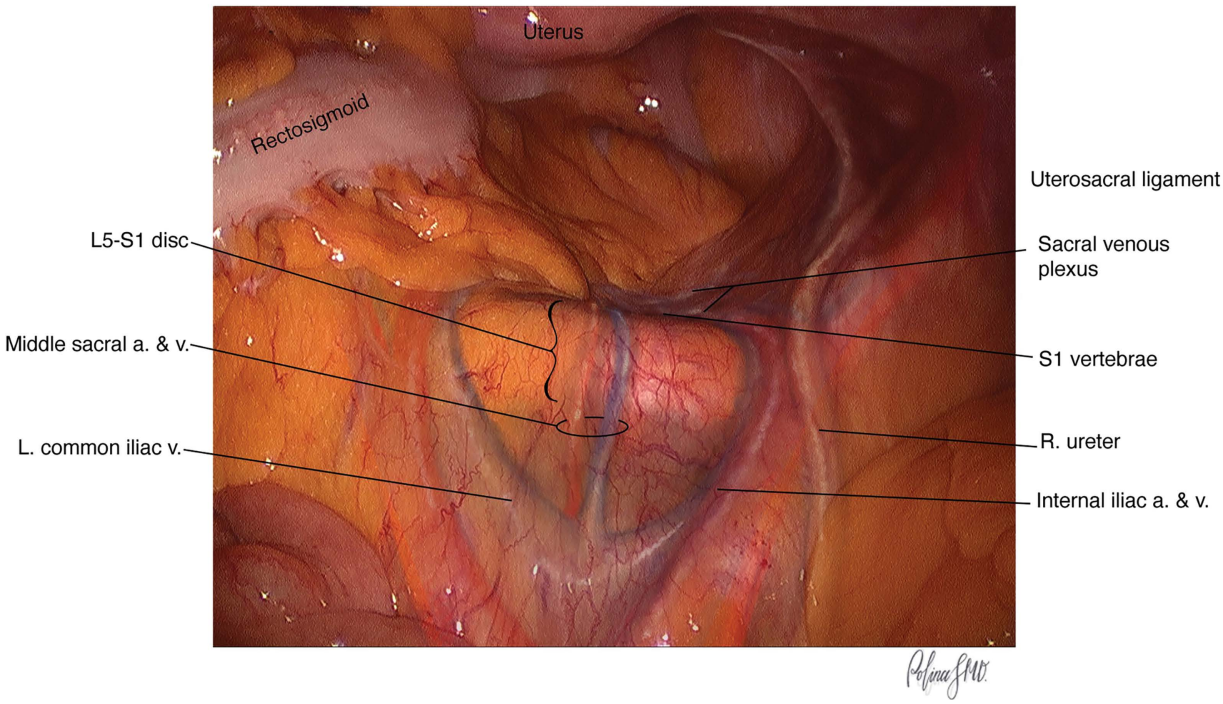


FIGURE 2.4 Presacral anatomy.

2.1.3 Presacral Space

Surgical entry into the presacral space is required for sacrocolpopexy and other procedures such as presacral neurectomies, lymphadenectomy, and tumor resection.

The presacral space is a retroperitoneal space located between the rectosigmoid and the posterior abdominal wall peritoneum anteriorly, and the sacrum posteriorly (Figure 2.4). It extends from below the aortic bifurcation to the pelvic diaphragm muscles, with lateral boundaries formed by the common and internal iliac vessels, as well as the fascia covering the piriformis muscle and lumbosacral nerve plexus. Within this space, there is a substantial adipose tissue layer containing the superior hypogastric plexus, hypogastric nerves, and the sacral sympathetic trunk. The sacral venous plexus, primarily formed by connections between the median and lateral sacral veins, lies adherent to the ventral surface of the sacrum. Control of bleeding in this region can be challenging due to the veins retracting into the sacral foramina. The middle sacral artery, arising from the posterior and distal part of the abdominal aorta, courses posterior to the left common iliac vein to reach the presacral space. The anterior surface of the first sacral vertebra is the preferred site for mesh fixation during sacrocolpopexy, considering the proximity of critical structures such as the ureter, iliac vessels, and the first sacral nerve. Surgeons

often use the area cephalad to the "true" sacral promontory (i.e., overlying the L5-S1 disc) for graft fixation, but caution must be exercised to avoid complications (2–4). Precise identification of the ligament and the left common iliac vein is crucial when placing sutures or metal tacks above the sacral promontory. Understanding the 60-degree drop between the anterior surfaces of L5 and S1 vertebrae helps with intraoperative localization of the anatomically correct promontory and avoids the L5-S1 disc.

2.1.4 Pelvic Brim

The pelvic brim, located over the sacroiliac joint, serves as the entry point for several important structures into the pelvic cavity. These structures vertically course over the pelvic brim and then rotate to form the pelvic sidewall. Progressing posteriorly to the sacroiliac joint, the following structures are encountered: the peritoneum, the ovarian vessels within the infundibulopelvic ligament, the ureter passing over the bifurcation of the common iliac artery, the common iliac vein, the medial edge of the psoas muscle, the obturator nerve positioned over the parietal fascia above the sacroiliac joint capsule, and, in a more medial position, the lumbosacral trunk coursing from the lumbar plexus to the sacral plexus overlying the piriformis muscle in the pelvis (Figure 2.5). Because of the close relationship of the infundibulopelvic ligament to the ureter, identification of the ureter and lifting of the ligament away from the path of the ureter is critical to prevent injury during oophorectomy procedures.

2.1.5 Pelvic Sidewall

The pelvic sidewall can be divided into three surgical layers based on avascular planes. The first layer consists of the parietal peritoneum, which includes the ureter within its own visceral fascial capsule. When the peritoneum is incised and retracted medially, the ureter moves with it. The second layer encompasses the internal iliac artery and vein, along with their anterior visceral branches, all enveloped within visceral connective tissue containing lymph tissue and visceral hypogastric nerves. The third layer comprises the parietal fascia over the obturator internus muscle, which includes the obturator artery, nerve, and vein. Additionally, it involves the external iliac artery and vein along the medial aspect of the psoas muscle, positioned over the bony arcuate line of the ilium. Blunt dissection allows for the separation of these layers without damaging blood vessels. The second surgical layer can be identified by tracing the path of the obliterated umbilical artery back to the superior vesical artery within the broad ligament, and then to the terminal root of the internal iliac artery, with the uterine artery branching off at this junction.

2.1.6 Base of the Broad Ligament

The base of the broad ligament refers to the anatomical region where the cardinal ligament inserts into the pericervical ring of the endopelvic fascia, providing upper vaginal support (5, 6). Within this region, the ureter travels in an oblique fashion underneath the uterine artery, approximately 1.5 cm lateral to the cervix. It is a critical area where the ureter bends, making a "knee-bend" to turn anteriorly and medially across the

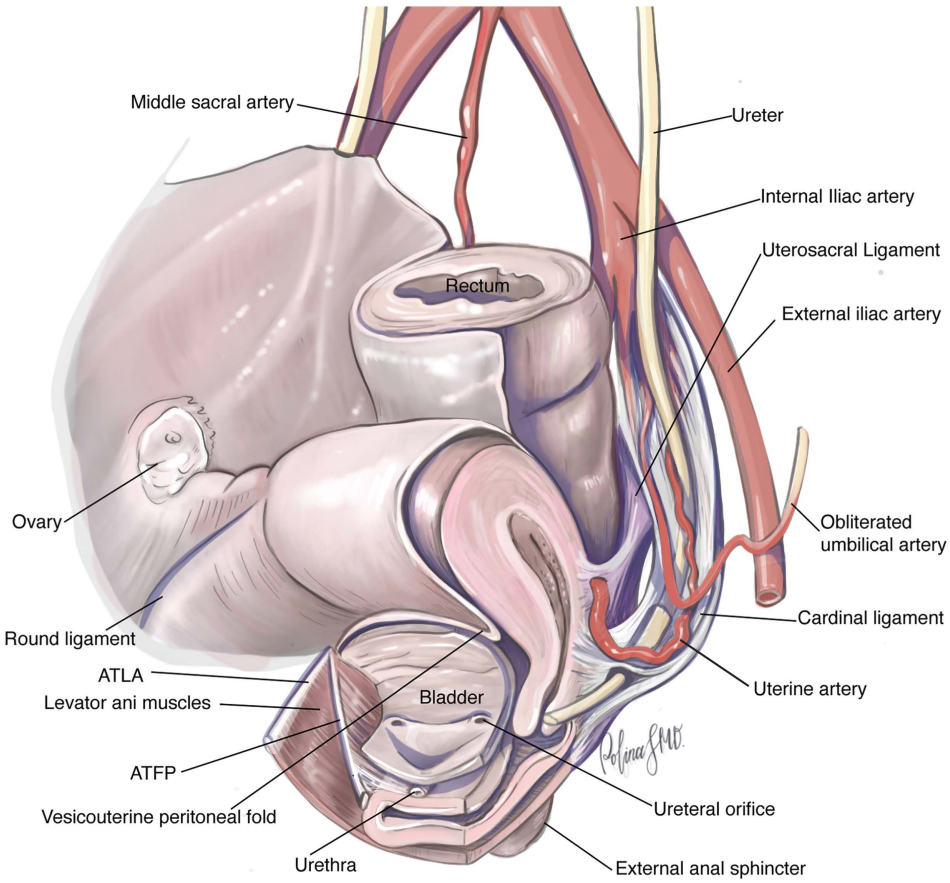


FIGURE 2.5 Potential surgical spaces of the female pelvis.

anterolateral fornix of the vagina before entering the bladder. This knee-bend is situated about 2 cm medial and anterior to the ischial spine (7, 8). It is also referred to as the parametrium, which is adjacent to the cervicouterine junction. The area lateral to the vagina is known as the upper paracolpium (5, 6).

2.1.7 Extraperitoneal Surgical Spaces of the Female Pelvis

2.1.7.1 Pararectal Space

The pararectal space is located posterior to the base of the broad ligament. It can be accessed by dissecting the ureter medially away from the internal iliac artery and vein, behind the origin of the uterine artery. The base of the broad ligament forms its anterior border, while the internal iliac artery and the ureter serve as its lateral and medial borders, respectively. The uterosacral ligament is also present within this space.

2.1.7.2 Paravesical Space

The paravesical space lies anterior to the base of the broad ligament and is bordered medially by the bladder and laterally by the fascia of the obturator internus muscle. It leads into the lateral retropubic space. Within the paravesical space, the area lateral to the obturator nerve is referred to as the obturator space. The obturator lymph nodes can be harvested from this region.

2.1.7.3 Retropubic Space

The retropubic space, also known as the prevesical space or the space of Retzius, is a potential space between the back of the pubic bone and the anterior portion of the bladder. It contains areolar tissue and a visceral bladder capsule. The obturator internus muscle and its parietal fascia form the lateral border, while the anterior border is formed by the bony ridge of the ilium, where the obturator nerve, artery, and vein are located. The floor of the space is the pubocervical fascia. Care must be taken when working in this space to avoid damaging the delicate perivesical venous sinuses (9).

2.1.7.4 Vesicovaginal Space

The vesicocervical space begins below the vesicouterine peritoneal fold, which represents the loose attachments of the peritoneum in the vesicouterine pouch. This space extends inferiorly as the vesicovaginal space, which reaches the junction of the proximal and middle thirds of the urethra. Below this point, the urethra and vagina fuse (10). These spaces are filled with loose connective tissue or visceral fascia, facilitating dissection during hysterectomy to separate the bladder from the cervix and anterior vaginal walls. Care must be taken not to dissect too vigorously and laterally to prevent injury to the ureter and vasculature within the bladder pillars.

2.1.7.5 Rectovaginal Space

The rectovaginal space is bounded superiorly by the cul-de-sac peritoneum and the uterosacral ligaments, laterally by the iliococcygeus muscles, posteriorly by the visceral fascial capsule surrounding the rectum, and anteriorly by the visceral fascial capsule surrounding the posterior aspect of the vagina (Figure 2.6). The rectovaginal septum, located behind

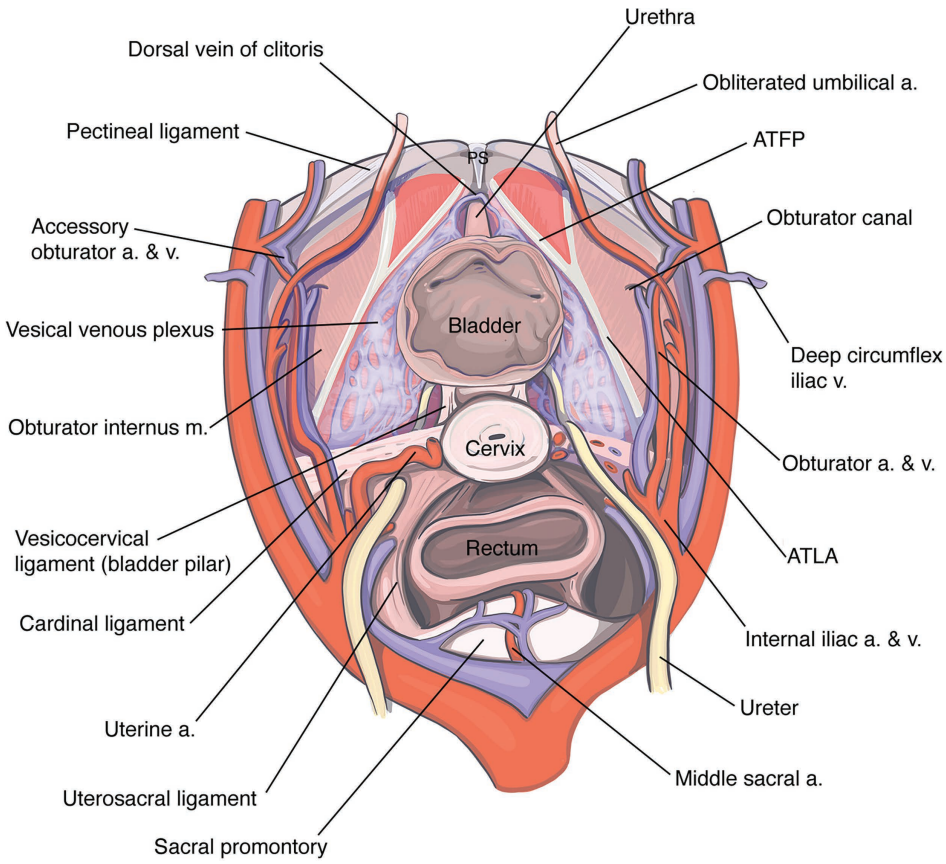


FIGURE 2.6 The cardinal and uterosacral ligaments and relative relationships to blood vessels and the ureter.

the vagina, can be dissected away from it. This space is often utilized for rectocele repair (11).

2.1.8 Pelvic Blood Supply

The pelvic organs receive their blood supply from the visceral branches of the internal iliac artery and direct branches of the abdominal aorta. The internal iliac artery divides into two divisions: the posterior division gives rise to the iliolumbar, lateral sacral, and superior gluteal arteries, while the anterior division gives rise to the internal pudendal, obturator, and inferior gluteal arteries. The anterior division also supplies the pelvic viscera, including the uterus, vagina, rectum, and bladder, through branches such as the uterine, vaginal, middle rectal, and superior vesical arteries. The superior rectal artery, a branch of the inferior mesenteric artery, contributes to the blood supply of the rectum, while the ovarian arteries contribute to the blood supply of the uterus and adnexa. There are important anastomoses between the aorta and internal iliac arteries, including those between the median and lateral sacral arteries and between the lumbar and iliolumbar arteries (Figure 2.7).

2.1.9 Pelvic Innervation

The autonomic nervous system in the pelvis includes the superior and inferior hypogastric plexuses and hypogastric nerves. The pelvic viscera and perineal erectile structures are innervated by fiber extensions from the inferior hypogastric plexus. The superior hypogastric plexus is an extension of the aortic and inferior mesenteric plexuses and primarily contains sympathetic and sensory fibers from the uterus. It divides into the right and left hypogastric nerves, which join parasympathetic fibers to form the inferior hypogastric plexus. The inferior hypogastric plexus contains sympathetic and parasympathetic fibers that accompany the branches of the internal iliac artery to the pelvic viscera. It is divided into the vesical, uterovaginal, and middle rectal plexuses (12) (Figure 2.8). The pudendal nerve provides motor and sensory innervation to the perineal region and is important for urinary and anal continence, as well as sexual function (13).

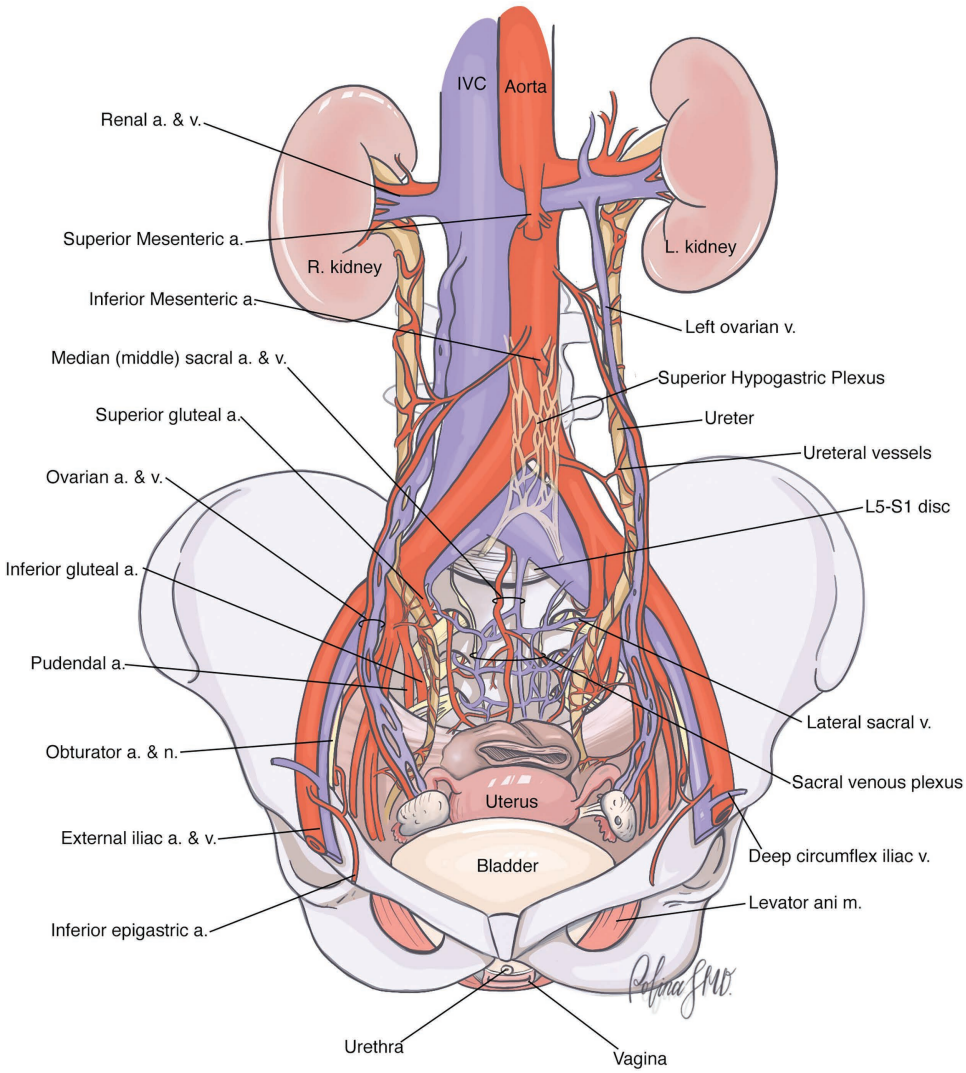


FIGURE 2.7 Blood supply of the female pelvis.

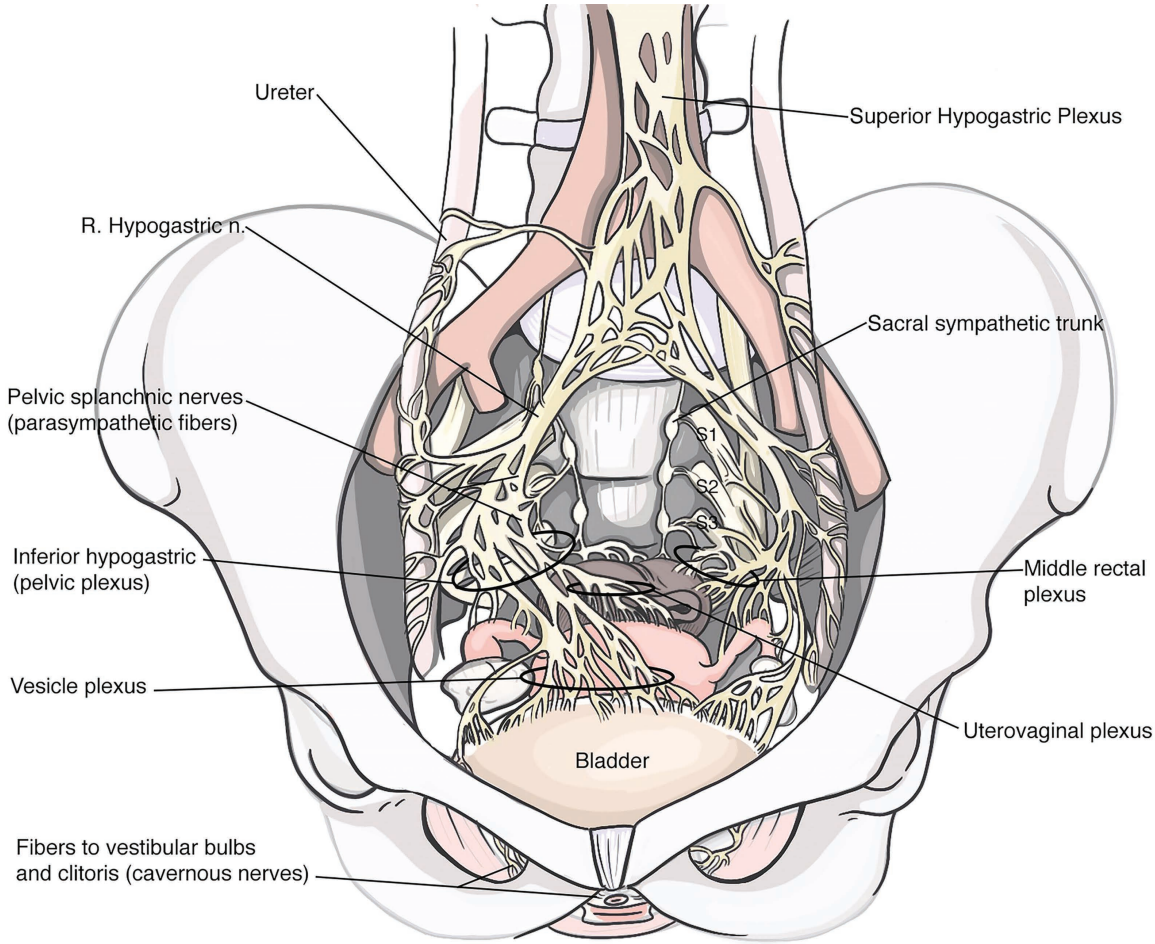


FIGURE 2.8 Neuroanatomy of the female pelvis.

2.2 Principles of Safe Surgical Dissection

Meticulous surgical dissection in minimally invasive gynecologic surgery is vital for optimal outcomes and reduced complications. These techniques, however, are only effective if the surgeon possesses an excellent understanding of the anatomy of the female pelvis. By thinning, stretching, and carefully opening visceral connective tissues, surgeons can identify vital structures while minimizing bleeding and tissue damage. Progressing millimeter by millimeter ensures accuracy, step-by-step control, safe exposure, and minimal blood loss. Expert techniques include "grasp and tent," "push-spread," "traction-countertraction," gentle tissue wiping, and hydrodissection. Dissection should follow anatomical relationships, adapting techniques to each region. These techniques save time, enhance efficiency, and improve visualization. Surgeons should practice becoming familiar with their sight and feel (14).

References

1. Nezhat F et al. Laparoscopic appraisal of the anatomic relationship of the umbilicus to the aortic bifurcation. *J Am Assoc Gynecol Laparoscop*. 1998;5(2):135–140.
2. Florian-Rodriguez ME et al. First sacral nerve and anterior longitudinal ligament anatomy: clinical applications during sacrocolpopexy. *Am J Obstet Gynecol*. 2017;217:607.e1–607.e4.
3. White AB et al. Optimal location and orientation of suture placement in abdominal sacrocolpopexy. *Obstet Gynecol*. 2009;113:1098–1103.
4. Good MM et al. Preventing L5-S1 discitis associated with sacrocolpopexy. *Obstet Gynecol*. 2013;121:285–290.
5. Ramanah R et al. Anatomy and histology of apical support: a literature review concerning cardinal and uterosacral ligaments. *Int Urogynecol J*. 2012;23:1483–1494.
6. Balgobin S et al. Standardized terminology of apical structures in the female pelvis based on a structured medical literature review. *Am J Obstet Gynecol*. 2020;222:204.e1–204.e18.
7. Rahn DD et al. Anatomic relationships of the distal third of the pelvic ureter, trigone, and urethra in unembalmed female cadavers. *Am J Obstet Gynecol*. 2007;197:668.e1–668.e4.
8. Jackson LA et al. Gross and histologic anatomy of the pelvic ureter: clinical applications to pelvic surgery. *Obstet Gynecol*. 2019;133:896–904.
9. Hamner JJ et al. Gross and histologic relationships of the retropubic urethra to lateral pelvic sidewall and anterior vaginal wall in female cadavers: clinical applications to retropubic surgery. *Am J Obstet Gynecol*. 2018;219:597.e1–597.e8.
10. Hinata N et al. The urethral rhabdosphincter, levator ani muscle, and perineal membrane: a review. *Biomed Res Int*. 2014:906921.

11. Maldonado PA et al. Posterior vaginal compartment anatomy: implications for surgical repair. *Female Pelvic Med Reconstr Surg*. 2020;26(12):751–757.
12. Ripperda CM et al. Anatomic relationships of the pelvic autonomic nervous system in female cadavers: clinical applications to pelvic surgery. *Am J Obstet Gynecol*. 2017;216:388.e1–388.e7.
13. Jackson LA et al. Anatomy, histology, and nerve density of clitoris and associated structures: clinical applications to vulvar surgery. *Am J Obstet Gynecol*. 2019;221(5):519.e1–519.e9.
14. Rogers RM, Jr. How to become a competent surgeon: learning the skills of surgical dissection & the applied knowledge of surgical anatomy. In: Pasic RP et al., eds. *Practical Manual of Minimally Invasive Gynecologic and Robotic Surgery: A Clinical Cook Book 3E*. CRC Press; 2022.

3 PHYSIOLOGY OF THE FEMALE REPRODUCTIVE TRACT

Archana Ayyar, Emily Marra, Lauren Griebel, and Rebecca Flyckt

3.1 Introduction

Understanding the physiology of the female reproductive system and its associated organs is essential when planning any gynecologic surgery, and this knowledge is also critical to interpreting intraoperative findings and surgical pathology reports appropriately. In addition to informing medical and surgical decision making, familiarity with reproductive physiology is important when counseling patients on treatment options and their different side effects. This chapter will summarize the relevant physiology of the hypothalamic–pituitary–ovarian axis and describe the hormonal regulation of the menstrual cycle. Through clinical correlations, this chapter will highlight relevant examples of pathophysiology that are commonly encountered in gynecologic office and surgical practice.

3.2 Relevant Anatomy

3.2.1 Hypothalamus and Pituitary

The hypothalamus is located at the base of the brain, inferior to the third ventricle, superior to the pituitary gland, and posteriorly to the optic chiasm (1). The hypothalamus is often deemed the "control center" for the endocrine system (2). It is responsible, through hormonal communication, for the physiologic regulation of endocrine functions in the thyroid, adrenals, and reproductive organs. The hypothalamus also serves to regulate non-endocrine systems such as temperature, appetite, and the autonomic nervous system (i.e., visceral motor system). The hypothalamus communicates with the anterior pituitary via the hypophyseal portal system, and the hypothalamus produces and secretes thyrotropin-releasing hormone (TRH), prolactin-releasing hormone (PRH), gonadotropin-releasing hormone (GnRH), corticotropin-releasing hormone (CRH), and growth hormone-releasing hormone (GHRH) (2). These hypothalamic hormones subsequently cause the anterior pituitary release of thyroid-stimulating hormone (TSH), prolactin, follicle-stimulating hormone (FSH) and luteinizing hormone (LH), adrenocorticotropic hormone (ACTH), and growth hormone (GH), respectively. The hypothalamus also communicates with the posterior pituitary via nerves to release antidiuretic hormone (ADH) and oxytocin, both of which are initially produced in the hypothalamus (see Table 3.1).

TABLE 3.1 Hormones and Their Associated Organs

Hormone	Organ of Origin	Organ of Release
TRH	Hypothalamus	Hypothalamus
PRH	Hypothalamus	Hypothalamus
GnRh	Hypothalamus	Hypothalamus
CRH	Hypothalamus	Hypothalamus
GHRH	Hypothalamus	Hypothalamus
TSH	Anterior Pituitary	Anterior Pituitary
Prolactin	Anterior Pituitary	Anterior Pituitary
FSH	Anterior Pituitary	Anterior Pituitary
LH	Anterior Pituitary	Anterior Pituitary
ACTH	Anterior Pituitary	Anterior Pituitary
GH	Anterior Pituitary	Anterior Pituitary
ADH	Hypothalamus	Posterior Pituitary
Oxytocin	Hypothalamus	Posterior Pituitary

Abbreviations: *TRH*: thyroid-releasing hormone. *PRH*: prolactin-releasing hormone. *GnRH:* gonadotropin-releasing hormone. *CRH*: corticotropin-releasing hormone. *GHRH*: growth hormone-releasing hormone. *TSH*: thyroid-stimulating hormone. *FSH*: follicle-stimulating hormone. *LH*: luteinizing hormone. *ACTH*: adrenocorticotropic hormone. *ADH*: antidiuretic hormone.

3.2.2 Ovarian Anatomy

The tissues that make up the ovary are comprised of three layers: surface, cortex, and medulla (2). The surface consists of a single layer of cuboidal epithelium, often referred to as the ovarian surface epithelium. The cortex is comprised of ovarian follicles containing ovarian follicles and oocytes, surrounded by their granulosa cells, theca cells, and connective tissue. The medulla is primarily connective tissue filled with neurovascular bundles and is the deepest layer.

3.2.2.1 Clinical Correlate

Anti-Müllerian hormone (AMH) and inhibin are produced by the granulosa cells of the ovarian antral and pre-antral follicles. AMH is a marker of ovarian reserve, although it does not predict fertility success in couples initiating attempts at conception (3, 4). AMH is often used as a measure of ovarian reserve in women undergoing fertility treatments, and it can be used to predict oocyte and embryo yield with IVF as well as required doses of gonadotropins for ovarian stimulation. AMH also inhibits primordial follicle growth and FSH-induced follicle growth, making it relevant for women with polycystic ovary syndrome (PCOS) and oligo-ovulation, who typically have high AMH levels (5). The higher the AMH levels, the less likely a patient is to respond to ovulation induction agents such as clomiphene citrate for purposes of conception (6). Inhibin (another ovarian marker) is elevated in ovarian granulosa cell tumors due to its production in granulosa cells, making it a useful tumor marker for this diagnosis (7).

3.2.2.2 Clinical Correlate

When performing ovarian cystectomy, it is best to make initial incision on the contralateral side of the ovary away from the hilum (8). Incisions near the hilum are more likely to produce difficult-to-control bleeding, and aggressive hemostatic techniques at the level of the hilum can result in devascularization of the ovary itself. In addition, when performing cystectomy, electrosurgery should be used sparingly on the cortex of the ovary and, if incision is needed, it should be performed sharply when possible without electrosurgery. This is the site of ovarian follicles and excessive electrosurgery damage can decrease ovarian reserve (8).

3.2.3 Uterine Physiology

The wall of the uterus can be divided into three distinct layers: endometrium, myometrium, and perimetrium (3). The

DOI: 10.1201/9781003312109-3

perimetrium contains connective tissue and is the outermost layer of the uterine wall. The myometrium is the middle layer and consists of smooth muscle. This layer contracts during the menstrual cycle, with orgasm, and during labor (3). The endometrium is the innermost layer. Although typically included in discussions of the hypothalamic–pituitary–ovarian (HPO) axis, the uterus, specifically the endometrium, is a key responder to the hormones produced in this feedback system (9). The endometrium can be further divided into two layers, the functionalis layer (superficial two-thirds) and the basalis layer (deep one-third) (9). The goal of the functionalis layer is to create an environment that is optimized for blastocyst implantation, and thus this is the layer that undergoes cyclic changes with the menstrual cycle in response to the HPO axis. In an incredible example of regenerative medicine, the stem cells of the stratum basalis layer rebuild the functionalis layer anew after each menstrual cycle (10).

3.3 Menstrual Cycle

The normal length of a menstrual cycle is between 21 and 35 days (11). Most of the variation in cycle length results from normal variation in the follicular phase, whereas the luteal phase tends to be stable at 14 days. In addition to the length of the menstrual cycle, the amount of blood loss encountered in a typical cycle (average of 30 mL) should be discussed routinely with patients. A blood loss of 80 mL or greater has been associated with anemia and is considered abnormal (11). However, this kind of quantitative cutoff has limited clinical utility as it is very challenging for patients to estimate blood loss (12). For both girls and adolescents, the menstrual cycle has been regarded as an additional vital sign by both the American College of Obstetricians and Gynecologists and the American Academy of Pediatrics (12, 13). Further evaluation for excessive bleeding is indicated if the patient needs to change their menstrual products every 1–2 hours, if there is concern for hemophilia, or if cycles occur 90 days or more apart (12). 5 years after menarche, menstrual cycles become increasingly regular and tend to reach adult cycle lengths and intervals (13).

The coordination of the menstrual cycle is dependent on the hypothalamic–pituitary–ovarian axis. The menstrual cycle (Figure 3.1) is divided into two phases that can be described by either ovarian or uterine attributes. The ovarian cycle is divided into the follicular phase that precedes ovulation and the luteal phase afterwards (14). Similarly, the uterine cycle is separated into the proliferative phase, which describes the endometrium before ovulation, and the secretory phase afterwards (14).

3.4 Endocrinology of the Hypothalamus–Pituitary–Ovarian Axis

The menstrual cycle is dependent on multiple organs that communicate hormonally. If the menstrual cycle were a symphony, the hypothalamus would be the conductor. GnRH manages the HPO axis. The neurons that synthesize GnRH originate in the olfactory bulb and migrate to the arcuate nucleus, at which point the neurons become hormonally active (8). GnRH, as stated previously, acts on the anterior pituitary to release FSH and LH stores (2). GnRH has a short half-life

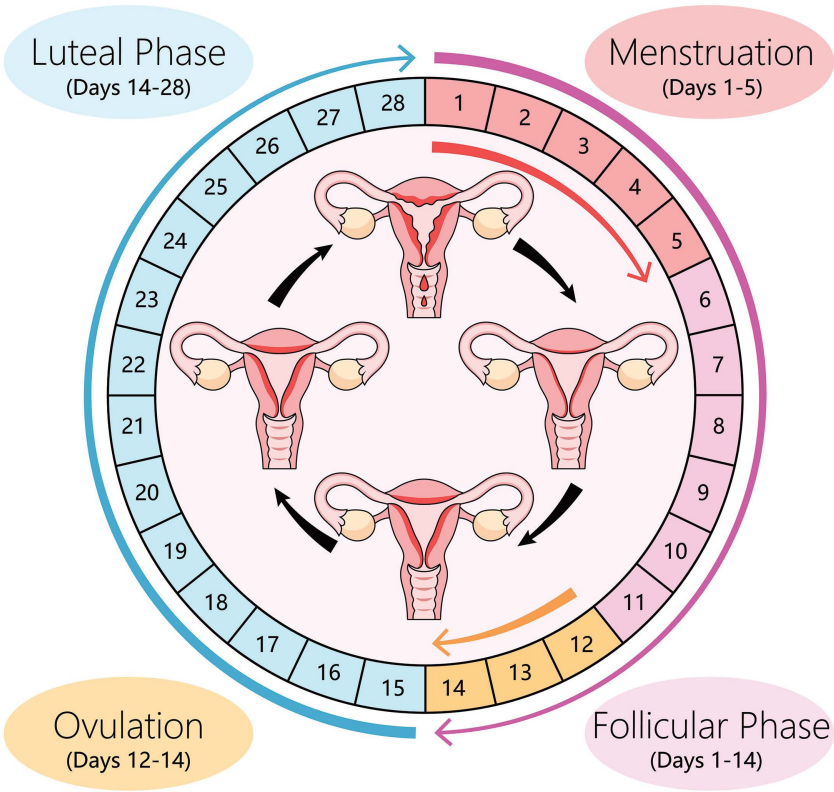


FIGURE 3.1 Stages of the menstrual cycle. (From Shutterstock, under license.)

and controls the HPO axis through pulsatile release. Moreover, the specific frequency and amplitude of GnRH release impacts the release of FSH/LH from the pituitary. Low- versus high-frequency GnRH pulses can preferentially instruct the pituitary to release FSH versus LH, respectively (14). FSH and LH then act on the ovary to produce androgens and estradiol. The feedback of ovarian steroids on the hypothalamus and pituitary is detailed later.

Dopamine does not impact FSH/LH directly at the pituitary but acts on the hypothalamus to inhibit GnRH release (8). However, dopamine does act at the level of the pituitary to inhibit prolactin release. Interestingly, dopamine is a precursor to norepinephrine, which has a stimulatory effect on GnRH release. Additionally, neuropeptide Y (NPY) stimulates the release of GnRH and increases appetite (9). NPY further potentiates the pituitary response to GnRH. Without estrogen present, NPY inhibits GnRH secretion. NPY is thought to be a surrogate marker for a body's energy capacity to support a pregnancy (14).

Other mediators involved in the menstrual cycle include follistatin, activin, and inhibin A and B. Activin is a peptide that is secreted from granulosa cells and augments FSH secretion and suppresses prolactin, ACTH, and GH secretion (2). Additionally, activin increases the number of FSH receptors on granulosa cells, further supporting FSH's actions (2). Follistatin, released from follicular fluid and the pituitary, binds activin to suppress FSH activity (14). When FSH binds to granulosa cells, it stimulates the production of inhibin B. Inhibin B is higher in concentration before ovulation and is produced from both granulosa cells and the pituitary (2). Inhibin B then communicates with the pituitary to decrease FSH release. After ovulation, inhibin A is secreted after ovulation by the corpus luteum. Although inhibins share similar structure with activin, inhibin A and B both suppress FSH secretion.

3.4.1 Clinical Correlate

The multiple positive and negative feedback loops of the endocrine system give physicians an opportunity to influence a patient's menstrual cycle if needed clinically. GnRH's short half-life and pulsatility plays an important role in the release of FSH/LH to then orchestrate the menstrual cycle (15). Prolonged exposure to GnRH at the pituitary initially causes a surge in release of FSH/LH ("flare" effect), however eventually causes downregulation and desensitization of the GnRH receptor at the pituitary (15). Thus, by providing a medication that is a GnRH agonist with a longer half-life, a provider can cause suppression of systemic gonadotropins and allow for temporary cessation of ovarian function and menses. GnRH antagonists have been studied as well and have the added benefit of avoiding the initial surge of gonadotropins seen with GnRH agonists (16). Examples of GnRH agonists and GnRH antagonists are detailed in Table 3.2. Furthermore, aromatase inhibitors block the conversion of androgens to estradiol and can cause a hypoestrogenic state. As endometriosis lesions express aromatase, aromatase inhibitor treatment (usually in combination with hormonal suppression of ovulation) may benefit endometriosis patients by suppressing local estradiol production within the endometriotic lesions themselves (17).

3.4.2 Ovarian Cycle

3.4.2.1 Follicular Phase

During the follicular phase, folliculogenesis occurs and drives the recruitment of immature antral follicles and the eventual selection of a dominant follicle (2). The selection of the dominant follicle occurs in days 5–7 of the menstrual cycle (14). The dominant follicle is the follicle that goes on to ovulate and is typically the largest, usually measuring approximately 1.7–2.5 cm prior to ovulation (2).

TABLE 3.2 GnRH Agonists and Antagonists

Name	Type	Half-Life	Potency	Route
GnRh	-	2–4 minutes	-	IV, SC
Leuprolide	GnRh Agonist	1.5 hours	Medium	SC, IM Depot
Buserelin	GnRH Agonist	1.5 hours	Low	SC, Intranasal
Goserelin	GnRH Agonist	4.5 hours	High	SC Implant
Elagolix	GnRH Antagonist	4–6 hours	High	PO

Abbreviations: *GnRH*: gonadotropin-releasing hormone. *IV*: intravenous. *SC*: subcutaneous. *IM*: intramuscular. *PO*: oral.

Source: See further Ref 2.

Increases in FSH level allows for the selection of one dominant follicle (18). The dominant follicle depends on both FSH and LH release from the pituitary. LH primarily acts on the theca cells and FSH acts on the granulosa cells in what is known as the two cell theory (8). Theca cells allows for progesterone and androgen production which is then converted to estradiol using aromatase in the granulosa cells (9). Rising estradiol levels inhibit GnRH production and stimulate proliferation of the endometrium. In the early follicular phase, declining FSH secretion leads to atresia of the non-dominant follicles that had been initially recruited for that cycle, further promoting the selection of only one dominant pre-ovulatory follicle per month (2).

3.4.2.2 Early Luteal Phase

Rising estradiol levels produced by the dominant follicle eventually reach a peak concentration approximately one day before ovulation. In the late follicular phase, there is a switch from negative to positive feedback of estradiol on the anterior pituitary gland. Once a critical level of estradiol is reached, the LH surge occurs. This promotes follicle rupture and subsequent oocyte release (ovulation), by stimulating both prostaglandin release and the production of proteolytic enzymes (2). This marks the transition into the luteal phase.

Ovarian follicles are arrested at the prophase stage of meiosis I at the time of birth. Resumption of meiosis occurs in response to the LH surge. This is then arrested in the metaphase stage of meiosis II until the oocyte is fertilized with sperm. This then allows for completion of meiosis II (8).

3.4.2.3 Middle to Late Luteal Phase

Following ovulation and the disruption of the dominant follicle, the remaining granulosa and theca cells form the corpus luteum. If embryo implantation has occurred, the corpus luteum continues to produce progesterone, which supports the pregnancy until the placenta is able to produce progesterone and provide support for the pregnancy (19). Human Chorionic Gonadotropin (hCG) produced from the pregnancy rescues the corpus luteum from regression (20).

β-hCG stimulates the corpus luteum to continue to produce progesterone and support the early gestation. In the absence of implantation of a fertilized oocyte, circulating progesterone

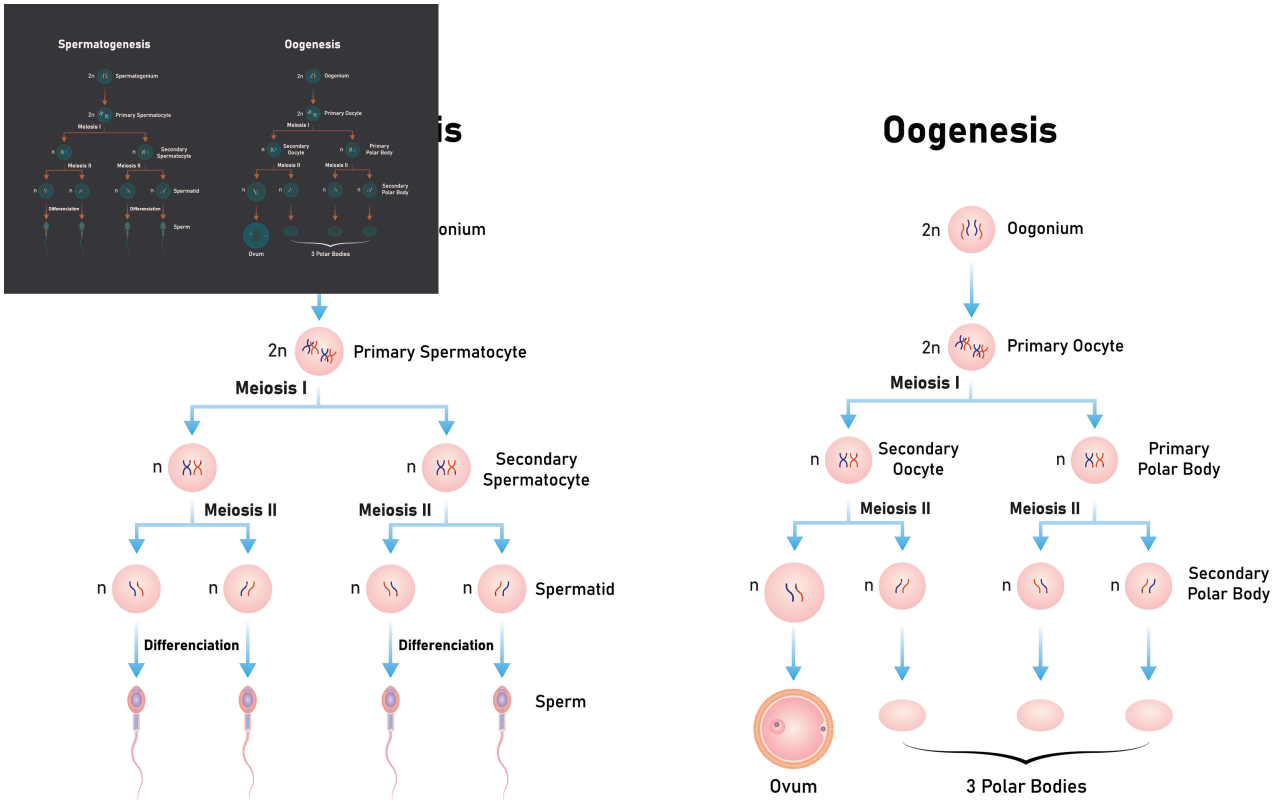


FIGURE 3.2 Oogenesis. (From Shutterstock, under license.)

levels decrease. This late luteal decline in estrogen and progesterone levels leads to the onset of menses, typically approximately 14 days after the LH surge (20).

3.4.2.3.1 Clinical Correlate

The "female athlete triad" is characterized by disordered eating resulting in insufficient energy availability, amenorrhea, and decreased mineral bone density (21). Changes in menstruation and bone health are driven by negative feedback from physical and nutritional stressors, leading to hypothalamic hypogonadism. Follicle recruitment and ovulation do not occur, leading to a deficiency in ovarian estradiol production and a lack of endometrial proliferation (21). After a progesterone challenge, patients will typically have scant or no withdrawal bleeding as there is insufficient endometrial tissue present to shed.

3.4.3 Uterine Cycle

3.4.3.1 Proliferative Phase

During the proliferative phase of the menstrual cycle, the functionalis layer responds to estrogen production from the growing ovarian follicle by increasing mitotic activity in order to thicken the endometrium (22). Within the stroma of the endometrium, spiral arteries extend to just below the surface of the endometrium (2). At this point in time, these arteries are not branched or coiled.

3.4.3.2 Secretory Phase

The secretory phase of the uterus begins after ovulation. The endometrium is heavily influenced by changes in both estrogen and progesterone levels. Embryo implantation typically occurs at around menstrual cycle days 21–22 in a person with regular 28-day cycles. If implantation does not occur, stimulation of the corpus luteum by hCG does not occur, and systemic progesterone and estrogen levels decrease as the corpus luteum degenerates (22). The endometrium stops proliferating and there is a decline in DNA synthesis. There is increased tortuosity of the glands and the spiral arteries begin to demonstrate significant coiling. The spiral arteries will further vasoconstrict, causing tissue necrosis (21). This, in addition to enzymatic degradation, instigates the process of apoptosis, which leads to endometrial tissue breakdown and menstrual shedding (23).

3.4.3.3 Clinical Correlate

In patients with chronic anovulation, such as polycystic ovarian syndrome, there is no systemic increase or subsequent withdrawal of progesterone as would occur with normal ovulation (24). Thus, there is no cessation of the proliferative phase. Chronic low levels of ovarian estrogen stimulate many oncogenes which allow for growth of the endometrium (25). Progesterone normally suppresses estrogen's effect on these oncogenes. Thus, a patient with anovulation does not have a method of counteracting tissue proliferation, which then increases the risk of developing hyperplasia or malignancy of the endometrium. Patients with chronic oligomenorrhea should have endometrial sampling performed to evaluate for underlying precancerous or cancerous lesions, especially if there are other risk factors for hyperplasia or cancer (e.g., obesity, pre-diabetes, PCOS, etc.) (11).

3.4.3.4 Clinical Correlate

During menstruation, there is a balance between clotting and fibrinolysis. In order to minimize blood loss,

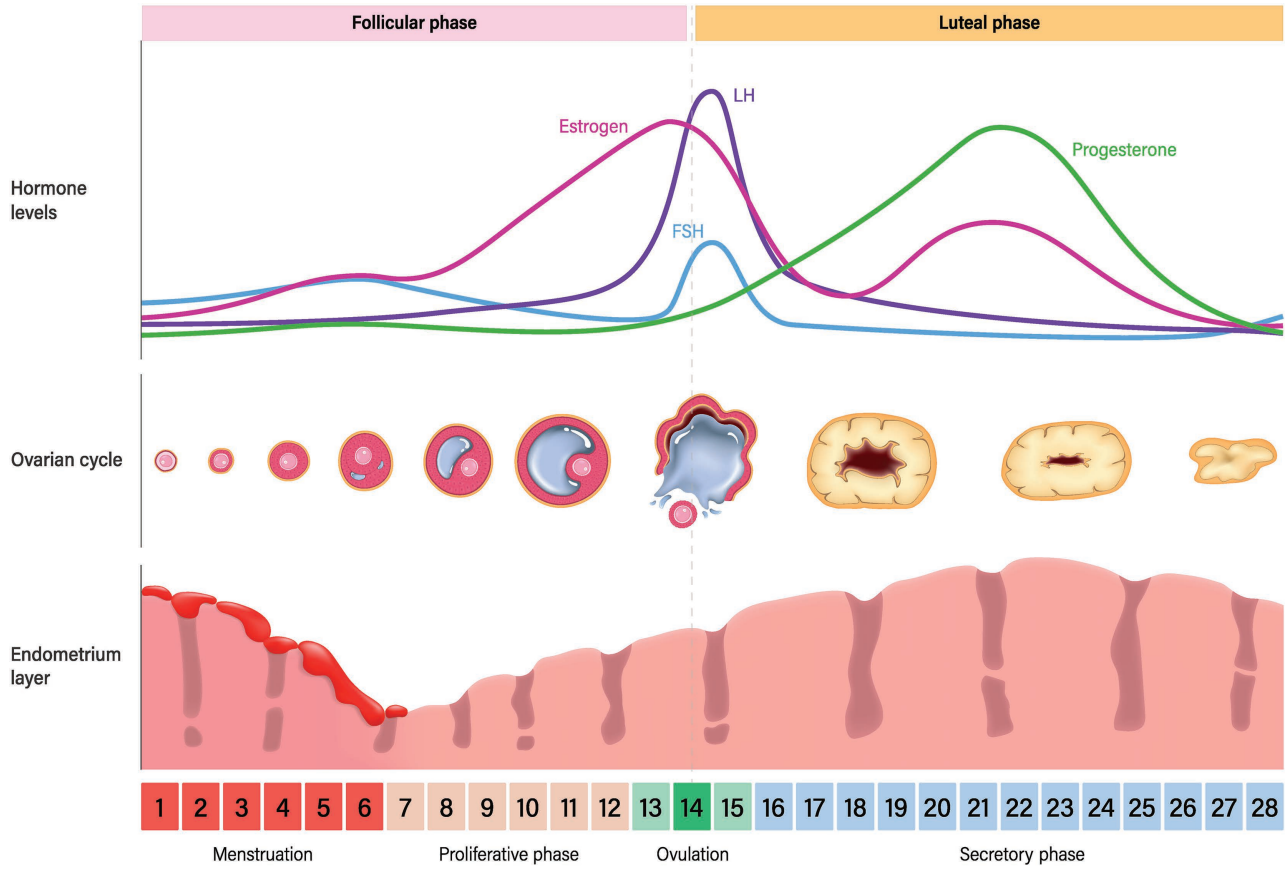


FIGURE 3.3 Hormonal changes in the menstrual cycle. (From Shutterstock, under license.)

thrombin-platelet plugs form at the shedding surface of the endometrium (26). Multiple factors, including plasminogen activators, are used in this process. If this plug does not form properly or the patient has a platelet dysfunction, they can experience menorrhagia. Plasminogen activators convert plasminogen to plasmin, which then degrades fibrin clots. Tranexamic acid (TXA) can be used to treat heavy menstrual bleeding by inhibiting plasminogen from converting to plasmin, thus preventing the fibrinolysis and decreasing the volume of menstrual blood loss (27).

3.4.4 Conclusion

The menstrual cycle involves a complex interplay between the hypothalamus, pituitary, ovary, and uterus. From the pulsatile release of GnRH to the release and downstream impact of FSH and LH, each step of the menstrual cycle is meticulously coordinated to allow for folliculogenesis, ovulation, and endometrial proliferation. By understanding of the anatomy of the reproductive organs and the intricacies of the menstrual cycle, clinicians are equipped to diagnose and medically or surgically manage common underlying gynecologic conditions.

References

1. Daniel PM. Anatomy of the hypothalamus and pituitary gland. *J Clin Pathol Suppl*. 1976;7:1–7.
2. Gingold JA et al. Hypothalamic-pituitary-ovarian axis and control of the menstrual cycle. In: Falcone T et al., eds. *Clinical Reproductive Medicine and Surgery*, 4th edn. Cham: Springer; 2022.
3. Practice Committee of the American Society for Reproductive Medicine. Testing and interpreting measures of ovarian reserve: a committee opinion. *Fertil Steril*. 2012;98(6):1407–1415.
4. Steiner AZ et al. Association between biomarkers of ovarian reserve and infertility among older women of reproductive age. *JAMA*. 2017;318(14):1367–1376.
5. Rudnicka E et al. Anti-Müllerian hormone in pathogenesis, diagnostic and treatment of PCOS. *Int J Mol Sci*. 2021;22(22):12507.
6. Lanham MSM et al. Elevated anti-Müllerian hormone (AMH) levels decrease odds of response to ovulation induction with letrozole or clomiphene citrate. *Fertil Steril*. 2014;102(3).
7. ACOG Committee on Practice Bulletins – Gynecology. Practice bulletin 174: evaluation and management of adnexal masses. *Obstet Gynecol*. 2016;128(5):e210–e226.
8. Hoffman BL et al., eds. *Williams Gynecology*, 4th edn. McGraw-Hill; 2020.
9. Ferenczy A et al. Histology of the human endometrium: from birth to senescence. *Ann NY Acad Sci*. 1991;622:6–27.
10. Cousins FL et al. Endometrial stem/progenitor cells - their role in endometrial repair and regeneration. *Front Reprod Health*. 2022;3:811537.
11. ACOG Committee on Practice Bulletins – Gynecology. Practice bulletin 128: diagnosis of abnormal uterine bleeding in reproductive-aged women. *Obstet Gynecol*. 2012;120(1):197–206.

12. ACOG Committee opinion. 651: menstruation in girls and adolescents: using the menstrual cycle as a vital sign. *Obstet Gynecol*. 2015;126(6):e143–e146.
13. AAP Committee on Adolescence et al. Menstruation in girls and adolescents: using the menstrual cycle as a vital sign. *Pediatrics*. 2006;118(5):2245–2250.
14. Fritz MA et al., eds. *Clinical Gynecologic Endocrinology and Infertility*, 8th edn. Wolters Kluwer Health/Lippincott Williams & Wilkins; 2011.
15. Moghissi KS. A clinician's guide to the use of gonadotropin-releasing hormone analogues in women. *Medscape Womens Health*. 2000;5(1):5.
16. Griesinger G et al. GnRH-antagonists in reproductive medicine. *Arch Gynecol Obstet*. 2005;273(2):71–78.
17. Bulun SE et al. Aromatase and endometriosis. *Semin Reprod Med*. 2004;22(1):45–50.
18. Schipper I et al. The follicle-stimulating hormone (FSH) threshold/window concept examined by different interventions with exogenous FSH during the follicular phase of the normal menstrual cycle: duration, rather than magnitude, of FSH increase affects follicle development. *J Clin Endocrinol Metab*. 1998;83(4):1292–1298.
19. Holesh JE et al. Physiology, ovulation. In: *StatPearls* [Internet]. Treasure Island: StatPearls Publishing; 2023.
20. Denschlag D et al. Das Corpus Luteum [The corpus luteum]. *Ther Umsch*. 2002;59(4):159–162.
21. Coelho AR et al. The female athlete triad/relative energy deficiency in sports (RED-S). *Rev Bras Ginecol Obstet*. 2021;43(5):395–402.
22. Makieva S et al. Inside the endometrial cell signaling subway: mind the gap(s). *Int J Mol Sci*. 2018;19(9):2477.
23. Jain V et al. Uterine bleeding: how understanding endometrial physiology underpins menstrual health. *Nat Rev Endocrinol*. 2022;18(5):290–308.
24. ACOG Committee on Practice Bulletins – Gynecology. Practice bulletin 194: polycystic ovary syndrome. *Obstet Gynecol*. 2018;131(6):e157–e171.
25. Rodriguez AC et al. Estrogen signaling in endometrial cancer: a key oncogenic pathway with several open questions. *Horm Cancer*. 2019;10(2–3):51–63.
26. Davies J et al. Endometrial haemostasis and menstruation. *Rev Endocr Metab Disord*. 2012;13(4):289–299.
27. Leminen H et al. Tranexamic acid for the treatment of heavy menstrual bleeding: efficacy and safety. *Int J Womens Health*. 2012;4:413–421.

4 EPIDEMIOLOGY, RESEARCH METHODS, STATISTICS, AND OUTCOME MEASUREMENTS

Ritchie Delara and James Symanowski

4.1 Introduction: Biostatistics in the Healthcare Domain

A key aspect of biostatistics in the healthcare domain regarding investigator-sponsored research (ISR) is early collaboration between the sponsor-investigator and the biostatistician beginning at the initial idea phase. A sponsor-investigator (SI) initiates, develops, and oversees the ISR and conducts the clinical investigation alone or with other local institutional principal investigators (PIs). Early collaboration is important regardless of study type. Designing a research study includes choosing a research topic; formulating a research question; writing the hypothesis, background, and rationale; and developing measurable primary and secondary objectives. Next, a study design is determined based on the study objectives. Early collaboration between the SI and the biostatistician is important regardless of the intended funding source (e.g., grant, industry, or institutional).

In this chapter, an overview of types of study designs is provided, including the basic concepts of power and sample size calculations. Study endpoints typically utilized in clinical research and the basic concepts of hypothesis testing are also described. This chapter is focused on quantitative research as it pertains to SIs.

4.2 Types of Human Subjects Research

ISR study types can be categorized into studies requiring participant-informed consent and studies that are consent-exempt, which are inherently classified as observational studies. Consent-based studies are further classified as interventional clinical trials or observational trials. Interventional clinical trials prospectively assign human subjects to one or more protocol-directed interventions to evaluate the effects of those interventions on health-related biomedical or behavioral outcomes. Consent-based observational trials typically involve a nonstandard of care information acquisition such as biospecimen collection and analysis, patient-reported surveys, and device trackers. In observational trials, the investigator records information and analyzes data which may be correlated with clinical factors or outcomes, but participants are not assigned to an arm of therapy or any intervention. Figure 4.1 illustrates the types of human subject research.

4.3 Observational Studies

Non-interventional research studies generally do not require informed consent from research subjects. Observational studies involving informed consent include a research protocol that does not dictate patient care or management. Patients are managed clinically per standard of care practices, and data abstracted from the electronic medical record (EMR) are entered into the EMR per standard practice. Protocols for observational studies are written with a request for a waiver of informed consent. Importantly, safeguards are written into these protocols to protect personal health information (PHI) and to comply with Health Insurance Portability and Accountability Act (HIPAA) standards.

A *case report*, also known as a case study, is a descriptive study that documents three or fewer unusual or emerging clinical cases. Presenting signs and symptoms, evaluation, diagnosis and management, clinical course, and prognosis are commonly described. In contrast, a *case series* includes four or more clinical cases or groups of cases. Disadvantages of case reports and case series include susceptibility to bias, challenges in reproducibility and replicability, and lack of generalizability. While their quality of evidence is considered low, case reports and case series can provide anecdotal or real-world evidence that catalyzes new hypotheses and develops higher caliber research designs.

A *cohort study* design is used to determine rates of an outcome compared between groups exposed or not exposed to a factor of interest (Figure 4.2). Cohort studies can be prospective or

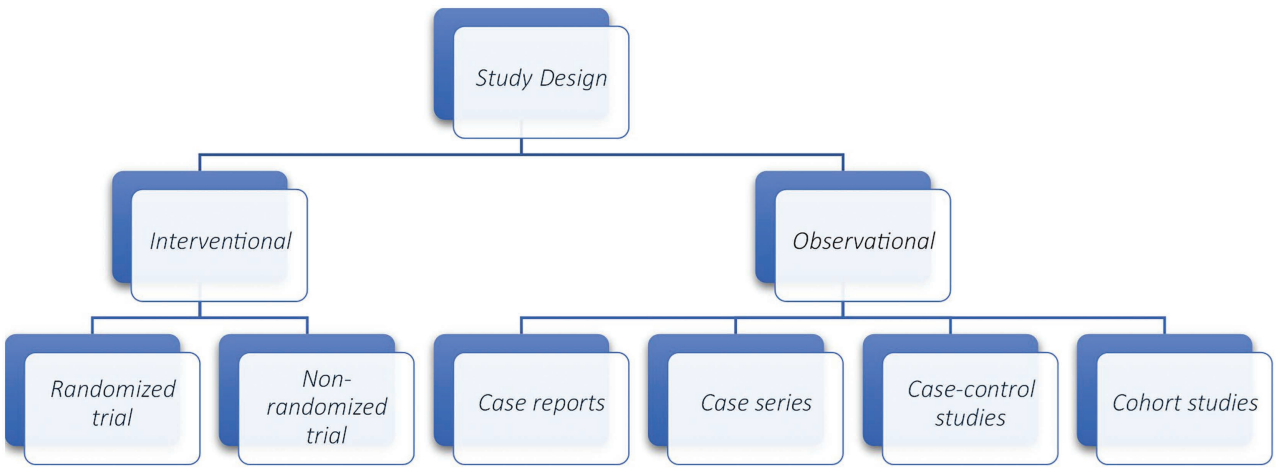


FIGURE 4.1 Study types.

DOI: 10.1201/9781003312109-4

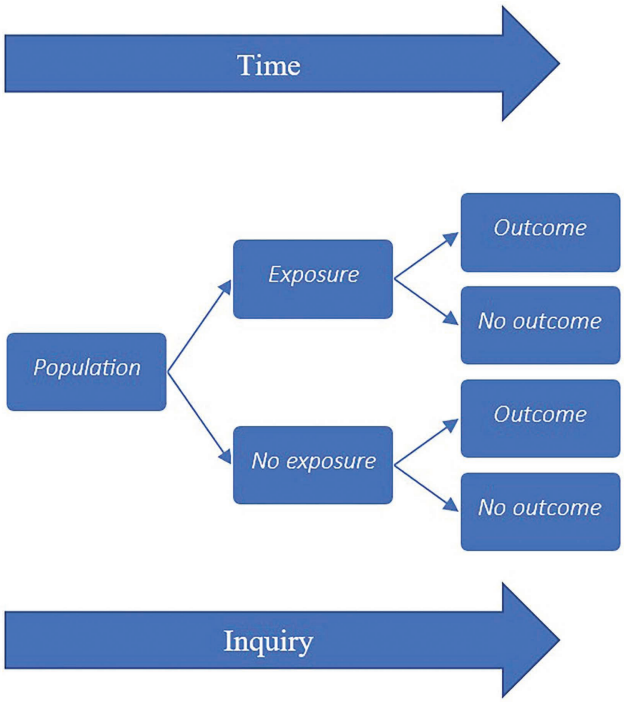


FIGURE 4.2 Cohort study.

retrospective in design. A *prospective cohort study* shares some similarities to a *randomized controlled trial* in that subjects are followed over time to determine rates of an outcome. The main difference between these two prospective study designs is that randomized trials randomly allocate subjects to a treatment or intervention and are managed under protocol-directed treatment and/or procedures, whereas prospective cohort studies group patients into cohorts based on either standard of care or shared decision making. Prospective cohort studies are thus susceptible to bias due to baseline *confounding factors* (or confounders) among subjects in their respective treatment groups (1).

A *case-control study* identifies a group of subjects with an outcome of interest and a control group without the outcome of interest, then evaluates exposures retrospectively (Figure 4.3). Case-control studies are best used for rare outcomes. Exposures can be ascertained by using existing records or interviewing subjects, so are prone to recall bias. In case-control studies, an *odds ratio* (OR) can be used to describe the relationship between exposure and outcome.

Systematic reviews and *meta-analyses* retrieve data from all relevant trials answering the same research question and combine them. When the information or data are combined, the result is a systematic review. When the data are combined and statistically analyzed, the result is a meta-analysis. The highest quality meta-analyses consist of data compiled from randomized controlled trials or prospective cohort studies.

Evidence-based medicine utilizes a hierarchy of study design, or levels of evidence. Levels of evidence classify and standardize quality in research studies and can be rated from level I to V in order of descending quality (Figure 4.4).

- *Level I evidence*: Systematic reviews, meta-analyses, randomized controlled trials, and prospective cohort studies with statistical power > 80% and adequate follow-up.
- *Level II evidence*: Randomized trials and prospective cohort studies with less than adequate follow-up, retrospective studies, and systematic reviews of level II studies.
- *Level III evidence*: Case-control studies.
- *Level IV evidence*: Case series and case reports.
- *Level V evidence*: Expert review.

4.4 Interventional Studies and Clinical Trial Design

Interventional research studies include protocols that dictate some aspect of patient care or management. Protocol-directed

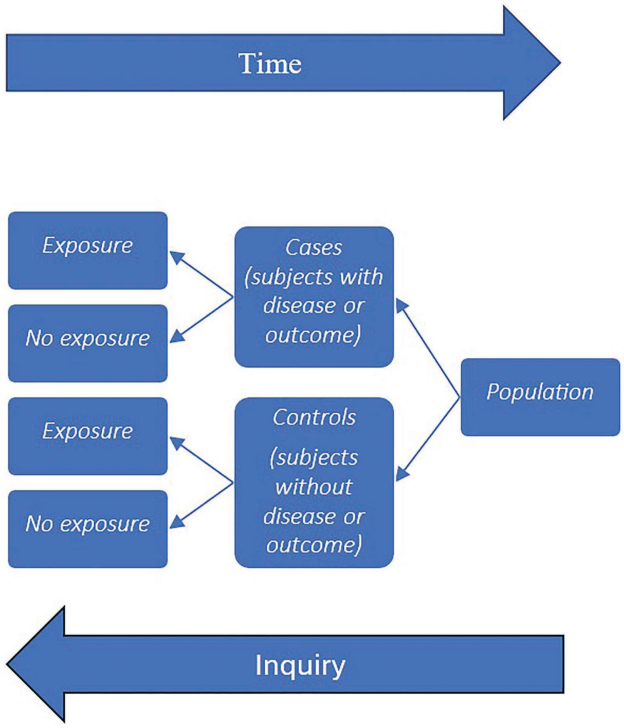


FIGURE 4.3 Case-control study.

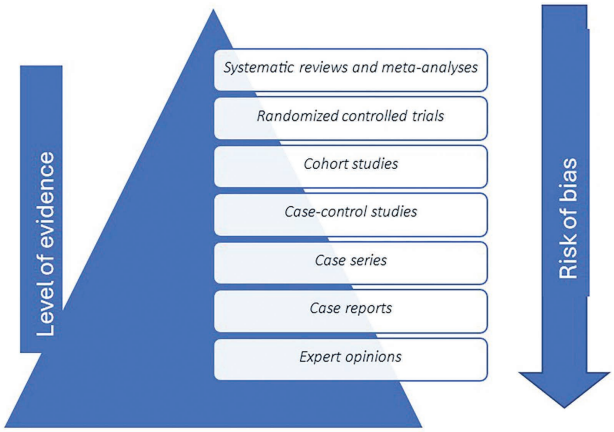


FIGURE 4.4 Levels of evidence.

interventions include systemic therapy, surgical procedures, biospecimen collection, symptom management procedures, and imaging procedures. All treatments and subject procedures may be protocol-directed, or these studies can be a blend of protocol-directed treatments and/or procedures with standard of care treatments and/or procedures. Documented informed consent is typically required.

Clinical trial designs for interventional studies can be categorized into three phases (phase I, phase II, and phase III clinical trials). If the primary intervention involves systemic therapeutics, the goal of a phase I clinical trial is to establish a maximum tolerated dose (MTD) of the investigational regimen. Phase I trials can be conducted based on rule-based designs or model-based designs. Rule-based designs, like the 3+3 traditional model, examine a specific dose in three patients, and if no dose-limiting toxicities are reached, the next dose level is investigated with three additional patients. This pattern is repeated until the MTD is reached, which is typically the dose level below the level with unacceptable toxicity. When the number of preplanned dose levels is large, typically greater than three, this model performs poorly. Accelerated dose escalation may be utilized in this circumstance. Model-based designs optimize conduct and minimize the number of subjects enrolled through the continual reassessment method, dose escalation with overdose control, or Bayesian optimal interval design.

After a recommended dose is established, the next step in intervention is a phase II clinical trial. This type of trial examines one or more specific scenarios (e.g., tumor histology) with a signal identified from the phase I trial or with preclinical rationale. The phase II clinical trial establishes efficacy in a specific setting. Phase II trials can be designed as a single arm trial using a historical control, as a randomized controlled trial, or as a randomized multi-arm rank and select design.

A phase III clinical trial compares an experimental arm to the accepted standard of care and is typically larger and more definitive. These trials may incorporate an interim futility analysis to minimize the number of subjects required. Alternatively, a group sequential analysis may be performed. Phase III trials may be designed as superiority, non-inferiority, or equivalence trials.

When designing a clinical trial in any phase, the study design includes many components prior to the determination of power and sample size calculations, including for primary objective, primary endpoint, explicit inclusion and exclusion criteria, and the study conduct context. The sample size portends the statistical power of a study. The *statistical power* signifies the probability that the results obtained will be statistically significant if the investigational treatment effect sizes are true. An acceptable statistical power typically ranges from 70% to 90%. Power is represented as $(1-\beta)$ where "beta" represents the false negative rate. The false negative rate is the probability the study fails to show statistically significant results if the assumed investigational treatment effect size is true. The false negative results are called the *b error* or *type II error*.

The *p value* is the probability that the differences observed between treatment outcomes are due to chance alone. A *p* value of 0.05 indicates that there is a 5% chance that the differences observed between treatment outcomes are due to chance. In other words, we accept that 5% of the time the study shows a significant difference between treatment outcomes when in fact there is no difference. This *alpha error*, or *type I error*, occurs when we conclude that the null hypothesis is false when in fact it is true. A *null hypothesis* (H0) states that the observed difference in outcomes is due to chance alone and not due to the effect of the treatment or intervention.

4.5 Types of Data

There are four common types of outcome data: continuous, categorial, count or rate, and time to event (2, 3).

4.5.1 Ordinal Data

Continuous (or ordinal) *data* are numerical measurements, such as temperature and body mass index. Continuous data can be presented using a central tendency. *Central tendency* is the measure of the centrality of the distribution of the data. Measures of central tendency are *mode*, *median*, and *mean*. Mode (Mo) represents the most frequent or most common value in the data set. Mode, however, is not the best measure of central tendency, as it can vary from sample to sample. Median is the middle value. In other words, if data are organized in numerical order, the median is the value in the middle. Mean (M), the average value, is calculated by dividing the summation of values (x) by the number of cases (N). The mean is calculated using the equation:

$$M = \frac{\sum x}{N}$$

In most cases, the mean is the preferred measured of central tendency. However, if there are several outliers within the data set, the median is a more appropriate measure of central tendency. An outlier is a value not similar to the rest of the values in the data set, which is outside of or abnormally distanced from the rest of the values. The mean but not the median is usually impacted by outliers, so the median is a more appropriate measure of central tendency, specifically if there are several outliers within the sample.

The distribution of data describes the shape of the data plotted on a histogram (3). The shape of the distribution can be *symmetric* or *asymmetric* (or skewed). The skew affects the mode, median, and mean. When the distribution is symmetric (normal, or Gaussian), the measures of central tendency (mode, median, and mean) coincide. In contrast, the values in the tail of an asymmetric distribution represent the outliers. When there are outliers, the mean moves in the direction of the outlier, or toward the tail of the distribution. When the mean is lower than the mode, the distribution is negatively skewed (Figure 4.5a), whereas when the mean is higher than the mode, the distribution is positively skewed (Figure 4.5b).

In addition to measures of distribution, measures of variation can be used to describe data (4). Variation can be presented as a *range*, *interquartile range*, *standard deviation*, and *standard error*. The range of a data set is the amount of spread between the extremes of data, and it represents the difference between the largest value and the smallest value. A more robust approach to describing range is interquartile range (IQR), which divides the distribution of data into four quartiles, with the second quartile representing the median. IQR represents the distance between the first and third quartile.

Standard deviation (SD) measures the variability within a sample population. A large SD suggests variability in the data, whereas a small SD suggests that the data are clustered close to the sample mean. The formula for standard deviation is

$$\sigma = \sqrt{\frac{\sum (x_i - \mu)^2}{N}}$$

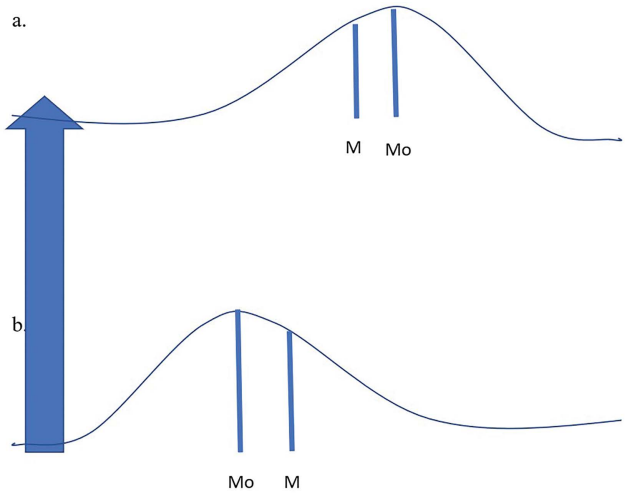


FIGURE 4.5 Distribution of data: (a) The distribution is negatively skewed; (b) the distribution is positively skewed.

where σ is the standard deviation of the population, x_i represents each value from the population, μ is the population mean, and N is the size of the population. In contrast, the standard error of the mean (SEM) measures the variability among multiple samples of a population. The SE represents the precision of the estimated sample mean. The formula for standard error of the mean is

$$SEM = \frac{\sigma}{\sqrt{n}}$$

where sigma is the standard deviation and n is the sample size.

Standard deviation is not a function of the sample size, so it remains constant despite population size. SEM is a function of the sample size (Figure 4.6). If the sample size increases, the SEM decreases and thus represents a more accurate estimation of the true mean of the population.

4.5.2 Nominal Data

Categorical (or nominal) *data* can be divided into groups or categories such as gender, ethnicity, educational level, and employment status. Categorical data can be dichotomous (or binary) such that the outcome can be one of only two possible outcomes. When there are more than two, categorical data have or do not have a natural order. *Ordered categorical* data, like gynecologic cancer staging, have a natural order, whereas *nominal categorical* data, like types of common benign ovarian cysts, do not have a natural order.

Nominal data can be presented as a rate and/or proportion. The *rate* measures the frequency or event count divided by interval time. For example, the number of wound infections that occur in one year is a wound infection rate. A *proportion* is a ratio of two quantities. For example, the number of patients who experienced an iatrogenic bladder injury in a cohort of 100 patients after hysterectomy is a proportion, which can be expressed as a percentage. These proportions can be compared between populations or interventions.

4.5.3 Count Data

Count data is the number of experienced events. Certain events can occur more than once; for example, a patient can be diagnosed with a urinary tract infection (UTI) on several occasions. Therefore, describing these data as count data rather than dichotomous (that is, UTI or no UTI) is preferred. Count data can be used for rare and common events. Count data of common events can be treated as continuous data, whereas count data of rare events are referred to as Poisson data and can be analyzed using rates.

4.5.4 Time-to-Event Data and Survival Analyses

Time-to-event (TTE) *data* is the amount of time until an *event of interest* (or outcome) occurs. When the event of interest is death, TTE data can be appropriately summarized using survival analyses. There are several ways to estimate the survival function or a survival curve: non-parametric analyses such as Kaplan–Meier and log-rank test, and semi-parametric analyses such as simple (univariate) or multiple (multivariate) Cox proportional hazard regression. The *Kaplan–Meier method* estimates the probability of surviving beyond a certain point in time (t), or the probability that the event has not or will not occur at time t. The Kaplan–Meier method is not to be confused with Kaplan–Meier curve, which is a graphical representation of the survival function using probabilities estimated by the Kaplan–Meier method.

The *log-rank test* is used to compare two Kaplan–Meier curves and determines if there is a statistically significant difference between survival curves (i.e., reject the null hypothesis). While a log-rank test assesses for statistical significance, it

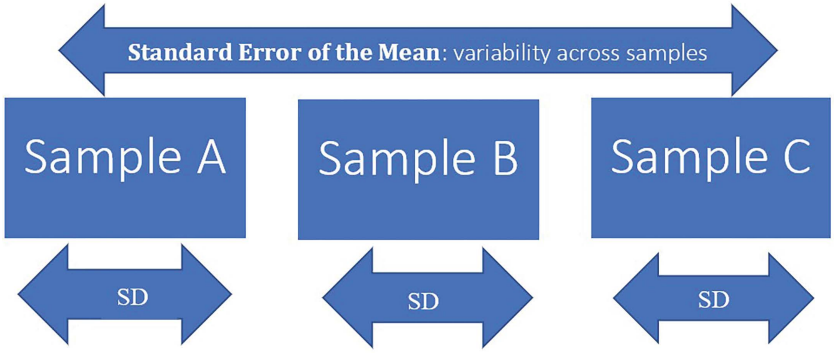


FIGURE 4.6 The difference between standard error of the mean and standard deviation (SD).

cannot test or control for the effects of more than one variable on survival time, and it does not estimate the *effect size* (or the magnitude of difference between treatment groups).

Cox proportional hazards regression analysis is used to test or control for several independent variables. In the Cox proportional hazards regression model, the effect of the treatment or intervention is presented as a *hazard ratio* (HR). HR measures instantaneous risk and can continuously vary. An HR is represented by the slope of a survival curve, and thus demonstrates either similarities or divergence between survival curves.

$$HR = \frac{hazard\ in\ treatment\ arm}{hazard\ in\ control\ arm}$$

HR describes the likelihood that an exposed subject will or will not experience an event at any given point in time (t) compared to a subject not exposed. An HR of 1.0 means no divergence, i.e., the likelihood of the event of interest was equally likely at any given point in time. For example, if the HR was 2.0, then at any given point in time there were twice as many patients in the treatment arm that experienced an event compared to the control arm. If the HR was 0.5, then at any given point in time, half as many patients in the treatment arm experienced an event compared to the control arm.

Not all study subjects experience the prespecified event or outcome, so those patients become censored. In other words, *censoring* refers to incomplete observed survival times. There are many types of censoring mechanisms. *Left censoring* occurs when the event of interest occurred for the subject prior to the start of the study observation period, so the time-to-event interval may be shorter than the observation time. *Right censoring*, which is more common in survival studies, occurs when the observation period is terminated before the event occurs, so the time-to-event interval may be longer than the observation time. Right censoring can occur when subjects are monitored for a fixed period of time (Type I, or time censoring); when a study is halted after a prespecified number or level of events have been achieved (Type II, or failure censoring); or when a subject drops out for a reason other than the event of interest (random censoring).

Censoring in survival analyses can be non-informative or informative. *Non-informative*, or *ignorable*, *censoring* occurs when subjects drop out of the study for reasons unrelated to the study, whereas *informative*, or *non-ignorable*, *censoring* occurs when subjects drop out for reasons related to the study. Informative censoring may be exemplified in a study comparing objective response rate after chemotherapy treatment. If subjects in the control arm experience more recurrences and are lost to follow-up because the control treatment is ineffective, and participants in the experimental arm remain on the study, the results would be biased in favor of the subjects who received the experimental treatment and remained on the study. An unbiased analysis of survival requires non-informative censoring, thereby assuming that censored subjects will have the same probability of experiencing the event of interest as the subjects who remained in the study.

4.5.5 Effect Measures

Effect measures are used to compare outcomes data between two treatment groups and illustrate the magnitude of treatment effect. Effect measures can be divided into difference (or absolute) measures and ratio (or relative) measures. The mean difference (difference in means between two groups) is an example of a difference measure, and are calculated using a 2×2 table.

An *odds ratio* (OR) is an example of a relative measure (5). The OR is the odds of an outcome or event $\left(\frac{a}{b}\right)$ divided by the odds of a non-event $\left(\frac{c}{d}\right)$.

$$odds\ ratio\,(OR) = \frac{odds\ of\ an\ event\ in\ cases\ group}{odds\ of\ an\ event\ in\ control\ group} = \frac{a/b}{c/d} = \frac{ad}{bc}$$

The *relative risk* (RR; also called risk ratio) is another example of a relative measure. The RR is the probability of the event occurring in the exposed $\left(\frac{a}{a+b}\right)$ and non-exposed $\left(\frac{c}{c+d}\right)$ groups (6).

$$relative\ risk\,(RR) = \frac{probability\ of\ contracting\ disease\ if\ exposed}{probability\ of\ contracting\ disease\ if\ not\ exposed} = \frac{\left(\frac{a}{(a+b)}\right)}{\left(\frac{c}{(c+d)}\right)}$$

Both odds ratio and relative risk can be used to estimate risk, but the choice depends on the study design and the type of planned statistical analyses (7). Odds ratio can be used in any study design, but it is particularly useful in assessment of case-control studies and meta-analyses. An OR of 1.0 means that there is neither an increase nor decrease in risk; OR < 1.0 means the exposure variable reduces risk of the event; and OR > 1.0 means the exposure variable increases risk of the event. OR can be adjusted to account for the effects of confounders in multivariate analyses. However, when the exposure and/or disease is common, OR does not give a good approximation of the relative risk, and in such cases OR can overestimate the true association between exposure and outcome.

Conversely, relative risk can be used when the sample has been randomly selected, such as in a cohort or cross-sectional study, and is only used when bivariate analyses are to be performed. RR should not be calculated for case-control study designs. Relative risk represents a multiplication of the risk. In other words, a RR of 2 for an exposure implies that events that occur from exposure are two times more likely than from non-exposure. Relative risk can also be interpreted as $100\times(RR-1)\%$. For a RR of 2, the exposure increases the risk of events by 200%. Conversely, a RR of 0.5 implies that the exposure decreases the risk of events by $100\times(1-RR)\%$ = 50%, or a *relative risk reduction* of 50%. It is challenging to interpret an OR in the same manner, and so a simpler approach is to convert an OR to a RR then interpret the RR. The OR can be converted to RR using the formula

$$RR = \frac{OR}{(1-P)+(P\times OR)}$$

where P represents the incidence of an outcome in the unexposed group, expressed as a fraction.

The *risk difference* (RD; also called *absolute risk reduction* or *attributable risk*) is an example of an absolute measure. The RD is the difference in the observed risk of events between the

exposed and unexposed groups, and it can vary depending on the baseline risk of a population. The RD can be calculated using the formula:

$$RD = \text{risk of event in exposed group} - \text{risk of event in unexposed group}$$
$$= \frac{a}{a+b} - \frac{c}{c+d}$$

The *number needed to treat* (NNT) is the number of patients needed to treat to prevent one bad outcome, such as death. For example, if a drug treatment has an NNT of 100, that means 100 patients will need to be treated to prevent one bad outcome. NNT can be obtained from the RD (or the absolute risk reduction, ARR) (8).

$$NNT = \frac{1}{ARR}$$

4.6 Bias

Bias is a tendency to produce an untrue value or event by systematically favoring one or more outcomes over others. There are several types of bias, which can be classified by the stage of research in which they occur: pre-trial, during trial, or post-trial (9, 10).

Pre-trial bias includes selection bias and confounder bias. *Selection bias* can occur when investigators use improper procedures or inconsistent criteria for selecting a sample population (11). In addition, selection bias can occur when not all subjects selected for study participation complete and return questionnaires; these non-responders may have different data compared to responders. As a result, the study population does not represent the target population or the overall population. *Confounder bias* is the presence of confounders that may interact with certain exposures. Confounders can mask a true association between exposure and outcome, and some can falsely demonstrate an apparent outcome when no association between exposure and outcome truly exists.

Examples of biases that occur during a trial include recall bias and observer bias. *Recall bias* occurs when patients self-report past exposures or outcomes, limiting reliability and reproducibility to limited to patient recollection of events. *Observer bias* occurs when the investigator is aware of disease status and treatment group, and their ability to interview the patient and collect or analyze data is compromised.

Post-trial bias includes *publication bias*, which occurs when studies with significant results are more easily published than those with negative (non-significant or inconclusive) results.

Bias can negatively impact research study results and conclusions. While some bias can be avoidable, some cannot. It is critical to identify biases and their sources and assess their potential impact on the conclusions of the study.

References

1. Ledet E et al. *Clinical Research for Surgeons*. Stuttgart, New York: Thieme; 2009.
2. Higgins JPT et al. *Cochrane Handbook for Systematic Reviews of Interventions*. Oxford: Cochrane Collaboration; 2022.
3. Hammond FMD. *Handbook for Clinical Research: Design, Statistics, and Implementation*. Demos Medical; 2014.
4. Campbell MJ et al. *VleBooks. Statistics at Square One*, 11th edn. Chichester: John Wiley; 2009.
5. Grimes DA et al. Making sense of odds and odds ratios. *Obstet Gynecol*. 2008;111(2 Pt 1):423–426.
6. Steinberg WJ et al. *Statistics Alive!* 3rd edn. Los Angeles: SAGE; 2020.
7. Peat J et al. *Medical Statistics: A Guide to Data Analysis and Critical Appraisal*. Chichester: John Wiley; 2005.
8. Bacchieri A et al. Fundamentals of clinical research: bridging medicine, statistics, and operations. In: *Statistics for Biology and Health*. Milan: Springer; 2007.
9. Pannucci CJ et al. Identifying and avoiding bias in research. *Plast Reconstr Surg*. 2010;126(2):619–625.
10. Delgado-Rodriguez M et al. Bias. *J Epidemiol Community Health*. 2004;58(8):635–641.
11. Coggon D et al. *Epidemiology for the Uninitiated*. BMJ Publishing Group; 1993.

5 PERIOPERATIVE CONSIDERATIONS AND ENHANCED RECOVERY AFTER SURGERY (ERAS)

Gregg Nelson, Jennifer Mateshaytis, Simrit K. Warring, and Sean C. Dowdy

5.1 Introduction

Enhanced Recovery After Surgery (ERAS) is a global surgical quality improvement initiative aimed at improving outcomes through evidence-based interventions that minimize the surgical stress response and normalize physiology perioperatively (1). The implementation of ERAS pathways has been shown to result in both clinical and economic benefits (1, 2). Key outcome measures of a successful ERAS program include reduction in length of stay (LOS) and postoperative complications, which have been demonstrated in both benign and malignant gynecologic procedures (3). As with other surgical disciplines, much of the original evidence for ERAS in gynecologic surgery has been centered on patients undergoing laparotomy (4–6). Recently however, there has been an increasing focus on the role of ERAS in patients undergoing gynecologic procedures performed through a minimally invasive surgery (MIS) route (7, 8). The purpose of this chapter is to (i) review the core components of ERAS, with particular emphasis on those most relevant to MIS (modern fasting guidelines, role of bowel preparation, premedications/prophylaxis, early urinary catheter removal, early feeding, and opioid-sparing analgesia), (ii) highlight keys to successful development of a same-day discharge program, and (iii) review the key outcome studies evaluating the benefit of ERAS in the MIS population.

5.2 Core Components of ERAS in Minimally Invasive Gynecologic Surgery

The recommendations for a minimally invasive gynecologic surgery ERAS protocol are shown in Table 5.1. Highlights of this protocol are described in this section.

5.2.1 Modern Fasting/Carbohydrate Loading

The overnight fasting rule, or "NPO after midnight" is an example of a practice which is based in historical surgical dogma, despite there being no evidence to support this approach. Prolonged fasting leads to significant patient discomfort, and importantly metabolic derangements that can negatively affect clinical outcomes (9). To the contrary, modern fasting guidelines, which allow clear fluids up until 2 hours and solid food until 6–8 hours before surgery, are endorsed by anesthesiology societies worldwide (10, 11). Compared with the standard "NPO at midnight" policy, a review of 22 randomized clinical trials (RCT) found no evidence to suggest that a shortened fluid fast resulted in increased aspiration risk, regurgitation, or related morbidity (12).

Across several surgical disciplines, ingestion of a preoperative beverage containing 50 g of carbohydrate 2–3 hours before induction of anesthesia has been shown to decrease the catabolic response induced by overnight fasting and surgery (13), reduce postoperative insulin resistance, improve bowel function, and shorten hospital stay (14). However, the evidence for carbohydrate loading specific to minimally invasive gynecologic surgery is less clear. Ren et al. randomized 144 women scheduled for elective laparoscopic gynecologic surgery to either ERAS care or conventional care. ERAS was associated with a 1-day reduction in length of stay, and multivariate regression analysis identified carbohydrate loading as an independent factor leading to early discharge (15). Conversely, Cho and colleagues randomly assigned patients undergoing laparoscopic gynecologic surgery to a midnight fasting group or a carbohydrate loading group. There was no difference found between groups in either length of stay or quality of recovery scores (16).

5.2.2 Avoidance of Mechanical Bowel Prep

Historically, mechanical bowel preparation (MBP) was used in surgery as it was thought to result in a decrease in anastomotic leak and infection rates, easier handling of the bowel, and improved visualization (9, 17). This practice however is associated with patient distress, dehydration, and a lack of evidence, particularly in the minimally invasive gynecologic surgery literature.

Yang et al. compared the effect of MBP using oral sodium phosphate solution versus a single enema on the quality of the surgical field in patients undergoing minimally invasive gynecologic surgery (18). No significant differences were found between the groups with respect to evaluation of the surgical field, bowel handling, or surgical difficulty, however severe adverse effects (e.g., abdominal bloating, weakness, dizziness, overall discomfort) were significantly greater in the oral solution group. In a similar RCT of MBP versus enema in minimally invasive pelvic reconstructive surgery, Adelowo and colleagues reported initial improvement in the quality of the surgical field in the MBP, but this benefit was not sustained at the conclusion of the surgery (19). Notably, patients in the MBP group reported more overall discomfort and negative preoperative side effects. Ozturk et al. investigated the effect of MBP versus no MBP on intraoperative visualization, bowel handling, and overall ease of surgery in elective minimally invasive gynecologic surgery and, like the previous studies, found no differences between the groups (20).

In a large database study of nearly 225,000 hysterectomies performed between 2006 and 2017, Kalogera and colleagues examined whether MBP alone, oral antibiotics alone, or a combination were associated with decreased rates of surgical site infections or anastomotic leaks compared to no bowel preparation (21). The main conclusion of the study was that use of bowel preparation did not decrease rates of surgical site infection, anastomotic leak, or major morbidity following benign or malignant hysterectomy, regardless of surgical approach.

5.2.3 Premedications and Prophylaxis

Premedication with multimodal preemptive analgesia is an important preoperative element in ERAS pathways to prevent pain receptor activation during surgery (22). Prior to surgery, analgesia agents with varying mechanisms of action are given with the goal to reduce postoperative narcotic medication requirements. This includes nonopioid pharmacologic agents (e.g., acetaminophen, cyclooxygenase-2 inhibitors, dexamethasone) and locoregional anesthetics (7). Preoperative gabapentin

DOI: 10.1201/9781003312109-5

has limited value in ERAS protocols especially in the elderly (8) and recent evidence suggests that the risk may outweigh the benefit, especially in MIS (23). Postoperative nausea and vomiting (PONV) are the leading cause of unexpected hospital admissions following outpatient surgery (24). Efforts to decrease PONV is imperative as MIS and same-day discharge (SDD) become more common. Risk factors for PONV include gynecologic/laparoscopic surgery, female sex, postoperative opioid use, and duration of surgery > 30 minutes (25). Most patients undergoing minimally invasive gynecologic surgery have at least three risk factors and therefore should receive multiple preventative agents from different classes. These agents have an additive effect; therefore, combination therapy is preferred. Preoperative dexamethasone has been shown to have analgesic properties and therefore serves as both pain and nausea prophylaxis (26). A meta-analysis found that single intermediate-dose dexamethasone has opioid-sparing effects, whereas high-dose dexamethasone has opioid-sparing effects and is associated with decreased pain scores (27). Transdermal scopolamine patches have been found to provide an additive benefit when used with antiemetic medications in the prevention of PONV for high-risk patients (28). Thromboprophylaxis with low-molecular-weight heparin in addition to sequential compression devices for high-risk patients should be considered (8, 29), and extended prophylaxis is of limited value in MIS patients (8). Appropriate antimicrobial prophylaxis should be given within 1 hour prior to incision and an increased dosage should be administered for patients with obesity (6).

5.2.4 Early Urinary Catheter Removal

ERAS pathways support early urinary catheter removal within 24 hours after surgery (6, 8). Often catheter removal can occur immediately after MIS to facilitate early discharge. Urinary retention (UR) following surgery is a leading risk factor for prolongation of LOS and may result in need for recatheterization (30). Multiple studies have assessed the optimal timing of early catheter removal while weighing risks of UR, urinary tract infection (UTI), and increased LOS. SDD criteria following MIS should include a voiding trial to assess for postoperative UR. Efforts toward time-efficient acute phase recovery include immediate removal and use of retrograde fill voiding trials (31). Immediate removal after an uncomplicated laparoscopic hysterectomy has been shown to be safe and associated with low rates of UR (31). A prospective RCT including vaginal and abdominal routes of hysterectomy did not show a significant difference in recatheterization or UTI for patients with immediate versus next-day removal (32). A recent multicenter RCT following minimally invasive sacrocolpopexy did not show a difference in risk for recatheterization with immediate versus overnight removal (33). Earlier catheter removal has been associated with shorter time to first void, passing a larger volume of urine at first void, requiring less recatheterization for UR, and shorter hospital LOS (34). A more recent metanalysis of RCTs in gynecologic surgery, which included abdominal, laparoscopic, and vaginal surgery, compared immediate, ≤ 6 hour, or > 6 hour postoperative catheter removal. This study found that removal at ≤ 6 hours was most beneficial and associated with less UR and fewer UTIs (35).

5.2.5 Early Feeding

Early feeding with oral fluid and solid intake within 24 hours following gynecologic surgery is supported by ERAS guidelines (5–7, 36). This applies to surgeries that include bowel resection (37). While recovering from anesthesia, patients are encouraged to drink fluids. After patients reach the postoperative floor, a regular diet should be offered. No specific regimen is recommended, and patients should be allowed to determine the volume and type of oral intake. Various studies have also found that early feeding does not increase postoperative complications rates, such as anastomotic leaks and wound or pulmonary complications (38, 39). There is some evidence that early feeding is associated with a mild increase in postoperative nausea, but this was not associated with vomiting, abdominal distention, or need for nasogastric tube use (5). Importantly, early feeding protocols are associated with high patient satisfaction (40).

5.2.6 Opioid-Sparing Analgesia

Postsurgical pain management is an important aspect of recovery and patient experience. Although opioids are an important modality to treat pain, their use should be minimized as much as possible recognizing common side effects such as nausea and constipation, and the fact that 6%–10% of patients issued a prescription for opioids demonstrate persistent opioid use and potential long-term dependence (41, 42).

Postsurgical pain should be managed using a multimodal approach of nonopioid and opioid medications (43). We recommend using scheduled oral acetaminophen and NSAIDS unless contraindicated, supplemented with oral opioids if necessary. Ketorolac is very effective for postoperative pain and is often used as first-line treatment in the first 24 hours after surgery. IV opioids such as Dilaudid may be used for breakthrough pain unresponsive to oral medications (44). If more than three doses of IV opioid are required, patient-controlled analgesia (PCA) may be considered, although this is unlikely to be required for patients undergoing MIS. Nonpharmacologic options such as acupuncture, massage, aromatherapy, and cognitive behavioral therapy should also be offered as outlined by Joint Commission standards.

Following hospital dismissal, a tiered prescribing approach should be used for opioids, guided by surgical procedure in outpatients, and observed opioid requirements in the last 24 hours of hospitalization for patients requiring admission (45). Of note, > 50% of patients require no opioids after MIS; therefore, no opioid prescriptions may be required for many patients at dismissal (46). For patients who do require opioids, no more than three to ten tablets are often necessary. The wide variation in opioid requirements may be due in part to variations in pharmacogenomics; further investigations are required to define the impact and cost-effectiveness of such testing (47).

5.3 Same-Day Discharge (SDD) Program

Same-day discharge (SDD) – defined as discharge on the same calendar day as the surgery – in patients undergoing minimally invasive gynecologic surgery is a recent trend aligned with ERAS principles (8). SDD programs in the minimally invasive gynecologic patient population are safe and effective, with low risk of readmission or complications (48–50). There are multiple patient and healthcare system benefits to this disposition strategy (7, 51). Importantly, patient satisfaction is high, with studies suggesting that greater than 90% of patients would recommend SDD (52–54).

Several interventions have been identified to address barriers and improve rates of SDD. While there are no consensus criteria in the literature, a process to select candidates

TABLE 5.1. Recommendations for a Minimally Invasive Gynecologic Surgery ERAS Protocol

Preoperative	
Bowel preparation	▫ No mechanical bowel preparation
Modern fasting guidelines	▫ Light snack allowed up to 6 h before procedure ▫ Clear fluids allowed up to 2 h before procedure
Carbohydrate loading	▫ Complex carbohydrate (e.g. maltodextrin) drink 2 h prior to surgery
Preoperative medications	▫ Acetaminophen 1000 mg PO once ▫ Celecoxib or Ibuprofen 400 mg PO once ▫ Antiemetic agents (combination therapy preferred, e.g., dexamethasone, aprepitant)
VTE prophylaxis	▫ Heparin 5000 U SC given preoperatively or after induction ▫ Sequential compression devices placed prior to induction of anesthesia
Antimicrobial prophylaxis	▫ Chlorhexidine-alcohol for skin cleansing ▫ Cefazolin 2 g IV before incision (3 g for weight >120 kg)
Intraoperative	
Nausea and vomiting prophylaxis (example antiemetics to choose from)	▫ Droperidol 0.625-1.25 mg IV end of surgery ▫ Ondansetron 4 mg IV end of surgery ▫ Promethazine 6.25-12.5 mg IV end of surgery
Best surgical practices	▫ Avoidance of peritoneal drains and nasogastric tubes
Maintenance of normothermia	▫ Use of active warming device and warmed fluids
Fluid therapy	▫ Use of lactated ringers as opposed to normal saline ▫ Aim for euvolemia (very restrictive or liberal fluid regimes to be avoided)
Postoperative	
Diet	▫ Solid diet started as soon as possible after surgery
Analgesia	▫ Acetaminophen 1000 mg PO q6h (should not exceed 4000 mg/24 h from all sources) ▫ Ibuprofen 400 mg PO q6h (unless contraindications exist) If scheduled acetaminophen/ibuprofen ineffective (or if contraindications): ▫ Oxycodone 5-10 mg PO q4 h prn ▫ Tramadol 100 mg PO q4-6 h prn ▫ Opioid IV (e.g., hydromorphone 0.5 mg IV q30 min prn) only if PO opioid medications ineffective within 30 min
Nausea and vomiting prophylaxis	▫ Ondansetron 4 mg PO q6 h prn nausea ▫ Prochlorperazine 10 mg IV q6h breakthrough nausea after 30 min Ondansetron
Fluid therapy	▫ Fluids at 40 mL/h postoperatively (typical duration <6 h) ▫ Peripheral lock IV when patient drinking
Urinary catheter removal	▫ Remove urinary catheter immediately after surgery (in operating room) or within 6 h postoperatively unless contraindications exist
Active mobilization program	▫ Ambulate as soon as possible after surgery
Discharge protocol	▫ Aim for Same-Day Discharge unless contraindications exist ▫ Avoid narcotic prescription if possible

for SDD is necessary (7, 53, 54). In the preoperative phase of care, ensuring SDD candidates are booked with surgical start times early in the day and focusing on patient education and expectation setting have been identified as key to facilitating SDD (7, 53, 54). Intraoperatively, strategies such as removing the Foley catheter at the conclusion of the operation have led to improved SDD rates. Postoperatively, using predefined discharge criteria, ensuring adherence to ERAS protocols (such as management of nausea, adequate pain control with minimal use of narcotics), and facilitating further patient education (including expectations upon discharge and processes for contacting the care team) result in increased SDD success (7, 53, 54). Finally, stakeholder engagement and buy-in is an important component of successful SDD programs – ownership of the process by all members of the care team facilitates ongoing adherence to interventions (7, 54).

5.4 Outcomes of ERAS in MIS

The evidence in support of ERAS programs in the context of minimally invasive gynecologic surgery is relatively new and still evolving – until recently it was unclear if patients derived most of their benefit from the surgical approach itself or the additional ERAS perioperative interventions. Based on several recent studies, it appears ERAS protocols further enhance the benefits offered by MIS; there have been notable benefits in the domains of opioid use, SDD, health-related quality of life (HRQoL), patient satisfaction, and cost savings.

A retrospective cohort analysis of women undergoing MIS non-hysterectomy procedures was conducted to compare ERAS versus conventional postoperative care protocols (55). The authors demonstrated improvement in immediate perioperative outcomes and no impacts on 30-day complications with the introduction of an ERAS protocol. In an RCT, Ren et al. similarly demonstrated the benefit of a comprehensive ERAS program for patients undergoing MIS procedures (ovarian cystectomy, myomectomy, hysterectomy), showing reduction in LOS, improved patient quality of life, and no difference in 30-day morbidity, readmission rate, or costs to the healthcare system (15).

Several recent studies have evaluated the impact of ERAS on opioid use in minimally invasive gynecologic surgery. A retrospective study by Weston et al. assessed opioid use and postoperative pain in gynecologic oncology patients undergoing MIS according to ERAS versus a historical cohort (56). After controlling for possible confounding variables (age, BMI, operative time, LOS, cancer diagnosis, surgical approach), the ERAS group required fewer morphine equivalents intraoperatively and postoperatively and had lower reported pain scores compared with the non-ERAS control group. Levytska et al. similarly compared ERAS and non-ERAS cohorts undergoing MIS – in the ERAS cohort there was a statistically significant reduction in the prescription of opioids as well as a significant reduction in patient phone calls and provider visits for pain (57). Taken together, this evidence suggests that ERAS programs are an effective means of reducing opioid use in patients undergoing minimally invasive gynecologic surgery.

Several studies have evaluated the impact of ERAS programs on the success of SDD. In one study looking at ERAS vs non-ERAS postoperative care for patient undergoing minimally invasive gynecologic surgery, the rate of SDD was higher (49% vs 39%) and the rate of readmission was lower (2.0% vs 5.6%) in the ERAS cohort (57). These rates of SDD are much lower than what has been reported elsewhere in the literature, but this study was not specifically designed with an SDD protocol in mind – rather, the improved rate of SDD noted by the authors is solely due to the impact of the ERAS program components. To the same effect, Peters et al. reported a 9.4% improvement in SDD in their ERAS MIS group; again, this study was not designed with the intention to improve rates of SDD specifically, however by virtue of ERAS interventions the rate of SDD spontaneously increased (55). Finally, Kim et al. applied the foundational aspects of ERAS perioperative care in their quality improvement initiative to improve rates of SDD among gynecologic oncology patients undergoing MIS. After implementation they saw a significant increase in successful SDD from 29% to 75% and reported no difference between the groups in terms of readmissions, presentations to the emergency department, return to the operating room, 30-day perioperative complications, and mortality (53).

ERAS programs have been shown to improve HRQoL and patient satisfaction. In a study by Kilpio et al., the authors evaluated HRQoL (15D questionnaire, General Health Questionnaire-12) at baseline and one month after MIS (hysterectomy) following ERAS postoperative management or conventional perioperative care (58). ERAS appeared to have a positive impact on recovery after MIS in the dimensions of sleeping, discomfort and symptoms, depression, distress, and vitality. In another study, Ren et al. reviewed patient quality of recovery (Quality of Recovery Scale-15) with a statistically significant improvement in the ERAS cohort (15). Finally, Kim et al. evaluated patient satisfaction as it relates to SDD and postoperative ERAS management – all patients in the post-intervention group completed satisfaction surveys: 89% of patients rated their experience as "very good" or "excellent" (53).

Lastly, although clinical outcome improvements are a priority for both clinicians and patients, it is also important to quantify costs savings to the healthcare system which result from ERAS implementation. These cost implications are often what healthcare managers and administrators consider most when making decisions on whether to adopt surgical quality improvement programs. When examining the cost impact of ERAS in several surgical programs implemented across an entire healthcare system, Thanh et al. found that ERAS was associated with a return-on-investment range of 1.05–7.31 (every dollar invested in ERAS would bring $1.05 to $7.31 in cost avoidance) (59). Modesitt and colleagues implemented an ERAS protocol specifically in minimally invasive gynecologic surgical patients and calculated cost savings of $671 per patient (60). In a similar study conducted in Canada, Mitric et al. found that ERAS applied to minimally invasive gynecologic oncology patients led to a 17% total cost reduction and savings of $2063 per patient (61).

5.5 Conclusion

ERAS is a global surgical quality improvement initiative that has now moved beyond its origins in open surgery and is becoming embedded within the realm of minimally invasive gynecologic surgery. There is evidence that ERAS offers benefits for patients over and above that which is obtained by MIS itself. Surgeons are encouraged to adopt as many components of ERAS as possible, and in doing so, clinical outcome improvements for patients and healthcare savings will be realized.

References

1. Ljungqvist O et al. Enhanced recovery after surgery: a review. *JAMA Surg*. 2017;152(3):292–298.
2. Ljungqvist O et al. ERAS-Value based surgery. *J Surg Oncol*. 2017;116:608–612.
3. Bisch SP et al. Outcomes of enhanced recovery after surgery (ERAS) in gynecologic oncology – a systematic review and meta-analysis. *Gynecol Oncol*. 2021;161:46–55.
4. Nelson G et al. Guidelines for pre- and intra-operative care in gynecologic/oncology surgery: Enhanced Recovery After Surgery (ERAS®) Society recommendations – Part I. *Gynecol Oncol*. 2016;140(2):313–322.
5. Nelson G et al. Guidelines for postoperative care in gynecologic/oncology surgery: Enhanced Recovery After Surgery (ERAS®) Society recommendations – Part II. *Gynecol Oncol*. 2016;140(2):323–332.
6. Nelson G et al. Guidelines for perioperative care in gynecologic/oncology: Enhanced Recovery After Surgery (ERAS) Society recommendations - 2019 update. *Int J Gynecol Cancer*. 2019;29:651–668.
7. Stone R et al. Enhanced recovery and surgical optimization protocol for minimally invasive gynecologic surgery: an AAGL white paper. *J Minim Invasive Gynecol*. 2021;28:179–203.
8. Nelson G et al. Enhanced Recovery After Surgery (ERAS®) Society guidelines for gynecologic oncology: addressing implementation challenges – 2023 update. *Gynecol Oncol*. 2023;173:58–67.
9. Nelson G et al. Enhanced recovery pathways in gynecologic oncology. *Gynecol Oncol*. 2014;135:586–594.

10. Practice guidelines for preoperative fasting and the use of pharmacologic agents to reduce the risk of pulmonary aspiration: application to healthy patients undergoing elective procedures: an updated report by the American Society of Anesthesiologists Task Force on preoperative fasting and the use of pharmacologic agents to reduce the risk of pulmonary aspiration. *Anesthesiol*. 2017;126:376–393.
11. Smith I et al. Perioperative fasting in adults and children: guidelines from the European Society of Anaesthesiology. *Eur J Anaesthesiol*. 2011;28(8):556–569.
12. Brady M et al. Preoperative fasting for adults to prevent perioperative complications. *Cochrane Database Syst Rev*. 2003:CD004423.
13. Nygren J et al. Preoperative oral carbohydrate therapy. *Curr Opin Anaesthesiol*. 2015;28:364–369.
14. Smith MD et al. Preoperative carbohydrate treatment for enhancing recovery after elective surgery. *Cochrane Database Syst Rev*. 2014;8.
15. Ren Y et al. A full enhanced recovery after surgery program in gynecologic laparoscopic procedures: a randomized controlled trial. *J Minim Invasive Gynecol*. 2021;28:1610–1617.
16. Cho EA et al. Preoperative oral carbohydrate loading in laparoscopic gynecologic surgery: a randomized controlled trial. *J Minim Invasive Gynecol*. 2021;28:1086–1094.
17. Wells T et al. Preoperative bowel preparation in gynecologic oncology: a review of practice patterns and an impetus to change. *Int J Gynecol Cancer*. 2011;21(6):1135–1142.
18. Yang LC et al. Mechanical bowel preparation for gynecologic laparoscopy: a prospective randomized trial of oral sodium phosphate solution vs single sodium phosphate enema. *J Minim Invasive Gynecol*. 2011;18(2):149–156.
19. Adelowo AO et al. The use of mechanical bowel preparation in pelvic reconstructive surgery: a randomized controlled trial. *Female Pelvic Med Reconstr Surg*. 2017;23:1–7.
20. Ozturk UK et al. The effect of mechanical bowel preparation on the surgical field in laparoscopic gynecologic surgeries: a prospective randomized controlled trial. *J Invest Surg*. 2022;35:1604–1608.
21. Kalogera E et al. Use of bowel preparation does not reduce postoperative infectious morbidity following minimally invasive or open hysterectomies. *Am J Obstet Gynecol*. 2020;223(2):231.e1–231.e12.
22. Chao L et al. Enhanced recovery after surgery in minimally invasive gynecologic surgery. *Obstet Gynecol Clin North Am*. 2022;49:381–395.
23. Huynh TQ et al. Preoperative gabapentin for minimally invasive hysterectomy: a randomized controlled trial. *J Minim Invasive Gynecol*. 2021;28:237–244.e2.
24. Gold BS et al. Unanticipated admission to the hospital following ambulatory surgery. *JAMA*. 1989;262:3008–3010.
25. Gan TJ et al. Fourth consensus guidelines for the management of postoperative nausea and vomiting. *Anesthes Analges*. 2019;131:411–448.
26. Blanton E et al. Non-opioid pain management in benign minimally invasive hysterectomy: a systematic review. *Am J Obstet Gynecol*. 2017;216:557–567.
27. De Oliveira GS et al. Perioperative single dose systemic dexamethasone for postoperative pain: a meta-analysis of randomized controlled trials. *J Am Soc Anesthesiol*. 2011;115:575–588.
28. Kalogera E et al. Enhanced recovery pathway in gynecologic surgery: improving outcomes through evidence-based medicine. *Obstet Gynecol Clin North Am*. 2016;43:551–573.
29. ACOG Committee Opinion 750: perioperative pathways: enhanced recovery after surgery. *Obstet Gynecol*. 2018;132:e120–e130.
30. Scheib SA et al. Enhanced recovery after surgery in gynecology: a review of the literature. *J Minim Invasive Gynecol*. 2019;26:327–343.
31. Dedden SJ et al. Immediate catheter removal after laparoscopic hysterectomy: a retrospective analysis. *Eur J Obstet Gynecol Reprod Biol*. 2020;250:76–79.
32. Dunn TS et al. Are in-dwelling catheters necessary for 24 hours after hysterectomy? *Am J Obstet Gynecol*. 2003;189:435–437.
33. Aslam MF et al. When to remove the indwelling catheter after minimally invasive sacrocolpopexy? CARESS (CAtheter REmoval after Sacrocolpopexy Surgery). *Urogynecol*. 2020;26:120–127.
34. Ind TEJ et al. Midnight removal of urinary catheters – improved outcome after gynecological surgery. *Int Urogynecol J*. 1993;4:342–345.
35. Huang H et al. The timing of urinary catheter removal after gynecologic surgery: a meta-analysis of randomized controlled trials. *Medicine*. 2020;99:e18710.
36. Charoenkwan K et al. Early versus delayed oral fluids and food for reducing complications after major abdominal gynaecologic surgery. *Cochrane Database Syst Rev*. 2014;2014(12):CD004508.
37. Minig L et al. Early oral versus "traditional" postoperative feeding in gynecologic oncology patients undergoing intestinal resection: a randomized controlled trial. *Ann Surg Oncol*. 2009;16:1660–1668.
38. Lewis SJ et al. Early enteral feeding versus "nil by mouth" after gastrointestinal surgery: systematic review and meta-analysis of controlled trials. *BMJ*. 2001;323:773–776.
39. Han-Geurts IJ et al. Randomized clinical trial of the impact of early enteral feeding on postoperative ileus and recovery. *Br J Surg*. 2007;94:555–561.
40. Kalogera E et al. Enhanced recovery in gynecologic surgery. *Obstet Gynecol*. 2013;122(2 Pt 1):319–328.
41. Hessami K et al. Perioperative opioid dispensing and persistent use after benign hysterectomy: a systematic review and meta-analysis. *Am J Obstet Gynecol*. 2022;229(1):23–32.e3.
42. Santosa KB et al. New persistent opioid use among older patients following surgery: a Medicare claims analysis. *Surgery*. 2020;167:732–742.
43. Ong CK et al. Combining paracetamol (acetaminophen) with nonsteroidal antiinflammatory drugs: a qualitative systematic review of analgesic efficacy for acute postoperativepain. *Anesth Analg*. 2010;110:1170–1179.
44. Nelson G et al. Enhanced recovery after surgery (ERAS®) in gynecologic oncology – practical considerations for program development. *Gynecol Oncol*. 2017;147(3):617–620.
45. Glaser GE et al. Outcomes and patient perspectives following implementation of tiered opioid prescription guidelines in gynecologic surgery. *Gynecol Oncol*. 2020;157:476–481.
46. Kim SR et al. Implementation of a restrictive opioid prescription protocol after minimally invasive gynecologic oncology surgery. *Int J Gynecol Cancer*. 2021;31(12):1584–1588.
47. Rocco R et al. Use of pharmacogenetic data to guide individualized opioid prescribing after surgery. *Surgery*. 2019;166:476–482.
48. Lee SJ et al. The feasibility and safety of same-day discharge after robotic-assisted hysterectomy alone or with other procedures for benign and malignant indications. *Gynecol Oncol*. 2014;133:552–555.
49. Fountain CR et al. Promoting same-day discharge for gynecologic oncology patients in minimally invasive hysterectomy. *J Min Invasive Gynecol*. 2017;24:932–939.
50. Nensi A et al. Implementation of a same-day discharge protocol following total laparoscopic hysterectomy. *J Obstet Gynaecol Can*. 2018;40:29–35.
51. Korsholm M et al. Systematic review of same-day discharge after minimally invasive hysterectomy. *Int J Gynaecol Obstet*. 2017;136:128–137.
52. Gale J et al. Early discharge after laparoscopic hysterectomy: a prospective study. *J Obstet Gynecol Can*. 2018;40:1154–1161.
53. Kim SR et al. Enhanced recovery after minimally invasive gynecologic oncology surgery to improve same day discharge: a quality improvement project. *Int J Gynecol Cancer*. 2022;32:457–465.
54. Mateshaytis J et al. Improving the rate of same-day discharge in gynecologic oncology patients with endometrial cancer undergoing minimally invasive robotic surgery: a quality improvement initiative. *J Minim Invasive Gynecol*. 2022;29:1184–1193.

55. Peters A et al. Enhanced recovery after surgery outcomes in minimally invasive nonhysterectomy gynecologic procedures. *Am J Obstet Gynecol*. 2020;223(2):234.e1–234.e8.
56. Weston E et al. The impact of an enhanced recovery after minimally invasive surgery program on opioid use in gynecologic oncology patients undergoing hysterectomy. *Gynecol Oncol*. 2020;157(2):469–475.
57. Levytska K et al. Enhanced recovery after surgery (ERAS) protocol is associated with lower post-operative opioid use and a reduced office burden after minimally invasive surgery. *Gynecol Oncol*. 2022;166(3):471–475.
58. Kilpiö O et al. Health-related quality of life after laparoscopic hysterectomy following enhanced recovery after surgery protocol or a conventional recovery protocol. *J Minim Invasive Gynecol*. 2021;28(9):1650–1655.
59. Thanh N et al. Return on investment of the Enhanced Recovery After Surgery (ERAS) multiguideline, multisite implementation in Alberta, Canada. *Can J Surg*. 2020;63(6):E542–E550.
60. Modesitt SC et al. Enhanced recovery implementation in major gynecologic surgeries: effect of care standardization. *Obstet Gynecol*. 2016;128(3):457–466.
61. Mitric C et al. Cost-analysis of an enhanced recovery program after minimally invasive gynecologic oncology surgery. *Int J Gynecol Cancer*. 2022;32(Suppl 3):A1–A274.

6 PRINCIPLES OF LAPAROSCOPIC AND ROBOTIC SURGERY

Megan Cesta and Natalie Wallace

6.1 Operating Room Setup

6.1.1 Surgical Team and Patient Safety Culture

Surgical suites should be tailored towards minimally invasive surgery and provide benefits such as improved safety, efficiency, and ergonomics for the surgeon and operating room staff. A team-centered approach to patient care and safety culture are important pillars of a successful operating suite. Surgical teams should consist of the primary surgeon and qualified assistant, circulating nurse, scrub technician, and anesthesia personnel. All staff should receive training in critical communication. The World Health Organization implemented a surgical safety checklist in 2009 which has been demonstrated to reduce morbidity and readmission rates (1, 2).

6.2 Room Setup and Ergonomics

Laparoscopy carries unique physical risks to the surgeon. Considerations to minimize physical risk include table mobility, monitor position, and instrument design (3). Optimal surgical suite setup provides improved surgical ergonomics. Suites should be equipped with multiple video monitors placed strategically throughout the room to allow for the surgeon and assistants to have optimal views without sacrificing posture or positioning throughout the case. Attention should be paid that surgeons maintain appropriate posture with lowering the shoulders, avoiding forward neck movement and improper leg loading (4). With respect to robotic-assisted surgeons, unique ergonomic considerations are trunk mobility and wrist and finger movements. Robotics may confer decreased surgeon muscle work load for the obese patient (5).

Mechanical booms and video monitors should be suspended from the ceiling in order to reduce the amount of equipment and cords on the operating room floors, thus avoiding crowding or tripping hazards. Booms can house a multitude of equipment such as electrosurgical units, gas lines, video capturing devices, and insufflators. Ceiling mounts are also useful for overhead lighting. Overhead lamps with light emitting diode (LED) working elements have improved lifespan over traditional incandescent or halogen lights.

Also equally important for laparoscopy is an operating table that can be placed in steep Trendelenburg position with considerations given to weight limits that may accommodate patients with elevated BMI. The da Vinci® Xi Surgical System incorporates integrated table motion allowing for the patient to be repositioned as the surgeon is operating (Intuitive Surgery, Mountain View, California). Additionally, tables should have side rails to allow for the attachment of booted stirrups.

Operating suites may be designated minimally invasive suites with integrated technology (Figure 6.1). Minimally invasive suites often have multiple mobile booms such as OR1™ (Karl Storz Endoscopy, Tuttlingen, Germany). The video imaging, insufflation, and electrosurgical units are all located on mechanical booms that can move within the operating suite. Video monitors and lighting systems are strategically located on booms as well for mobility and ergonomics. If an operating suite is not designated specifically for minimally invasive surgery, the necessary equipment is usually housed within a mobile tower connected to a video monitor for ease of transportation between suites.

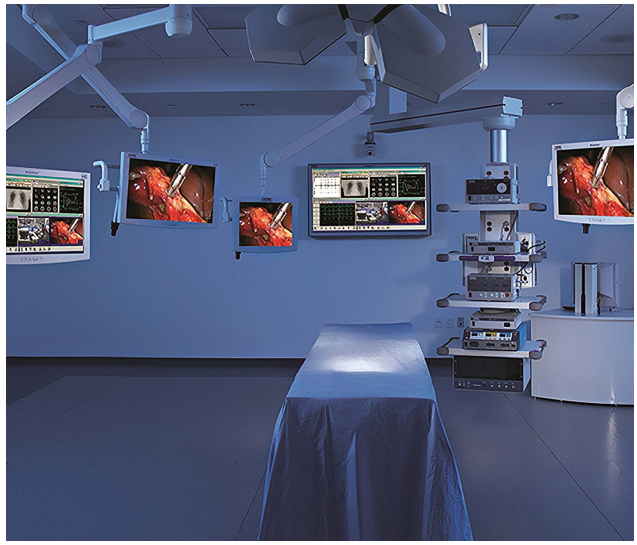


FIGURE 6.1 Minimally invasive surgical suite with equipment arranged for maximum ergonomics. (From Pasic RP et al. Instrumentation and equipment. In: *Practical Manual of Minimally Invasive Gynecologic and Robotic Surgery*, 3rd edn., CRC Press, Boca Raton, FL, 2018, with permission.)

6.3 Imaging

A wide array of imaging systems is available. Typical systems include high-definition (HD) video monitors, an image and video capturing device, HD digital cameras, a light source, and a laparoscope.

6.3.1 Video Monitors

Video monitors and cameras are an important aspect of laparoscopy. HD monitors and video cameras are the current standard. Optimal placement of monitors consists of two mobile video monitors attached to ceiling mounts. Each monitor is placed lateral to the patient's legs on either side. This allows for both surgeon and assistant to maintain appropriate posture throughout the surgery. A third wall monitor may be mounted along the wall above the patient's head to facilitate visualization during vaginal portions of procedures such as hysteroscopy or cystoscopy. If only one video monitor is available it should be placed between the patient's legs.

6.3.2 Camera Head and Image Capturing

Video cameras incorporate a solid-state microchip processor. The camera head functions to capture the image provided by the laparoscope and feed it through a capturing device which allows for video recording, recording still images as well as relaying the live image to the video monitors. Cameras

DOI: 10.1201/9781003312109-6

produce high-definition resolution measured in pixels (p), and surgical systems are typically equipped with 720 p and 1080 p cameras. The newest advances in imagery are 4K resolution and three-dimensional. These systems provide almost 4000 pixels of horizontal and over 2000 pixels of vertical resolution (Olympus Surgical America, Orangeburg, New York).

6.3.3 Light Sources

Light sources provide illumination to the surgical field which in turn enhances the image quality. The most common light source used today is a high-intensity xenon lamp light source in which the light is then transmitted through fiberoptic cables and attached to the laparoscope. Xenon allows for the emission of true white light, and the fiberoptic cables can reach extreme temperatures. Caution must be exercised as unprotected light sources can release enough heat to cause patient burns or ignite surgical draping. Fiberoptic cables must be stored and handled with care as the delicate fibers are prone to breakage if the light cord is wound too tight or dropped. This breakage can result in decreased light transmission. It is important to note that blood on the surgical field may absorb light emitted and decrease visualization, therefore maintaining a clean surgical field is an important component of adequate visualization.

6.3.4 Laparoscopes

Laparoscopes contain lenses strategically positioned at the tip of the scope and throughout the laparoscope to create images which are then converted digitally by the camera head and eventually sent to an LED monitor. Alternatively, some laparoscopes transmit images via a camera chip at the tip of the endoscope (Olympus Surgical America, Orangeburg, New York). These advances provide for increased resolution and high-definition images and even 3D image conversion in some systems. Laparoscope size can vary, and selection of size will determine the amount of light produced and visual acuity (Figure 6.2). The most common sizes are 5 mm and 10 mm laparoscopes. Microlaparoscopes range from 2 mm to 3 mm and are useful in diagnostic laparoscopy. Additionally, 8 mm operative laparoscopes allow for an operating channel which is incorporated into the scope. The da Vinci® Xi system also uses and 8 mm laparoscope. Angle of view is also an important consideration when choosing a laparoscope. A 0° forward viewing laparoscope provides a straight view of the operation and is commonly used, whereas a 30° deflected-angle laparoscope may provide improved visual angles for pathologies such as large fibroid uterus. Increased skill and attention is required for use of an angled view laparoscope as the field of view must constantly be adjusted and maintained. It is important to note that the light post always faces opposite the field of view when using an angled laparoscope.

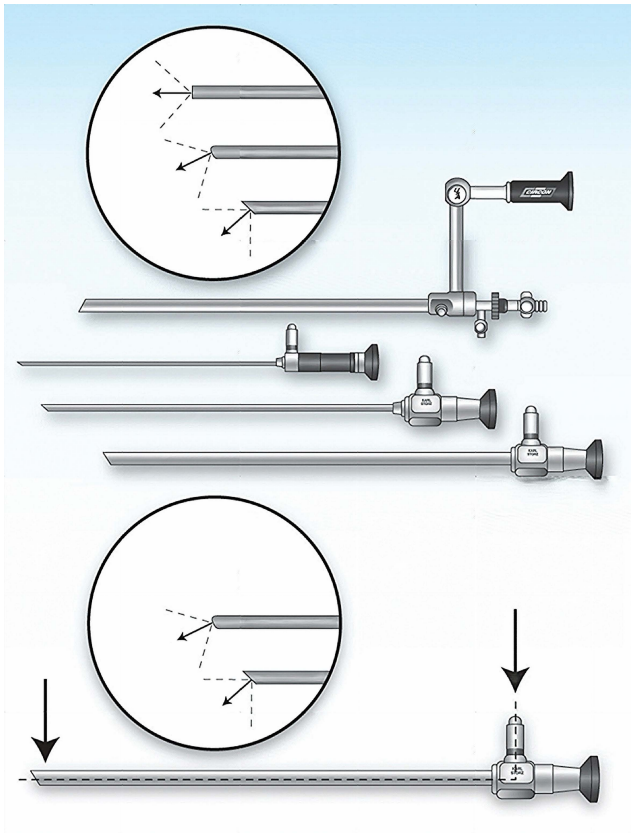


FIGURE 6.2 Laparoscopes in various sizes and viewing angles. (From Pasic RP et al. Instrumentation and equipment. In: *Practical Manual of Minimally Invasive Gynecologic and Robotic Surgery*, 3rd edn., with permission.)

6.4 Devices

6.4.1 Insufflators

A carbon dioxide (CO_2) insufflator is a machine that can rapidly deliver a constant flow rate of CO_2. The insufflation of CO_2 allows for the creation of space within the abdomen and pelvis in which the surgeon can work. Insufflators can be equipped with many features. The most basic features include an adjustable flow rate as well as gas and pressure sensors. These features can be very helpful when establishing pneumoperitoneum, for example if an opening pressure with a Veress needle is above 10 mmHg, there is a high likelihood the needle is incorrectly positioned and may be located in the preperitoneal space, omentum, or liver. Each machine provides a digital readout of the flow pressure, abdominal pressure, and total volume of CO_2 used. Gynecologic laparoscopy typically takes place using a pressure of 15 mmHg. Lower pressures like 12 mmHg can be used for patients who experience respiratory difficulties during surgery. Pressure can be temporarily elevated to 25 mmHg to assist in port placement. This temporary increase in pressure puts more distance between the abdominal wall and underlying organs. Insufflators also may have the capability to deliver heated gas which assists with patient euthermia and decreasing laparoscope fogging. Additionally, there are insufflators that can deliver continuous rates of CO_2 flow while simultaneously suctioning smoke.

6.4.2 Electrosurgical Unit

The electrosurgical unit (ESU) is often housed on the same boom as video capturing and light equipment. This very important piece of equipment converts standard electricity, which is approximately 60 Hertz (Hz), to the electrosurgical frequency range of approximately 300 KHz–3.3 MHz (Figure 6.3). Surgical instruments that use electrosurgical energy will pair with the ESU from the same manufacturer. The ESU typically processes advanced algorithms unique to each instrument to determine the amount of energy and duration of application of the energy to the target tissue. Typical units have the ability to connect to both bipolar and monopolar devices simultaneously. For monopolar devices, the surgeon is able to control the wattage settings from the ESU.

FIGURE 6.3 The ValleyLab™ F10 Energy Platform electrosurgical unit. (By courtesy of Medtronic, Boulder, Colorado.)

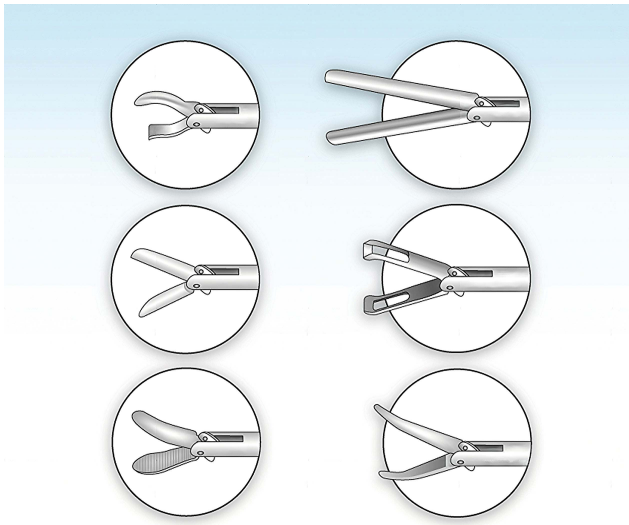


FIGURE 6.4 Laparoscopic instruments. (From Pasic RP et al. Instrumentation and equipment. In: *Practical Manual of Minimally Invasive Gynecologic and Robotic Surgery*, 3rd edn., with permission.)

6.5 Instruments

A full complement of instruments should be available to surgeons for every procedure. The standard set of instruments should include graspers, dissectors, and energy, cutting, suction, and irrigation devices.

Laparoscopic graspers have a multitude of designs and functions. The design of the instrument will help dictate the type of tissue it is meant to handle. Basic categories include traumatic and atraumatic graspers (Figure 6.4). Tissue that is more resistant to puncture such as uterus and ovary are able to be grasped with traumatic graspers. These types of graspers have more jaws that compress tissue, thereby securing it within the instrument. Tissue that is delicate and susceptible to puncture and tearing such as the bowel and fallopian tubes should only be handled with atraumatic graspers such as bowel graspers. These instruments will have blunt tissue edges and may leave more room between the jaws so as not to compress the tissue. Instruments may also come equipped with a locking mechanism. This is helpful for traumatic graspers which are more commonly used to retract for longer periods of time. Dissecting instruments such as Maryland dissectors do not have a locking capability. The handles of instruments should also include an ergonomic design with a rotating shaft. This is crucial to maintaining appropriate ergonomics. Also significant for ergonomics is the length of the instrument shaft. Most laparoscopic procedures are performed using 34 cm instruments while considerations such as obesity may require use of longer 44 cm instruments.

Uterine manipulation is a key component of gynecologic laparoscopy. It allows for improved exposure of the anterior and posterior pelvis while also providing adjustable tissue tension and traction. Uterine manipulators are composed of an intrauterine tip or probe that often has an inflatable balloon which fixates this portion of the device in the uterine cavity. The probe is attached to a handpiece operated by the surgeon or assistant. Many of these devices have a joint at the junction of the tip and handpiece that allow for articulation of the cervicouterine junction such as the RUMI® II System (Cooper Surgical, Shelton, Connecticut; Figure 6.5). This provides the capability to retroflex the uterus and anteriorly deflect the cervix and vice versa. Other uterine manipulators provide the uterine tip and handpiece as one single device such as Kronner Manipujector Uterine Manipulator (Cooper Surgical, Shelton,

FIGURE 6.5 (a) RUMI® II System manipulator with articulating cervicouterine joint for improved uterine manipulation.

FIGURE 6.5 (b) Kronner Manipujector Uterine Manipulator with balloon tip to secure placement. (Both by courtesy of Cooper Surgical, Shelton, Connecticut.)

Connecticut; Figure 6.6). These may or may not incorporate a colpotomizer cup into the design. For simple laparoscopic procedure, a probing tenaculum can be used but has a defined uterine tip that cannot be adjusted for cavity length. The ALLY Uterine Positioning System® is attached to the caudal portion of the surgical bed and can be pneumatically positioned and held in place without the need for an assistant to manipulate.

Historically, irrigation was performed using a syringe attached to a hollow instrument tip that was introduced into the abdomen. Suction devices are hollow instruments that can be attached to wall suction in which they are constantly active. This can be problematic as the rate of suction can rapidly decrease pneumoperitoneum. Suction devices that attach to wall suction also may have trumpet valves that allow for the surgeon to turn on and off the suction flow. Suction and irrigation are now frequently combined into one piece of equipment. A handpiece is attached to a hollow instrument. The handpiece is connected via dual lumen tubing to a pump which is then connected to irrigation fluid. The electric pump allows for controlled irrigation flow rates. The other lumen is then connected to a suction unit thereby combining the two functions into one piece of equipment. Suction is best operated in short bursts so as to not reduce the pneumoperitoneum.

Energy devices incorporate many functions such as vessel sealing and tissue transection and dissection. The most common electrosurgical devices used for tissue sealing are advanced bipolar devices. These devices have different jaw types with blunt, dolphin (pointed), and Maryland (curved) tips. It is important to know the specific parameters such as thermal spread, maximum vessel sealing diameter, and burst pressure for each instrument. Advanced bipolar devices use complex algorithms to determine the precise time and energy needed to seal tissue that is being grasped. Conversely, traditional bipolar energy devices allow for tissue sealing and are controlled by the surgeon via use of a foot pedal. These devices deliver steady electrosurgical energy at the surgeon's chosen wattage and must also be turned off by the surgeon. Additionally, ultrasonic energy devices also allow for vessel sealing and tissue transection. These devices contain an active blade that oscillates rapidly creating thermal energy from kinetic energy. They have the unique capability to "drill" into tissue. There is currently one device available that incorporates both ultrasonic and bipolar energy into a single device. Monopolar energy can be used as a single tip instrument such as a laparoscopic L-hook or the energy can be applied to laparoscopic scissors or Maryland dissectors (Figure 6.7).

FIGURE 6.6 The ALLY Uterine Positioning System™ is an adjustable hands-free uterine manipulator that ensures cephalad traction and allows for static uterine positioning. (By courtesy of Cooper Surgical, Shelton, Connecticut.)

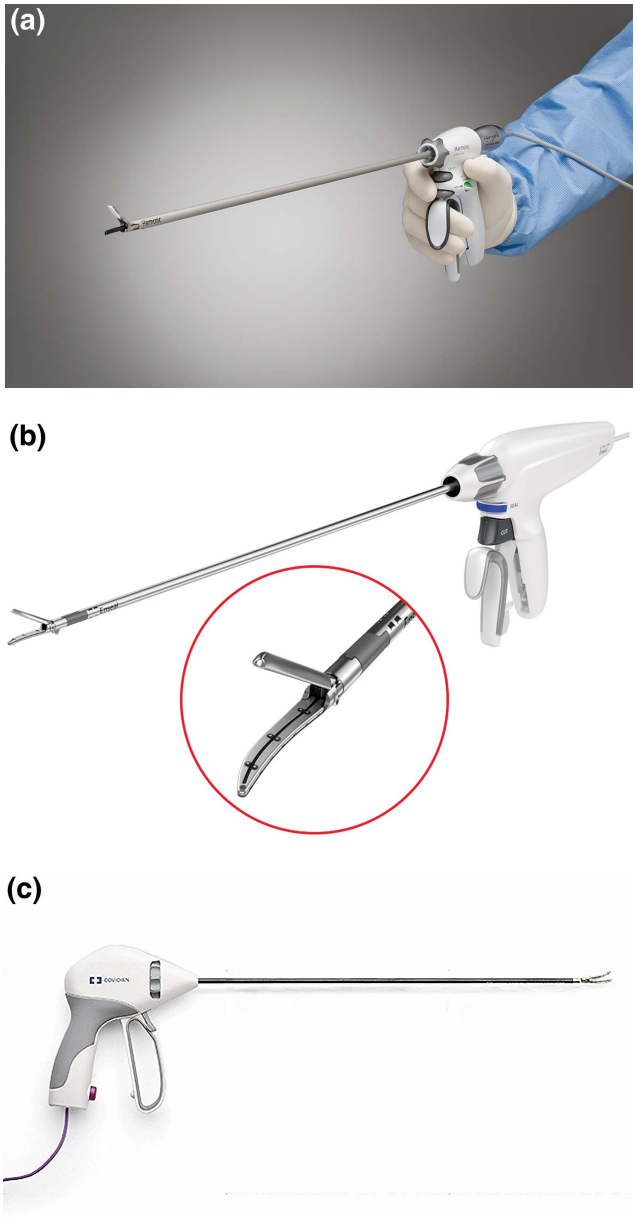


FIGURE 6.7 (a) The HARMONIC ACE™+7 Ultrasonic Shears (by courtesy of Ethicon Endosurgery, Cincinnati, Ohio). (b) ENSEAL™ X1 Curved Jaw Tissue Sealer (by courtesy of Ethicon Endosurgery, Cincinnati, Ohio). (c) LigaSure™ Maryland Jaw Sealer/Divider (©2021 Medtronic. All rights reserved. Used with the permission of Medtronic).

6.6 Robotics

The da Vinci® Xi Surgical System has three components: the surgeon's console, the patient cart, and the vision cart. The patient-side cart has four robotic arms, the center of which typically holds the camera. The arms allow for seven degrees of motion, allowing the surgeon to manipulate with greater dexterity and articulation than traditional laparoscopy. Additional benefits of robotic surgery include the ability to have 3D visualization and improved ergonomics for the surgeon.

6.6.1 Surgeon Console

The surgeon console has many different functions. It houses a 3D vision screen which provides a wide view of the surgical field. This unit contains a lap bar which allows the surgeon to rest their arms while using the master controls. This bar also contains an interactive touch pad that allows for adjusting the camera viewing angle, accepting or giving control of instruments, and moving the various parts of the console to adjust for surgeon body habitus. The master controls for wrist and hands (the master controls contain loops that secure the surgeon's middle finger and thumb), while the index finger rests atop this portion of the device. Pedals are located at the bottom of the device and allow the surgeon to control multiple functions with their feet. Controls include application of bipolar or monopolar energy depending on which EndoWrist instruments are being used. There is also the ability to control the camera and switch control of the robotic arms. A very useful feature is the ability of the system to pair with an assistant or teaching console; this useful feature permits the instruments to be switched from surgeon to surgeon (Figure 6.8).

6.6.2 Patient Side Cart

The patient side cart is the portion of the robotic system that houses the wristed instruments and attaches to the trocars within the patient's abdomen. This system contains four robotic arms which descend from a mobile boom. The entire cart is mobile, and thus it is typically docked or brought to the bedside and affixed to the robotic trocars after abdominal entry and port placement has been performed. Ports are typically placed 8–10 cm lateral to each other and 2 cm deviated in the vertical axis. The camera port is placed 10–20 cm cephalad to the target anatomy. The da Vinci® Xi system uses a uniform 8 mm trocar throughout all port sites. The surgeon has the option of using three or four robotic ports per case. Specialized EndoWrist instruments also allow for single site surgical functionality. Once docked, the camera is inserted and the system performs a "targeting function" which aligns the boom to the optimal surgical angle. The side cart is most commonly side docked at a 90° angle for gynecologic procedures.

The wristed instruments are available in many different configurations and energy sources and include bipolar forceps, Maryland dissectors, scissors, tenaculum, and needle drivers. Assistant laparoscopic ports are useful for suction and irrigation functions as well as the introduction of needles into the surgical field.

6.6.3 Vision Cart

The vision cart is a mobile tower that contains the input for the endoscope. At the top it holds an interactive touch screen that displays the surgical field of view. The electrosurgical unit is also contained within the vision cart. This cart is often placed at the foot of the bed.

6.7 Patient Positioning and Nerve Injury

Proper patient positioning is an essential part of any procedure. Depending on the procedure being performed, positioning of the patient can vary widely to allow for access to the organs and/or area being operated on. In addition to allowing access to the surgical field, proper positioning also prevents any neurovascular injuries to the patient as well as proper ergonomics for the surgeon and their assistant(s).

Injuries to nerves due to improper positioning can be very distressing to patients, causing either sensory deficits, motor deficits, or both. Damage to the nerve can occur from stretching forces or compression. These forces can occur in a variety of ways, including improper positioning, use of retractors, stirrups, and shoulder braces. A more uncommon cause of nerve

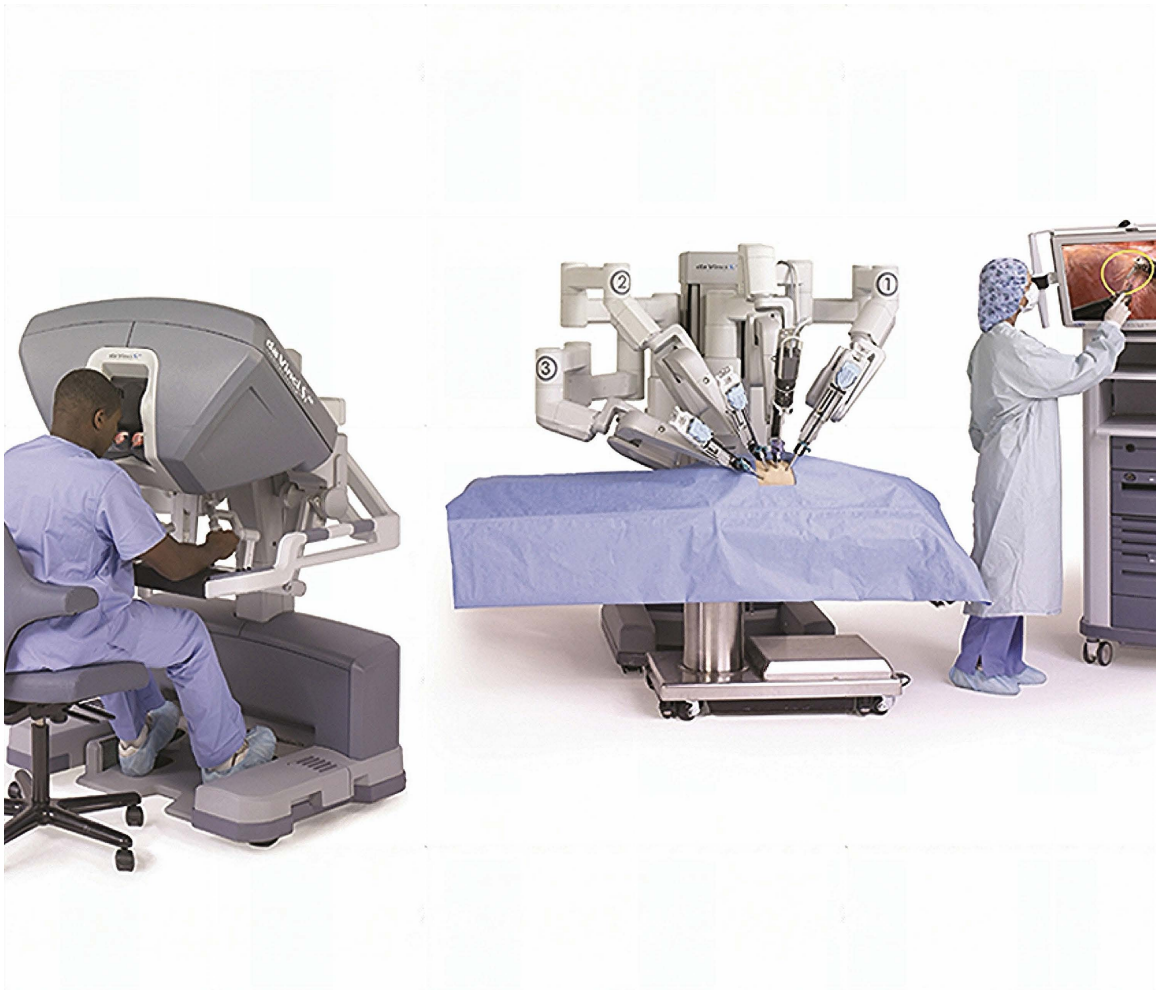


FIGURE 6.8 The da Vinci® Xi Surgical System surgeon console, patient side cart, and vision cart. (From Pasic RP et al. Instrumentation and equipment. In: Pasic RP et al., *Practical Manual of Minimally Invasive Gynecologic and Robotic Surgery*, 3rd edn., with permission.)

injury is entrapment, which can occur during fascial closure. In the majority of cases, nerve damage is transient and self-resolving, however severe injuries have been known to occur and cause permanent damage. Risk factors for nerve injuries at the time of surgery include a large body mass index and prolonged time in Trendelenburg and/or lithotomy position.

The overall incidence of nerve injuries that occur during gynecologic surgery is very low, about 1.8% (6). The nerves most commonly damaged are the lateral femoral cutaneous and femoral nerves. However, the brachial plexus and lumbosacral plexus are also very vulnerable to damage during gynecologic surgery because they are superficial and have many compression points along their paths.

When a patient presents with signs and symptoms concerning a nerve injury after surgery, a history and physical exam is all that is routinely needed for diagnosis. Most injuries will spontaneously resolve with conservative treatment. The mainstay of treatment is physical therapy and avoiding positions that aggravate symptoms. Other treatment options include symptomatic treatment with medications such as, tricyclic antidepressants, and antiepileptics. If the injury is thought to be secondary to entrapment from material such as a suture, surgical decompression is an option as well. Overall, about 73% of injuries will completely resolve within 10 months (7), however, the time to resolution can vary with the severity of injury.

6.7.1 Lower Limb

The lumbosacral plexus houses the nerves that innervate the lower limbs and abdominal wall, making them vulnerable to injury at the time of surgery. The lumbar plexus is composed of the L1–L4 spinal nerves, whereas the sacral plexus is made up of the S1–S3 spinal nerves. Due to the fact that most gynecologic procedures are performed in lithotomy position with the feet and legs in either booted stirrups or candy cane stirrups, there are many points at which compression and/or stretching of nerves can occur. This can predispose the patient to potential neuropathies to the lower extremities (Table 6.1).

The ilioinguinal and iliohypogastric nerves are purely sensory nerves and course over the transversus abdominis and internal oblique muscles on the anterior abdominal wall. This puts them at risk of damage from compression or even entrapment during surgery from retractors, trocar placement, and fascial closure. Damage to these nerves at the time of surgery can lead to paresthesias and pain that can radiate suprapubically, into the thigh, and even into the labia.

TABLE 6.1 Lower Extremity Neuropathies

Nerve	Mechanism of Injury	Signs and Symptoms
Ilioinguinal Iliohypogastric	Compression from retractors, trocar placement, and fascial closure	• Paresthesias to suprapubic region, thigh, and/or labia
Femoral	Extreme hip flexion, retractors	• Quadriceps weakness • Paresthesias to anterior thigh • Absent patellar reflex
Sciatic	Extreme hip flexion	• Paresthesias to posterior thigh, calf, and sole of the foot • Inability to extend thigh • Inability to flex leg • Absent Achilles reflex
Common Peroneal	Compression at fibular head	• Foot drop • Inability to dorsiflex foot • Paresthesias to lateral lower leg
Lateral Femoral Cutaneous	Extreme hip flexion	• Paresthesias to lateral thigh
Obturator	Retroperitoneal dissection	• Inability to adduct thigh • Paresthesias to medial thigh
Pudendal	Sacrospinous ligament suspension	• Paresthesias to perineum, clitoris, labia, and buttock • Incontinence from weakness of pelvic floor muscles

The femoral nerve is the largest nerve that comes off of the lumbar plexus. It runs below the inguinal ligament, which is a common site for compression, especially in high lithotomy position with extreme hip flexion. Signs of injury can include quadriceps weakness and numbness of the anterior thigh as well as an absent patellar reflex. This nerve can also be damaged where it runs over the psoas muscle when using self-retaining retractors during surgery.

The sciatic nerve is the largest nerve in the human body. It is susceptible to stretch injury with the hips in hyperflexion or improper high lithotomy. This causes numbness over the posterior thigh, calf, and sole of the foot, as well as inability to extend the thigh or flex the leg. Injury can also cause an absent Achilles reflex. The lateral femoral cutaneous nerve is injured in a similar way, which can result in paresthesias over the lateral thigh.

When the patient's legs are placed in booted stirrups, a common site of compression if positioned incorrectly is at the fibular head. Compression at this bony prominence on the lateral part of the knee against the fin of the stirrup can damage the common peroneal nerve. The common peroneal nerve is responsible for dorsiflexion of the foot and sensation to the lateral lower leg. Damage to this nerve will often present as a foot drop, which is evident when a patient ambulates after surgery.

Other lower extremity nerves at risk for injury include the obturator nerve and pudendal nerve. The obturator nerve supplies motor innervation to the thigh adductor muscles and is at risk during retroperitoneal dissection within the obturator space. Injury can also cause paresthesias to the medial aspect of the thigh. The pudendal nerve arises from the sacral plexus and provides sensory innervation to the perineum, clitoris, labia, and buttock as well as motor innervation to the pelvic floor muscles. It traverses near many ligaments and bony prominences putting it at risk for injury and entrapment. Damage can cause weakness to the pelvic floor muscles, leading to urinary and/or fecal incontinence. Pudendal neuralgia, which can cause significant pain in the distribution of the pudendal nerve, has been described after sacrospinous ligament suspension if the nerve is within the suspension stitch.

6.7.2 Upper Limb

While injuries to the brachial plexus at the time of gynecologic surgery are rare, they can be some of the more serious to occur. The brachial plexus comprises the C5–T1 spinal nerves and supplies both motor and sensory function to the upper extremities. There are many bony prominences in close proximity to the course of the various nerves that branch off from the brachial plexus. Entrapment of compression at these locations place the nerves at risk for injury along their various paths (Table 6.2). The use of shoulder braces, while effective at preventing caudad sliding on the operating table, does confer an increased risk of brachial plexus injuries due to compression (6). If the shoulder braces are used, they should be positioned laterally over the acromion, and medial placement should be avoided since it can cause compression to the brachial plexus.

The ulnar nerve comes off the medial cord of the brachial plexus and runs next to the medial epicondyle of the elbow in the olecranon groove, putting it at high risk for compression. To prevent injury, padding should be placed over the bony prominences of the elbows. Damage to the ulnar nerve presents as the "claw hand," with the inability of the patient to make

TABLE 6.2 Upper Extremity Neuropathies

Nerve	Mechanism of Injury	Signs and Symptoms
Ulnar	Compression near medial epicondyle	• "Claw hand" • Inability to make a fist • Paresthesias to medial 4th digit and entire 5th digit
Median	Hyperextension of elbow	• Weakness with flexion of wrist and fingers • Paresthesias to first 2.5 digits
Radial	Compression at humerus	• Wrist drop • Weakness with extension of forearm and wrist • Paresthesias to first 3.5 digits

a fist as well as numbness to the medial aspect of the fourth digit and entire fifth digit.

The median nerve is another that can be damaged at the time of surgery; it is formed from the medial and lateral cords of the brachial plexus. The most common mechanism of injury to the median nerve is stretching forces from hyperextension of the elbow, which can result in weakness with flexion of the wrist and fingers, as well as numbness to the first two and a half digits.

The radial nerve is the last nerve discussed from the upper extremity. It comes off the posterior cord of the brachial plexus and is responsible for extension of the forearm and wrist as well as sensation to the lateral three and a half fingers. Damage to the radial nerve can occur from compression of the humerus.

To help mitigate the risk of injury to the upper extremity nerves at the time of surgery, the patient's arms should be either in a supinated or neutral position. If using arm boards, the arms should not be abducted more than 90°. Commonly a patient's arms are tucked at their sides at the time of surgery, if so, padding should be used over the bony prominences at the shoulder, elbow, and wrist to prevent injury to the nerves previously discussed.

6.7.3 Lithotomy Position

In gynecologic surgery, the most common positioning during surgery will be lithotomy position, which is a supine position with the legs separated, flexed, and supported in raised stirrups. This position was originally used to remove stones from the urinary system in urologic procedures, but is now used for many urologic, rectal, and gynecologic procedures as it allows for access to the urinary system and rectum, as well the vulva, vagina, and cervix.

The standard lithotomy position is dorsal lithotomy, which was described earlier. Most surgeons now use padded booted stirrups to position the legs of the patient as opposed to candy cane stirrups. Studies have shown that candy cane stirrups have been associated with an increased risk of postoperative neuropathy as well as decreased physical function 6 weeks after vaginal surgery versus those positioned with booted stirrups (8, 9).

When using booted stirrups, the patient's heel should be all the way back in the boot to ensure that the posterior aspect of the leg is not being compressed against the boot. The knee should also be in line with the patient's contralateral shoulder, as this prevents injury to the common peroneal nerve between the boot and fibular head. Allen® Yellofin® (Hill-Rom Holdings Inc, Chicago, Illinois) stirrups are commonly used and have a starting weight limit of 350–500 lb. Bariatric model stirrups such as the Ultrafins® have a higher weight limit, up to 800 lb.

There are many variations to the traditional dorsal lithotomy position depending on the angle of the hip flexion. The level of hip flexion is measured based on the degree between the patient's posterior thigh and the operating table (Figure 6.9).

With standard or dorsal lithotomy, the patient's hips are flexed 60°–170°, knees are flexed 90°–120°, and hips are abducted 90° or less. Low lithotomy is defined as when the patient's lower legs are parallel to the operating table with a hip flexion of 40°–60°. High lithotomy is when the patient's hips are flexed to 110°–120° and the lower legs are flexed. When patients are not properly positioned in lithotomy, there is an increased risk of injuries to the nerves of the lower extremities, including the femoral, lateral femoral cutaneous, peroneal, sciatic, and obturator nerves (10).

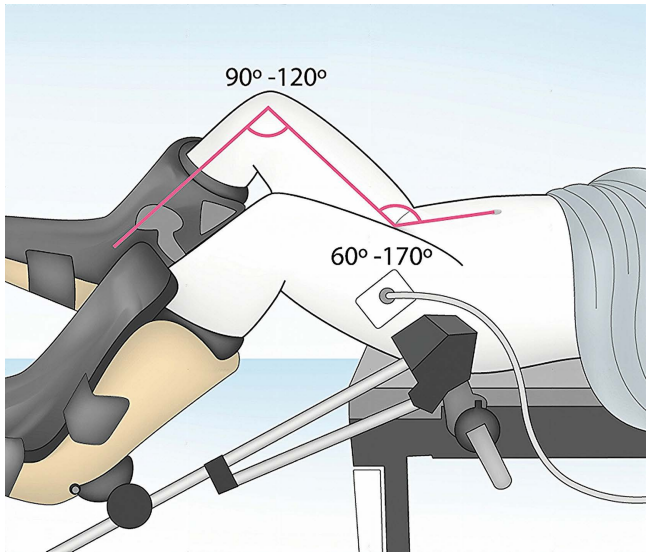


FIGURE 6.9 Dorsal lithotomy patient position and the appropriate degrees of hip and knee flexion. (From Rogers R. The Art of the Competent Surgeon. In: Pasic RP et al. *Practical Manual of Minimally Invasive Gynecologic and Robotic Surgery*, 3rd edn., with permission.)

6.7.4 Obesity Considerations

When it comes to obesity, there are many considerations to take into account, including weight limits of equipment and positioning accommodations that differ from a nonobese patient. Obese patients are at greater risk of neurovascular injuries during surgery so proper positioning is essential. When using stirrups, the lateral knee pad is removed for obese patients to prevent compression of the common peroneal nerve against the fibular head. Extra care should be taken to pad any areas prone to compression as the anatomy can be distorted in obese patients to help prevent injuries in this high-risk population. Surgical bed extenders can be placed on the lateral portions of the bed to accommodate greater width and provide arm support. Air transfer mats such as HoverMatt® are useful to aid in safe patient transfer post-anesthesia (HoverTech International, Allentown, Pennsylvania).

6.7.5 Anti-Slip Devices

The majority of laparoscopic gynecologic surgery will be performed in the Trendelenburg position or steep Trendelenburg position. This placement can cause the patient to shift cephalad on the operating table and thus place the patient at risk of nerve stretching and compression of the lumbosacral and brachial plexuses. To prevent this movement or "slipping," many anti-slip devices have been developed and are used in the operating room as standard of care. These devices include gel foam, memory foam, egg crate padding, bean bags, and shoulder braces, among others. When comparing anti-slip devices, studies have shown that the currently used devices are all comparable in the amount of slide and there was no significant difference in the rate of neuropathies between them (11).

Devices such as gel foam, memory foam, and egg crate padding are all ones that are placed underneath the patient to prevent slip. The Pink Pad® Trendelenburg Patient Positioning System falls under this category (Xodus Medical, New Kensington, Pennsylvania). They are single use devices and have to be replaced for each patient (Figure 6.10).

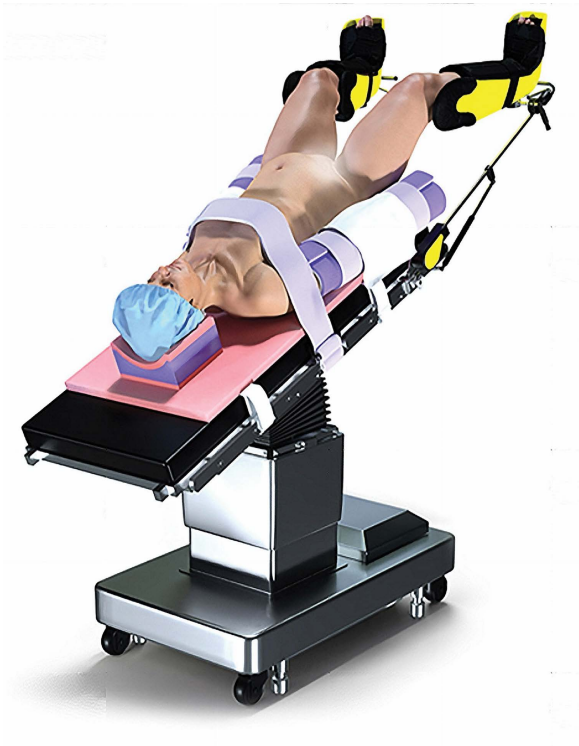


FIGURE 6.10 The Pink Pad® Trendelenburg Patient Positioning System prevents patient slippage while in steep Trendelenburg position and also decreases pressure points. (Used with permission of the Pink Pad by Xodus Medical, Inc.)

There are many devices and systems on the market for use in steep Trendelenburg. One type are bean bag positioners, which include the Hug-U-Vac Steep Trend Positioner, which is a large pliable bean bag with vacuum valves (Hill-Rom Allen Medical, Acton, Massachusetts). Once the patient is positioned in the Hug-U-Vac, suction is applied and the bean bag "molds" to the patient, allowing for individualized positioning for each patient without continuous suction required. However, there is a 500 lb. weight limit with the Hug-U-Vac, limiting its use for more obese patients.

The TrenGuard™ Trendelenburg Patient Restraint is a system with foam bolsters and pillows that does not require additional foam underlay pads or chest straps (D.A. Surgical, Newbury, Ohio; Figure 6.11). This system has the highest weight limit currently on the market at 550 lb. As discussed previously, shoulder braces are not routinely used to prevent slip while in Trendelenburg due to the increased risk of brachial plexus injuries and the many other devices available currently. If shoulder braces are used, care should be taken not to place them medially on the shoulder as this can lead to increased risk of nerve injury.

FIGURE 6.11 (a) TrenGuard™ Trendelenburg Patient Restraint: Here the foreground lateral stabilizing pillow is semi-transparent so the cervical notch bolster can be seen. (b) The semi-reusable HYBRID version. (By courtesy of D. A. Surgical, Newbury, Ohio.)

6.8 Abdominal Entry and Trocar Placement

Abdominal entry is a crucial component of laparoscopic surgery. There are multiple methods to choose from and important contributing factors include a patient's surgical history, body habitus, and the pathology being treated. The safest entry technique has been shown to be whichever technique the surgeon is most comfortable performing (12). The most common anatomical locations for entry include the umbilicus and the abdominal left upper quadrant. Alternate access points include the right upper quadrant and the Lee–Huang point.

The umbilicus is one of the most common sites of laparoscopic entry. The surgeon must be aware of relevant underlying anatomy as the umbilicus typically is located at the third (L3) and fourth (L4) lumbar vertebra. It is important to note the bifurcation of the aorta is typically at the level of (L4) (13). At the base of the umbilicus the fascial layers are fused, and this area is devoid of muscle thus creating a very thin layer of tissue to traverse in order to gain access to the abdominal cavity. Factors that may alter the location of the umbilicus include extremes of

body mass index. A large panniculus may distort the relevant anatomy. Additionally history of abdominoplasty may also alter the natural location of the umbilicus. The surgeon must also be aware of any preexisting hernia at this location.

Left upper quadrant entry is typically achieved through Palmer's point. Palmer's point was first described by Raoul Palmer in the 1970s and is located along the right midclavicular line 3 centimeters below the inferior costal margin. Relevant underlying anatomy include the stomach, liver, spleen, and large and small bowel. An orogastric tube should be placed on suction to decompress the stomach to avoid injury at Palmer's point. Conditions such as splenomegaly and hepatomegaly could result in injury of either organ during entry at this site. Patients with a history or gastrostomy tube are not candidates for Palmer's point entry.

The Lee–Huang point is located along the midline of the abdomen between the umbilicus and xiphoid process (14). This point of entry has been useful in gynecologic surgery with large pelvic pathologies such as fibroids and pelvic malignancy.

6.8.1 Direct Trocar Placement

Direct trocar placement is a technique used for abdominal entry at the umbilicus. It involves the surgeon placing the trocar by feel rather than with visual guidance. The surgeon grasps the abdominal wall with the goal of elevating the umbilicus off the underlying bowel and vasculature. In this abdominal entry technique the surgeon uses one hand placing the thumb and fingers on the abdominal wall on opposite lateral sides at the level of the umbilicus. The trocar is then placed through a skin incision at a parallel angle to the sacrum to avoid any vascular or visceral entry.

6.8.2 Direct Visual Entry

Direct visual entry is a very common entry technique that is employed commonly at Palmer's point and at the umbilicus. Specialized laparoscopic trocars are used that allow for the laparoscope to be placed in the obturator. As the trocar is advanced through the tissue the separate abdominal wall layers are visualized. Once intra-abdominal entry is visualized the obturator is removed and laparoscope is inserted through the trocar to confirm visualization of bowel and omentum, then insufflation can begin. Using the direct visual entry technique at Palmer's point requires no manipulation of the abdominal wall, whereas entry at the umbilicus requires manual elevation of the abdominal wall.

6.8.3 Indirect Entry

Indirect or closed entry involves insufflation of the abdominal cavity prior to trocar placement. This is accomplished via placement of a Veress needle. A Veress needle contains spring-loaded action that provides tactile feedback (Figure 6.12). This action "springs" when the needle enters the abdominal cavity and there is no longer resistance against the tip of the needle. When performed at Palmer's point placement involves three "pops" or layers that provide resistance when the needle is placed. These layers are the external oblique fascia, internal oblique fascia, and the peritoneum. At the base of the umbilicus the muscle and fascial layers are fused and thus only two "pops" are encountered, the fused layer and the peritoneum. At the umbilicus, the angle of the Veress needle insertion varies depending on the patient's body habitus. In the nonobese patient, the Veress needle is inserted at a 45° angle so that it is in parallel to the sacrum and avoids major vasculature. In obese patients, the needle is inserted at a 90° angle so that it passes through the thinnest portion of tissue at the base of the umbilicus.

FIGURE 6.12 Veress needle for indirect entry methods. (By courtesy of Ethicon Endosurgery, Cincinnati, Ohio.)

Entry can be confirmed by attaching the CO_2 insufflation and entry pressures under 10 mmHg, noting slightly higher pressure may be observed in the obese patient. If initial entry pressure is higher than 10 mmHg, the needle should be drawn back to ensure it is not in the omentum. If pressure remains high, insufflation should be stopped and the needle removed. Elevated pressures can indicate the needle is in the incorrect location such as abdominal wall, preperitoneal spaces, or even potentially in an intra-abdominal organ such as the liver. Alternatively, a water drop test can be performed. This test involves attaching a small syringe to the Veress needle and injecting the water into the Veress needle. The water should flow freely into the abdominal cavity. If counter pressure is encountered, the needle is presumed to be preperitoneal or possibly against an intra-abdominal organ. Rarely, the water can falsely flow easily into the preperitoneal space. Once intra-abdominal entry is confirmed, the needle must be held steady in place to prevent the tip of the needle moving, which could cause organ or vascular injury. After insufflation, the needle is removed and entry can be established by placing a trocar at the desired location.

6.8.4 Open Entry

Open entry, first described by Harrith Hasson in 1971, involves cutting down into the peritoneum at the umbilicus to gain abdominal cavity access (12, 15). In the Hasson technique the skin is incised at the umbilicus and a Kocher clamp is used to grasp the fascia at the base of the umbilicus, a second clamp is walked approximately 1 centimeter inferiorly on the fascia, and the layer is elevated and incised. The fascial edges are tagged with suture to facilitate incision closure at the end of the procedure. The peritoneum is grasped and elevated and incised. A specialized blunt trocar is placed through the incision and the trocar is secured to the fascial sutures. Pneumoinsufflation is then undertaken (Figure 6.13).

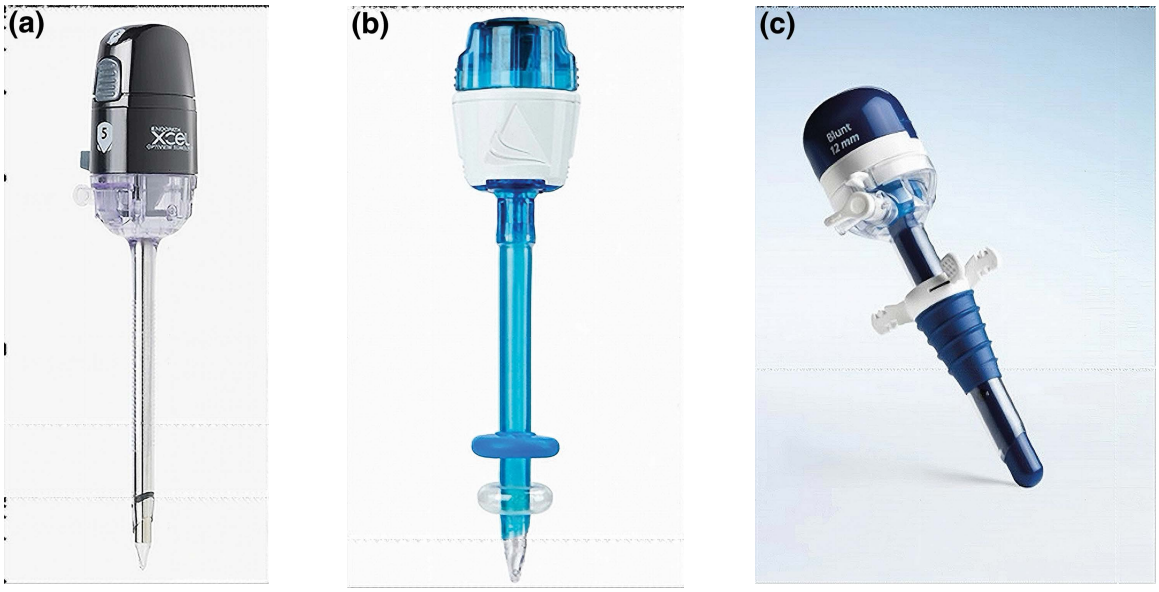


FIGURE 6.13 (a) ENDOPATH XCEL® Trocar with OPTIVIEW® which allows for placement of the laparoscope within the tricar to facilitate direct visual entry (by courtesy of Ethicon Endosurgery, Cincinnati, Ohio). (b) Kii® Advanced Fixation Trocar with balloon for improved abdominal wall access (by courtesy of Applied Medical, Rancho Santa Margarita, California). (c) VersaOne™ Blunt Trocar which facilitates Hasson access (by courtesy of Medtronic, Boulder, Colorado).

6.9 Tissue Retrieval

Tissue retrieval is an integral step for minimally invasive gynecologic procedures. Historically, pelvic pathology specimens were removed intact through laparotomy incisions. With advances in minimally invasive gynecologic surgery, tissue retrieval has evolved with newer techniques that allow for extracting larger specimens through smaller incisions. With the capabilities to now perform laparoscopic procedures for larger pathologies such as hysterectomy for fibroid uterus and cystectomy for large adnexal cysts, the need has presented for contained or in-bag tissue extraction. Principles of contained tissue extraction are:

1. Reduce the risk of extrapelvic implantation and wound contamination, such as in cases of parasitic fibroid and port site endometrioma.
2. Decrease exposure or spillage of benign pathologies to the pelvis, thus decreasing the risk of complications including peritonitis and postoperative ileus like in the setting of mature cystic teratomas.
3. Prevent metastasis of potentially malignant specimens and avoid spillage and possible upstaging of malignancies such as ovarian cancer.

During minimally invasive hysterectomy, tissue is commonly extracted through the vagina if possible. Sutures placed in the cervix prior to hysterectomy allow for traction of the specimen after colpotomy and facilitate vaginal delivery of the uterus and adnexa. Additionally, ring forceps or tenacula can be used to grasp and retrieve specimens. In the event of large specimens, transvaginal manual morcellation is common, as is removal through minilaparotomy (16). During vaginal natural orifice transluminal endoscopic surgery (vNOTES) procedures, the uterus or adnexa are removed through the vagina. In the case of vNOTES adnexal surgery, specimens are removed through the posterior vaginal wall at the site of colpotomy.

For large pathologies in which removal cannot be accommodated via natural orifice extraction, multiple tissue extraction systems are available for assisted removal. Contained extraction requires placing the tissue into a bag system. The bag is then partially delivered through the vagina or minilaparotomy incision and the specimen is morcellated. This can be accomplished via scalpel or electromechanical morcellation. Knowledge of the various containment bags and surgical pathology is crucial for successful minimally invasive extraction.

Laparoscopic specimen retrieval bags are widely available and are produced in single use and multi-use formats. The surgeon must consider multiple characteristics when choosing a retrieval system. Bag selection should be performed taking into consideration the following components:

1. Bag volume
2. Bag shape and taper
3. Mouth dimensions
4. Incision/trocar size

Bag volume is the total volume of tissue that a bag can contain when completely full. Bag shape and ball fit are important characteristics in relation to pathology. Bags can have a gradual, steep, or continuous taper. Depending on the taper, wide or more spherical pathologies may not be able to rest in the base of the bag. An additional consideration is the type of incision or trocar through which the bagging system will be deployed.

The most common port sizes for retrieval systems are 5 mm, 10 mm, and 15 mm (Figure 6.14). It is important for the surgeon to note that trocar size does not necessarily correlate with bag mouth dimensions or bag volume. Thus, it is important for the surgeon to be familiar with the tissue

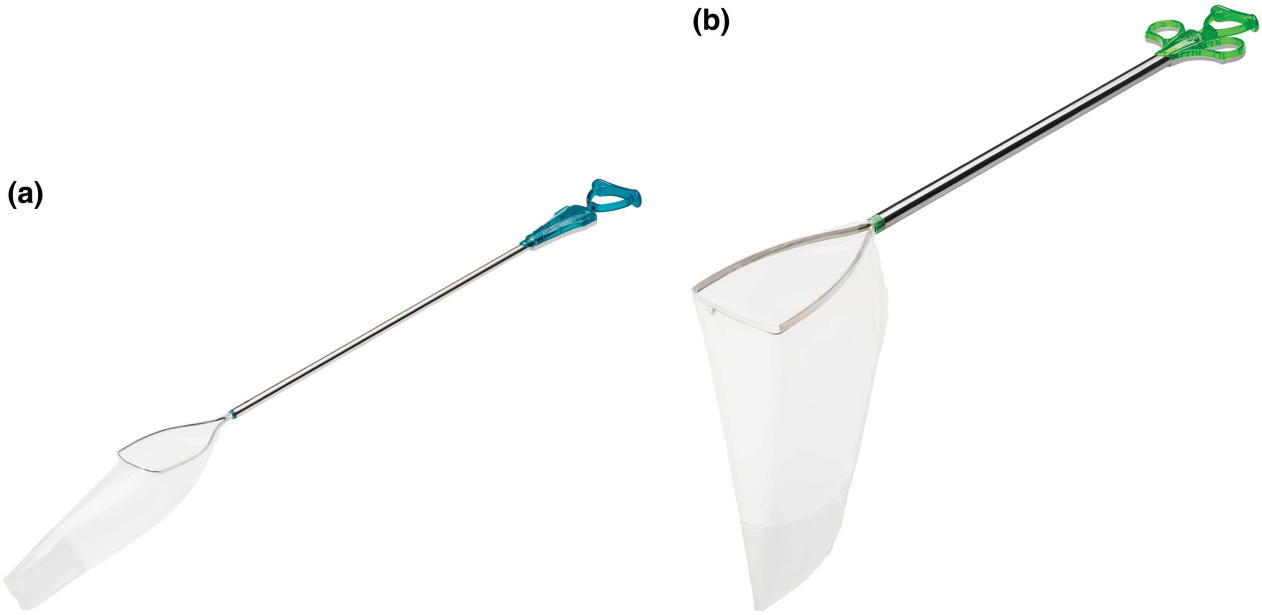


FIGURE 6.14 (a) The Inzii® 10 mm standard specimen retrieval bag with a volume of 225 mL. (b) The Inzii® 12–15 mm specimen retrieval bag with a volume of 1600 mL. (By courtesy of Applied Medical, Rancho Santa Margarita, California.)

FIGURE 6.15 The Alexis Contained Extraction System requires a 2.5 cm incision and affords the ability to extract larger specimens. (By courtesy of Applied Medical, Rancho Santa Margarita, California.)

retrieval systems available to them. Tissue retrieval systems that do not require port sites for introduction can be placed through a minimum of a 2.5 cm incision or a minilaparotomy (Figure 6.15). Retrieval bags are typically composed of polyurethane, polypropylene, or nylon. Nylon is the strongest of these synthetic polymers and the bag can tolerate more force. Polypropylene and polyurethane are slightly less durable and more susceptible to tearing forces.

After the specimen retrieval system is deployed and the specimen is placed in the bag, retrieval is undertaken. The bag is typically delivered through an incision such as colpotomy or minilaparotomy. Tissue extraction is then performed typically via manual morcellation or electromechanical morcellation (EMM).

Manual morcellation is the use of a scalpel to remove the tissue in smaller pieces. Common techniques are extracorporeal C-incision tissue extraction technique (ExCITE) and paper roll technique. The ExCITE technique involves incising the tissue in a curvilinear fashion whereas the paper roll technique requires the scalpel to move in linear fashion. Each method reduces the bulk of the pathology into manageable strips to facilitate removal from a smaller incision. Electromechanical morcellator employs the use of a mechanical device.

Power morcellation is the use of powered devices to either "peel" or "core" the specimen to be more easily removed from the abdominal cavity. Traditionally, this was done within the abdomen or pelvis without containment in a bag, however the FDA released a warning for power morcellation in 2014 against the use of power morcellators in women undergoing myomectomy or hysterectomy for the treatment of fibroids. This warning arose from the possible spread of unsuspected leiomyosarcoma during morcellation that could potentially lead to the upstaging of disease. The FDA's most recent recommendations are to only use power morcellation in appropriately selected patients without risk factors for leiomyosarcoma and only with the use of a tissue containment system.

Using a tissue containment system prevents the possible spread of cells throughout the abdominal and pelvic cavity. However, studies have shown that even with contaminants bags remaining intact, there was still risk of leakage of fluid and possibly cells from the specimen noted (17). With numerous containment bags on the market, it was found that the presence of leakage during power morcellation varied widely between brands (18). Currently, the only FDA-approved device is the Olympus Contained Tissue

Extraction System, which is specifically designed for containment and power morcellation during gynecologic procedures (Olympus Surgical America, Orangeburg, New York). The Olympus PneumoLiner is the containment bag for the system, which allows for intra-abdominal insufflation and provides a barrier to prevent the leakage of tissue and fluid.

References

1. McCarroll ML et al. Development and implementation results of an interactive computerized surgical checklist for robotic-assisted gynecologic surgery. *J Robot Surg*. 2015;9(1):11–18.
2. World Health Organization. *WHO surgical safety checklist*. 2009. Available at: www.who.int/teams/integrated-health-services/patient-safety/research/safe-surgery/tool-and-resources.
3. Catanzarite T et al. Ergonomics in surgery: a review. *Female Pelvic Med Reconstr Surg*. 2018;24(1):1–12.
4. Rosenblatt PL et al. Ergonomics in the operating room: protecting the surgeon. *J Minim Invasive Gynecol*. 2013;20(6):744.
5. Moss EL et al. Impact of obesity on surgeon ergonomics in robotic and straight-stick laparoscopic surgery. *J Minim Invasive Gynecol*. 2020;27(5):1063–1069.
6. Abdalmageed OS et al. Nerve injuries in gynecologic laparoscopy. *J Minim Invasive Gynecol*. 2017;24(1):16–27.
7. Cardosi RJ et al. Postoperative neuropathies after major pelvic surgery. *Obstet Gynecol*. 2002;100(2):240–244.
8. Whitis AM et al. Postoperative lower extremity neuropathy with boot stirrups compared with candy cane stirrups. *Obstet Gynecol*. 2021;137(5):916–923.
9. Gupta A et al. Candy cane compared with boot stirrups in vaginal surgery: a randomized controlled trial. *Obstet Gynecol*. 2020;136(2):333–341.
10. Barnett JC et al. Laparoscopic positioning and nerve injuries. *J Minim Invasive Gynecol*. 2007;14(5):664–673.
11. Das D et al. Evaluation of positioning devices for optimization of outcomes in laparoscopic and robotic-assisted gynecologic surgery. *J Minim Invasive Gynecol*. 2019;26(2):244–252.e1.
12. Ahmad G et al. Laparoscopic entry techniques. *Cochrane Database Syst Rev*. 2019;1(1):CD006583.
13. Berger AA et al. 3D vascular anatomy of the presacral space: impact of age and adiposity. *Int Urogynecol J*. 2019;30(3):401–407.
14. Lee CL et al. A new portal for gynecologic laparoscopy. *J Am Assoc Gynecol Laparosc*. 2001;8(1):147–150.
15. Hasson HM. A modified instrument and method for laparoscopy. *Am J Obstet Gynecol*. 1971;110(6):886–887.
16. Kim R et al. Current methods of tissue extraction in minimally invasive surgical treatment of uterine fibroids. *JSLS*. 2022;26(3):e2022.00036.
17. Cohen SL et al. Contained tissue extraction using power morcellation: prospective evaluation of leakage parameters. *Am J Obstet Gynecol*. 2016;214(2):257.e1–257.e6.
18. Herman A et al. In vitro leakage testing of tissue containment bags when subjected to power morcellation forces. *J Minim Invasive Gynecol*. 2020;27(3):655–664.

7 PRINCIPLES OF VAGINAL SURGERY AND vNOTES

Ali Azadi, Jan Baekelandt, and Greg Marchand

7.1 Introduction

The vaginal approach is a natural orifice surgical technique used for a variety of gynecological conditions. As incisions through the vaginal wall do not cause visible scarring and recovery from vaginal procedures is generally faster than laparotomy, vaginal surgery is considered minimally invasive surgery. From the vaginal approach multiple procedures can be performed in addition to hysterectomy, allowing the possibility to treat comorbid conditions such as pelvic organ prolapse, urinary incontinence, and adnexal masses. Moreover, the vaginal approach not only provides access to the intraperitoneal cavity but also allows for entry into retroperitoneal spaces.

The history of vaginal hysterectomy dates to as early as 50 BC. In the early 18th century, the first planned vaginal hysterectomy was reported. By the mid-19th century, there were several reports of emergency vaginal hysterectomies in cases such as postpartum uterine inversion. Remarkably, over the past century, most hysterectomies have been performed using the abdominal approach (1).

According to the 2017 ACOG committee opinion, a strong recommendation is made for the use of minimally invasive approaches in hysterectomy whenever possible, going as far as to call vaginal hysterectomy the "Approach of Choice" when feasible. Because of its advantages over laparotomic hysterectomy and scar-free cosmesis, the vaginal approach is often the preferred approach among all minimally invasive techniques (2).

A comprehensive 2015 Cochrane review further supports the preference for vaginal hysterectomy over abdominal, laparoscopic, and robotic-assisted approaches. The review supported several benefits of the vaginal approach including fewer visceral injuries, reduced fistula formation, less postoperative pain, shorter operating times, shorter hospital stays, higher levels of patient satisfaction, and greater cost-effectiveness (3).

Given the strong evidence and multiple recommendations from professional organizations, it is paramount that all minimally invasive gynecologic surgeons have familiarity with vaginal techniques, including vaginal hysterectomy without laparoscopic or robotic assistance. The vaginal approach should be considered and offered to patients based on their clinical indications whenever possible.

Despite the strong wording supporting the vaginal approach, surgeons need to be aware that such recommendations for minimally invasive approaches were largely based on meta-analysis of randomized controlled trials that did not stratify all gynecological pathologies. In these reviews, benign diseases such as endometriosis, fibroids, and pelvic organ prolapse were often lumped together in data synthesis. Therefore, while these recommendations make sense as general guidelines, individual patient circumstances, such as coexisting pathologies and unique symptomatology or anatomy could shift the favored technique to another modality. As a result, consideration of the factors individual to each patient is critical when choosing a minimally invasive technique.

As far as contraindications to vaginal hysterectomy, no absolute contraindications have been identified by any meta-analyses or named by any major scientific organizations. However, individual surgeon preferences can play a significant role in the choice of surgical approach. In some cases, surgeons may prefer an abdominal approach when they encounter pathologies such as large uterine size, large adnexal masses, lack of mobility and lack of descent of the uterus, anticipation of severe adhesions, and concern for extrauterine involvement of pathologies such as in malignancies and advanced endometriosis.

Over the past decade, the feasibility of using laparoscopy to perform a total hysterectomy entirely through the vaginal approach, also called transvaginal natural orifice transluminal endoscopic surgery or vNOTES, has been demonstrated in several case series. In these procedures, the conventional steps of a vaginal hysterectomy are followed but performed endoscopically with standard reusable endoscopic instruments and a vaginally introduced single-port device (4, 5).

vNOTES procedures are becoming increasingly common, as many surgeons recognize that this approach combines many of the advantages of traditional laparoscopic surgery with the enhanced cosmesis and benefits of vaginal surgery. Although originally vNOTES was initially utilized mainly for hysterectomy and adnexal surgery, recently vNOTES techniques have been described for much more complex urogynecological and oncological procedures (6, 7).

It is worth noting that over the same period in the past decade, there has been an increase in the percentage of laparoscopically performed hysterectomies compared to vaginal and open abdominal approaches. Currently in the United States, only 13% of hysterectomies are performed vaginally, while 68% are performed with some form of laparoscopic or laparoscopic robotic-assisted approach (8).

Multiple factors can affect a surgeon's decision in choosing the route of hysterectomy. The list includes but is not limited to the surgeon's training and experience, patient profile, uterine size and mobility, uterine pathology, involvement of pathology outside of the uterus, the anticipation of adhesions, adnexal pathologies, parity, necessary concurrent procedures, chronic pelvic pain, and the presence of endometriosis. However, with advanced techniques, most experts do not consider factors such as nulliparity, uterine size, and adnexal pathology as absolute contraindications to vaginal surgery (8). Preoperative imaging may also provide additional relevant information to assist the surgeon in choosing the best surgical route.

7.2 Preoperative Considerations

Informed consent is essential with a detailed discussion of the risks and benefits specific to the planned surgery. At a minimum, this consent should entail the commonly experienced risks and complications of the anticipated procedure, as well as alternative approaches that could be considered. The benefits of the chosen technique should be discussed, as should the possibility of changing the approach in order to address unanticipated pathology. In patients with symptomatic vaginitis, evaluation and treatment are recommended prior to surgery. Cervical dysplasia screening tests should be updated.

DOI: 10.1201/9781003312109-7

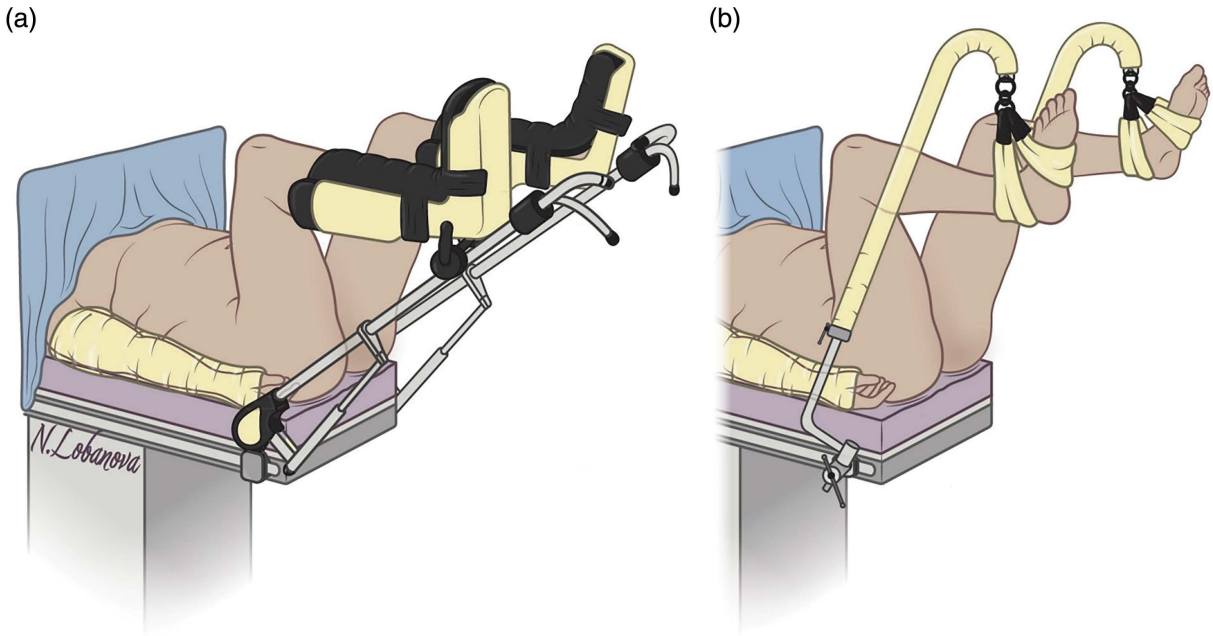


FIGURE 7.1 Positioning for vaginal surgery: (a) Boot stirrups; (b) candy cane stirrups.

7.2.1 Positioning

Vaginal surgery is commonly performed with the patient in the dorsal lithotomy position. "Candy cane" and "Allen" or "boot" stirrups are commonly used (Figure 7.1). A recent randomized controlled trial demonstrated that women undergoing vaginal surgery positioned in boot-type stirrups have significantly improved physical function six weeks post-surgery compared to those positioned in candy cane–type stirrups. Proper patient positioning is not only essential for surgical success but critical to prevent complications such as pressure ulcers and nerve injuries. Nerve injuries can occur due to excessive compression or stretching during positioning. Femoral, tibial, sciatic, and peroneal nerves can potentially be affected. These neuropathies can persist for months after vaginal surgeries (9,10). Chapter 19 (Principles of Neuropelveology) provides a more comprehensive overview of nerve injuries that can occur during gynecologic surgery.

When a concomitant laparoscopic procedure is planned, or when a potential need for conversion to laparoscopy is likely, consideration of proper patient positioning becomes crucial as outlined in the following:

1. *Tucking Arms and Padding*: Arms are tucked to the patient's sides and pads are used underneath the patient to prevent sliding. This helps maintain stability and minimize the risk of injury.
2. *Avoiding Brachial Plexus Injury*: Care must be taken with proper padding to avoid pressure or stretching of the brachial plexus while securing the arms. Sliding should be avoided while the patient's arms are tucked as it may cause injury to the brachial plexus by stretching.
3. *Patients with Limited Mobility*: In patients with limited mobility such as history of joint replacement, one may allow the patient to position herself while awake to allow positioning within range of motion.
4. *Buttock Position*: Some surgeons prefer to have the patient's buttocks overhanging the end of the table to enhance exposure. Caution should be taken to ensure coccyx and sacrum have adequate support on the bed to avoid injury.
5. *Sequential Compression Devices (SCDs)*: The use of SCDs is recommended in accordance with many established guidelines. SCDs help prevent deep vein thrombosis (DVT).

7.2.2 Preparation, Exposure, Visualization, Light, and Retractors

7.2.2.1 Prepping and Draping

We recommend the insertion of a Foley catheter after completion of draping. This type of catheter facilitates easy catheter removal for cystoscopy at any time during the procedure, ensuring the continued use of the same catheter without contamination concerns. Additionally, a three-way Foley catheter enables bladder backfilling when the surgeon requires a full bladder for anatomical verification.

While patient safety and comfort at the time of surgery are paramount, surgeons should also prioritize ergonomics during vaginal surgery to avoid fatigue. The use of table-mounted retractors and cameras has been found to be helpful to some surgeons for better ergonomics and to reduce the need for additional assistants in soft tissue retraction (11) (Figure 7.2).

Achieving adequate exposure during vaginal surgery is essential. There are multiple retractors that can be used during vaginal surgery, each having its own advantages and limitations. Selection of the proper retractor allows maximum exposure at various stages of the surgery (Figure 7.3).

In order to maximize visualization, some surgeons will use headlamps or light sources attached to suction devices

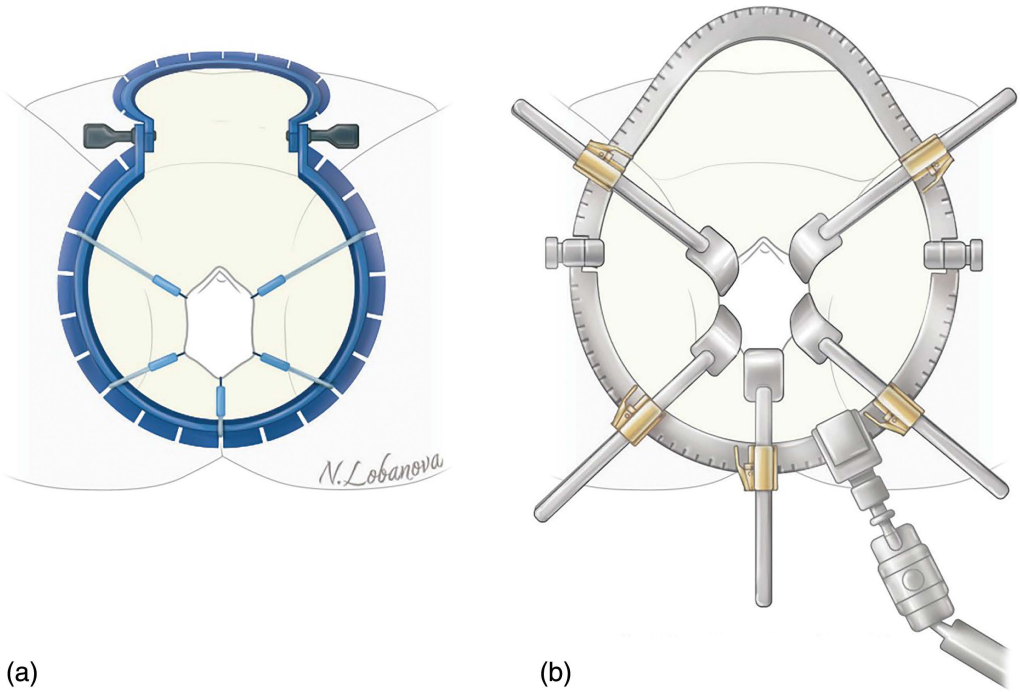


FIGURE 7.2 Vaginal self-retractors: (a) Lone Star retractor; (b) Magrina–Bookwalter retractor.

FIGURE 7.3 Retractors used in vaginal surgery (e.g., Breisky, right angle, Deaver, Sims, and Jackson retractors, heavy weight speculum, bivalve speculum).

or retractors. Regardless of the chosen technique and instruments, maximum exposure is critical for safe and successful vaginal surgery.

7.3 Description of a Vaginal Hysterectomy

7.3.1 Incision (Figure 7.4a)

After the cervix is grasped and pulled forward, a diluted solution of either vasopressin or a local anesthetic with epinephrine is injected circumferentially at the cervicovaginal junction. This injection serves a dual purpose, aiding in achieving hemostasis and hydrodissection. In some cases, an anesthetic may also be injected into the uterosacral ligaments to ensure effective analgesia. Subsequently, an incision is made with a scalpel or by using electrosurgery using Bovie circumferentially to incise epithelium and underlying muscularis. It is worth noting that an elliptical incision, as opposed to circular, is often preferred as it provides better access. Following the incision, the vaginal epithelium and muscularis are dissected away from the cervix or pubocervical fascia using sharp and/or blunt movements. It is important to note that the specific order of entry into the anterior and posterior cul-de-sac may vary depending on the surgeon's individual preferences and the unique requirements of the procedure.

7.3.2 Entry to Posterior Cul-de-Sac (Figure 7.4b)

To facilitate access into the posterior cul-de-sac, the cervix is pulled forward and upward while the posterior vaginal wall is grasped with an allis clamp and pulled downward. Occasionally, Trendelenburg positioning can aid the movement of the small bowel out of the cul-de-sac. The surgeon can palpate the area of intended entry between two fingers to minimize the chance of inadvertent injury to the bowel. Sharp scissors can be used to enter the cul-de-sac. The handle of scissors should be dropped to maintain a safe angle and avoid rectal injury. After intraperitoneal entry is obtained, a long retractor is placed in the incision.

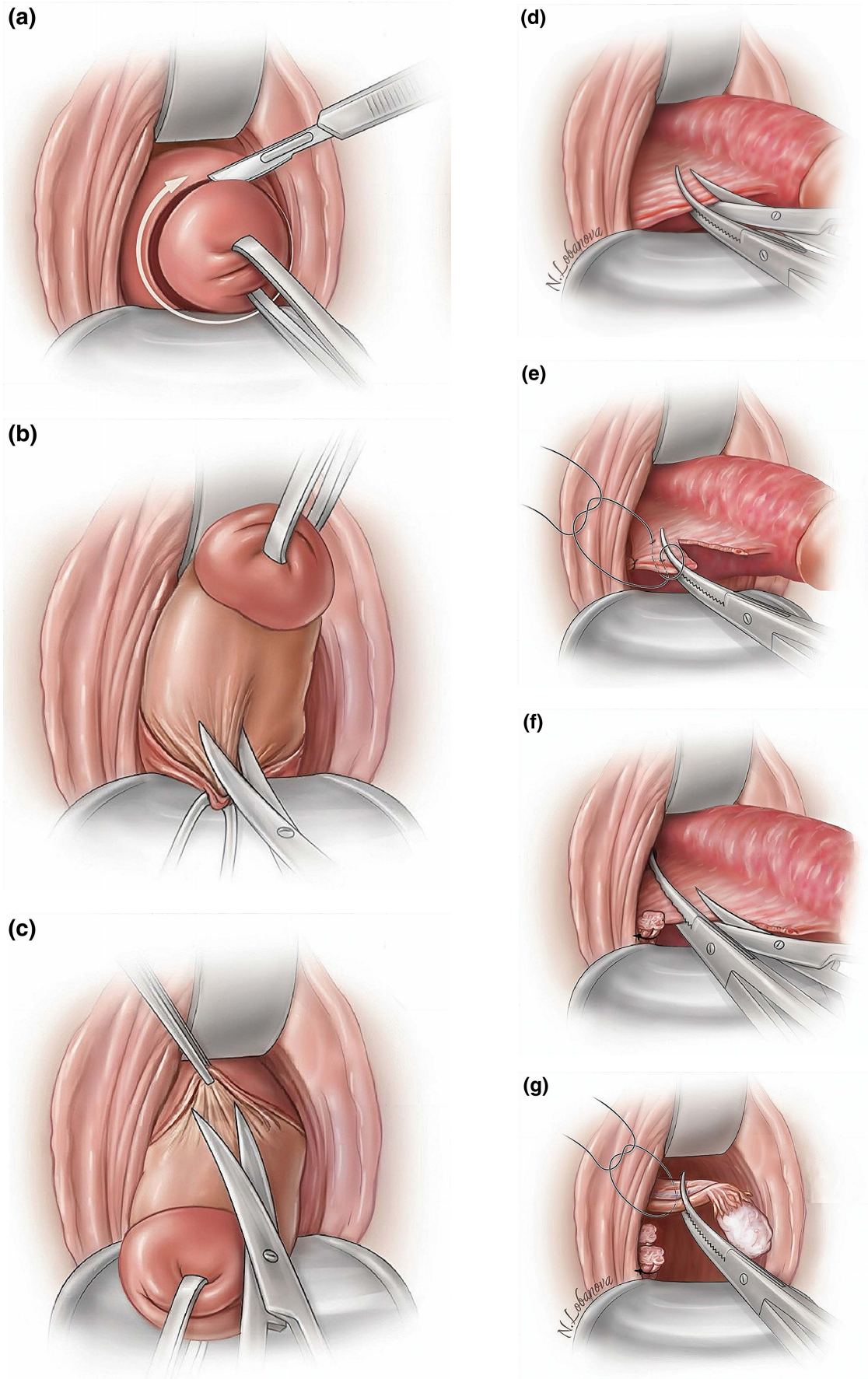


FIGURE 7.4 Steps of vaginal hysterectomy: (a) Incision is made circumferentially at cervicovaginal junction. (b) Entry to posterior cul-de-sac. (c) Anterior colpotomy. (d) Transection of the uterosacral ligaments. (e) Suture ligation of the uterine artery. (f) Clamping the utero-ovarian ligaments. (g) Clamping the infundibulopelvic ligaments.

7.3.3 Entry to Anterior Cul-de-Sac (Figure 7.4c)

For many surgeons, before entering the anterior cul-de-sac, it is common practice to transect the uterosacral ligaments. This allows for more uterine descent to aid in the anterior entry. Some surgeons prefer to have the patient's full bladder at this stage, as it helps identify the vesicovaginal fold to reveal the ideal point of entry. To proceed, the peritoneum is grasped with a fine instrument and pulled upward under traction. While maintaining traction, a sharp entry with Metzenbaum scissors is made. To ensure the bladder's integrity before continuing the procedure, the surgeon can palpate the bladder inferiorly and identify the Foley catheter over the intact bladder. A Deaver retractor can be placed anteriorly for better visualization for the rest of the procedure.

7.3.4 Transection of Uterosacral and Cardinal Ligaments (Figure 7.4d)

The uterosacral ligaments can be clamped using a heavy instrument such as a Heaney clamp.

The pedicle can be transected, and suture ligated. The pedicle is often tagged to provide traction on the uterosacral ligament later in the case. It is important to be mindful of the variation in uterosacral anatomy and make necessary adjustments to the technique as required. Studies using high-definition MRI imaging have shown that uterosacral ligaments can attach to the cervix, vagina, or both as normal variants of anatomy (12).

Alternatively, advanced vessel sealing devices can be used for ligament division and ligation. When using such devices, it is crucial to adhere to safety protocols similar to those followed in laparoscopic cases. Notably, surgeons must exercise caution regarding the thermal spread of these devices to avoid injury to nearby structures such as the ureters, bladder, and rectum.

7.3.5 Clamping and Ligation of Uterine Arteries (Figure 7.4e)

After transecting and securing the uterosacral ligaments, the uterine vessels are clamped and transected. The clamp usually includes the anterior and posterior leaves of the broad ligament peritoneum. While transfixation sutures can provide security, it is important to avoid inserting the needle in a vascular pedicle. The use of advanced vessel sealing devices for this step may result in sealing of the anterior and posterior leaves of the broad ligament, which may improve hemostasis.

7.3.6 Transection of Broad, Utero-Ovarian, and Round Ligaments (Figure 7.4f)

Transection of the broad, utero-ovarian, and round ligaments involves a sequential process of clamping, cutting, and suture ligation. It is important to avoid excessive traction to prevent avulsion. It is advisable to avoid any gaps when suturing to optimize hemostasis. Some surgeons may prefer using energy devices for efficiency. For vascular pedicles such as the utero-ovarian ligaments, we recommend using the free tie and transfixation suture. To minimize the risk of damage to sliding bowels and enhance visualization, Trendelenburg positioning can be utilized. Some cases may also require packing the bowels to create a clear surgical field.

7.3.7 Extraction Techniques

While removal of a large specimen can be challenging, vaginal morcellation techniques such as attempting to split the uterus in half ("bivalving"), intramyometrial coring, vaginal myomectomy, and use of a strong retrieval bag have been described to help facilitate this process. In cases where malignancy is suspected, the specimen must be removed intact or encapsulated in a protective bag or liner.

7.3.8 Adnexal Surgery (Figure 7.4g)

Opportunistic salpingectomy, performed alongside a hysterectomy, is recommended for cancer risk reduction (13). If indicated, salpingo-oophorectomy can usually be safely performed via the vaginal approach. The infundibulopelvic ligaments can be clamped with Heaney clamps. Free ties can be applied on the vascular pedicle proximal to the clamp. Typically, the pedicle between the clamp and tie will be suture ligated for better security and hemostasis. Some surgeons may prefer to use advanced energy devices as an alternative. We emphasize that with proper techniques, the need for adnexal surgery should not preclude women from having vaginal surgery as a minimally invasive option.

7.3.9 Apical Suspension

Apical support of the pelvic organs is typically disrupted during hysterectomy at the time of transection of uterosacral and cardinal ligaments. Although the true risk of developing pelvic organ prolapse after hysterectomy is not precisely known, it is important to note that the route of hysterectomy itself does not impact the risk of developing pelvic organ prolapse (14).

There is currently limited data supporting the routine use of high uterosacral ligament suspension or McCall culdoplasty during hysterectomy (15, 16). However, we recommend that surgeons assess the patient's preoperative symptoms, especially if uterine descent is a consideration for choosing a vaginal approach. The presence of uterine descent may indicate symptomatic prolapse which requires proper apical suspension at the time of surgery. In lieu of performing a formal suspension or culdoplasty procedure, a commonly used acceptable technique is to tag the uterosacral ligaments and incorporate the higher portion of uterosacral ligaments into the vaginal cuff with delayed absorbable sutures. This can act as a treatment or to prevent prolapse.

In cases of more advanced pelvic organ prolapse, it is important to be aware of the development of de novo stress urinary incontinence when the prolapse is reduced. Proper workup and planning are required to avoid developing urinary incontinence after surgery.

7.3.10 Cystoscopy and Rectal Examination

The practice of performing routine cystoscopy at the time of hysterectomy has been a subject of debate. However, most experts concur that it offers valuable benefits in detecting immediate bladder and ureteral injuries and has limited risk of complication. Surgeons should be aware that injuries that are delayed in presentation, such as thermal damage from energy devices, are notorious for being undetectable at the time of immediate postoperative cystoscopy.

Given the potential risk of rectal injury during posterior colpotomy, vaginal cuff closure, and apical suspension, we recommend that the surgeon perform a rectal examination following hysterectomy to verify integrity of rectum.

7.4 Perioperative Complications

The surgeon should be aware of the potential complications associated with gynecological procedures, such as vaginal hysterectomy. Common complications for vaginal hysterectomy

are similar to other approaches, and a partial list appears as follows (17):

1. Hemorrhage
2. Bladder Injury
3. Ureteral Injury
4. Bowel Injury
5. Conversion to Open or Laparoscopy
6. Nerve Injury
7. Cuff Dehiscence
8. Vaginal Cuff Abscess
9. Urinary Retention
10. Fallopian Tube Prolapse
11. Fever
12. Fistula
13. Ileus
14. Bowel Obstruction
15. Venous Thromboembolic Events
16. Dyspareunia
17. Urinary Tract Infections

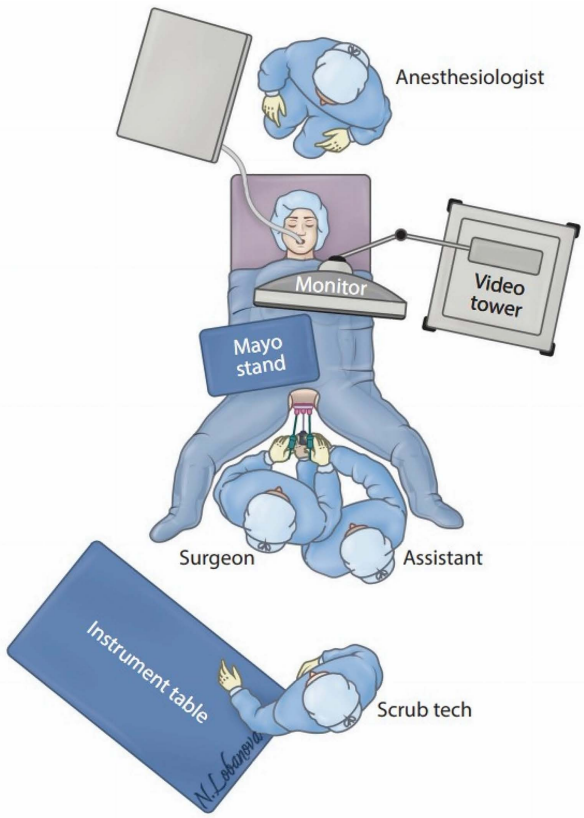


FIGURE 7.5 Room setup for vNOTES.

7.5 vNOTES

In this approach, a special port similar to single-site laparoscopic surgery is used. Access to the peritoneal cavity is provided after anterior and posterior colpotomy is performed during vaginal hysterectomy. A single colpotomy (generally posterior) alone can provide such access if a hysterectomy is not planned. The port will provide pneumoperitoneum and allow access to laparoscopic instruments similar to abdominal laparoscopy. The remaining steps of the procedure are completed laparoscopically from the transvaginal approach and following the same steps of vaginal surgery (Figures 7.5, 7.6, and 7.7)

vNOTES has gained popularity since its introduction in 2012 (5). While long-term data is limited, existing studies suggest similar safety outcomes compared to traditional laparoscopy. Some of these studies have reported potential benefits such as reduced postoperative pain, shorter operating times, and faster recovery (18, 19).

7.5.1 Benefits of vNOTES

Surgeons may find that vNOTES combines the advantages of vaginal surgery with the benefits of laparoscopic surgery. This innovation could influence a shift in the declining rate

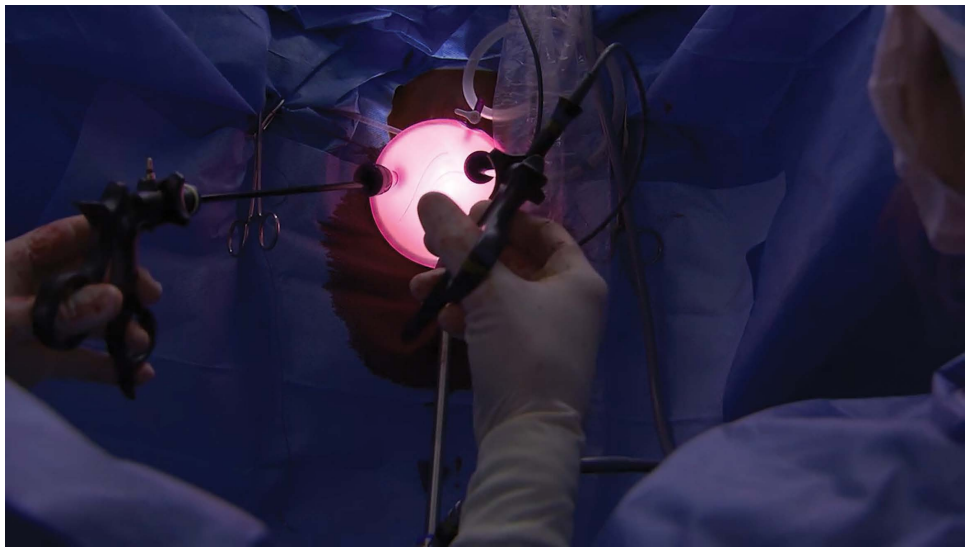


FIGURE 7.6 Port placed vaginally to allow laparoscopic access for vNOTES.

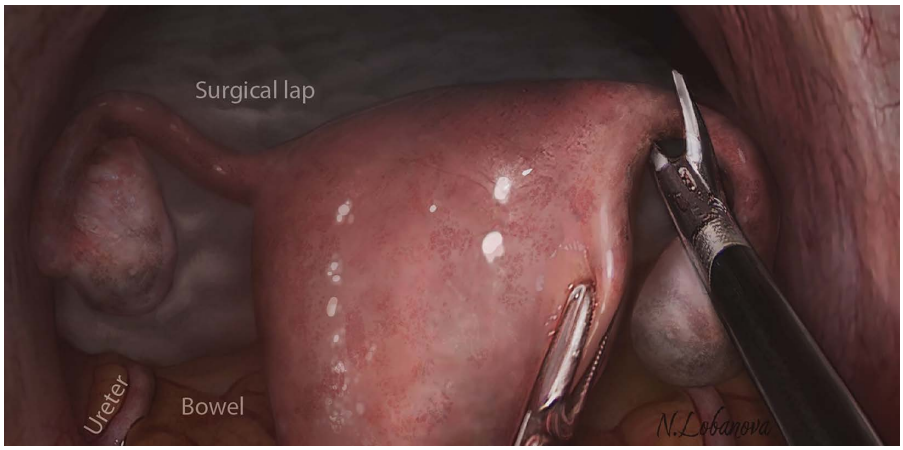


FIGURE 7.7 Laparoscopic view and illustration of last steps of hysterectomy via vNOTES.

of traditional laparoscopic surgery or even of vaginal surgery. However, like any other new innovation, physicians should be aware of the lack of long-term data and patients need to be counseled properly.

Some of the potential advantages of vNOTES include:

- *Improved Visualization*: Enhanced by magnification and the use of an angle scope.
- *Adhesion Avoidance*: Patients who have previously undergone upper abdominal surgery may benefit from vNOTES.
- *Minimal Trendelenburg Position*: In contrast to traditional laparoscopy, vNOTES often requires less use of the Trendelenburg position, which can be particularly advantageous in obese patients and patients in which increased intracranial pressure should be avoided.
- *Reduced Risk of Instrumental Injury*: vNOTES may minimize the risk of instrument-related injuries occurring outside the visualized field.

Only one-third of instruments are typically in view during traditional laparoscopy. Visceral and vascular mechanical injuries have been reported in traditional abdominal laparoscopy during introducing instruments to the field and electrical injuries can occur due to a variety of mechanisms including insulation defects, open activation, direct coupling, and capacitive coupling.

Non-visualized parts of instruments in vNOTES are not in contact with bowel and major vessels, compared to traditional laparoscopy. Therefore, there is potentially less chance of mechanical and electrical injury from instruments.

- *Easier Adhesiolysis and Access to the Adnexa*: The vaginal approach can often yield a less hindered approach to the adnexa, often eliminating the challenges to visualization that more cephalad adhesions can present. Often adhesiolysis that would have been essential to completing a procedure from the abdominal approach simply does not need to be undertaken to complete a vNOTES technique.
- *Better Ergonomics*
- *Avoiding Abdominal Scars, Improved Cosmesis*: vNOTES generally only requires colpotomy, which leaves no visual scars.

The recent advancement of vNOTES is expanding its applicability to more complex urogynecological and oncological cases. Moreover, the introduction of robotic vaginal natural orifice transluminal endoscopy represents a promising development. This approach combines the advantages of robotic surgery with the benefits of a vaginal approach, potentially improving patient outcomes and surgeons' enhanced precision during complex procedures (20).

References

1. Baskett TF. Hysterectomy: evolution and trends. *Best Practice Res Clin Obstet Gynaecol*. 2005;19(3):295–305.
2. Committee opinion 701: choosing the route of hysterectomy for benign disease. *Obstet Gynecol*. 2017;129: e155–e159.
3. www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD003677.pub6/full.
4. Baekelandt J. Total vaginal NOTES hysterectomy: a new approach to hysterectomy. *J Minim Invasive Gynecol*. 2015;22:1088–1094.
5. Su H et al. Hysterectomy via transvaginal natural orifice transluminal 378 endoscopic surgery (NOTES): feasibility of an innovative approach. *Taiwan J Obstet Gynecol*. 2012;51:217–221.
6. Hurni Y et al. Omentectomy for oncological surgical staging by transvaginal natural orifice transluminal endoscopic surgery (vNOTES): a preliminary study. *Front Surg*. 2023;10.
7. Zoorob D et al. Urogynecologic applications for the vaginal natural orifice transluminal endoscopic surgical approach. *J Gynecol Surg*. 2023;40(2).
8. Morgan DM et al. Nationwide trends in the utilization of and payments for hysterectomy in the United States among commercially insured women. *Am J Obstet Gynecol*. 2018;218:425.e1–425.e18.
9. Irvin W et al. Minimizing the risk of neurologic injury in gynecologic surgery. *Obstet Gynecol*. 2004;103(2):374–382.
10. Gupta A et al. Candy cane compared with boot stirrups in vaginal surgery. *Obstet Gynecol*. 2020;136(2):333–341.
11. Woodburn KL et al. Vaginal surgery: don't get bent out of shape. *Am J Obstet Gynecol*. 2020;223(5):762–763.
12. Umek WH et al. Quantitative analysis of uterosacral ligament origin and insertion points by magnetic resonance imaging. *Obstet Gynecol*. 2004;103(3):447–451.
13. Hanley GE et al. Opportunistic salpingectomy for ovarian cancer prevention. *Gynecol Oncol Res Pract*. 2015;2:5.

14. Dallenbach P et al. Risk factors for pelvic organ prolapse repair after hysterectomy. *Obstet Gynecol*. 2007:110:625.
15. Barber E et al. The effectiveness of McCall culdoplasty following vaginal hysterectomy in advanced stages of uterine prolapse. *Int Urogynecol J*. 2021;32(8):2143–2148.
16. Bushra M et al. Long-term experience with modified McCall culdoplasty in women undergoing vaginal hysterectomy for pelvic organ prolapse. *J Obstet Gynaecol Canada*. 2021;43(10):1129–1135.
17. Özel B. Vaginal hysterectomy: indications, avoiding complications. In: *Handbook of Gynecology*. Cham: Springer; 2023:833–847.
18. Baekelandt J et al. Hysterectomy by transvaginal natural orifice transluminal endoscopic surgery versus laparoscopy as a day-care procedure: a randomized controlled trial. *BJOG*. 2019;126:105.
19. Marchand G et al. Systematic review and meta analysis of vNOTES versus laparoscopic hysterectomy. *AJOG Global Reports*. 2024:100320.
20. Lowenstein L et al. Robotic vaginal natural orifice transluminal endoscopic hysterectomy for benign indications. *J Minim Invasive Gynecol*. 2021;28:1101.

8 ENERGY SYSTEMS IN LAPAROSCOPY*

Andrew I. Brill

Electricity is produced when valence electrons are freed from atoms of conductive materials. When these electrons are set in motion in the same direction an electric current (I) is produced that is measured in amperes. Opposite charges on the ends of the conductor cause the electrons to flow in one direction toward the positive terminal. The difference in potential between the positive and negative poles provides the electromotive force or voltage (V) to drive the current through the conductor (Figure 8.1).

Current that flows in one direction through a circuit is called direct current (DC). When alternating current (AC) flows through a circuit, the movement of electrons reverses direction at regular intervals, which is expressed as cycles per second (Hertz). Since the effects of current on the load are all that is important, the periodic reversal of current flow does not undo its work.

The amount of current that flows through a circuit is determined by the electromotive force (voltage) across the circuit and the resistance that circuit provides to the current. Resistance (R) is the difficulty that a material presents to the flow of electrons and is measured in ohms. Resistance of biologic tissues varies depending upon the water content. It is very high in desiccated tissue, moderate in lipid-rich adipose tissue, and very low in vascular tissue. Resistance for alternating current is expressed as impedance due to the induction of additional resistive phenomena (inductance) that include the effects of imploding electrostatic fields and the oppositional electromotive force of out-of-phase magnetic fields.

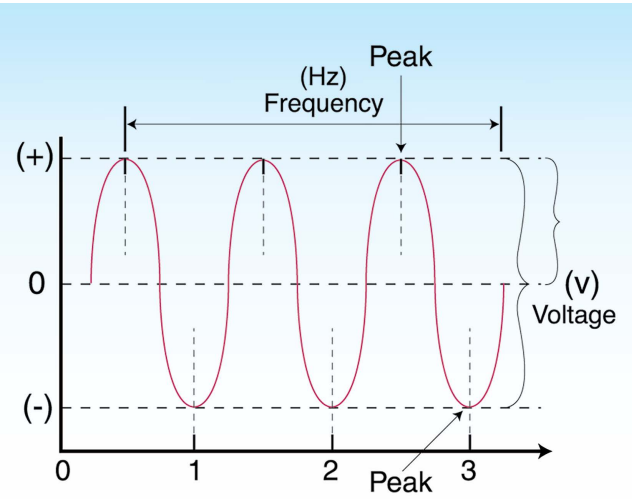


FIGURE 8.1 The difference in potential between the positive and negative poles provides the electromotive force (voltage) to drive the current through the conductor.

Current is directly proportional to the voltage and inversely proportional to the resistance, as expressed by Ohm's law:

$$I = V / R$$

Therefore, greater resistance requires greater voltage and, with a fixed resistance, greater voltage creates greater current. When the switch of an electrical circuit is left open (i.e., when the resistance is infinite) as when keying an electrosurgical electrode without tissue contact, it is logical that the energy source will work at maximum voltage. This means that an electrosurgical generator produces the highest voltage across the electrode when it is activated remotely from the tissue surface without current flow. In order to better understand the basic principles of the electrical current, the analogy of electric current to water flow is presented in Figure 8.2.

Power is the rate of doing work and is expressed in watts (W). It represents the total quantity of electrons moved and the pressure gradient against which the movement occurred, as expressed by the equation:

$$W = I \times V$$

Inserting Ohm's law:

$$W = I^2 \times R \text{ and } W = V^2 / R$$

Therefore, power to tissue increases as a function of both the square of the voltage and the square of the current.

The ratio of voltage to current is primarily responsible for the electrosurgical effects on tissue (Table 8.1).

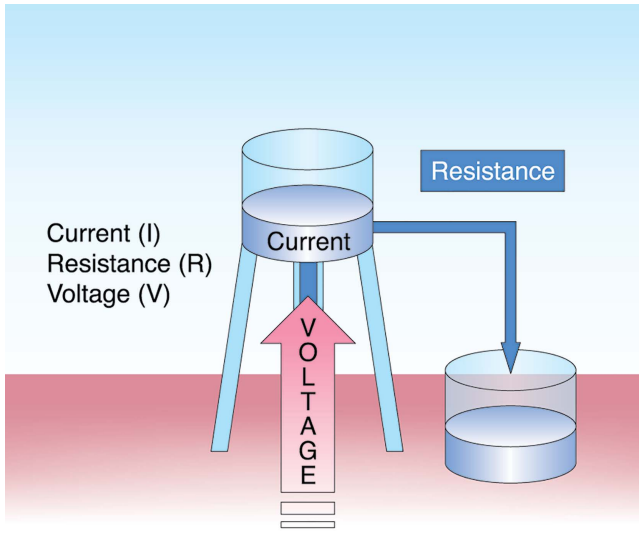


FIGURE 8.2 The analogy of electric current to water flow.

* This chapter is an updated version of Brill AI. Energy Systems in Laparoscopy, in Pasic RP et al., eds. *Practical Manual of Minimally Invasive Gynecologic and Robotic Surgery: A Clinical Cook Book*, 3rd Edn. CRC Press, 2018.

DOI: 10.1201/9781003312109-8

TABLE 8.1: The Effects of Increased Voltage

GREATER VOLTAGE
↓
GREATER FORCE
↓
GREATER RISK

Regarding electrosurgical tissue effects, other important factors are time (duration of current application) and power density. The power density represents the amount of energy applied per unit of surface and time and can be represented in the following way:

$$\text{Power density} = \frac{\text{Power output/Time}}{\text{Surface area}}$$

This equation demonstrates that if time is kept constant, power density only depends upon the wattage and surface area of the active electrode. Changes in power density can therefore be achieved by changing the power output or the contact area. Indeed, to maximize power density a higher energy output is paired with a small contact electrode (Figure 8.3).

8.1 Principles of Electrosurgery

8.1.1 Current

Using current that reverses its direction periodically, electrosurgery is exclusively performed with high-frequency alternating current. The frequency with which current changes direction is measured in cycles per second or Hertz (Hz). Since electrosurgery only relies on the effects of current on the load (tissue), this periodic reversal does not undo the tissue effects. Normal household current has a frequency of 60 Hz (cycles per second). Low-frequency alternating current causes tetanic neuromuscular activity by rapidly reversing depolarization of neuromuscular tissue (Faradic effects). These effects do not occur at frequencies greater than 100,000 cycles per second (Hz), where the net positional change of cellular ions is minimal. Justifiably, then, electrosurgery is typically performed using alternating currents ranging between 500,000 Hz and 3 million Hz (Figure 8.4).

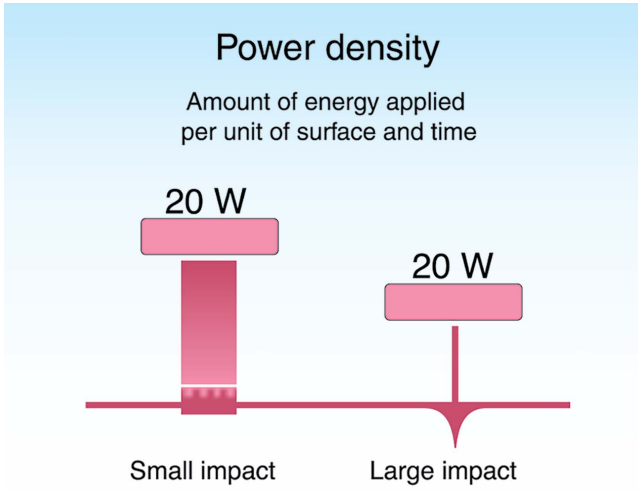


FIGURE 8.3 Power density.

8.2 Bipolar and Monopolar Instruments

In reality, all radiofrequency (RF) electrosurgery is "bipolar"; the difference is the location and purpose of the electrodes. Bipolar electrosurgical instruments utilize two terminals (electrodes), typically of equal size, that are extremely close by virtue of being situated across from one another at the end of the instrument. Rather than the patient being part of the electrical circuit, the current is conducted only through the tissue between the distal electrodes (Figure 8.5). When monopolar instruments are used, current is passed through the patient's body by applying two differently shaped electrodes at locations distant from one another. In this type of system, the surgical (often called "active")

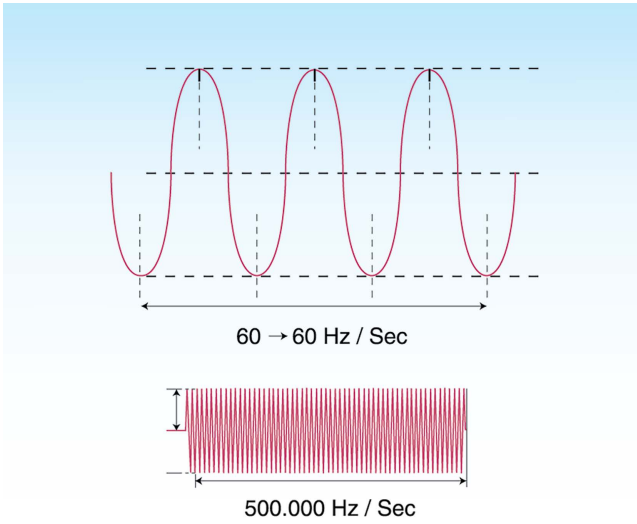


FIGURE 8.4 Electrosurgery alternating current ranges.

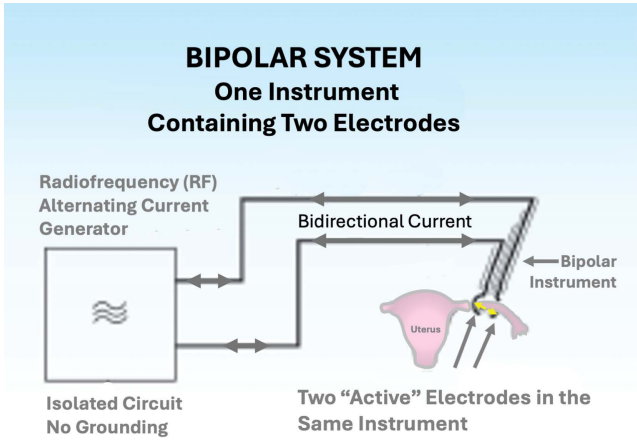


FIGURE 8.5 Bipolar system.

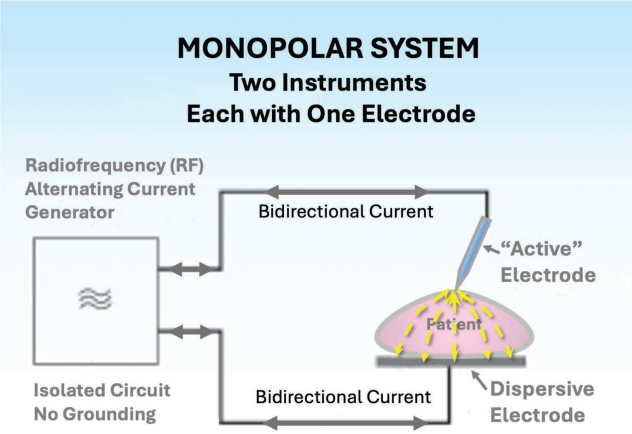


FIGURE 8.6 Monopolar system.

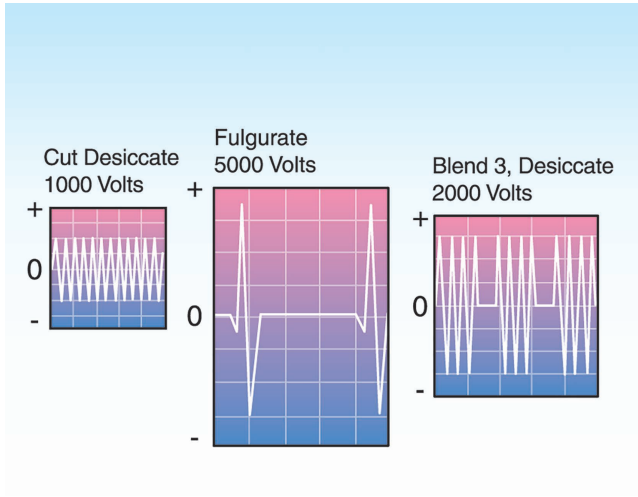


FIGURE 8.8 The conservation of energy across modes.

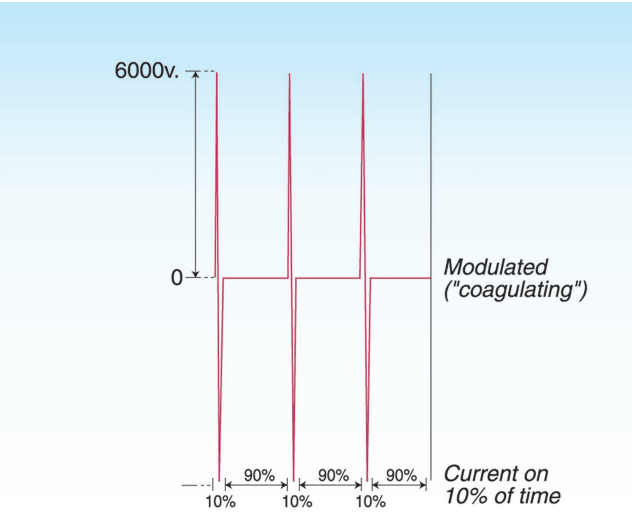


FIGURE 8.7 Modulation.

electrode has a much smaller area of contact with the underlying tissue than the second ("dispersive") electrode. Consequently, with generator activation, a tissue effect can occur adjacent to the active electrode due to the high power (or current) density. The large size of the second, dispersive electrode, essentially "defocuses" the energy, lowering the power density, so a tissue effect doesn't occur with generator activation (Figure 8.6).

8.3 Waveforms

Although most contemporary electrosurgical generators have front-panel controls labeled "cut," "blend," and "coag," these terms are not necessarily related to the actual tissue effects. The variety of choices simply reflects different degrees of waveform modulation (damping) that can be incrementally produced by the generator's solid-state circuitry. Modulation is the periodic interruption of current flow (Figure 8.7). The "cut" mode of the generator produces an unmodulated (undamped) pure sine wave with a relatively low peak voltage. The "coag" mode produces the most modulated waveform that correspondingly has the highest peak voltage. Therefore, for equal power settings, increasing waveform modulation (i.e., switching from "cut" to "blend" to "coag") causes the peak voltage to proportionally increase, i.e., energy must be conserved (Figure 8.8).

8.4 The Dispersive Electrode

The dispersive electrode or pad is used in conjunction with an active electrode, but for monopolar systems, is placed remote from the surgical site on the patient's skin. While it receives the same current and wattage of the active electrode, the area of the dispersive pad is such that the current is dissipated, so no thermal injury occurs. It is important to note that in the isolated circuits used in contemporary RF electrosurgery, the patient is NOT grounded, a feature that provides a significant measure of safety against current diversion issues. While some call this instrument a "return" or "neutral" electrode, this concept is faulty. First, with current generated with alternating polarity (alternating current), the direction of the current is constantly reversing (typically 300,000–500,000 times per second, or 300–500 KHz). Second, the same RF energy passing through the active electrode is the same as that passing through the dispersive electrode, so the notion of a neutral electrode is inaccurate.

Although the dispersive electrode pad is designed to provide a pathway with low impedance and low power density, preventing thermal injury to the skin, its misapplication can result in catastrophic thermal injury. The rules for proper usage aim to minimize impedance while maximizing the surface area for the current to disperse, preventing injury to the skin. Impedance is primarily reduced by selecting a site with sufficient water content for conduction. Areas of skin with hyperkeratosis or hair and those that overlie dense fat deposits (e.g., buttocks) should be avoided, while hair-free or shaved skin over larger muscles is preferred (e.g., upper thigh). Impedance is further reduced by choosing a site as close as possible to the active electrode (Figure 8.9). The surface area of the dispersive electrode must

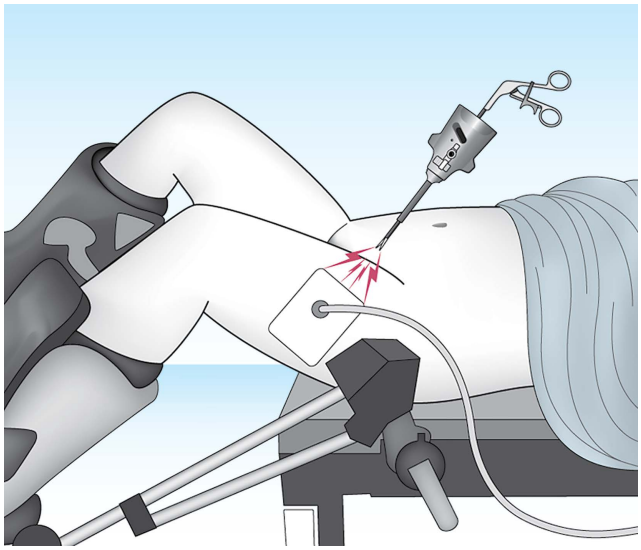


FIGURE 8.9 Depicted here, the current concentration (current or power density) created when the system is activated is high enough to cause a therapeutic tissue effect adjacent to the active electrode but is dissipated under the dispersive electrode, so no thermal effect is experienced. Impedance is reduced by choosing a site as close as possible to the active electrode.

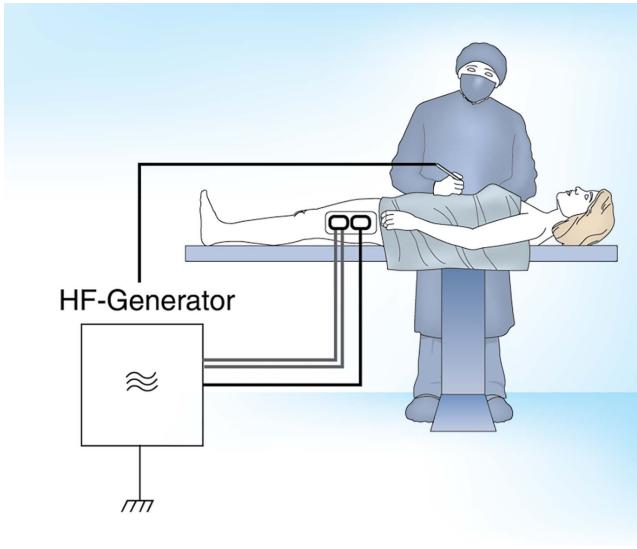


FIGURE 8.10 A dispersive electrode monitoring system monitors the pad's connection to the generator and the degree of contact with the patient.

be large enough to permit the current to be widely dispersed. Tissue heating is intimately related to current density that is inversely related to the square of the surface area, and the rise in tissue temperature is directly proportional to the square of the current. Therefore, small decrements in the surface area between the dispersive pad and the skin can result in dramatic thermal effects to the underlying tissues. A uniform, unalterable application ensures a large surface area. Areas with bony prominences are prone to movement on patient repositioning (such as the back and buttocks) and should be avoided. Since the edge of the dispersive electrode pad closest to the active electrode tends to concentrate the current, the longer edge of the pad should be placed toward the operative site.

Contemporary electrosurgical generators are equipped with an automatic alarm and shutdown mechanism that activates when the connection between the generator and the dispersive electrode is not intact. However, this does not monitor the adequacy of contact between the pad surface and the patient. Since the impedance to current flow through the dispersive electrode is relatively low until most of the pad has peeled away, any drop in electrosurgical effectiveness should alert the surgeon to check the dispersive electrode application.

Dispersive electrode monitoring systems (sometimes mislabeled as "return electrode monitoring systems" or REMs) that monitor both the dispersive pad's connection to the generator and the degree of contact with the patient are commercially available. Typically, the dispersive pad is split into two functional halves; a small current is generated to flow through the first half, through the contiguous skin and tissue, and then via the other half to the generator, which electronically monitors the local impedance. If the impedance threshold is exceeded due to separation from the skin, current generation from the generator is stopped, and an alarm is sounded (Figure 8.10). This innovation in dispersive pad technology completely eliminates the risk of thermal damage from a dispersive electrode that has peeled from the skin to a degree that the current density electrode.

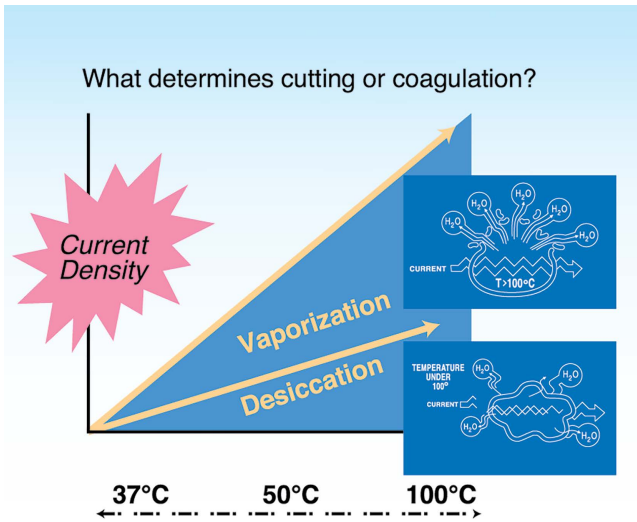


FIGURE 8.11 Factors determining cutting or coagulation.

8.5 Tissue Effects of Electrosurgery

Owing to the impedance, electrical energy when applied to the tissue is transferred to thermal energy, and the tissue effect of this thermal energy directly depends on the temperature inside of the tissue and the time required to reach that temperature (Figure 8.11). Electrosurgical energy produces three distinct effects on tissue: cutting, fulguration, and desiccation.

By varying the rate and extent of the thermodynamic effects of electric current in biological tissue, high-frequency electrosurgery is used to cut and/or coagulate. Although the efficiency of hemostasis is related to the depth of coagulation, it is of paramount importance that no more tissue suffers thermal damage than is absolutely needed. The art of electrosurgery is

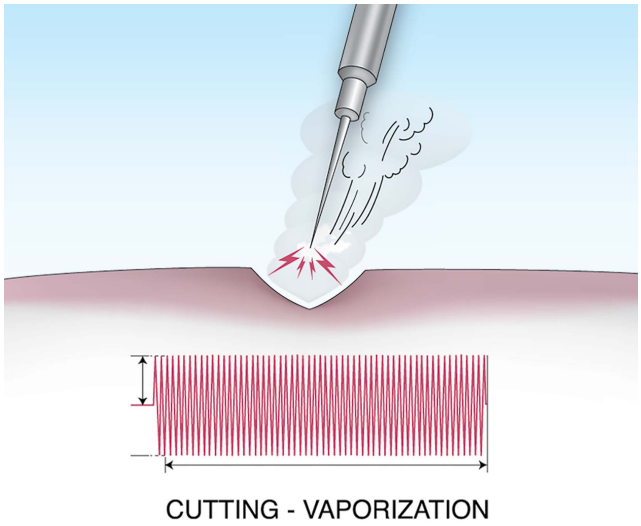


FIGURE 8.12 Formation of a plasma cloud.

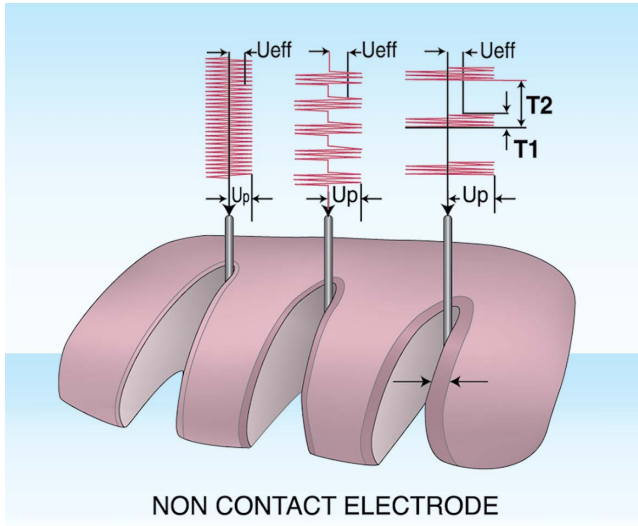


FIGURE 8.13 Non-contact electrode.

balancing between the need for absolute hemostasis and the least amount of deep coagulative necrosis.

8.5.1 Cutting (Electrosection)

The cutting of tissue occurs when there is sufficient voltage (at least 200 V) between the electrode and the tissue to produce an electric arc, which concentrates the current to specific points along the tissue surface. The open circuit creates an electric field that ionizes the intervening air. An avalanche of colliding and accelerating charged ions forms a plasma cloud that gives off light and sound as the ions pass to lower energy states to produce an electric arc (Figure 8.12). The extremely high current density delivered by the arc rapidly superheats the cellular water to temperatures greater than 600°C. Explosive cellular vaporization ensues secondary to the production of highly disruptive pressure (steam occupies six times the volume of liquid water!) and acoustic forces. Arcing is then enhanced by an envelope of steam vapor that becomes instantly ionized. The use of the unmodulated "cut" waveform helps sustain this envelope by producing an uninterrupted current that continuously maintains the same pathways for arc formation. However, since the "cut," "blend," and "coag" outputs all provide peak voltages greater than 200 V, any generator setting can be utilized to perform electrosection. In any case, tissue contact eliminates the steam envelope and abolishes the cutting arc.

In general, the depth of coagulation along the cut edges increases with increasing voltage and length or intensity of the electric arcs. Therefore, an unmodulated "cut" waveform produces a cut with the least amount of coagulative necrosis at the edges, whereas waveforms with greater modulation and higher peak voltages (i.e., higher "blend" and the "coag" settings) result in substantially larger zones of coagulation (Figure 8.13).

When using conventional electrosurgical generators, the smallest volume of coagulation during electrosection is assured by employing the thinnest possible electrodes (i.e., edge rather than surface), using the unmodulated "cut" waveform with low peak voltage, and cutting as rapidly as possible using a single pass of the electrode. Deeper coagulation occurs when opposite parameters are applied. A higher "blend" (i.e., blend 2 or 3) or the "coag" waveform may be selectively employed during the electrosection of highly vascular tissues (e.g., leiomyoma) to provide a significant measure of hemostasis along the cut margins.

A new breed of electrosurgical generators incorporates automatic control circuits to ensure that the intensity of the electric arcs and the output voltage are kept constant (constant voltage generator). This makes the depth of coagulation relatively independent of the cutting rate and depth, as well as the magnitude of the output current. Thus, the distance of coagulation remains constant regardless of the magnitude of the output current. With this type of equipment, the operator can move the electrode as quickly or slowly as desired and at any angle without significantly affecting the depth of coagulation.

8.5.2 Desiccation and Coagulation

Contact of tissue with the surface of an active electrode leads to conduction of current with a low current density (Figure 8.14). Resistive heating is produced by the high-frequency agitation of intracellular ionic polarities. As the tissue is slowly heated to temperatures above 50°C and maintained, irreversible cellular damage is initiated by deconfiguration of regulatory proteins followed by the denaturation of cellular proteins (white coagulation). Further heating to 100°C leads to complete evaporation of cellular water (desiccation), hemostasis secondary to the contraction of blood vessels and the surrounding tissues, and conversion of collagens to glucose that has an adhesive effect between the tissue and electrode. Temperatures above 200°C cause carbonization and charring. The prudent application of monopolar electrosurgery to tissue is continuously moderated by monitoring for the terminal evanescence of steam formation and tissue whitening; tissue charring, sticking, and smoke are indicative of overzealous coagulation (Figure 8.15).

Until the tissue reaches a temperature of 100°C and is completely desiccated, the rise in tissue temperature is directly proportional to the tissue resistance (degree of desiccation), time of current flow, and the square of the current density. Therefore, temperature change is more rapid at superficial depths and evolves more gradually with larger surface electrodes.

As the tissue is progressively desiccated, current flow is moderated by a zone of electrically insulated steam vapor that forms between the electrode and tissue. The flow of current will eventually cease based on the output voltage. At lower voltages

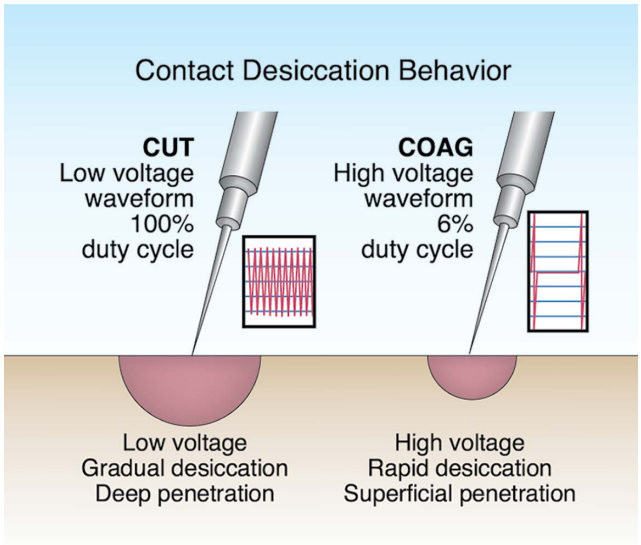


FIGURE 8.14 Contact desiccation behavior.

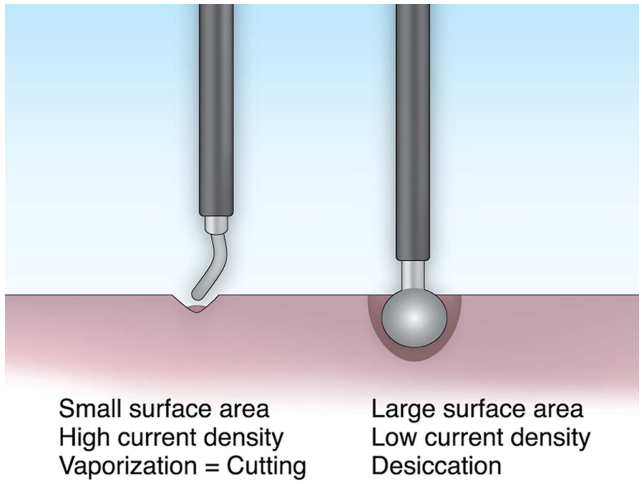


FIGURE 8.15 Vaporization and desiccation.

using the unmodulated "cut" waveform, the coagulative process continues until the tissue is entirely dried out (soft coagulation). Continued application of current after completion of the evaporative phase leads to tissue adherence. Therefore, soft coagulation should ideally be terminated at the time of vapor formation.

At higher voltages when using modulated waveforms (especially with smaller electrodes and higher current densities), the vapor layer and desiccated tissue are punctured by electric arcs (forced coagulation) causing further coagulation until the coagulum is so thick it cannot be penetrated. Tissue becomes carbonized, sticky, and precariously unstable. This results in deeper coagulation at the expense of greater force, intense arcing, and increased temperature generation (Figure 8.16).

During soft coagulation, the lower voltage of the "cut" waveform heats the tissue more slowly so heat can flow into deeper tissue layers. Hence, it can be said that soft coagulation is more effective coagulation. Since the reduction of abnormal uterine bleeding after endometrial ablation is related to the degree of destruction of the basalis layer and superficial myometrium, it can be formally argued that the unmodulated "cut" waveform should be used during hysteroscopic electrocoagulation of the endometrium.

In consideration of all the physical parameters that govern the behavior and effects of high-frequency alternating electric current in biological tissue, laparoscopic monopolar electrosurgery should ideally be performed using the unmodulated "cut" waveform for cutting and deep coagulation of tissue. Any electrode configured with both a flat surface and an edge (e.g., spatula electrode, electrosurgical scissors) can be used as an all-purpose electrosurgical tool with this waveform. The concentration of current at the edge or tip of the electrode provides arcing and hemostatic cutting of tissue. Blunt dissection, tissue traction, coaptation of small blood vessels, and contact coagulation can all be effectively accomplished using the flat surface (see Figure 8.15).

8.5.3 Fulguration

Electric arcs generated by modulated waveforms with higher peak voltages (fulguration) can superficially coagulate a broad

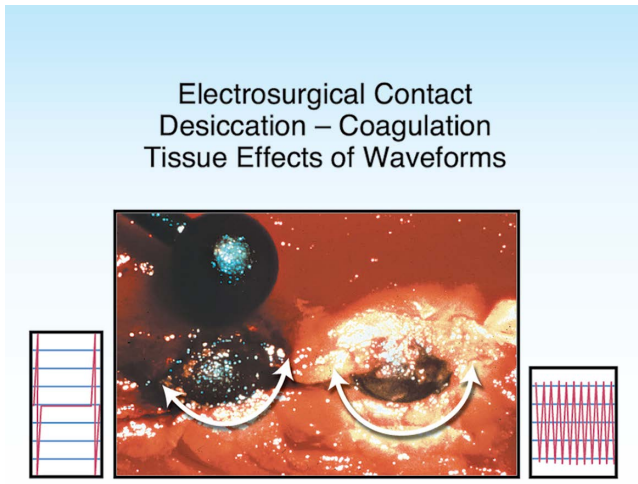


FIGURE 8.16 Higher voltages using modulated waveform.

surface of tissue with open vessels as large as 2 mm. Current modulation allows the steam envelope to dissipate between the interruption of sparks, causing the electric arcs to strike the tissue surface in a widely dispersed and random fashion, thereby preventing tissue cutting. Although the higher voltage sparks are larger and create broad areas of charring (to > 500°C) and tissue destruction, current flow is limited to the superficial tissue layers due to rapid desiccation and the buildup of tissue resistance. Fulguration is relatively useless in the presence of a wet surgical field due to the diffusion of current by saline rich blood.

Teleologically, then, the only selective indication for using the highly modulated "coag" waveform during monopolar electrosurgery is for the superficial coagulation of tissue along a large surface area (Figure 8.17). Exemplary needs for fulguration during laparoscopic surgery include the myometrial bed after myomectomy, the base of the ovarian cortex after cystectomy, and for oozing veins. Since thermal effects are kept quite superficial

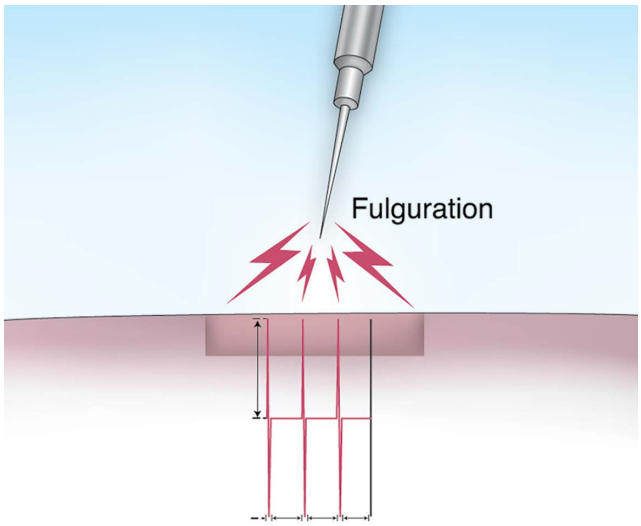


FIGURE 8.17 Fulguration.

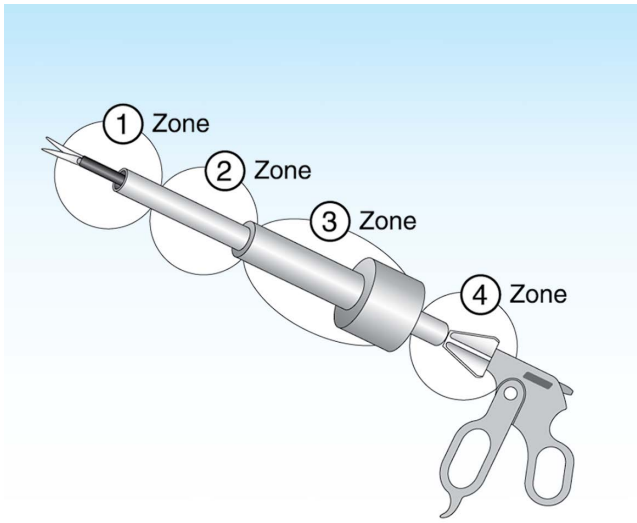


FIGURE 8.18 Zones of potential conduction.

by the rapid surface desiccation, fulgurative current may be the best choice to superficially electrocoagulate areas of endometriosis over vital structures such as the bladder and ureter.

The argon beam coagulator (ABC) is a true fulgurating electrosurgical device that utilizes the flow of argon gas through an electrode device to form a comparatively longer bridge of electric arcs to the tissue. This gas is easier to ionize than air, allowing the electric arcs to create a more uniform surface coagulation effect. The high flow of gas (4 L/min) displaces oxygen and nitrogen as well as pooled blood, which focuses the effective surface area and reduces the formation of smoke, carbonization, and tissue buildup on the tip of the electrode.

8.6 Problems with Monopolar Systems during Laparoscopic Surgery

Contrary to the open surgical environment during laparotomy, the bulk of most instruments and nearly all surrounding intra-abdominal structures are not visualized during any laparoscopic procedure. Furthermore, nearly all of the potential conductors during laparoscopic electrosurgery are also out of the surgeon's field of view. Intended and unintended couriers of direct or induced currents include the abdominal wall, metallic trocar sheaths and instruments, the operating laparoscope, contiguous visceral tissues, and the active electrode (which is the only part of the circuit under view!) (Figure 8.18). It comes as no surprise that most accidental electrosurgical burns during laparoscopic surgery are undetected at the time of injury.

8.6.1 Insulation Failure

Insulation failure occurs secondary to breaks or holes in the insulation caused by physical abruption during use (such as during passage through an incompletely engaged trumpet cannula) or during normal reprocessing procedures. Completely intact insulation (especially on disposable instrumentation) can be breached by very high voltage (e.g., during open circuit activation or using a modulated "coag" waveform). Any break or breach in insulation may provide an alternate pathway for the flow of current. If the defective portion of insulation contacts tissue during electrode activation, an electric arc will bridge directly from the electrode through the defect to this tissue (Figure 8.19). Thermal damage will occur if the current density is high enough to significantly heat the tissue. Since these defects are usually out of the field of view, this type of injury usually occurs undetected at the time of insult.

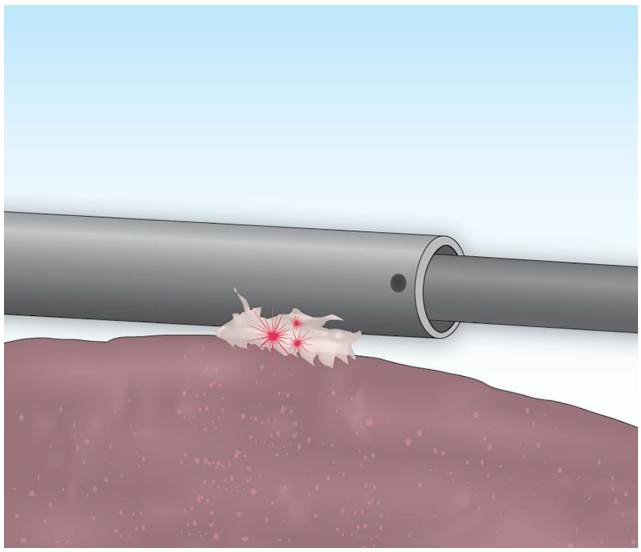


FIGURE 8.19 Defective portion of insulation contacting tissue during electrode activation.

Insulation failure can be minimized by periodically inspecting the insulation covering of all laparoscopic electrodes (especially at the shoulder) for small cracks and defects. Disposable monopolar electrodes should not be reused. The risk of high voltage can be eliminated by using the unmodulated "cut" waveform and avoiding open circuit activation.

8.6.2 Direct Coupling

Direct coupling of current occurs when an activated electrode makes unintended contact with another metal object in the area of the surgical field. Accidental electrode contact with a suction-irrigator probe, the operating laparoscope, or a metal cannula creates an alternate pathway that is normally

conducted up through a metal trocar to the abdominal wall and back to the dispersive electrode. However, if any of these devices are isolated from direct contact with the abdominal wall by an insulator (e.g., plastic cannula or self-retaining device) the current may take an alternate pathway through a point of contact with adjacent tissue (Figure 8.20). Again, if the current density is high, thermal damage may occur.

Direct coupling can be avoided by never activating the generator when the electrode is touching or in near proximity to another metal object in the surgical field.

8.6.3 Capacitive Coupling

Capacitance is the property of an electrical circuit to store energy. Any device that creates capacitance is called a capacitor. A capacitor exists whenever two conductors that have different potentials are separated by an insulator. A difference of potential or voltage will exist between two conductors that have differing numbers of free electrons (an overall negative charge on the conductor with excess, and a positive charge on the electron-deficient conductor). Although separation by an insulator prevents the flow of electrons between these conductors, the potential difference nevertheless creates an attraction or electrostatic force between them. This force results in an electric field and creates a reservoir of stored energy. When an alternating current flows through a circuit, the applied voltage and flow of current periodically changes direction. This means that a capacitor with alternating current is continuously "charged" in alternating directions. With each reversal of current flow, the energy of the stored electric field is discharged. Although no actual current flows through the capacitor, the charged current from capacitance completes the circuit and in essence conducts the alternating current. Since the amount of capacitance is directly proportional to the voltage, capacitance is greatest during open circuit activation and with highly modulated current such as the "coag" waveform.

Capacitive coupling is the induction of stray current to a surrounding conductor through the intact insulation of an active electrode. In fact, all of the necessary ingredients for the localized genesis of capacitance are provided by an activated monopolar electrode that is passed through a conductive sheath.

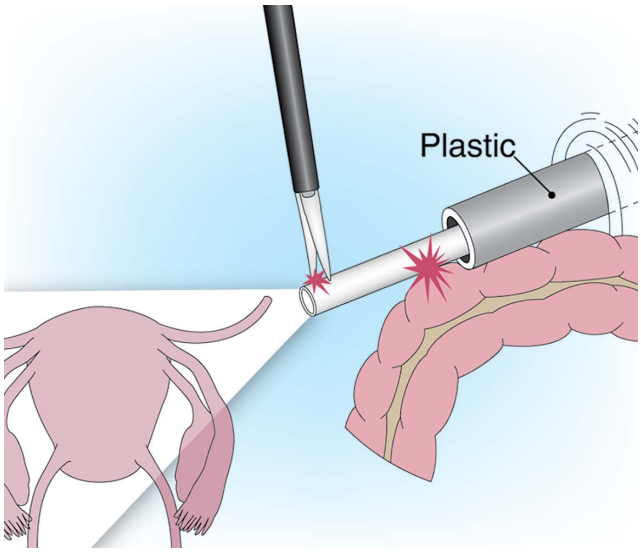


FIGURE 8.20 Current taking an alternate pathway through a point of contact with adjacent tissue.

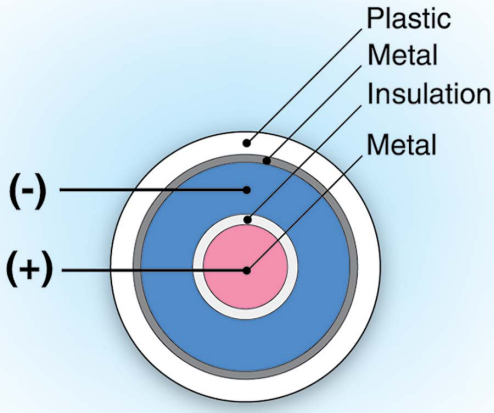


FIGURE 8.21 Conductors.

Two conductors of differing potentials, the active electrode and the metal sheath (e.g., trocar sheath, working channel of an operating laparoscope, irrigator-aspirator probe) are separated by the insulation of the electrode (Figure 8.21). On activation, up to 80% of the generator current is induced on the metal sheath by capacitance. Normally this stray current is safely transferred to the dispersive electrode by conduction through the large area of contact between the metal trocar sheath and the abdominal wall. The magnitude of capacitance is greater with higher voltage, smaller cannulas, and longer electrodes. Furthermore, the induced current will persist until the electrode is deactivated or it is conducted via an alternate pathway.

If a metal trocar sheath is attached to the abdominal wall by a nonconductive plastic device (e.g., hybrid trocar [metal/plastic] or plastic self-retaining screw device), the induced current becomes electrically isolated from the abdominal wall. Contact between the cannula and a visceral structure provides an alternate pathway for the stray current to discharge (Figures 8.22 and 8.23). Significant thermal damage will occur if the current density is sufficiently concentrated by a small area of contact. A similar phenomenon of capacitive coupling and current isolation may occur during activation of an electrode placed through the working port of an operating laparoscope, which is isolated from the abdominal wall by an all-plastic cannula. In either case, the thermal injury is usually out of the surgeon's field of view.

Capacitance is minimized by using an unmodulated "cut" waveform and avoiding open circuit activation (i.e., minimizing voltage). An all-metal system will suffice for the safe conduction of capacitively coupled current back to the dispersive electrode. Hybrid cannula systems (mixtures of plastic and metal) should not be used to house monopolar electrosurgical devices.

8.7 Electrosurgery with Bipolar Instruments

During electrosurgery with monopolar instruments, a high density of electrons is created at the active electrode and is ultimately dispersed by the broad surface of the dispersive electrode. The pathways between these electrodes and the generator vary in a myriad of conductive pathways.

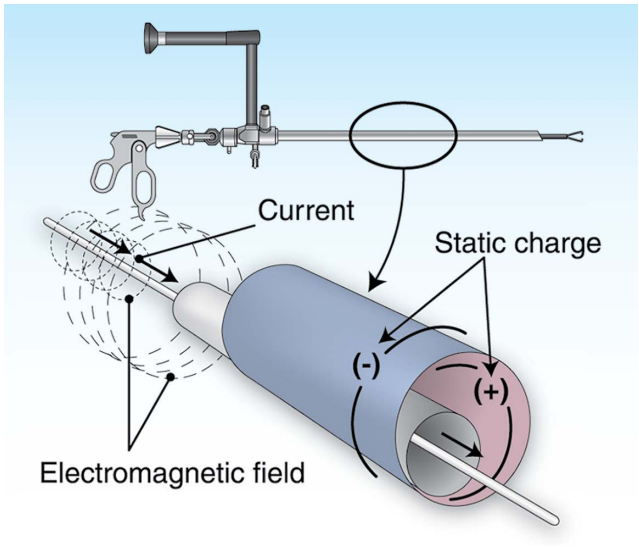


FIGURE 8.22 Capacitance.

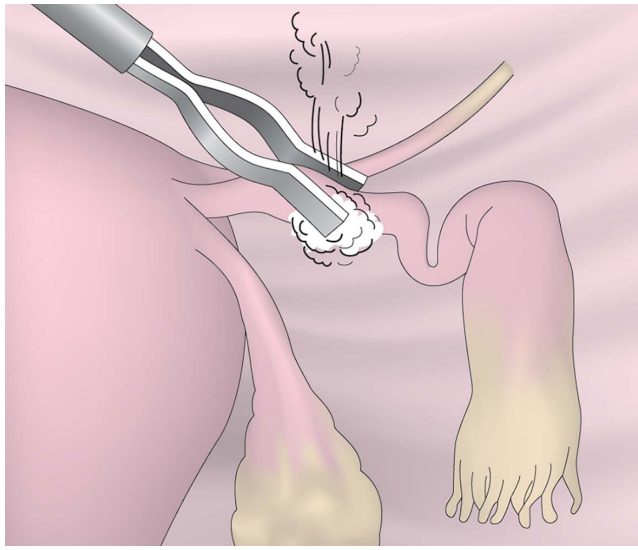


FIGURE 8.24 Unmodulated "cut" waveform.

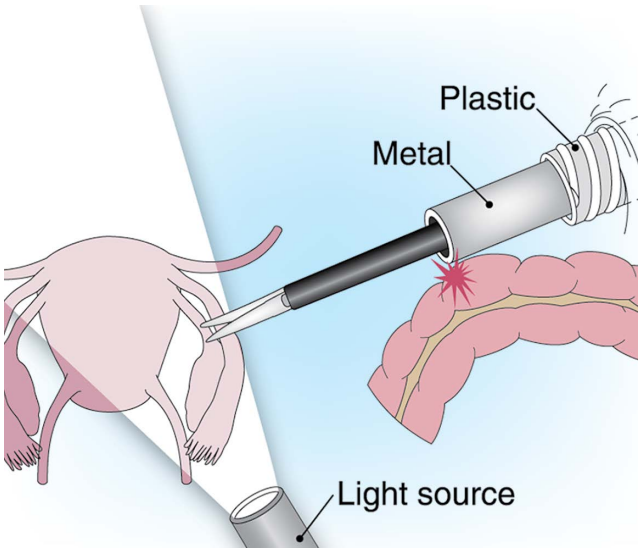


FIGURE 8.23 Contact providing an alternate pathway for discharge.

Bipolar instruments are created with two electrodes, and while most such instruments (e.g., bipolar forceps or scissors) both electrodes are "active," in some instances, one is dispersive or at least not designed to create a tissue effect (Figure 8.24). Rather than coursing through the patient, the flow of alternating current is symmetrically distributed through the tissue between the poles, reversing direction every one-half cycle. This eliminates the risk of capacitive coupling and alternate current pathways. Power requirements are significantly less than with monopolar instruments due to the current concentration between the poles. Therefore, an unmodulated "cut" waveform with low peak-to-peak voltage is the generator output during bipolar electrosurgery (Figure 8.24). These factors typically limit thermal effects to desiccation and tissue coagulation. Laparoscopic scissors and shears depicted as bipolar cutting devices are usually mechanical cutting devices that simultaneously desiccate at the edge of the cutting electrodes. Using advanced solid-state technology, true bipolar electrosurgical cutting can be accomplished by means of bipolar cutting electrodes paired to a dedicated low-voltage electrosurgical generator. The 5 mm PK Cutting Electrode (Olympus) consists of a retractable active needle electrode paired with a dispersive electrode collar near the distal tip. A tissue-cutting effect is generated when both electrodes are in contact with the tissue and are drawn across the tissue surface during activation. Olympus later introduced a Plasmaspatula™ 5 mm cutting-coagulation spatula electrode consisting of multiple conductive surfaces covering the distal electrode that can be manipulated and keyed to either cut or coagulate tissue. Since the PK electrosurgical generator produces a low-voltage output, the high impedance posed by very desiccated or fatty tissues may preclude vaporization with either of these novel bipolar electrodes.

Bipolar electrosurgical forceps can be used for laparoscopic tubal sterilization by sequentially grasping and desiccating the midportion of the fallopian tube and adjacent mesosalpinx with the Kleppinger or similar forceps. Failure of this method usually results from incomplete destruction of the tubal lumen with persistent viability of the endosalpinx. Complete desiccation is best ensured by including the vascular portion of the tube in the forceps, coagulating at least 3 cm of contiguous areas along the ampullary portion of the tube, using relatively low power (25 W) and an inline ammeter to ensure that the tissue is completely desiccated (Figure 8.25).

The localization of current between the poles of the instrument during bipolar electrosurgery offers several distinct advantages. Thermal damage is generally limited to a discrete volume of tissue. The bipolar forceps can be used to coapt and thermally weld blood vessels. The concentrated current and small distance between the poles makes it possible to desiccate tissue that is immersed in fluid. The apparent disadvantages of this modality arise when open blood vessels are retracted or tissue pedicles are very thick.

Although the flow of current and primary thermal effects are restricted to the tissue between the poles, this does not remove the risk of thermal effects to tissue that is distant from the operative site. In fact, the net thermal effects are also governed by the physical parameters described during monopolar

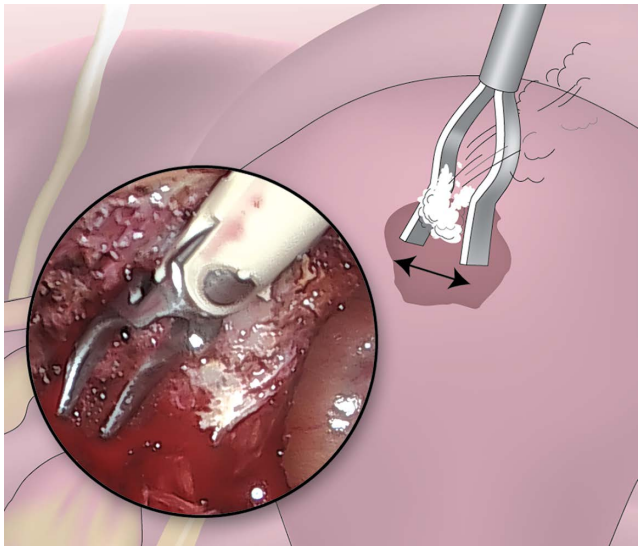


FIGURE 8.25 Complete desiccation.

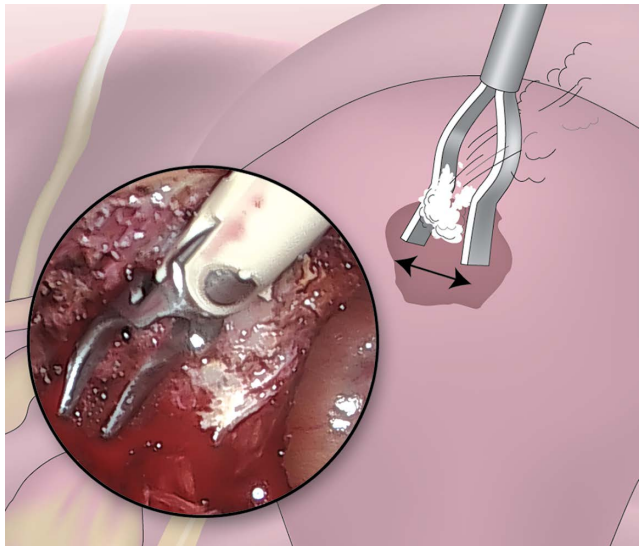


FIGURE 8.26 Lightly "painting" the tissue surface for directed hemostasis.

electrosurgery. The application of bipolar current leads to the gradual desiccation of the intervening tissue. The rate of tissue coagulation at any given power is moderated by the applied surface area of the poles, the thickness of the pedicle, the formation of a vapor layer between the poles and tissue, and the evanescing degree of tissue hydration. Impedance is maximal when the vapor phase is abolished as the tissue is completely desiccated. If the current is further applied and maintained more than several seconds, a secondary thermal bloom occurs to surrounding tissues from a correspondingly rapid rise in tissue temperature. Thus, tissues at some distance from the operative site may undergo subtle but irreversible thermal damage (e.g., the pelvic ureter during overzealous bipolar desiccation of the uterine artery).

During laparoscopic surgery, other than tubal sterilization, the spread of thermal damage during bipolar desiccation should be minimized by terminating the flow of current at the end of the vapor phase, cooling the surrounding tissues with irrigating solution, applying current in a pulsatile rather than continuous fashion, avoiding the use of an inline ammeter to determine the endpoint of desiccation, and securing vascular pedicles by using a stepwise process that alternates between partial desiccation and incremental cutting. The smallest depth of coagulative necrosis will occur when the sides or tips of a slightly open forceps are used to lightly "paint" the tissue surface for directed hemostasis (Figure 8.26).

8.7.1 Taking the Judgment out of Bipolar Electrodesiccation

Rather than using the judgment of the surgeon to assess the thermal endpoint during bipolar desiccation, newer bipolar devices can now think for you. The latest advance in bipolar electrosurgery is the introduction of three novel ligating-cutting devices that minimize electromagnetic force by delivering electrical energy as high current and low voltage output. Once tonal feedback from a dedicated generator confirms complete desiccation of the tissue bundle, the pedicle is cut by advancing a centrally set mechanical blade. By directly responding to incremental increases in tissue resistance during coaptive desiccation, total energy delivery with these devices is dramatically less than conventional bipolar systems (300 V versus 1200 V!). Comparatively, then, carbonization, tissue sticking, smoke, incomplete desiccation, and lateral thermal damage are all significantly reduced with these new devices. All produce sufficient energy and vascular coaptation to reliably seal both ovarian and uterine arteries.

Relying on the breakthrough that vessel wall fusion can be achieved using electrical energy to denature collagen and elastin in vessel walls to reform into a permanent seal, the 5 mm and 10 mm LigaSure™ Laparoscopic Vessel Sealing Device (Covidien) applies a high coaptive pressure to the coapted tissue bundle during the generation of tissue temperatures under 100°C; hydrogen cross-links are first ruptured and then denature resulting in a vascular seal that has high tensile strength.

A second device, the 5 mm and 10 mm PK Cutting Forceps (Olympus Medical Systems Corporation) utilizes advanced solid-state generator software to deliver pulsed energy with continuous feedback control. The cycle stops once it senses that tissue response is complete; the cool-down phase ensures collagen and elastin matrix reforms without tissue fragmentation. Electrical energy delivery in this fashion results in more uniform tissue heating and in less average and total energy delivery when compared to conventional bipolar systems.

A third device, the 5 mm EnSeal™ Laparoscopic Vessel Fusion System (Ethicon, Endosurgery, Inc., Cincinnati, Ohio) is an innovative bipolar instrument that for all practical purposes displaces the command of the electrosurgical generator into the distal jaw materials of the instrument. This "smart electrode" contains a set of plastic jaws embedded with nanometer-sized spheres of nickel that conduct a locally regulated current. Tissue temperatures never exceed 120°C due to the progressive generation of resistance in the plastic jaws. With this device, desiccation is facilitated by simultaneously advancing a mechanical blade that both cuts and squeezes the tissue bundle to eliminate tissue water. Reducing tissue water during heating at the coaptive interface further addresses lateral thermal spread by reducing the production of percussive steam during tissue desiccation and vaporization. This device now articulates up to 110 degrees, facilitating a perpendicular

approach to vascular pedicles and greater access to tissue in deep and tight spaces.

8.8 Harmonic Scalpel and Hybrid Devices

The harmonic scalpel is an ultrasonically activated laparoscopic device that provides mechanical energy to cut and coagulate tissue. A piezoelectric crystal housed in the handpiece vibrates the tip of a titanium blade at 55,500 times/second over a variable excursion of 50–100 μm. Energy is transmitted through tissue primarily in a linear fashion, parallel to lines of force. Hydrogen bonds that maintain the configuration of tissue proteins are ruptured, gradually leading to a denatured protein coagulum up to 2 mm without significant desiccation or charring. Mechanical vibration and cavitational fragmentation of tissue parenchyma produce tissue cutting. Steam bubbles that form as the vaporization threshold is reduced by local changes in atmospheric pressure concurrently separate tissue planes in front of the tip. Available 5 mm blades include a hook and curved electrodes for cutting and coagulating. The LCS-B5 is a 5 mm harmonic scalpel shear with a straight cylindrical active blade. Its shape is continuous circumferentially. The ACE™ (Ethicon, Endosurgery, Inc., Cincinnati, OH) is a 5 mm harmonic scalpel shear with a curved active blade. The curved blade has an increased amplitude compared to the straight blade, giving it an increased longitudinal motion, leading to increased cutting speed. The new ACE™ harmonic scalpel provides better hemostasis and cutting.

A 10 mm laparoscopic coagulating shears (LCS) provides coaptive coagulation and cutting by securing tissue between a grooved plastic pad and a 15 mm multipurpose rotational blade with sharp, blunt, and flat surfaces. By employing various combinations of blade configurations, blade excursion, and tissue tension, specific tissue effects are created with this device. Operationally, cutting should be considered the obverse of coagulation. Cutting velocity is proportional to blade excursion, tissue traction, and blade sharpness and inversely related to density and elasticity of tissue. Coagulation is inversely related to tissue tension, blade sharpness, blade excursion, and cutting speed. Thus, the fastest cutting occurs when tissue is placed on tension and firmly squeezed, lifted, or rotated with the sharp side of the blade set at maximum excursion. Effective coagulation is best accomplished by relaxing tissue tension, minimizing blade excursion, and using a blunt edge or flattened surface. Although a zone of coagulation of less than 1 mm is typically created by coaptive incision with the LCS, it remains proportional to blade excursion, application time, and applied pressure.

Several companies have now introduced new laparoscopic instrumentation that similarly employ ultrasonic energy to cut and coagulate tissue. The biophysical principles dictating the interaction between living tissue and ultrasound described earlier are the same for these devices. However, these devices lack impedance feedback to moderate ultrasound transmission and are only approved for sealing vessels up to 5 mm in diameter. Manufactured as a cordless ultrasonic device driven by a battery pack, Sonocision (Medtronic, Minneapolis, Minnesota) has the added benefit of eliminating an associated power cord. A hybrid device, Thunderbeat™ (Olympus Surgical America), has been introduced to the surgical armamentarium, the first surgical device to combine advanced bipolar electrosurgery and ultrasonic energy into a single multifunctional hand instrument, allowing surgeons to simultaneously seal and cut vessels up to and including 7 mm in size.

Bibliography

Amaral JF et al. Depth of thermal injury: ultrasonically activated scalpel vs electrosurgery. *Surg Endosc*. 1995;9(2):226.

Corson SL et al. Laparoscopic laser treatment of endometriosis with the Nd: YAG sapphire probe. *Am J Obstet Gynecol*. 1989;160:718–723.

D'Arsonval MA. Action physiologique des courants alternaifs. *Soc Biol*. 1891;43:283–286.

Erbe Elcktromedzin. *Operating Instructions Manual. Erbotom ACC 450*. Tubingen, Germany; 1990.

Ewing J. *A Treatise on Tumors*, 2nd edn. Philadelphia: WB Saunders; 1922:17.

Friedman J. The technical aspects of electrosurgery. *Oral Surg*. 1973;36:177–187.

Hambley R et al. Wound healing of skin incisions produced by ultrasonically vibrating knife, scalpel, electrosurgery, and carbon dioxide laser. *J Dermatol Surg Oncol*. 1988;14:1213–1217.

Honig WM. The mechanism of cutting in electrosurgery. *IEEE Trans Biomed Eng BME*. 1975;22:58–62.

Kelly HA et al. *Electrosurgery*. Philadelphia: WB Saunders; 1932.

Luciano A et al. Essential principles of electrosurgery in operative laparoscopy. *J Am Assoc Gynecol Laparosc*. 1994;1:189–195.

Luciano M et al. A comparison of thermal injury, healing patterns, and postoperative adhesion formation following CO2 laser and electromicrosurgery. *Fertil Steril*. 1987;48:1025–1029.

McCarus SD. Physiologic mechanism of the ultrasonically activated scalpel. *J Am Assoc Gynecol Laparosc*. 1996;3:601–608.

Nduka C et al. Cause and prevention of electrosurgical injuries in laparoscopy. *J Am Coll Surg*. 1994;179:161–170.

Nezhat C et al. Surgical treatment of endometriosis via laser laparoscopy. *Fertil Steril*. 1986;45:778–783.

Phipps JH. Thermometry studies with bipolar diathermy during hysterectomy. *Gynaecol Laparosc*. 1994;3:5–7.

Reich J et al. CO2 laser used through the operating channel of laser laparoscopes: in vitro study of power and power density losses. *Obstet Gynecol*. 1991;77:40–47.

Ryder RM et al. Bladder and bowel injury after electrodesiccation with Kleppinger bipolar forceps: a clinicopathologic study. *J Reprod Med*. 1993;3:595–598.

Semm K. Endocoagulation: a new field of endoscopic surgery. *J Reprod Med*. 1976;16:195–203.

Sigel B et al. The mechanism of bleed vessel closure by high frequency electrocoagulation. *Surg Gynecol Obstet*. 1965;121:823–831.

Tucker RD et al. The effect of bipolar electrosurgical coagulation waveform on a rat uterine model of fallopian tube sterilization. *J Gynecol Surg*. 1992;8:235–241.

Tulandi T et al. Histopathological and adhesion formation after incision using ultrasonic vibrating scalpel and regular scalpel in the rat. *Fertil Steril*. 1994;61:548–560.

Vaincaillie TG. Electrosurgery at laparoscopy: guidelines to avoid complication. *Gynaecol Endosc*. 1994;3:143–150.

Wattiez A et al. Electrosurgery. *In: Operative Endoscopy*. Oxford: Blackwell Science; 1995:81–92.

9 IMAGING AND IMAGING-GUIDED INTERVENTIONS IN MINIMALLY INVASIVE GYNECOLOGIC SURGERY

Scott W. Young

9.1 Introduction

Diagnostic imaging is an indispensable tool in minimally invasive gynecologic surgery. Preoperative imaging is of particular importance for selecting the appropriate operative techniques, evaluating the extent of disease, predicting operative times, and identifying potential complications. Imaging plays an integral role in informed patient consent. Imaging may provide intraoperative identification of disease that may be laparoscopically occult (1) and postoperative evaluation of surgical success and potential complications. Imaging guided procedures are also critical in the minimally invasive diagnosis and management of gynecologic conditions. This chapter will explain the variety of imaging modalities and their acquisition, utility, and reporting in the context of minimally invasive gynecologic surgery.

9.2 Ultrasound

Ultrasound is the primary imaging modality used in gynecologic imaging, routinely characterizing disorders of the adnexa, uterus, and urinary bladder. Expert use broadens its application to include assessment of many other structures including the urethra, ureters, bowel, pelvic ligaments, pelvic floor muscles, and vagina. Grayscale ultrasound imaging, often referred to as B-mode imaging, is the most basic and commonly used form of ultrasound. It produces two-dimensional images of internal structures by sending high-frequency sound waves into the body and then recording the echoes of these sound waves as they reflect off internal tissues.

The ultrasound probe contains piezoelectric crystals which, when an electric current is applied, vibrate and produce high-frequency sound waves that are transmitted into the body. As these sound waves travel through different tissues, a portion is reflected back to the probe at different strengths depending on the acoustic properties of the tissue. These returning echoes are detected by the same piezoelectric crystals that send the sound waves. The piezoelectric crystals convert the returning echoes into electrical signals. The time it takes for the echoes to return helps to determine the depth of the structure, while the strength of the echo can give information about the characteristics of the tissue. The ultrasound machine processes these electrical signals and constructs an image based on the amplitude and time delay of the returning echoes. Structures that reflect more sound waves back to the probe appear as lighter (hyperechoic) areas on the image, while structures that do not reflect sound waves as well appear darker (hypoechoic) or black (anechoic). The image is displayed in real time in grayscale. Fluid-filled structures (like blood vessels and cysts) typically appear black because they do not reflect many sound waves, whereas denser structures like bones and very low-density substances such as gas appear white due to the high reflection of the sound waves.

Ultrasound video clips are valuable tools in the evaluation and management of many gynecologic conditions. In pelvic floor dysfunction, they provide dynamic visualization of the pelvic floor muscles, allowing for the assessment of muscle function, anatomy, and coordination (2, 3). The recording and review of video clips is particularly useful for understanding the relationship between pelvic structures. For example, a twisting of the ovarian vasculature, the whirlpool sign, is often best appreciated on video images (4). Dynamic ultrasound also plays a key role in evaluating the ovarian and uterine mobility in the setting of deep endometriosis (5). Transducer and/or manual displacement of these structures has excellent predictive value for posterior cul-de-sac obliteration and periovarian adhesions. Transducer pressure is also useful when distinguishing ovarian from tubal and other adnexal observations. The ability to displace a structure away from the ovary is helpful in diagnosing tubal ectopic pregnancy and other tubal pathologies.

Color Doppler ultrasound is an imaging technique that is used to visualize blood flow within vessels and other structures. It combines the traditional grayscale (B-mode) ultrasound with information on blood flow by utilizing the Doppler effect, which is the change in frequency of a wave in relation to an observer moving relative to the source of the wave. Similar to grayscale ultrasound, the ultrasound probe sends high-frequency sound waves into the body. As these sound waves hit moving blood cells, they are reflected back with a change in frequency proportional to the speed and direction of blood flow. This change in frequency is known as the Doppler shift. The ultrasound machine processes the Doppler shift and calculates both the velocity and direction of blood flow.

The velocity and direction of blood flow are encoded in colors, usually with one color (such as red) representing flow towards the transducer, and another color (such as blue) representing flow away from the transducer. The colors are then superimposed on the grayscale image to provide both anatomical and flow information. Different shades or intensities of the colors represent different speeds of blood flow (6). Color Doppler is useful in the assessment of blood flow in the differentiation of leiomyoma from adenomyoma. Leiomyomas show circular displacement of surrounding blood flow, whereas adenomyoma is characterized by translesional vascularity. The subjective intensity of color flow plays a role in the prediction of malignancy in the International Ovarian Tumor Analysis (IOTA) group and Ovarian-Adnexal Reporting & Data System (O-RADS™) adnexal mass classification schemes (7). Color Doppler should be used with caution in the diagnosis of ovarian torsion. In part due to the ovary's dual blood supply, both arterial and venous flow may remain intact despite torsion of the vascular pedicle. The diagnosis should rely on ovarian enlargement with stromal edema and other grayscale morphologic features such as peripherally displaced follicles and ovarian malposition or presence of a whirlpool sign (8).

Spectral Doppler quantitatively evaluates blood flow velocities. It displays the flow velocities over time and is especially useful for evaluating blood flow through specific vessels and for detecting velocity and directional abnormalities such as stenosis and reflux. It also characterizes blood flow throughout the cardiac cycle, evaluating the systolic upstroke, vessel elasticity,

DOI: 10.1201/9781003312109-9

and relative amount of diastolic flow which can inform tissue resistance or venous outflow obstruction.

3D ultrasound is an advanced ultrasound technique that generates three-dimensional images of anatomy. Most current 3D ultrasound systems use specialized probes that automatically acquire 2D planes in a volume over a certain angle or region. This is known as volume acquisition. This dataset is processed by the ultrasound machine, which reconstructs the slices into a single three-dimensional volume. After the 3D volume is reconstructed, volume rendering techniques are used to visualize this data in a meaningful way. These techniques can include the adjustment of slice thickness, brightness, contrast, and texture to highlight different structures.

The sonographer can manipulate the 3D image on the ultrasound machine, rotating it and viewing it from different angles. Some machines also allow for the visualization of the interior of hollow structures by virtually "cutting" through the surface (such as in the visualization of the inside of an adnexal cyst or a blood vessel). 3D ultrasound provides additional information compared to 2D ultrasound and is particularly useful in areas where spatial relationships are important, such as in fetal imaging, evaluation of uterine anomalies, IUD assessment, and evaluation of the endometrial–myometrial interface in the setting of adenomyosis or FIGO 0–3 fibroids (4).

Contrast-enhanced ultrasound (CEUS) uses microbubble contrast agents to improve the visualization of blood flow in the microvasculature. It is particularly useful for evaluating organ perfusion and for characterizing lesions. Ultrasound contrast agents have an unusually high safety profile and may be administered repeatedly (9). Elimination of agents is largely respiratory, without risk of renal dysfunction. Contrast reactions are very rare. CEUS may have a future use in characterizing gynecologic malignancies and can be helpful in guiding biopsy by highlighting tumor areas that are non-necrotic.

A variety of other ultrasound techniques are currently available that have very high sensitivity to blood flow which are not dependent on Doppler techniques. These techniques are vendor-specific and proprietary. Such images are sometimes produced by amplifying the subtle grayscale echoes off moving blood cells while simultaneously repressing static structures, creating images similar in appearance to those created by CEUS.

Saline infusion sonohysterography (SIS), hysterosalpingo-contrast sonography (HyCoSy), and hysterosalpingo-foam sonography (HyFoSy) are ultrasound-based diagnostic procedures used to evaluate the uterine cavity and fallopian tubes.

SIS involves the introduction of sterile saline solution into the uterine cavity via a thin catheter, while performing a transvaginal ultrasound. The saline distends the uterine cavity, providing better visualization of the endometrium and the identification of any abnormalities such as polyps, fibroids, and adhesions within the uterine cavity (10).

HyCoSy and HyFoSy are similar to SIS but use a contrast or foam agent instead of saline to evaluate both the uterine cavity and the patency of the fallopian tubes. This procedure involves the introduction of a contrast medium into the uterine cavity and fallopian tubes while performing transvaginal ultrasound. The passage of the contrast medium through the tubes can be visualized, helping to assess tubal patency (11). There are different types of contrast agents used in HyCoSy/HyFoSy, including echogenic (bubble-containing) fluids and gel-based agents.

Hysterosalpingography (HSG) is a radiographic procedure to investigate the shape of the uterine cavity and the shape and patency of the fallopian tubes. It involves the injection of an iodine-based contrast medium through the cervix into the uterine cavity. X-ray images are then taken to outline the cavity and fallopian tubes. HSG uses ionizing radiation, while SIS and HyCoSy are based on ultrasound and do not involve radiation exposure (12, 13).

9.3 Magnetic Resonance (MR)

Magnetic resonance (MR) uses strong magnetic fields and radio waves to generate images of the body's internal structures. When a patient is placed in an MR scanner, the strong magnetic field causes the protons in the water molecules of the body to align with the magnetic field. Excitation involves application of a pulse of radiofrequency (RF) energy, which temporarily knocks the protons out of alignment. Once the RF pulse is turned off, the protons begin to return to their original alignment (relaxation) within the magnetic field. As they do this, they emit RF signals. RF coils pick up these emitted signals. The signals received by the RF coils are processed by a computer to generate an image. The time it takes for the protons to realign with the magnetic field and the varying amounts of RF energy that are emitted as they do give MR images their contrast and allow tissue differentiation. MR does not use ionizing radiation, which makes it safer for repeated imaging and imaging of sensitive populations such as pregnant women. MR is an invaluable tool for the evaluation of benign and malignant gynecologic conditions. It offers excellent soft tissue contrast and the ability to acquire images in multiple planes, which is particularly helpful in assessing the complex anatomy of the pelvis.

In MR, different sequences can be used to generate images with varying contrast and characteristics. The main sequences commonly used, especially in the context of gynecologic imaging, are T1-weighted, T2-weighted, and T2-weighted fat-suppressed sequences, as well as diffusion-weighted imaging (DWI).

T1-weighted images are generated by using a relatively short repetition time (TR) and echo time (TE). This emphasizes the T1 relaxation time of tissues. In T1-weighted images, fat appears bright, and water appears dark. T1WI is useful for assessing the myometrium and for detecting hemorrhagic cysts and endometriomas, which can appear bright due to the presence of blood products (14). T1-weighted imaging is the most common sequence used in contrast-enhanced MRI. Gadolinium-based contrast agents primarily shorten the T1 relaxation time of the tissues, causing them to appear brighter on T1-weighted images. Post-contrast T1-weighted images are typically acquired with fat suppression (to suppress the bright signal from fat) to maximize the visibility of the enhancement.

T2-weighted images use a longer TR and TE, which emphasizes the T2 relaxation time of tissues. Water appears bright, and fat appears relatively bright compared to other soft tissues in T2-weighted images. High-resolution T2-weighted images (especially those produced on high field strength [3T] MR) without fat suppression are crucial for diagnosing deep endometriosis. The high contrast resolution of T2-weighted images is particularly adept at differentiating between soft tissues, which is essential for identifying endometriosis implants against the background of surrounding pelvic structures. T2-weighted images can highlight the presence of fibrosis and adhesions, which are common in deep endometriosis (15). T2WI is invaluable in gynecologic imaging for evaluating the endometrium, assessing ovarian cysts, and characterizing

adnexal masses. It is particularly helpful in depicting high fluid content, as in cases of hydrosalpinx or cysts (16).

T2-weighted fat-suppressed imaging combines T2-weighted imaging with fat suppression techniques. Fat suppression can be achieved through different methods such as short tau inversion recovery (STIR) or using frequency-selective fat saturation pulses. This is important in general gynecologic imaging to suppress the high signal from fat and improve the visualization of structures adjacent to fat, such as ovarian lesions.

Diffusion-weighted imaging exploits the microscopic motion of water molecules to generate contrast. It is particularly useful in gynecologic imaging for characterizing adnexal masses and for the detection of smaller lesions. It has applications in the assessment of tumors, as malignant tumors often restrict diffusion more than do benign tissues (17).

MR can be useful in the staging of cancers of the endometrium, cervix, and ovaries (18, 19). Its high contrast resolution is beneficial in detecting and characterizing small tumors, assessing myometrial invasion, and detecting lymph node involvement. MR can be used to guide surgical and radiation therapy planning by providing detailed images of the tumor and surrounding structures. It helps in delineating the tumor margins and identifying critical structures nearby. MR is used to monitor the response of gynecological cancers to chemotherapy or radiation therapy, including size reduction and changes in the characteristics of tumors. For patients who have undergone treatment for gynecologic cancers, MR is used to monitor for recurrence, especially in detecting small or subtle recurrent tumors.

MR is often used for further characterization of adnexal masses that are occasionally indeterminate on ultrasound, helping to differentiate benign from malignant masses (20). MR may differentiate between functional cysts, dermoid cysts, and other benign cysts (21).

MR is considered the gold standard for imaging uterine fibroids. It provides detailed information on the number, size, location, and type of fibroids, which is crucial for treatment planning, including surgery or uterine artery embolization (22). MR is highly sensitive in diagnosing adenomyosis with excellent interobserver agreement. It helps in distinguishing adenomyosis from fibroids and assessing the extent of disease, which can guide treatment options (23).

MR can be used to evaluate Müllerian duct anomalies and other congenital anomalies of the female reproductive tract, which may be associated with infertility or obstetrical complications (24). However, 3D ultrasound often provides similar information (25, 26).

9.4 Computed Tomography (CT)

Computed tomography (CT) uses X-rays to create cross-sectional images of the body. Within the CT scanner, an X-ray tube generates X-ray beams. These beams are directed through the patient's body to a detector on the opposite side. As the X-rays pass through the body, they are attenuated or absorbed to different degrees by different tissues. For example, bone absorbs more X-rays than soft tissue. The detectors measure the number of X-rays that reach them after passing through the body and convert this into electrical signals. The X-ray tube and detectors rotate around the patient, and many measurements are taken from different angles. A computer processes the electrical signals to calculate the number of X-rays absorbed by each volume point (or voxel) in a cross-section of the body. This data is reconstructed to produce a two-dimensional grayscale image of a slice of the body. Each pixel in the image represents a voxel in the body, with the brightness of each pixel representing the density of tissue at that point. Multiple cross-sectional images are stacked together to create a three-dimensional representation of the body. These can be viewed individually or rendered into a 3D image (27). Because CT scans involve the use of X-rays, there is exposure to ionizing radiation, which has potential risks. Consequently, the utility of a CT scan must be weighed against these risks, especially in sensitive populations such as pregnant women and children.

CT is often helpful in the staging of gynecologic cancers, such as ovarian, cervical, and endometrial cancer. It helps determine the size and extent of the primary tumor, as well as whether there is a spread to nearby lymph nodes or distant organs. CT can be utilized to plan surgical or radiation treatments for gynecologic cancers. Additionally, it is used to monitor the response of tumors to chemotherapy or radiation therapy. For patients who have undergone treatment for gynecologic cancers, CT is often used to monitor for recurrence. While ultrasound is the first-line imaging modality for evaluating adnexal masses and MR is typically used for advanced characterization, CT can be useful when masses are large or have complex characteristics to provide additional information on their nature and extent (28). In cases of postoperative infection or tubo-ovarian abscess, CT can help in identifying collections of pus or fluid. CT and MR are useful in the assessment of gynecologic emergencies, particularly when first-line ultrasound imaging is indeterminate. Conversely, CT is often ordered in emergency departments as a first-line study for abdominal or pelvic pain. Many gynecologic emergencies, such as adnexal torsion, pelvic inflammatory disease, and symptomatic hemorrhagic corpus luteal cysts can be diagnosed on CT and do not necessarily require ultrasound for confirmation (29).

9.5 FDG PET-CT

FDG PET-CT is a hybrid imaging technique that combines positron emission tomography (PET) with computed tomography to provide both functional and anatomical information. FDG refers to fluorodeoxyglucose, which is a radiolabeled glucose analog commonly used as a tracer in PET imaging.

The patient is injected with a small amount of FDG, which is taken up by cells throughout the body. Because cancer cells are typically more metabolically active than normal cells, they take up more FDG. The patient waits (usually about 60 minutes) to allow the FDG to distribute throughout the body. As the FDG is metabolized, it emits positrons, which then collide with electrons. This collision results in the emission of gamma rays, which are detected by the PET scanner. The scanner collects data on the gamma rays and uses this information to create a three-dimensional map of tracer concentration. Almost simultaneously with the PET scan, a CT scan is performed. CT provides detailed anatomical information. The PET images, which show metabolic activity, are superimposed with the CT images that show anatomy. This fusion allows for the localization of areas of increased metabolic activity which is typically increased in cancerous tumors (30).

PET-CT is increasingly being used in the management of various gynecologic cancers, including ovarian, cervical, and endometrial cancers. Its utility lies in its ability to provide both functional and anatomical information, which is invaluable for initial staging, evaluating the response to therapy, and detecting recurrence.

In gynecologic cancers such as cervical and ovarian cancer, PET-CT can help in initial staging by identifying the primary tumor and detecting any metastatic spread to lymph nodes or distant organs.

PET-CT can be used to plan treatment, particularly in guiding radiation therapy. By identifying areas of increased metabolic activity, radiation therapy can be more precisely targeted. After chemotherapy or radiation therapy, PET-CT can be used to monitor the response of the tumor to the treatment. A decrease in the metabolic activity of the tumor can indicate a good response to the treatment. For patients who have undergone treatment for gynecologic cancers, PET-CT may be used to monitor for recurrence. It can pick up early changes in metabolic activity that may indicate the cancer is returning before structural changes are evident.

Similarly, but less widely available, PET-MR combines the individual advantages of PET and MR, improving the sensitivity for detecting local recurrence, pelvic lymph node, peritoneal, and bone metastases (31, 32).

9.6 Interventional Radiology in MIGS

9.6.1 Digital Subtraction Angiography (DSA)

Digital subtraction angiography (DSA) is a fluoroscopic technique used primarily to visualize blood vessels. Before injecting the contrast agent, an image (mask or pre-contrast image) of the area of interest is captured. This image contains background information that will be later subtracted from the image taken after the contrast agent is administered. A contrast agent, usually iodine-based, is injected into the blood vessels. This contrast agent is radiopaque, meaning that it absorbs X-rays more than the surrounding tissues, which makes the blood vessels appear much clearer on X-ray images. After the contrast agent is injected, real-time fluoroscopic images are taken. Using digital image processing techniques, the pre-contrast image is subtracted from the post-contrast images. This removes the background information (bones, organs, etc.) and leaves behind only the contrast-enhanced blood vessels. Improvements in clarity significantly reduce the radiation dose compared to conventional angiography (33).

Angiography and other interventional techniques have been increasingly employed in the management of various gynecologic conditions. These minimally invasive techniques can augment or offer an alternative to surgery.

One of the common uses of angiography in gynecology is for the treatment of uterine fibroids through uterine fibroid embolization (UFE). In UFE, a catheter is guided to the blood vessels supplying the fibroids, and an embolic agent is injected to block these vessels, which leads to the shrinkage of the fibroids. UFE has been demonstrated to be an effective alternative to surgical treatments for fibroids like myomectomy and hysterectomy (34). Similar to uterine fibroids, adenomyosis can also be treated using interventional radiology techniques like embolization to reduce symptoms (35).

In cases where medical management fails, angiography and embolization of the uterine arteries can be used to control bleeding in the setting of postpartum hemorrhage (36).

DSA is useful in the management of pelvic congestion syndrome (PCS) and May–Thurner syndrome (MTS). These are two distinct vascular conditions, but they can be related in certain cases due to their anatomical proximity and similar presentation of symptoms. PCS is a condition characterized by the presence of varicose veins in the pelvis, particularly around the ovaries. It is thought to be caused by the reflux of blood in the ovarian veins and is associated with chronic pelvic pain. This pain can be exacerbated during menstruation, after prolonged standing, and during or after sexual intercourse. MTS, also known as iliac vein compression syndrome, is a condition where the left iliac vein is compressed by the right iliac artery as they cross each other in the pelvis. This compression can lead to a decrease in blood return from the left leg, causing swelling, pain, and, in some cases, deep vein thrombosis (DVT) in the left lower extremity. The ovarian veins drain into the iliac veins, and if there is compression of the left iliac vein due to MTS, it could potentially exacerbate venous congestion in the pelvis. This, in turn, may worsen the symptoms of PCS (37).

PCS is often treated by ovarian vein embolization. This minimally invasive procedure aims to block the blood flow to the varicose veins in the pelvis, which are believed to be the cause of chronic pelvic pain associated with PCS. Once the abnormal veins are identified, small coils, plugs, or a sclerosing agent are delivered through the catheter to the target veins. This causes the veins to close off, preventing blood from pooling in the pelvis (38, 39).

Fluoroscopy is also used to guide wire placement and catheterization during fallopian tube recanalization (40).

Imaging guidance for biopsy in gynecology is essential for obtaining tissue samples from specific areas within the female reproductive system. This is used to diagnose various gynecological conditions, such as cancers, infections, and other abnormalities. The main imaging modalities used in guiding gynecological biopsies are ultrasound and CT.

Ultrasound is often the preferred method for guiding biopsies. It does not involve ionizing radiation and provides real-time imaging. Ultrasound can be used to guide biopsies of masses within the uterus, ovaries, or other structures in the pelvis.

In certain cases, particularly when masses are in areas difficult to reach with ultrasound guidance, CT guidance may be used. CT imaging can provide cross-sectional images of a larger area and is particularly useful for guiding biopsies of masses within the pelvic cavity that are near other critical structures or when bone or gas artifacts may obscure ultrasound visualization.

Pelvic abscess drainage may be performed under CT or ultrasound guidance. In transvaginal abscess drainage, ultrasound is used to guide the procedure. In the trocar method, a small drainage catheter mounted over a needle is placed in a single step. The simultaneous use of fluoroscopy to monitor drain placement is helpful, particularly when the Seldinger (needle-wire-dilator-catheter) technique is used to place a larger catheter. The patient is usually placed in the dorsal lithotomy position. The vagina is cleaned and local anesthetic is applied. A needle and/or a catheter is inserted through the vaginal wall into the abscess. The pus is drained out, and in some cases, a drainage catheter may be left in place for continuous drainage over a few days. The same methods may be used in a transrectal approach (41).

Ultrasound is commonly used intraoperatively for guidance during instrumentation of the uterus, usually from a transabdominal approach with a filled urinary bladder as an acoustic window. Transabdominal, transvaginal, or laparoscopic ultrasound may also be used to localize surgically occult disease. It can also guide needle or wire localization or injection of methylene blue dye to aid surgical identification of disease. Such guidance is helpful during resection of deep endometriosis, which may be visualized on preoperative ultrasound or MR but may nevertheless be difficult to identify at laparoscopy without extensive surgical dissection (42–44).

High-intensity focused ultrasound (HIFU) is a noninvasive therapeutic technique that uses ultrasound waves to focus on and heat specific tissues within the body. HIFU has been increasingly used for the treatment of uterine fibroids. The procedure involves focusing ultrasound waves on fibroids within the uterus. The energy from these waves is absorbed by the fibroids, which raises the temperature and causes coagulative necrosis, leading to the shrinkage of the fibroids over time. This procedure is minimally invasive, and patients can usually return to their normal activities shortly after treatment (45). HIFU can also be used for the treatment of adenomyosis. Similar to uterine fibroids, HIFU targets the affected tissue and causes thermal ablation without damaging the surrounding structures. Though not as widely adopted for adenomyosis as for fibroids, HIFU shows promising results in reducing the symptoms associated with adenomyosis, such as heavy menstrual bleeding and pelvic pain (46).

HIFU may be performed under ultrasound or MR guidance. However, MR provides higher resolution imaging and the ability to measure temperature changes, which can be important for application near thermally sensitive structures, such as the bowel (47).

9.7 Diagnostic Imaging Reporting and Communication in MIGS

Structured reporting in radiology involves using standardized templates or forms for the communication of imaging findings, as opposed to traditional free-text narrative reports. Structured reporting ensures that essential elements are consistently included in the report, which is particularly important in gynecologic imaging where there are numerous structures and potential pathologies that need to be assessed and documented. The structured format makes it easier to extract data for research and quality improvement purposes. Structured reports can improve communication with the MIGS surgeon by providing them with a concise and clear summary of the findings (48). This is particularly useful in the reporting of preoperative endometriosis imaging using MR or expert ultrasound (49). By using structured templates, trainees become familiar with the important elements that should be included in reports, helping them to develop comprehensive reporting habits. Structured reporting can ensure that data is collected and reported consistently across different centers, which is particularly important in multicenter trials assessing the efficacy of interventions for gynecologic conditions (50).

Other standardizations are essential in providing clear and consistent reporting. For the reporting of uterine fibroids, use of the FIGO classification rather than descriptive language allows for report simplification and clarity (51). The ultrasound assessment of adenomyosis should comment on the presence or absence of the Morphological Uterus Sonographic Assessment (MUSA) criteria (52). Adnexal masses should be characterized and reported using IOTA or O-RADS™ terminology (53–56). Accurate reporting in radiology is also dependent on how indications are provided. For example, the accuracy of diagnosing adenomyosis by ultrasound and MR is significantly improved when the interpreting physician is aware of adenomyosis as the clinical concern (57).

Two-way communication of imaging and operative findings can improve diagnostic accuracy. The MIGS surgeon should be aware of the sensitivity and specificity of any given imaging observation. For example, the sensitivity and specificity of deep endometriosis bowel nodules diagnosed by bowel-prepared transvaginal ultrasound approach 100%. If such a nodule is not detected initially at laparoscopy, efforts including additional dissection and intraoperative ultrasound would be appropriate (1, 58).

9.8 Conclusion

Diagnostic imaging and imaging-guided interventions play a crucial role in the minimally invasive management of benign and malignant gynecologic conditions. They inform preoperative diagnosis and surgical planning, intraoperative detection of disease, and postoperative assessment of surgical success and management of surgical complications. Interventional procedures may augment surgical management or provide a nonsurgical alternative when clinically appropriate. Standardization of imaging reports can improve communication between the interpreting physician and the MIGS surgeon to optimize operative outcomes.

References

1. Goncalves MO et al. Systematic evaluation of endometriosis by transvaginal ultrasound can accurately replace diagnostic laparoscopy, mainly for deep and ovarian endometriosis. *Hum Reprod*. 2021;36(6):1492–1500.
2. Dietz HP. Ultrasound imaging of the pelvic floor. Part II: three-dimensional or volume imaging. *Ultrasound Obstet Gynecol*. 2004;23(6):615–625.
3. Dietz HP. Ultrasound imaging of the pelvic floor. Part I: two-dimensional aspects. *Ultrasound Obstet Gynecol*. 2004;23(1):80–92.
4. Nelson TR et al. Three-dimensional ultrasound imaging. *Ultrasound Med Biol*. 1998;24(9):1243–1270.
5. Reid S et al. Prediction of pouch of Douglas obliteration in women with suspected endometriosis using a new real-time dynamic transvaginal ultrasound technique: the sliding sign. *Ultrasound Obstet Gynecol*. 2013;41(6):685–691.
6. Rubin JM et al. Power Doppler US: a potentially useful alternative to mean frequency-based color Doppler US. *Radiology*. 1994;190(3):853–856.
7. Roseland ME et al. Adnexal mass imaging: contemporary guidelines for clinical practice. *Radiol Clin North Am*. 2023;61(4):671–685.
8. Chang HC et al. Pearls and pitfalls in diagnosis of ovarian torsion. *Radiographics*. 2008;28(5):1355–1368.
9. Claudon M et al. Guidelines and good clinical practice recommendations for Contrast Enhanced Ultrasound (CEUS) in the liver – update 2012: a WFUMB-EFSUMB initiative in cooperation with representatives of AFSUMB, AIUM, ASUM, FLAUS and ICUS. *Ultrasound Med Biol*. 2013;39(2):187–210.
10. Bree RL et al. US evaluation of the uterus in patients with postmenopausal bleeding: a positive effect on diagnostic decision making. *Radiology*. 2000;216(1):260–264.
11. Exacoustos C et al. Hysterosalpingo-contrast sonography compared with hysterosalpingography and laparoscopic dye pertubation to evaluate tubal patency. *J Am Assoc Gynecol Laparosc*. 2003;10(3):367–372.
12. Luciano DE et al. Can hysterosalpingo-contrast sonography replace hysterosalpingography in confirming tubal blockage after hysteroscopic sterilization and in the evaluation of the uterus and tubes in infertile patients? *Am J Obstet Gynecol*. 2011;204(1):79 e1–79 e 5.
13. Luciano DE et al. Contrast ultrasonography for tubal patency. *J Minim Invasive Gynecol*. 2014;21(6):994–998.
14. Outwater EK et al. Ovarian teratomas: tumor types and imaging characteristics. *Radiographics*. 2001;21(2):475–490.
15. Bazot M et al. European society of urogenital radiology (ESUR) guidelines: MR imaging of pelvic endometriosis. *Eur Radiol*. 2017;27(7):2765–2775.

16. Thomassin-Naggara I et al. Contribution of diffusion-weighted MR imaging for predicting benignity of complex adnexal masses. *Eur Radiol*. 2009;19(6):1544–1552.
17. Gagliardi T et al. Diffusion-weighted magnetic resonance imaging in ovarian cancer: exploiting strengths and understanding limitations. *J Clin Med*. 2022;11(6).
18. Balleyguier C et al. Staging of uterine cervical cancer with MRI: guidelines of the European Society of Urogenital Radiology. *Eur Radiol*. 2011;21(5):1102–1110.
19. Rechichi G et al. Myometrial invasion in endometrial cancer: diagnostic performance of diffusion-weighted MR imaging at 1.5-T. *Eur Radiol*. 2010;20(3):754–762.
20. Thomassin-Naggara I et al. Adnexal masses: development and preliminary validation of an MR imaging scoring system. *Radiology*. 2013;267(2):432–443.
21. Sadowski EA et al. O-RADS MRI after initial ultrasound for adnexal lesions: AJR expert panel narrative review. *Am J Roentgenol*. 2023;220(1):6–15.
22. Vu KN et al. Evaluation of the routine use of pelvic MRI in women presenting with symptomatic uterine fibroids: when is pelvic MRI useful? *J Magn Reson Imaging*. 2019;49(7):e271–e281.
23. Bazot M et al. Role of transvaginal sonography and magnetic resonance imaging in the diagnosis of uterine adenomyosis. *Fertil Steril*. 2018;109(3):389–397.
24. Sugi MD et al. Mullerian duct anomalies: role in fertility and pregnancy. *Radiographics*. 2021;41(6):1857–1875.
25. Jayaprakasan K et al. Prevalence of uterine anomalies and their impact on early pregnancy in women conceiving after assisted reproduction treatment. *Ultrasound Obstet Gynecol*. 2011;37(6):727–732.
26. Marcal L et al. Mullerian duct anomalies: MR imaging. *Abdom Imaging*. 2011;36(6):756–764.
27. Abrahams RB et al. *Imaging Physics Case Review*. Elsevier; 2019:387.
28. Sala E et al. The added role of MR imaging in treatment stratification of patients with gynecologic malignancies: what the radiologist needs to know. *Radiology*. 2013;266(3):717–740.
29. Iraha Y et al. CT and MR imaging of gynecologic emergencies. *Radiographics*. 2017;37(5):1569–1586.
30. Czernin J et al. Improvements in cancer staging with PET/CT: literature-based evidence as of September 2006. *J Nucl Med*. 2007;48(Suppl 1):78S–88S.
31. Kitajima K et al. Value of fusion of PET and MRI in the detection of intra-pelvic recurrence of gynecological tumor: comparison with 18F-FDG contrast-enhanced PET/CT and pelvic MRI. *Ann Nucl Med*. 2014;28(1):25–32.
32. Tarcha Z et al. Added value of FDG PET/MRI in gynecologic oncology: a pictorial review. *Radiographics*. 2023;43(8):e230006.
33. Pavlicek W et al. Patient doses during digital subtraction angiography of the carotid arteries: comparison with conventional angiography. *Radiology*. 1982;145(3):683–685.
34. Goodwin SC et al. Uterine artery embolization for treatment of leiomyomata: long-term outcomes from the FIBROID Registry. *Obstet Gynecol*. 2008;111(1):22–33.
35. Popovic M et al. Uterine artery embolization for the treatment of adenomyosis: a review. *J Vasc Interv Radiol*. 2011;22(7):901–909; quiz 909.
36. Lee HY et al. Primary postpartum hemorrhage: outcome of pelvic arterial embolization in 251 patients at a single institution. *Radiology*. 2012;264(3):903–909.
37. Kibbe MR et al. Iliac vein compression in an asymptomatic patient population. *J Vasc Surg*. 2004;39(5):937–943.
38. Maleux G et al. Ovarian vein embolization for the treatment of pelvic congestion syndrome: long-term technical and clinical results. *J Vasc Interv Radiol*. 2000;11(7):859–864.
39. Asciutto G et al. Pelvic venous incompetence: reflux patterns and treatment results. *Eur J Vasc Endovasc Surg*. 2009; 38(3):381–386.
40. Kohi MP. Interventional radiologist's approach to fallopian tube recanalization. *Tech Vasc Interv Radiol*. 2021;24(1):100736.
41. McGahan JP et al. Sonographically guided transvaginal or transrectal pelvic abscess drainage using the trocar method with a new drainage guide attachment. *AJR Am J Roentgenol*. 2008;191(5):1540–1544.
42. Haverland R et al. Deep infiltrating endometriosis: using preoperative radiology for surgical planning. *J Minim Invasive Gynecol*. 2020;27(3):557–558.
43. McKee D et al. Intraoperative deep pelvic ultrasound for detection of ileocecal endometriosis. *J Minim Invasive Gynecol*. 2021;28(6):1125–1127.
44. Misal M et al. Ultrasound-guided spinal needle localization for resection of abdominal wall endometrioma. *J Minim Invasive Gynecol*. 2021;28(5):929–930.
45. Stewart EA et al. Clinical outcomes of focused ultrasound surgery for the treatment of uterine fibroids. *Fertil Steril*. 2006;85(1):22–9.
46. Zhou M et al. Ultrasound-guided high-intensity focused ultrasound ablation for adenomyosis: the clinical experience of a single center. *Fertil Steril*. 2011;95(3):900–905.
47. Kennedy JE. High-intensity focused ultrasound in the treatment of solid tumours. *Nat Rev Cancer*. 2005;5(4):321–327.
48. Franconeri A et al. Structured vs narrative reporting of pelvic MRI for fibroids: clarity and impact on treatment planning. *Eur Radiol*. 2018;28(7):3009–3017.
49. Mattos LA et al. Structured ultrasound and magnetic resonance imaging reports for patients with suspected endometriosis: guide for imagers and clinicians. *J Minim Invasive Gynecol*. 2019;26(6):1016–1025.
50. Brook OR et al. Structured reporting of multiphasic CT for pancreatic cancer: potential effect on staging and surgical planning. *Radiology*. 2015;274(2):464–472.
51. Shrivastava A et al. Role of MRI and FIGO staging in evaluation of fibroids – a pictorial review. *Maedica (Bucur)*. 2023; 18(1):121–126.
52. Harmsen MJ et al. Consensus on revised definitions of Morphological Uterus Sonographic Assessment (MUSA) features of adenomyosis: results of modified Delphi procedure. *Ultrasound Obstet Gynecol*. 2022;60(1):118–131.
53. Lu B et al. Comparison of contrast-enhanced ultrasound, IOTA simple rules and O-RADS for assessing the malignant risk of sonographically appearing solid ovarian masses. *J Gynecol Obstet Hum Reprod*. 2023;52(4):102564.
54. Shang J et al. Comparison of performance between O-RADS, IOTA simple rules risk assessment and ADNEX model in the discrimination of ovarian Brenner tumors. *Arch Gynecol Obstet*. 2023;08(3):961–970.
55. Vilendecic Z et al. Accuracy of IOTA simple rules, IOTA ADNEX model, RMI, and subjective assessment for preoperative adnexal mass evaluation: the experience of a tertiary care referral hospital. *Gynecol Obstet Invest*. 2023;88(2):116–122.
56. Levine D et al. Ovarian-adnexal reporting and data system for ultrasound: a framework for improvement. *Can Assoc Radiol J*. 2023;74(1):18–19.
57. Zanolli NC et al. Diagnostic accuracy of clinically reported adenomyosis on pelvic ultrasound and MRI compared to surgical pathology. *Clin Imaging*. 2022;82:117–120.
58. Ros C et al. Bowel preparation prior to transvaginal ultrasound improves detection of rectosigmoid deep infiltrating endometriosis and is well tolerated: prospective study of women with suspected endometriosis without surgical criteria. *Ultrasound Obstet Gynecol*. 2021;57(2):335–341.

10 SUTURE, MESH, AND GRAFTS

Meghan Hagedorn and Amy Park

10.1 Introduction

Suture and grafts enable restoration of normal anatomy through approximation of dissected tissues and reconstruction of damaged tissues, respectively. This chapter provides an overview of pertinent suture and graft materials, material properties, host responses, and typical uses within gynecologic surgery.

10.2 Suture

The United States Pharmacopeia (USP), which is a compendium of information that defines quality standards for medical products, characterizes suture by size, strand structure, and material properties. The USP designates suture size numerically using a whole number system which is centered on 0 and refers to the diameter of the suture strand. As the diameter increases from size 0, the USP size increases in numerical order by whole numbers. However, as the diameter decreases, the USP size designation changes progressively by increasing the number of zeros. For example, as the suture gets smaller, the progressive designation is 0, 00, 000, 0000, etc., which are written as 0, 1–0, 2–0, 3–0, 4–0, etc., where the first number denotes the additional number of zeros (1).

Suture is further characterized by the strand structure, which includes monofilament, braided or multifilament, and barbed options. Monofilament suture is made of a single, smooth strand of material, whereas a braided or multifilament suture consists of multiple strands of material braided together to make a singular, complex strand. Due to the braided nature of multifilament suture, microscopic interstices are created which are large enough to create a rough surface and allow ingress of bacteria. In comparison to multifilament, the smooth surface of the monofilament suture provides less risk of harboring bacterial organisms, allows for a smoother passage through tissue, elicits lower inflammatory response in the tissue, and ties down with less resistance. However, monofilament suture is more prone to crushing or crimping if not handled properly, which can weaken the suture. In contrast, the braided structure of the multifilament suture provides greater pliability, flexibility, and tensile strength, but also has a rougher surface which promotes tissue microtrauma and has been shown to favor bacterial adherence and biofilm formation when compared to monofilament (2). Coated multifilament sutures provide a smoother surface which allows for improved handling and decreases microtrauma of tissue. Barbed sutures are monofilament sutures with unidirectional or bidirectional barb-like projections on the surface which anchor the suture in the tissue. Since the entirety of the suture is anchored into the tissue, this resists suture migration, disperses tension across the wound, and eliminates the need for knots, which improves efficiency and reduces operating times (3, 4). However, most barbed suture is manufactured by making small cuts in the suture to create the barbs, which reduces the function diameter of the suture and thus reduces the tensile strength (5).

10.3 Suture Material Properties

Suture material is categorized by degradation properties (absorbable vs nonabsorbable) and by the source of the raw material (natural vs synthetic) used to produce the suture. Absorbable suture is defined by rapid degradation and loss of tensile strength during this process, whereas nonabsorbable suture can be permanent or semi-permanent and maintain tensile strength for a much longer period (6). More specifically, absorbable suture loses most of its tensile strength within 60 days of implantation, and suture that maintains most of its tensile strength after 60 days is considered nonabsorbable (1). The process by which suture is absorbed is dictated by the raw material from which it is made, i.e., natural versus synthetic. Natural suture is derived from natural, living sources, such as plants and animals, and is degraded and absorbed in the body through proteolytic enzymatic activity. In contrast, synthetic suture is manufactured from chemically derived polymers or synthetic compounds that are gradually broken down in the tissue through hydrolysis, and the by-products are absorbed by the surrounding tissues (Table 10.1).

10.3.1 Absorbable Natural Suture

10.3.1.1 Surgical Gut

Plain surgical gut (also known as plain gut, or catgut) is made from purified collagen strands derived from the submucosa of healthy ovine and bovine small intestines. The collagen strands are processed and spun to create monofilament sutures based on USP standards. Plain gut suture causes a moderate inflammatory tissue response resulting in rapid enzymatic degradation.

Chromic surgical gut (also known as chromic gut, or chromic catgut) is plain gut suture material that has been treated with a solution of chromium salt that results in a decreased inflammatory response, thus delaying degradation. The rate at which plain and chromic gut are degraded is highly dependent on the patient and tissue characteristics, such as presence of infection. Surgical gut suture is typically used for subcutaneous and soft tissue approximation when fast absorption is desired and strength is only needed for a short time. Use is not recommended for skin closures due to the inflammatory response and risk of scarring.

10.3.2 Absorbable Synthetic Suture

10.3.2.1 Poliglecaprone 25, Polyglactin 910, Polydioxanone

Poliglecaprone 25 (MONOCRYL) is made from a copolymer of glycolide and epsilon-caprolactone into a monofilament which is available in undyed and dyed violet options. Absorption occurs through hydrolysis and is quick, predictable, and within a similar time frame to chromic gut. Interestingly, the tensile strength retention profiles for the undyed and dyed suture are slightly different (Table 10.1). Poliglecaprone 25 is typically used for soft tissue and skin approximation when fast absorption is desired, strength is needed for a short time, and minimal inflammatory response is required.

DOI: 10.1201/9781003312109-10

TABLE 10.1 Suture Characteristics and Properties (1, 5, 7, 8)

Suture	Common Brand Names	Material Composition	Filament	Tissue Reactivity and Response	Absorption	Approximate Tensile Strength Half-Life	Time to Complete Absorption	Applications
Absorbable								
Natural								
Plain gut	SURGICAL GUT	Purified collagen (sourced from ovine and bovine small intestines)	Monofilament	Moderate	Proteolytic enzymatic activity	5–10 days	3–10 weeks	Subcutaneous and soft tissue approximation
Chromic gut	SURGICAL GUT Chromic	Purified collagen (sourced from ovine and bovine small intestines), treated with a solution of chromium salt to resist breakdown to prolong absorption and reduce tissue reactivity	Monofilament	Moderate (less than plain gut)	Proteolytic enzymatic activity	1–2 weeks	12 weeks	Soft tissue approximation and vessel ligation
Synthetic								
Poliglecaprone 25	MONOCRYL (Undyed)	Copolymer of glycolide and epsilon-caprolactone	Monofilament	Minimal	Hydrolysis	1 week	13–17 weeks	Soft tissue and skin approximation
	MONOCRYL (Dyed)	Copolymer of glycolide and epsilon-caprolactone, dyed violet	Monofilament	Minimal	Hydrolysis	1.5 weeks	13–17 weeks	Soft tissue and skin approximation where improved visualization of the suture is desired
Polydioxanone	PDS II	Polyester polymer	Monofilament	Slight	Hydrolysis	4–6 weeks	12–26 weeks	Soft tissue approximation, useful in tissue which requires extended structural support
Polyglactin 910	Coated VICRYL	90% glycolide, 10% L-lactide	Multifilament	Minimal	Hydrolysis	3 weeks	8–10 weeks	Soft tissue approximation and vessel ligation
	Coated VICRYL RAPIDE	90% glycolide, 10% L-lactide, treated with gamma rays to lower molecular weight	Multifilament	Minimal to moderate	Rapid hydrolysis	5–7 days	6 weeks	Superficial soft tissue and skin approximation
Nonabsorbable								
Natural								
Silk	PERMA-HAND SILK	Raw silk from silkworm moth larva	Multifilament	Acute inflammatory foreign body reaction	Very slowly degraded by enzymatic activity over time	6 months	2 years	Skin approximation and drain anchoring

(*Continued*)

TABLE 10.1 (Continued)

Suture	Common Brand Names	Material Composition	Filament	Tissue Reactivity and Response	Absorption	Approximate Tensile Strength Half-Life	Time to Complete Absorption	Applications
Synthetic								
Polypropylene	PROLENE	Isostatic crystalline stereoisomer of polypropylene	Monofilament	Minimal, encapsulation by fibrous connective tissue	N/A	No meaningful change over time	N/A	Soft tissue and skin approximation, vessel ligation, and infected wounds (minimizes sinus formation)
ePTFE	GORE-TEX	Expanded polytetrafluoroethylene	Microporous Monofilament	Minimal, encapsulation by fibrous connective tissue	N/A	No meaningful change over time	N/A	Soft tissue approximation and previously used for placement of prosthetic materials
Polyester	ETHIBOND EXCEL	Polyethylene terephthalate coated with polybutilate	Multifilament	Minimal, encapsulation by fibrous connective tissue	N/A	No meaningful change over time	N/A	Soft tissue approximation, vessel ligation, placement of prosthetic materials
	MERSILENE	Polyethylene terephthalate, uncoated	Multifilament	Minimal, encapsulation by fibrous connective tissue	N/A	No meaningful change over time	N/A	Soft tissue approximation, vessel ligation, placement of prosthetic materials

Polyglactin 910 (VICRYL) is a copolymer comprised of 90% glycolide and 10% L-lactide and coated with a mixture of calcium stearate and polyglactin 370 (equal parts copolymer of glycolide and lactide) and then braided into a multifilament suture strand. The coating acts as a lubricant for the suture to reduce tissue drag and provides a smoother tie down of knots, while the pliability of the suture and multifilament structure provides knot security and supports high-tension closures. Polyglactin 910 is dissolved through hydrolysis into glycolic acid and lactic acid, which are readily absorbed and metabolized by the body. The inflammatory tissue response is minimal, and the material is degraded slowly resulting in a slower loss of tensile strength compared to poliglecaprone 25, but faster than polydioxanone. Given the high knot security and pliability of the polyglactin suture, it is an excellent option for vessel ligation. Additionally, it is used for soft tissue approximation where a high-tension, secure closure is needed.

A modified version of Polyglactin 910, called VICRYL RAPIDE, is available which is treated with gamma rays to lower the molecular weight material that subsequently results in very fast absorption times that are comparable to surgical gut. The degradation and absorption processes are the same as VICRYL, but the tissue response is slightly more inflammatory resulting in a mild to moderate acute reaction. Use is only indicated for superficial soft tissue, mucosa, and skin approximation. Furthermore, this suture is best suited for wound closures that require a short duration of support and need to dissolve quickly, such as in episiotomy repairs.

Polydioxanone (PDS II) is constructed from a polyester polymer (p-dioxanone) into a monofilament which is specifically designed for delayed absorption and extended retention of tensile strength after implantation to allow for prolonged structural wound support. Polydioxanone creates only a slight inflammatory response as it is degraded and absorbed through hydrolysis and causes the least tissue reactivity of all absorbable suture. Due to the delayed absorption and tensile strength retention profile, this suture is ideal for high-tension closures (such as fascial reapproximation), soft tissue approximation which requires prolonged structural support, and in patients who are at high risk of delayed wound healing.

10.3.3 Nonabsorbable Natural Suture

10.3.3.1 Silk

Silk suture is fabricated from raw silk harvested from silkworm moth larva. Once harvested, the raw silk is processed, braided, and coated with wax or silicone. Silk suture offers excellent handling, knot tying, and knot security characteristics and thus is considered the standard by which all other suture is compared. Although considered nonabsorbable, silk suture elicits an acute inflammatory foreign body reaction resulting in fibrous tissue encapsulation followed by a protracted phase of enzymatic degradation. This prolonged degradation results in complete loss of tensile strength after approximately 1 year and eventually is undetectable in the tissue (1). Silk is primarily used for skin approximation and anchoring of drainage tubes with the intent of removal after the wound has healed or when the drain is pulled; however, it is not suitable for use in highly contaminated or infected tissue.

10.3.4 Nonabsorbable Synthetic Suture

10.3.4.1 Polypropylene and Polyester

Polypropylene (PROLENE) is made from a synthetic polymer of isostatic crystalline stereoisomer of polypropylene that is fabricated into a relatively inert monofilament suture material which does not adhere to tissue (1). The tensile strength of this permanent suture is preserved over time, and the material is not degraded. Overall, polypropylene elicits the least amount of tissue reactivity among all the synthetic nonabsorbable sutures, which makes it excellent for use in tissue in which the risk of sinus formation or extrusion should be minimized. Furthermore, it is well suited for use in contaminated or infected soft tissue wound closures.

Polyester sutures are produced primarily by using braided strands of polyethylene terephthalate, which are either uncoated or coated with a variety of materials that largely determine the properties of the suture. Specifically, uncoated versions of this suture include Mersilene and Dacron, which are difficult to handle and tie down, but offer excellent knot security (8). Ethibond is a coated version with polybutilate, which offers excellent handling, knot tying, and knot security characteristics. Tissue reactivity is minimal with polyester suture, and the tensile strength is retained over time. However, polyester suture has been shown to increase the risk of suture erosions and granulation tissue formation, and thus gynecologic use has decreased over time (9, 10).

10.4 Suture Selection

Special consideration must be given when selecting suture material that requires an understanding of the suture material properties, patient specific tissue properties, and the potential interactions between them. There are five parameters which can act as a guide to aid surgeons in appropriate suture selection: volume and density of tissue, wound tensile strength, wound healing time, tissue contamination, and tissue reactivity impact. In general, the smallest diameter suture which can adequately perform the intended purpose and support the target tissue should be used to minimize trauma to the tissue and the amount of foreign material in the body. Furthermore, the degree to which the wound needs support for healing, such as high-stress areas like abdominal fascia, perineum, and vaginal closure, or low-stress areas, such as skin, should also be considered. With respect to wound healing time, a suture material with an acceptable tensile strength half-life should be selected which will provide adequate support through the healing process. In patients who have impaired wound healing, such as in patients with vaginal atrophy due to postmenopausal state, chronic medical conditions, or chronic corticosteroid use, materials that maintain tensile strength over a prolonged period should be strongly considered (11–13). The degree of potential tissue contamination should also be considered as suture can become a nidus for infection. Finally, the impact of tissue reactivity as a response to the suture should also be considered. Preferably, the least reactive suture material should be selected for areas where tissue inflammation should be kept at a minimum. For example, in applications where optimal cosmetic results are desired or in tissue that has an increased risk of sinus formation, it may be more prudent to select absorbable or nonabsorbable synthetic monofilament suture material, such as poliglecaprone 25, polydioxanone, and polypropylene, as these materials are the least reactive in tissue and result in only slight to minimal inflammation post-implantation.

10.5 Grafts

Currently, there are four types of graft material available for use in gynecologic surgery: synthetic mesh and biologic

autografts, allografts, and xenografts. Synthetic mesh, like synthetic suture, is made from chemically derived synthetic compounds. Biologic grafts are sourced from natural origins, including humans and animals. A thorough understanding of host tissue response, graft material properties, risk of morbidity, and associated complications is essential in selecting the appropriate graft material to ensure the best outcome for patients.

10.5.1 Host Tissue Response

Tissue response to grafts is directly dependent on the structural and material properties of the grafts implanted. There are four categories of tissue response to grafts which have been previously described, including resorption, incorporation, encapsulation, and a mixed response which combines incorporation and encapsulation (14–16). A resorption response is defined by the replacement of the graft with new host connective tissue. Incorporation is a process in which host cells infiltrate the interstices in the graft that allows for neovascularization and deposition of fibroconnective tissue resulting in a mechanical anchoring of the graft to the host tissue. Encapsulation describes a similar process as incorporation, except the deposition of fibroconnective tissue is at the surface of the material resulting in a sheath-like capsule around the graft rather than intertwined into the mesh through pores as observed with incorporation. Mixed responses refer to a combination of incorporation and encapsulation processes.

10.5.2 Synthetic Mesh

Synthetic mesh material is made from chemically derived synthetic compounds which can be absorbable or nonabsorbable, as well as monofilament or multifilament in nature. The absorbable mesh currently available on the market is made from either polyglactin 910 or polyglycolic acid. Both materials elicit inflammatory reactions which result in hydrolysis of the material, during which time the graft is slowly replaced by host connective tissue. However, absorption times differ between polyglactin 910 and polyglycolic acid grafts, and they lose most of their strength around 30 and 90 days, respectively. Nonabsorbable synthetic mesh is made mostly from polypropylene, but other materials such as expanded polytetrafluoroethylene (ePTFE) and polyester are used. Furthermore, the synthetic mesh structure of woven strands gives rise to important structural properties, specifically porosity or pore size. Mesh weave designs which have pore sizes greater than 75 microns are considered macroporous, and designs with pore sizes smaller than 10 microns are considered microporous. Nonabsorbable synthetic mesh is classified into Types I, II, III, and IV, which are defined by pore size and filamentous structure (Table 10.2) (17–19).

10.5.3 Biologic Grafts

10.5.3.1 Autografts

Autografts are derived from tissue harvested from the patient's own connective tissue, most commonly from the tensor fascia lata or rectus abdominis anterior fascial sheath. Given autografts are derived from the patient's own tissue, there is no risk for host rejection or tissue erosion. Autografts are also cost-effective options as the tissue is harvested during the same procedure with minimal preparation of the tissue prior to implantation. However, the size and quality of the tissue may be limited based on the patient and site-specific anatomic constraints. The risk of morbidity associated with tissue harvesting includes but is not limited to an increased risk of pain, bleeding, need for blood transfusion, hematoma, wound infections, and incisional hernia (20, 21).

10.5.3.2 Allografts

Allografts are human cadaveric grafts harvested from donor tensor fascia lata or acellular dermal matrices (ADM). Harvesting of cadaveric tissue is performed aseptically and the tissue is processed to remove all cellular components to make the specimen nonimmunogenic. The tissue is then sterilized and preserved in a variety of ways based on the manufacturer's proprietary specifications, and thus details regarding those processes are limited to the public. Since allografts are harvested from cadaveric donors, the supply is dependent on available donor tissue, but does eliminate the risk of morbidity associated with host harvesting for autografts. All donors are screened and tested for blood-borne diseases, such as HIV or hepatitis, and are excluded as donors if considered high risk or test positive for the infection. However, this does not fully eliminate the risk of viral transmission (22)

10.5.3.3 Xenografts

Xenografts are nonhuman-derived grafts typically of bovine or porcine origin, specifically bovine pericardium and porcine intestine and dermis. Overall, tissue processing is similar to allografts such that the tissue is aseptically harvested, all cellular components are removed, and the specimen is sterilized and preserved. However, processing of various types of xenografts can differ by the addition of chemical cross-linking which essentially renders the tissue nonporous. The purpose of cross-linking is meant to prevent reabsorption by the host which ultimately promotes an encapsulation response at the surface of the graft similar to the tissue response seen in Type II synthetic mesh grafts (14). To address this concern, fenestrated cross-linked xenograft options are available which create functional pores that allow incorporation of host cells and connective tissue in the pores. This mixture of incorporation

TABLE 10.2 Synthetic Mesh Classifications (17–19)

Classification	Porosity	Filament	Material
Type I	Macroporous	Monofilament but may include absorbable multifilament components	Polypropylene (combination mesh material may also include poliglecaprone or polyglactin 910)
Type II	Microporous	Multifilament	Expanded polytetrafluoroethylene (ePTFE)
Type III	Macroporous with microporous or multifilament components	Multifilament	Polyethylene or polypropylene
Type IV	Submicroporous	Monofilament	Polypropylene

TABLE 10.3 Mesh Weight Categories

Weight Category	Density (g/m^2)
Heavy	> 90
Medium	50–90
Light	35–50
Ultra-light	< 35

and encapsulation results in a tissue response like Type III synthetic mesh.

10.6 Ideal Properties of Grafts

Due to the risks associated with biological grafts and available evidence which fails to show the benefit of use in pelvic reconstructive surgeries, synthetic mesh grafts are favored for use in gynecologic surgery (23, 24). Structural and material properties which are important to consider when selecting a synthetic mesh include filamentous construction, absorbability, density, and porosity. Synthetic meshes made of multifilament material, like multifilament suture, have microscopic interstices which are theoretically large enough to harbor bacteria, which may increase risk of infection. Therefore, like suture, monofilament mesh material is preferred in areas where infection risk is high and when using nonabsorbable material. Absorbable mesh materials are thought to provide lower risk of infection and pose less risk of adjacent viscera (19). However, once the material is absorbed, the replacement host tissue may not be as strong or durable as nonabsorbable mesh implants (25).

Density, also referred to as the weight of the mesh, is defined as the amount of material per square meter; thus, logically, the weight of mesh material is directly related to pore size. For example, mesh with larger pores results in less material per square meter, whereas small pore mesh results in more material present per square meter. Synthetic meshes are generally subdivided into heavy-, medium-, light-, and ultra-lightweight categories (Table 10.3) (26). The importance of pore size cannot be overstated; porosity not only impacts the weight of the mesh, but also the permeation of host cells, bacteria, blood vessels, and collagen fibers through mesh pores and the overall stiffness of the mesh (15, 27–29). Immune cells measure between 9 and 20 microns and bacteria typically measure less than 1 micron; thus, in microporous mesh designs, the micro pore size may allow bacteria to permeate the mesh weave but prevent infiltration of immune cells which increases the risk of infection (30). Stiffness, which is a mechanical property used to define the materials ability to resist deformation, has been shown to be directly related to a phenomenon known as stress shielding. Stress shielding occurs when two materials of differing stiffness are connected and the stiffer material "shields" the other material from stress and strain. Although this may sound like a desirable scenario, human tissue requires some level of stress to maintain structure and function; therefore, reduction in applied stress to tissue can lead to tissue degeneration. Furthermore, an in vivo study, which looked at how stiffness impacts host tissue response, found that stiffer meshes resulted in a decreased amount of important structural proteins (i.e., collagen and elastin), significant thinning of adjacent smooth muscle tissue, and findings suggestive of increased tissue injury (31). Stress shielding, and the resultant maladaptive degenerative response, is thought to be a key contributor to complications such as mesh exposures and erosions (32, 33). Although the perfect mesh material does not exist, based on the properties described earlier, the current consensus on the best mesh option available for pelvic surgery is ultralight or lightweight Type I synthetic mesh due to the macroporous, low-density, monofilament nature of the mesh.

References

1. Ethicon Inc. *Ethicon Wound Closure Manual*. Somerville, NJ: Ethicon; 2004.
2. Henry-Stanley MJ et al. Bacterial contamination of surgical suture resembles a biofilm. *Surg Infect*. 2010;11(5):433–439.
3. Zaruby J et al. An in vivo comparison of barbed suture devices and conventional monofilament sutures for cosmetic skin closure: biomechanical wound strength and histology. *Aesthet Surg J*. 2011;31(2):232–240.
4. Lin Y et al. The efficacy and safety of knotless barbed sutures in the surgical field: a systematic review and meta-analysis of randomized controlled trials. *Sci Rep*. 2016;6:23425.
5. Byrne M et al. The surgical suture. *Aesthet Surg J*. 2019;39(Suppl_2):S67–S72.
6. Maruccia M et al. *Textbook of Plastic and Reconstructive Surgery*. Springer; 2022.
7. Jones HW et al. *Te Linde's Operative Gynecology*. Wolters Kluwer; 2015.
8. WL Gore & Associates Inc. *The perfect close, Resource Library for GORE-TEX® Suture*. 2015. Available at: www.goremedical.com/resource/ab0101-en6 (Accessed Jul 9, 2023).
9. Yazdany T et al. Suture complications in a teaching institution among patients undergoing uterosacral ligament suspension with permanent braided suture. *Int Urogynecol J*. 2010;21(7):813–818.
10. Wong MJ et al. Uterosacral ligament vaginal vault suspension using delayed absorbable monofilament suture. *Int Urogynecol J*. 2011;22(11):1389–1394.
11. Nezhat C et al. Vaginal cuff dehiscence and evisceration: a review. *Obstet Gynecol*. 2018;132(4):972–985.
12. Hall G et al. Estrogen and skin: the effects of estrogen, menopause, and hormone replacement therapy on the skin. *J Am Acad Dermatol*. 2005;53(4):555–572.
13. Wilkinson HN et al. Epithelial arginase-1 is a key mediator of age-associated delayed healing in vaginal injury. *Front Endocrinol*. 2022;13:927224.
14. Trabuco EC et al. Xenograft use in reconstructive pelvic surgery: a review of the literature. *Int Urogynecol J Pelvic Floor Dysfunct*. 2007;18(5):555–563.
15. Bobyn JD et al. Effect of pore size on the peel strength of attachment of fibrous tissue to porous-surfaced implants. *J Biomed Mater Res*. 1982;16(5):571–584.
16. Bellón JM et al. Tissue response to polypropylene meshes used in the repair of abdominal wall defects. *Biomaterials*. 1998;19(7–9):669–675.
17. Amid PK. Classification of biomaterials and their related complications in abdominal wall hernia surgery. *Hernia*. 1997;1:15–21.
18. Birch C et al. The role of synthetic and biological prostheses in reconstructive pelvic floor surgery. *Curr Opin Obstet Gynecol*. 2002;14(5):527–535.
19. Ridgeway B et al. The use of synthetic mesh in pelvic reconstructive surgery. *Clin Obstet Gynecol*. 2008;51(1):136–152.
20. Blaivas JG et al. Surgery for stress urinary incontinence: autologous fascial sling. *Urol Clin North Am*. 2019;46(1):41–52.
21. Schimpf MO et al. Sling surgery for stress urinary incontinence in women: a systematic review and metaanalysis. *Am J Obstet Gynecol*. 2014;211(1):71.e1–27.
22. Simonds RJ et al. Transmission of human immunodeficiency virus type 1 from a seronegative organ and tissue donor. *N Engl J Med*. 1992;326(11):726–732.

23. Yurteri-Kaplan LA et al. The use of biological materials in urogynecologic reconstruction: a systematic review. *Plast Reconstr Surg*. 2012;130(5 Suppl 2):242S–253S.
24. Schimpf MO et al. Graft and mesh use in transvaginal prolapse repair: a systematic review. *Obstet Gynecol*. 2016;128(1):81–91.
25. Barbolt TA. Biology of polypropylene/polyglactin 910 grafts. *Int Urogynecol J Pelvic Floor Dysfunct*. 2006;17(Suppl 1):S26–S30.
26. Wang See C et al. Hernia mesh and hernia repair: a review. *Eng Regen*. 2020;1:19–33.
27. Shepherd JP et al. Uniaxial biomechanical properties of seven different vaginally implanted meshes for pelvic organ prolapse. *Int Urogynecol J*. 2012;23(5):613–620.
28. Pourdeyhimi B. Porosity of surgical mesh fabrics: new technology. *J Biomed Mater Res*. 1989;23(A1 Suppl):145–152.
29. Chu CC et al. Characterization of morphologic and mechanical properties of surgical mesh fabrics. *J Biomed Mater Res*. 1985;19(8):903–916.
30. Brun JL et al. Physical and biological characteristics of the main biomaterials used in pelvic surgery. *Biomed Mater Eng*. 1992;2(4):203–225.
31. Liang R et al. Vaginal degeneration following implantation of synthetic mesh with increased stiffness. *BJOG*. 2013;120(2):233–243.
32. Feola A et al. Deterioration in biomechanical properties of the vagina following implantation of a high-stiffness prolapse mesh. *BJOG*. 2013;120(2):224–232.
33. Knight KM et al. Mesh deformation: a mechanism underlying polypropylene prolapse mesh complications in vivo. *Acta Biomater*. 2022;148:323–335.

11 MEDICAL AND SURGICAL MANAGEMENT OF ECTOPIC PREGNANCY

Raanan Meyer, Kacey Hamilton, Mireille Truong, Matthew Siedhoff, and Kelly Wright

11.1 Introduction

Ectopic pregnancy is a condition in which a developing blastocyst implants outside the uterine cavity. It is a significant public health concern that affects women of reproductive age worldwide. The most common location of ectopic pregnancies is the fallopian tube, accounting for 96% of all ectopic gestations (1). Despite improved diagnostic methods leading to earlier detection and treatment of ectopic pregnancies, hemorrhage from ectopic pregnancy is still the leading cause of pregnancy-related maternal mortality in the first trimester, accounting for 4%–10% of all pregnancy-related deaths (2–5). In the developing world, EP constitutes a higher risk of maternal death compared to developed countries (6).

11.2 Incidence

Ectopic pregnancy accounts for approximately 2% of all reported pregnancies according to the Centers for Disease Control and Prevention (7). However, the true current incidence of ectopic pregnancy is difficult to estimate because patients are increasingly treated in an outpatient setting where events are not tracked (8). The incidence of ectopic pregnancy varies depending on multiple risk factors including age, race, reproductive history, and more. A study from the United States on emergency department data reported an increasing EP incidence between 2006 and 2013, from 7.0 to 8.3 per 1000 pregnancies (9). In the United Kingdom, an incidence of 11 per 1000 pregnancies has been reported (3). In IVF pregnancies, a much higher rate of 2.6%–8.6% EP was reported (10, 11). Increasing age is associated with higher incidence of EPs, peaking at 42 per 1000 women aged 40–49 years (12). Black women in the United States have a 1.46 relative risk of experiencing EP compared to white women, as well as a higher mortality risk (2, 13).

11.3 Etiology

EP results from interruption of the natural migration of the fertilized egg to the endometrium. Disruption of the normal tubal anatomy (from infection, surgery, or congenital anomalies), tubal dysfunction (malfunction or damage to ciliary activity), or inherent embryo factors may be the underlying causes of EP. Several risk factors for EP occurrence have been identified; however, in up to 50% of EP cases no identifiable risk factors are found (14).

11.4 Risk Factors

A history of a prior EP is associated with a 10% risk of recurrence with one previous occurrence, and 25% with two or more prior EPs, or up to eightfold compared with other pregnant women (14, 15). A history of pelvic inflammatory disease or other pelvic infections can cause tubal pathology and is associated with an odds ratio of more than three for EP occurrence (15, 16). Past chlamydia infection is associated with a greater than threefold risk of EP (15). Among women with EP, chlamydia was cultured in up to 30% (17). The risk of EP among women with infertility is two- to threefold compared with women without infertility (15). In vitro fertilization is associated with EP in some reports, with up to ninefold increased risk (11, 18, 19). However, the increased risk is probably attributed to tubal factors rather than the use of IVF itself (15). Intrauterine contraceptive devices are very effective in preventing EP occurrence. The risk of EP is one-tenth among women using IUDs compared with women not using contraception (18, 20). However, in the rare cases that pregnancy occurs, the risk of EP is higher compared with women not using contraceptives. Among users of oral contraceptives, patches, vaginal rings, or implants, the risk of contraceptive failure is also very low. In cases of failure, the reported risk of EP varies among studies, with some reporting lower risk compared with non-contraceptives users (20), while others report an up to fourfold higher risk among oral contraceptives users (15, 20, 21). Smoking causes alteration in ciliary motility and is associated with increased EP risk (1, 22). Other reported risk factors include increased maternal age, previous pelvic surgery, tubal sterilization, endometriosis, vaginal douching, and African American race (12, 13, 15, 23–25).

11.5 Fallopian Tube Ectopic Pregnancy

The most common EP location is the fallopian tube, accounting for more than 90% of cases (1). Within the tube, the most common sites of implantation are the ampulla (70%), isthmus (12%), and the fimbria (11%). Histologic findings in tubal EPs that may impair embryo transfer include chronic salpingitis in up to 90% of cases (26). This histologic finding includes attenuation and blunting of the plicae, and tubal wall infiltration by lymphocytes and plasma cells. Salpingitis isthmica nodosa, a condition in which the tubal mucosa penetrates the myosalpinx, is present in up to 57% of patients with tubal EPs (27). Several endocrine factors may be associated with premature embryo implantation (28).

The most common clinical manifestations of tubal EPs are abdominal pain and vaginal bleeding (29). However, tubal EP can also be asymptomatic. Abdominal pain originates from the distended tube and typically presents between 5 and 7 weeks of gestation. There are no pathognomonic pain characteristics. Pain is typically located in the pelvis and can be diffuse or located to one side. Tubal rupture is associated with abrupt, severe abdominal pain, as well as shoulder pain from diaphragmatic irritation by blood. Vaginal bleeding is typically preceded by amenorrhea. The bleeding is presumed to originate from sloughing of the decidualized endometrium, not from the tube itself.

Physical examination should initially include assessment of hemodynamic stability and confirmation of pregnancy (1). Abdominal examination may reveal tenderness, peritoneal signs, and/or a distended abdomen in ruptured EP cases. Cervical motion tenderness may be present, and a palpable mass may be present in 50% of cases (30). Clinically stable

DOI: 10.1201/9781003312109-11

patients should undergo a thorough examination to diagnose the pregnancy location, as discussed in the following sections. Unstable patients with a suspected EP should undergo a prompt surgical intervention.

11.6 Ultrasound

A transabdominal ultrasound may be performed to rule out intraperitoneal bleeding. If intraperitoneal bleeding is observed, the diagnosis of EP should be considered until proven otherwise. Transvaginal ultrasound (TVUS) is the most useful test and the modality of choice for determining pregnancy location. It should be performed as part of the initial evaluation of suspected EP and may need to be repeated based on the findings, β-hCG levels, and clinical presentation (31).

The presence of an adnexal mass, separated from the ovary, is the most common sonographic finding in EP. It is present in up to 89% of EP cases (32). The positive predictive value of this finding is 80% (31), and the pooled sensitivity and specificity are 67.3 and 94.9, respectively (33). The presence of gestational adnexal sac with a yolk sac or an embryo is diagnostic of EP, but is present in only 10%–17% of cases (34). A finding of an empty uterine cavity has a sensitivity of 81% and a specificity of 80% to detect EP (33). Pseudogestational sac is the collection of fluid within the endometrial cavity, mimicking an intrauterine pregnancy. This sonographic finding is a thickened decidual reaction surrounding an intrauterine fluid collection (33). Pseudosacs may occur in up to 15% of patients with EPs and may cause diagnostic confusion (35). The presence of free fluid in the posterior cul-de-sac has a sensitivity and specificity of 52% and 94%, respectively for the diagnosis of EP (33). A large amount of free fluid and debris may be consistent with ruptured EP. However, this sonographic finding is also found in other conditions including physiologic free fluid or ruptured adnexal cysts. The visualization of an intrauterine gestational sac with a yolk sac or an embryo refute the diagnosis of EP except in the rare cases of heterotopic pregnancies, discussed later in this chapter (36). In many cases, transvaginal ultrasound is not diagnostic because the pregnancy is too early to be diagnosed by ultrasound. This condition is called a "pregnancy of unknown location," and effort should be made to establish a definitive diagnosis of pregnancy location, as discussed later in this chapter (37).

11.7 Laboratory Testing

Initial laboratory testing should include a complete blood count, serum β-hCG level, Rhesus (Rh) blood type, and cross matching. Other laboratory testing may include renal and liver function tests, in preparation for possible methotrexate treatment for EP.

11.8 β-hCG

Serum β-hCG is the preferred test for pregnancy evaluation, rather than urine β-hCG. hCG can be detected in the serum six days after the luteinizing hormone (LH) surge. In normal intrauterine pregnancies, β-hCG levels rise in a curvilinear fashion until approximately 10 weeks of gestation, to a plateau of 100,000 mIU/mL (38). Single β-hCG levels should not be used to determine viability or location of a pregnancy because of the wide range of normal levels as pregnancy progresses (7). Rather, serial β-hCG levels should be used to differentiate between normal and abnormal pregnancies (39–41). In normal intrauterine pregnancies, β-hCG levels are expected to rise by 35%–53% over 48 hours (39, 40). Based on a 35% value, using two serial measurements will misclassify 7.7% of intrauterine pregnancies, while using three serial β-hCG measurements will decrease misclassification of an intrauterine pregnancy to 2.7% and lower the risk of unnecessary intervention. β-hCG level rise are dependent on the initial value, with slower rise when initial levels are high (42). For example, in initial levels of less than 1500 mIU/mL, the expected β-hCG level rise is 49%, compared with 33% for an initial β-hCG level of greater than 3000 mIU/mL. Abnormal β-hCG level rise is suspicious of an abnormal pregnancy, either early pregnancy loss or ectopic pregnancy. However, normal β-hCG rise patterns do not exclude the possibility of an ectopic pregnancy (43). Thus, serum β-hCG levels alone should not solely direct the clinical management of suspected EPs. History, physical examination, and ultrasound examinations should be used to make an accurate diagnosis (30).

β-hCG plateau or decline is usually suggestive of a nonviable pregnancy (7). β-hCG levels in EPs are expected to decline slower than intrauterine nonviable pregnancies (30). In a resolving pregnancy of unknown location, a β-hCG decline of 35%–50% at 2 days and 66%–87% at 7 days from first β-hCG measurement level is expected (44). A drop of 85% within 4 days or 95% within 7 days can rule out EPs nearly 100% of the time (45). These expected decline rates can aid in the management of suspected EPs but should be combined with clinical judgment to direct decision making.

11.9 Other Endocrine Markers

Serum progesterone levels are higher in intrauterine viable pregnancies than EPs or nonviable pregnancies (46). Serum progesterone levels greater than 25 mg/mL are associated with viable intrauterine pregnancies, while levels of < 5 mg/mL are associated with pregnancy failure (47–49). However, progesterone levels vary widely with limited discriminative capacity, and the threshold for the diagnosis of nonviable pregnancies or EPs has not been established. Thus, serum progesterone levels should not be used for clinical decision making in suspected EPs.

11.10 Pregnancy of Unknown Location

Pregnancy of unknown location (PUL) is a term used to describe a condition in which a positive pregnancy test is accompanied by a transvaginal ultrasound exam that does not demonstrate either intra- or extrauterine pregnancy (37). PUL should not be considered a final diagnosis, rather a definition used while efforts are made to establish a final diagnosis (36). Women with PUL, if clinically stable, should have repeat ultrasound and β-hCG measurements to achieve a final diagnosis and guide management (37, 39). Among women with PUL, the final diagnoses differ considerably among studies. Intrauterine pregnancies are diagnosed in 30%–47% of casesand EP in 6%–20%, and in 50%–70% of cases a final pregnancy location is not reported (50–56).

The β-hCG discriminatory zone is the serum level at which a gestational sac should be identified by transvaginal ultrasound (57, 58). The absence of a gestational sac in the presence of a

β-hCG measurement above the discriminatory level strongly suggests either an early pregnancy loss or an EP (7). Using a discriminatory level of > 3510 mIU/mL, 99% of gestational sacs should be visualized, compared with 80% in β-hCG levels of 1500 mIU/mL (58). Discriminatory zone levels should be used with caution, as 1% of viable pregnancies can still be not identified above a 3510 mIU/mL level, and other factors can affect detection rate including operator skill, ultrasound equipment quality, and uterine fibroids. Importantly, there is no discriminatory zone for EP, and β-hCG levels do not correlate with the EP sac size.

The initial management of patients with PUL depends on their hemodynamic stability and whether the pregnancy is desired. Unstable patients should receive immediate fluid resuscitation and surgical intervention. In a hemodynamically stable patient, shared decision making is important to guide further management.

In patients that desire pregnancy continuation, hCG levels and periodic TVUS should be performed (59). Serial β-hCG levels should be obtained typically every 48 hours. β-hCG rise in viable intrauterine pregnancies should be according to the levels described previously in this chapter. The optimal interval at which transvaginal ultrasound should be performed has not been defined. If β-hCG levels increase appropriately, TVUS should be performed once they reach the discriminatory zone. If β-hCG levels are declining by more than 50% at 48 hours, the pregnancy is likely resolving spontaneously. In such cases, expectant management with weekly β-hCG measurements can be taken until undetectable (59). Alternatively, active management can be considered. A randomized controlled trial showed that up to 40% of patients with PUL and low serum β-hCG levels managed expectantly will eventually undergo a medical or surgical intervention (60).

For patients who do not desire pregnancy continuation, both active and expectant management can be considered. Active management is associated with a higher chance of successful resolution and less change from the initial management strategy (61). Diagnostic uterine evacuation followed by examination of the contents for pregnancy tissue is typically performed (59). If chorionic villi are present, an intrauterine pregnancy can be confirmed. Absence of chorionic villi does not confirm the presence of EP, as curettage sensitivity is only 70%, and pipelle endometrial biopsy sensitivity is 30%–60% (58, 62, 63). If chorionic villi are not identified, serial β-hCG measurements should be done to ascertain pregnancy resolution (59). A fall of 15%–20% 24 hours after uterine evacuation suggests that the pregnancy was intrauterine. In such cases β-hCG levels should be followed weekly until indetectable (61). If β-hCG levels do not decrease appropriately, methotrexate should be offered (7, 64). Alternative active management options include empiric methotrexate or diagnostic laparoscopy if contraindications to methotrexate treatment exist and there is a high suspicion for EP (59).

11.11 Management of Ectopic Pregnancies

Management of EPs requires medical or surgical intervention, and in select cases, expectant management. The decision on management strategy should be guided by the clinical presentation, laboratory and imaging findings, and the patient's informed choice following a discussion on the risks and benefits of each approach (7).

11.12 Medical Management

Methotrexate (MTX) is the only recommended medical treatment of EPs (7). It is a folic acid antagonist that binds to and inhibits dihydrofolate reductase, inhibiting the formation of reduced folates and thymidylate synthetase, resulting in inhibition of purine and thymidylic acid synthesis, thus interfering with DNA synthesis, repair, and cellular replication. Its primary activity is in rapidly dividing cells such as malignant cells, trophoblasts, and fetal cells (65). Systemic methotrexate was originally used for the treatment of gestational trophoblastic disease and was first used to treat EP in 1982 (66, 67).

Compared with surgery, methotrexate has similar treatment efficacy and results in similar fertility outcomes (68, 69). Methotrexate treatment can be considered in hemodynamically stable patients who do not have contraindications to medical treatment (7). A practice committee of the American Society for Reproductive Medicine (ASRM) has outlined the following absolute contraindications to methotrexate treatment (70):

- Intrauterine pregnancy
- Evidence of immunodeficiency
- Moderate to severe anemia, leukopenia, or thrombocytopenia
- Sensitivity to MTX
- Active pulmonary disease
- Active peptic ulcer disease
- Clinically important hepatic dysfunction
- Clinically important renal dysfunction
- Breastfeeding
- Ruptured ectopic pregnancy
- Hemodynamically unstable patient

Relative contraindications include (70):

- Embryonic cardiac activity detected by transvaginal ultrasonography
- High initial β-hCG concentration (> 5000 mIU/mL)
- Ectopic pregnancy > 4 cm in size as imaged by transvaginal ultrasonography
- Refusal to accept blood transfusion
- Inability to participate in follow-up

Before MTX administration, a complete blood count (CBC), liver function tests, serum creatinine levels, blood type, and Rh status should be performed. In women with a history of pulmonary disease, a chest X-ray should be performed because of their increased risk of interstitial pneumonitis (70).

MTX is commonly administered intramuscularly. Oral MTX has been studied but data is limited and this route of administration is currently not recommended (7, 71). Three MTX treatment protocols have been published: single dose, two dose, and multiple dose (72–74). The treatment protocols are presented in Table 11.1.

11.13 Methotrexate Protocols Efficiency

11.13.1 Single Dose

Approximately 15%–20% of patients treated with the single-dose protocol will require an additional MTX dose because of insufficient β-hCG decline (75, 76). However, less

TABLE 11.1 Methotrexate Treatment Protocols (72–74)

Single-dose regimen

- Administer MTX 50 mg/m^2 IM on day 1
- Measure β-hCG level on posttreatment day 4 and day 7
  - If decrease > 15%, measure β-hCG levels weekly until reaching nonpregnant level
  - If decrease < 15%, readminister MTX 50 mg/m^2 IM and repeat β-hCG level
  - If β-hCG does not decrease after two doses, consider surgical management
- If β-hCG levels plateau or increase during follow-up, consider administering MTX for treatment of a persistent ectopic pregnancy

Two-dose regimen

- Administer MTX 50 mg/m^2 IM on day 1
- Administer second dose of MTX 50 mg/m^2 IM on day 4
- Measure β-hCG level on posttreatment day 4 and day 7
  - If decrease > 15%, measure β-hCG levels weekly until reaching nonpregnant level
  - If decrease < 15%, readminister MTX 50 mg/m^2 IM on day 7 and check β-hCG levels on day 11
  - If decrease 15% between day 7 and day 11, continue to monitor weekly until reaching nonpregnant levels
  - If decrease < 15% between day 7 and day 11, readminister dose of MTX 50 mg/m^2 IM on day 11 and check β-hCG levels on day 14
  - If β-hCG does not decrease after four doses, consider surgical management
- If β-hCG levels plateau or increase during follow-up, consider administering MTX for treatment of a persistent ectopic pregnancy

Fixed multiple-dose regimen

- Administer MTX 1 mg/kg IM on days 1, 3, 5, 7; alternate with folinic acid 0.1 mg/kg IM on days 2, 4, 6, 8
- Measure β-hCG levels on MTX dose days and continue until β-hCG has decreased by 15% from its previous measurement
  - If decrease > 15%, discontinue administration of MTX and measure β-hCG levels weekly until reaching nonpregnant levels
  - If β-hCG does not decrease after four doses, consider surgical management
- If β-hCG levels plateau or increase during follow-up, consider administering MTX for treatment of a persistent ectopic pregnancy

Abbreviations: β-hCG – human chorionic gonadotropin, IM – intramuscular, MTX – methotrexate

than 1% of patients will require more than two MTX doses (75). Success rate is dependent upon the initial β-hCG level (7, 77). Initial β-hCG < 5000 mIU/mL is associated with a 3.7% failure rate compared with 14.3% with initial β-hCG > 5000 mIU/mL.

11.13.2 Two Dose

In a meta-analysis of four randomized controlled trials, the two-dose protocol was associated with an 87% success rate (78).

11.13.3 Multiple Dose

The multiple-dose protocol was associated with 9.5% treatment failure rate in a meta-analysis of three randomized controlled trials (78).

11.13.4 Protocol Comparison

The reported overall success rate of MTX treatment ranges from 78% to 96% using the three protocols (68, 75, 79, 80). In a meta-analysis of seven randomized controlled trials, the single- and multiple-dose protocols had comparable treatment failure rates (9.5% vs 15.9%, respectively), but the multiple dose was associated with significantly higher adverse reactions rate (odds ratio [OR] 95% confidence interval [CI] 2.10 [1.24–3.54]) (78). In a systematic review, the single dose was less expensive than the multiple-dose protocol and patient acceptance was higher (81).

In the aforementioned meta-analysis, compared with the single-dose protocol, the success rate in the two-dose protocol was higher (OR 95% CI: 1.84 [1.13–3.00]), especially in a high β-hCG group, > 3000 mIU/mL (OR 95% CI: 3.23 [1.53–6.84]), and large gestational sac group, > 2 cm (OR 95% CI: 2.92 [1.23–6.93]) but was also associated with more adverse reactions (OR 95% CI: 1.53 [1.01–2.30]) (78). In conclusion, the two-dose protocol was superior to the single-dose protocol for the treatment of women at higher risk for failure.

11.13.5 Adverse Reactions

Adverse reactions to MTX treatment are dose dependent. The most common side effects are gastrointestinal (nausea, vomiting, stomatitis). In a meta-analysis including four randomized controlled trials, adverse reactions were reported in 22% of women treated with a single-dose and in 31% of women treated with a two-dose regimen. The multiple-dose regimen was associated with 41% adverse reaction rate (75). Liver enzyme elevation, alopecia, and pneumonitis are rare complications of MTX treatment. Liver enzyme elevation usually resolves following discontinuation of MTX (80, 82).

11.13.6 Combination Protocols

Mifepristone, a progesterone receptor antagonist, was studied as adjunct therapy to MTX. In a meta-analysis of three randomized controlled trials including 442 patients, the combination of MTX and mifepristone had similar success rates, operation rates, adverse reactions, and need for additional MTX dose compared with MTX alone (83). Gefitinib, a selective epidermal growth factor receptor inhibitor, was also studied as a combination therapy for EPs. In a randomized, placebo-controlled trial comparing gefitinib and MTX versus MTX alone for the treatment of tubal EPs, the addition of gefitinib resulted in similar rates of surgical intervention, time to resolution, and serious adverse events as MTX alone (84). However, the occurrence of diarrhea and rash was higher in the gefitinib groups.

11.13.7 Follow-Up after Methotrexate Treatment and Patient Instructions

Following MTX treatment, β-hCG levels may increase despite cessation of production by cytotrophoblast due to continued β-hCG production by syncytiotrophoblast (85, 86). A > 50% increase in β-hCG levels between days 1–4 may be

associated with a lower success rate; however, it should not affect management, as the 4–7 days change in β-hCG levels should guide management. β-hCG levels typically progressively decrease after the initial increase (31). After MTX treatment, the gestational sac may increase in size on ultrasound exam as well, likely due to hematoma formation. This phenomenon is not associated with treatment failure. There is no indication for routine ultrasound surveillance after MTX treatment because findings do not affect management (87, 88). β-hCG levels usually become undetectable within 2–4 weeks but could take up to 8 weeks after MTX treatment to resolve (75). Mild to moderate abdominal pain following MTX is expected due to tubal abortion or expansion because of hematoma formation. In contrast, severe abdominal pain may be a sign of tubal rupture, necessitating an ultrasound exam to rule out hemoperitoneum (89, 90). Immediate surgery is required in cases of tubal rupture.

The following patient recommendations by the ASRM have been published (70):

- Avoid intercourse until β-hCG is undetectable
- Avoid pelvic examinations and ultrasound during surveillance of MTX therapy
- Avoid sun exposure to limit risk of MTX dermatitis
- Avoid foods and vitamins containing folic acid
- Avoid gas-forming foods because they produce pain
- Avoid trying to conceive until β-hCG is undetectable

In addition, nonsteroidal anti-inflammatory drugs are usually avoided during therapy because these medications may decrease MTX efficacy (7).

Although some experts continue to recommend that women delay pregnancy for at least 3 months after the last dose of methotrexate, there is no evidence to support this time interval (91, 92). In a study comparing women conceiving < 6 months or ≥ 6 months after MTX treatment, there was no difference in the rates of fetal malformations or adverse outcomes (91).

Based on the available evidence, MTX treatment for EP does not adversely affect subsequent fertility or ovarian reserve (93, 94). In a prospective study of 25 women treated with MTX for EP, serum AMH levels before and after MTX treatment were similar, as well as cycle duration, gonadotropin requirements, E2 peak levels, number of oocytes retrieved, and total number of embryos obtained (93). A systematic review and meta-analysis of seven observational studies including 329 women reported similar results (94).

11.13.8 Expectant Management of Tubal Ectopic Pregnancies

Successful expectant management of EP is defined as reaching an undetectable level of β-hCG without complications or conversion to a treatment method. While medical or surgical treatments are the mainstay of EP treatment, expectant management can be considered in specific circumstances for tubal EPs. Mainly, candidates for expectant management should be asymptomatic and have a relatively low β-hCG level.

Spontaneous resolution in expectant management of EP depends upon the initial β-hCG level. For example, in a prospective observational study, 88% of patients with an initial β-hCG level of less than 200 mIU/mL experienced spontaneous resolution of the EP (95). In another prospective study, when initial β-hCG levels were 175–1500 mIU/mL, spontaneous resolution occurred in 66% of cases (96).

Several randomized controlled trials compared MTX to placebo for the treatment of tubal EP. A meta-analysis including two randomized controlled trials comparing MTX to placebo for the treatment of tubal EP in patient with β-hCG < 1500 IU/l, including a total of 103 patients, yielded no difference between groups in EP resolution, need for surgery, or time to resolution (97). Treatment success rates among patients managed expectantly was 80% compared to 83% among women treated with MTX. Avoidance of surgery was successful in 80% of women managed expectantly and 85% of women treated with MTX. Observational studies have reported similar results. In a literature review of 700 cases managed expectantly, spontaneous resolution occurred in 69% (98).

The National Institute for Health and Care Excellence (NICE) published guidelines for expectant management (99). According to the NICE, expectant management can be offered as an option for women who:

- Are clinically stable and pain free, and
- Have a tubal ectopic pregnancy measuring less than 35 mm with no visible heartbeat on transvaginal ultrasound, and
- Have serum β-hCG levels < 1000 IU/L or > 1000–1500 IU/L, and
- Are able to return for follow-up

A decrease of ≥ 15% from the previous value on days 2, 4, and 7 is adequate, and subsequent weekly β-hCG levels should be monitored. If levels decrease by < 15%, plateau or rise from the previous value, or in cases of severe abdominal pain or tubal rupture with hemoperitoneum, expectant management should be abandoned, and medical or surgical treatment should be initiated (7, 99).

11.13.9 Subsequent Fertility

Subsequent conception rates following expectant management appear to be similar to medical or surgical treatment. Overall, the reported intrauterine pregnancy rates range 63%–84% (100–103). Two of these studies compared fertility outcomes following expectant versus surgical management. In one study of 146 women who tried to conceive after the EP, the rate of intrauterine pregnancy was higher in the expectant management group compared to the salpingectomy group (84% vs 64%) (102). Another study on 97 women found no difference in intrauterine pregnancy rates following expectant or surgical management (65% vs 54%, respectively) (103).

11.14 Surgical Management

While medical management of ectopic pregnancy has benefits, including avoiding the inherent risks of surgery and anesthesia, it has a lower success rate and requires longer surveillance (68). Surgical management of ectopic pregnancy varies based on the pregnancy location as well as individual clinical scenarios and patient preferences. Surgical management is indicated in cases of suspected ruptured EP and with patients exhibiting hemodynamic instability or signs of ongoing intraperitoneal bleeding. Surgical management also may be required in stable patients who have contraindications to medical management or when medical management has failed. In clinically stable patients, the decision requires consideration of clinical, laboratory, and radiologic data and determination of patient treatment preference via thorough patient

counseling on the risks, benefits, alternatives, and expectations of the appropriate management options (7). It is also important to consider future fertility goals, as surgical management should be considered in patients who require concurrent surgery. For example, patients who desire permanent sterilization may opt for bilateral salpingectomy, or patients who are planning to undergo IVF may opt for salpingectomy for removal of any hydrosalpinx concurrently with treatment of the ectopic pregnancy.

Laparoscopy is the standard of care when surgery is required or opted for (68, 104, 105). Ample evidence exists to establish laparoscopic management of tubal ectopic pregnancy as the superior approach over laparotomy. In a randomized trial comparing abdominal salpingectomy and laparoscopic salpingectomy for the treatment of tubal pregnancy, laparoscopy decreased operative time, length of stay, and recovery time with no difference in resolution of ectopic pregnancy (104). Another randomized control trial comparing abdominal salpingostomy with laparoscopic salpingostomy noted a significant reduction in blood loss and hospital stay in the laparoscopy group, with no difference in rates of residual trophoblastic disease, tubal patency, or pregnancy rates postoperatively (105). Notably, laparoscopy was also more cost-effective (68).

Laparoscopy should be performed in the usual manner with the minimal number of access ports required to safely perform the procedure. Specimen retrieval should be done in a manner to prevent spillage of trophoblastic tissue. A posterior colpotomy or use of a single 10–12 mm port can be considered for retrieval depending on the size of specimen.

Upon entry a complete abdominal survey should be completed, the pelvis should be visualized, the ectopic identified, and hemostasis achieved with minimal tissue trauma. Hemostasis often occurs with resection of the pregnancy itself via salpingectomy or salpingostomy. In cases of nontubal pregnancy, organ preservation is typically achievable. Laparoscopic resection of the ectopic can frequently be completed and the organ in which implantation occurred can be repaired with absorbable suture. Electrosurgery can be employed for hemostasis as needed, though discrete and focal use is encouraged.

11.15 Salpingectomy versus Salpingostomy

Surgical treatment of tubal pregnancy is completed using salpingectomy (removal of the tube and the ectopic pregnancy it contains) or with salpingostomy (removal of the ectopic pregnancy from the tube with a linear incision). There is still some debate over the preferred procedure. Salpingostomy spares the tube with a potentially increased risk of persistent trophoblast tissue and recurrent ectopic pregnancy. Salpingectomy removes the tube, avoiding the risk of retained trophoblastic tissue and recurrent tubal pregnancy at the same site. Therefore, whether to perform salpingostomy or salpingectomy for the treatment of tubal ectopic pregnancy is guided by the clinical scenario, the current state of both the affected and unaffected tube, and the patient's fertility goals.

Importantly, randomized clinical trials (RCTs) that compare salpingectomy and salpingostomy for tubal ectopic management found no statistical difference in recurrent ectopic pregnancy or subsequent intrauterine pregnancy rates (106). These RCTs failed to demonstrate a significant difference in future fertility prospects for salpingectomy versus salpingostomy when the contralateral fallopian tube appeared healthy at the time of surgery (107, 108). However, cohort studies published on the same topic noted contrasting results (106). In the cohorts, there was a higher subsequent intrauterine pregnancy rate and a higher recurrent ectopic rate in the salpingostomy group. Additionally, there was a significantly higher rate of persistent trophoblastic tissue requiring intervention in the salpingostomy group.

Because there is no clear benefit of salpingostomy, salpingectomy is generally the preferred option (7, 109), especially in cases with significant tubal damage or heavy bleeding or in patients with a healthy contralateral fallopian tube (7). If the contralateral tube is damaged or surgically absent, a salpingostomy may be considered to preserve reproductive capacity for spontaneous pregnancy if the patient desires (7). Notably, subsequent pregnancy rates were higher in all groups when the contralateral fallopian tube appeared healthy at the time of surgery (106). In addition, if pelvic adhesions or contralateral tubal damage existed at the time of salpingectomy for tubal pregnancy, the subsequent pregnancy rate was significantly lower (108).

The majority of tubal pregnancies implant in the ampullary portion of the fallopian tube which is the area most favorable for salpingostomy. The isthmic portion is less favorable to salpingostomy as lower postoperative patency rates have been reported, as has an increased risk of significant bleeding (110). Because the risk of incomplete removal of trophoblastic tissue is higher in salpingostomy, serial β-hCG monitoring is recommended to ensure resolution of the pregnancy. If the β-hCG trend is concerning for retained products, a single methotrexate dose can be considered (111).

11.16 Other Ectopic Pregnancy Locations

11.16.1 Interstitial Ectopic Pregnancy

An EP that is located in the proximal segment of the fallopian tube, within the muscular uterine wall, is an interstitial EP. These EPs comprise 2%–4% of EPs (112). Risk factors for interstitial EPs are similar to tubal EPs except for ipsilateral salpingectomy (113). Most cases are diagnosed between 6 and 8 weeks gestation (113). These pregnancies are particularly dangerous because the location near the myometrium and uteroovarian ligament creates a unique potential for life-threatening hemorrhage. Mortality rates from interstitial pregnancy have been reported near 2.5%, significantly higher than other tubal ectopic pregnancies (114).

Interstitial pregnancy is often termed "cornual pregnancy," due to the location within the region of the uterine cornua. However, this term is nonspecific and simply describes implantation in the upper and lateral uterine cavity or within a uterine horn (115). Moreover, pregnancy implanted in a uterine horn is often referred to as a cornual pregnancy. Examples include a communicating horn of a bicornuate uterus (not considered an ectopic) or a noncommunicating rudimentary horn (considered an ectopic) (115).

Interstitial pregnancy can also be confused with angular pregnancy, which occurs when an embryo is implanted eccentrically in the endometrial cavity, as it is medial to the ostia (116). Angular pregnancies are technically within the uterine cavity and therefore not considered ectopic (115). Despite the terms interstitial, angular, and cornual pregnancy being used relatively interchangeably in the past, these are distinct entities with distinct prognoses (Figure 11.1).

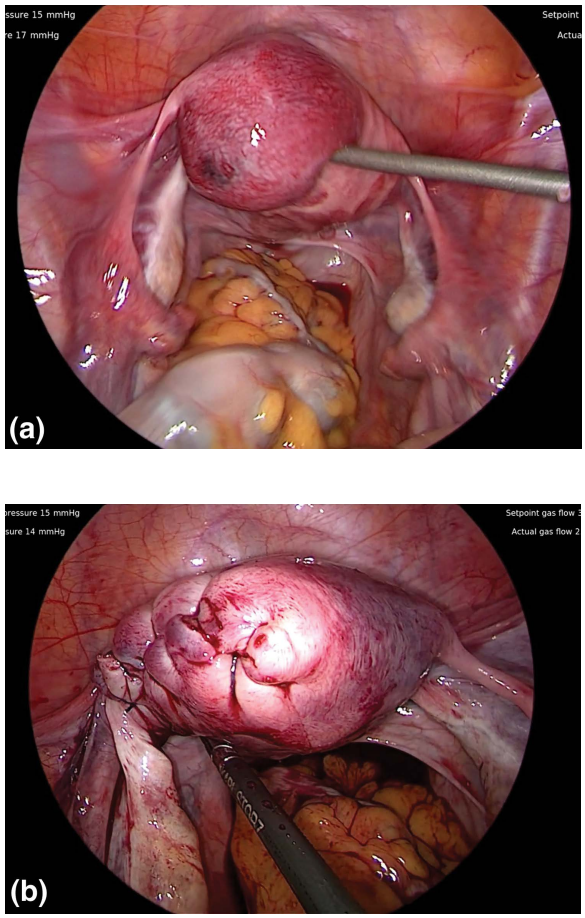


FIGURE 11.1 An interstitial ectopic pregnancy: (a) Prior to resection; (b) after suture repair.

Angular pregnancy should be monitored closely, but unlike interstitial pregnancy, requires consideration of expectant management as well as medical or surgical management. This is especially true in cases of desired pregnancy as normal term gestations have been reported in cases of angular pregnancy despite their eccentric implantation (115). Angular pregnancies end in miscarriage in 38% of cases (113). Later complications include persistent pelvic pain, vaginal bleeding, retained placenta, and uterine rupture (117). Although no specific treatment guidelines exist, it is believed that an angular pregnancy with increased thickness of surrounding myometrium is less likely to rupture. With advancements in pelvic imaging, angular and interstitial pregnancy can be diagnosed separately with unique criteria. Delineating these entities is important, given the prognostic differences (115).

Interstitial pregnancy can be diagnosed radiographically with the presence of the "interstitial line sign" (118). This is the separation of the gestational sac from the empty endometrial cavity, but instead within the interstitial portion of the fallopian tube; it can be noted as a thin echogenic line on transvaginal ultrasound. In comparison, an angular pregnancy can be diagnosed when the pregnancy is contiguous with the endometrial stripe despite its eccentric location (118). The endomyometrial mantle thickness is another distinguishing factor. Mantle thickness less than 5 mm supports interstitial ectopic pregnancy while a value more than 8 mm is suspicious for angular pregnancy (119). Pelvic magnetic resonance imaging (MRI) may be helpful in the diagnosis, and criteria are similar to those described in ultrasound (115, 120). During laparoscopy, interstitial ectopic pregnancy can be distinguished from angular pregnancy by the location of the gestational sac bulge (117). While the bulge of an interstitial pregnancy is lateral to the round ligament, the bulge of an angular pregnancy is medial to the round ligament and displaces the round ligament laterally.

Reported nonsurgical management including systemic of local methotrexate treatment and expectant management success rates range 70%–94% (112, 121). However, studies are of limited sample size due to the rarity of interstitial EPs. The most common MTX protocol for interstitial EP is the multidose regimen. Local methotrexate injection can be as effective as systemic methotrexate administration (112, 122, 123).

Surgical treatment of interstitial ectopic pregnancy is a frequently used approach given the high risk of hemorrhage in these cases. Surgery in clinically stable patients should be considered when medical management has failed or is not feasible, in recurrent interstitial EPs, or for those who decline blood transfusion (to minimize risk of hemorrhage secondary to rupture). Surgery is immediately indicated in those with signs of rupture, internal hemorrhage, or severe pain. Surgical management of interstitial pregnancy includes cornuotomy and cornual resection (usually with removal of the ipsilateral fallopian tube) (109). Hysterectomy is an option but is often unnecessary outside of emergent life-threatening hemorrhage. Laparoscopy remains the standard of care, and considerations for prevention of blood loss should be taken. Injection of dilute vasopressin into the surrounding myometrium, use of endoloops, ultrasonic energy, and temporary ligation of the uterine arteries and/or utero-ovarian ligament have been suggested as effective means of reducing blood loss and improving ease of resection and laparoscopic closure during cornuotomy or cornual resection (Figure 11.2) (124, 125).

Cornuotomy has been described as the creation of a linear incision over the ectopic pregnancy followed by resection of the EP without removing myometrium or fallopian tube (113), and the defect is closed. Cornuostomy is a similar procedure without closure of the defect but is generally not recommended given the unique potential for continued bleeding postoperatively. Laparoscopic cornual resection is essentially the laparoscopic equivalent of a cornual wedge resection. The interstitial pregnancy and the surrounding myometrium over the cornua are resected en bloc, then reapproximated via suture closure of the myometrium (113).

No conclusive evidence exists to support laparoscopic cornuotomy versus cornual resection, though both have been reportedly successful treatments (126). To date, most evidence is based on case reports and retrospective data. Some studies suggest cornuotomy confers a higher risk of residual pregnancy tissue requiring further treatment, but it has benefits of reduced operative time, intraoperative blood loss, and distortion of uterine anatomy (113, 126–128). In addition, a possible reduction in the risk of uterine rupture in subsequent pregnancies has also been reported (128).

Transcervical evacuation via hysteroscopy and suction curettage under ultrasound and/or laparoscopic guidance have been reported in case reports and case series. However, the transcervical approach is not commonly used due to the high risk of perforation and subsequent hemorrhage.

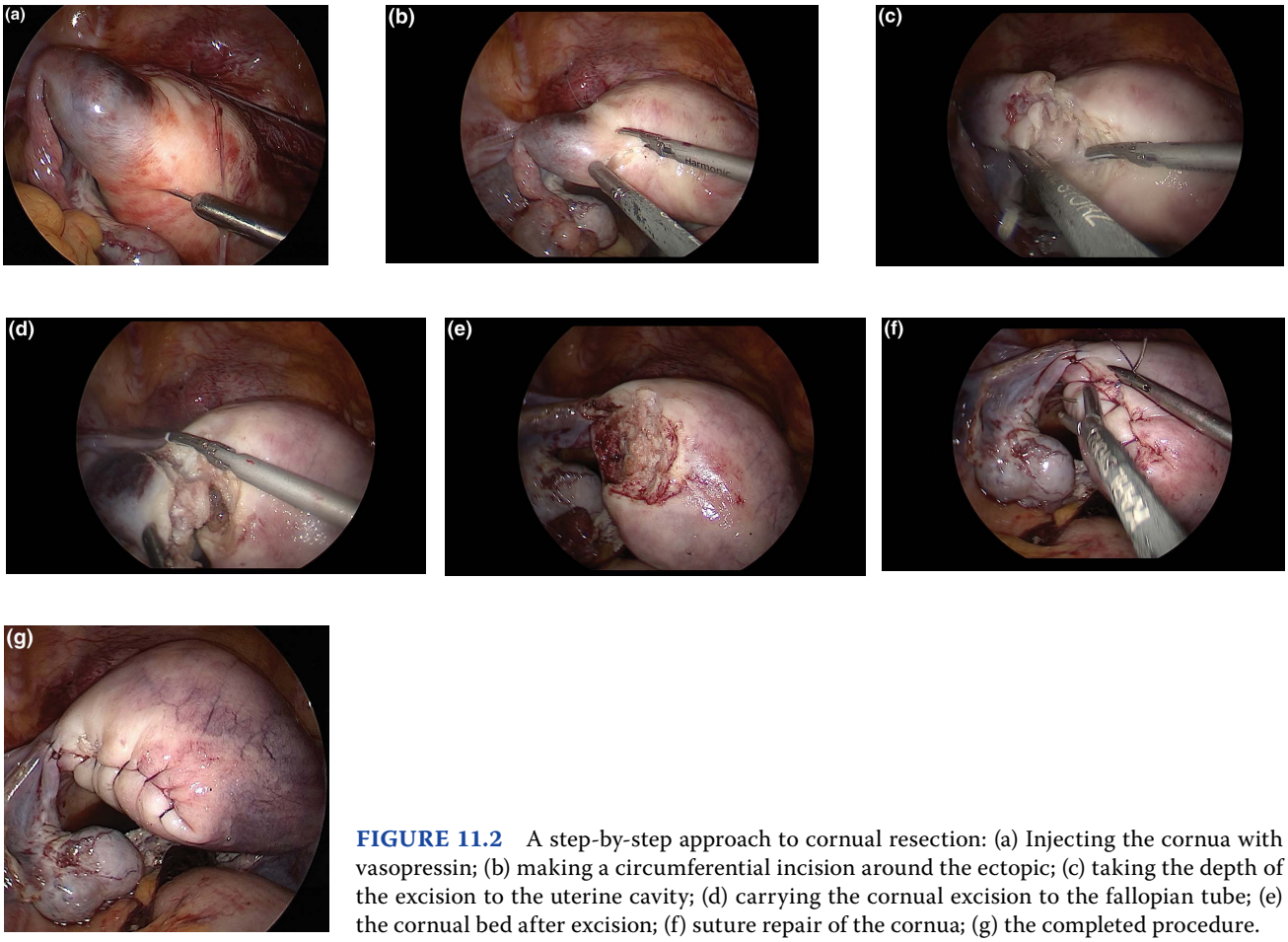


FIGURE 11.2 A step-by-step approach to cornual resection: (a) Injecting the cornua with vasopressin; (b) making a circumferential incision around the ectopic; (c) taking the depth of the excision to the uterine cavity; (d) carrying the cornual excision to the fallopian tube; (e) the cornual bed after excision; (f) suture repair of the cornua; (g) the completed procedure.

11.17 Cesarean Scar Pregnancies

Cesarean scar pregnancies (CSP) are pregnancies implanted on or in a scar from a prior cesarean delivery (Figure 11.3). The incidence of CSPs is rising due to an increase in cesarean section rates and is approximately 6% of EPs among women with prior cesarean deliveries (129, 130). CSPs are associated with an increased risk of uterine rupture in up to 13% when managed expectantly (131). Risk factors include prior CSP, other prior uterine surgeries, IVF, and manual removal of the placenta (132–134). One-third of patients are asymptomatic at presentation (135). Vaginal bleeding is the most common presenting symptom, in up to 90% of patients, followed by abdominal pain (130, 136). It has been suggested that CSP and placenta accreta spectrum (PAS) constitute a continuum of the same pathology, with CSP being a precursor of PAS (137–139).

The diagnosis is based on transvaginal ultrasound, preferably with Doppler. Sonographic criteria for the diagnosis of CSP include:

- An empty uterine cavity and closed, empty endocervical canal
- An early gestational sac close to the hysterotomy scar with a yolk sac, embryonic pole, or fetus
- An absent or thin myometrium between the gestational sac and the anterior uterine wall or the bladder
- Abundant Doppler flow around the gestational sac (140)

In hemodynamically stable CSP cases, management includes termination of the pregnancy, or, in select cases, expectant management including continuation of the pregnancy (141). If continuation of the pregnancy is decided, the management of CSPs is similar to PAS pregnancies. The optimal management in cases where termination of the pregnancy is chosen is unclear. Both medical and interventional treatments have been described, medical treatments of CSPs include local or intragestational injection of methotrexate. Systemic methotrexate treatment alone is not recommended due to the high risk of complications (142). Surgical treatment may be associated with a higher success rate. In one systematic review, pregnancy resolution rate was 62% for systemic or local methotrexate compared with 83% for surgical management (142, 143). In the case of fetal or embryo demise, expectant management can be considered, with up to 69% success rate (131). In such cases, weekly follow-up with serum β-hCG and transvaginal ultrasound is recommended until β-hCG levels are undetectable. Importantly, nonviable CSP can take several months to resolve spontaneously. Uterine aspiration can be used to hasten the CSP resolution (142).

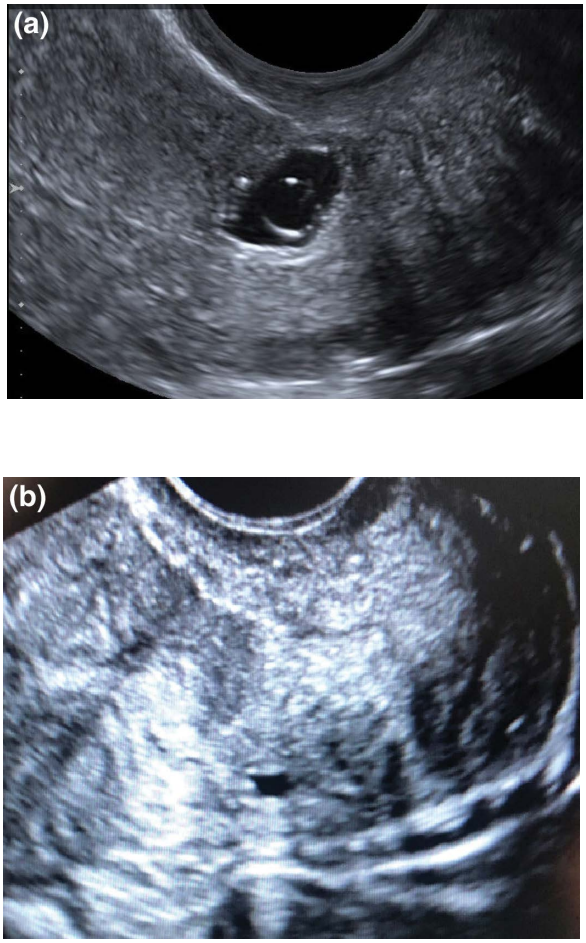


FIGURE 11.3 A cesarean scar ectopic pregnancy: (a) Preoperative images of the gestational sac in the cesarean scar, though no protrusion of the scar beyond the uterine serosa is seen; (b) intraoperative ultrasound immediately after suction curettage. The sac is removed and the scar is decompressed and no longer seen.

Surgical treatment of CSPs includes both laparoscopic and hysteroscopic approaches. There is limited data to support these approaches; mostly case reports exist thus far. As with any EP, patient status, clinical scenario, and future fertility goals should be considered. In addition, care should be taken in both approaches to reduce blood loss. Vasopressin, ligation of the uterine arteries (via uterine artery embolization or using temporary or permanent surgical ligation), and availability of electrosurgery for cautery should be considered. Hysteroscopic resection is useful given the direct visualization of the abnormal pregnancy. Hysteroscopic suction morcellators and/or resectoscopes can be useful in this approach. Care should be taken to prevent perforation in these cases. Laparoscopic resection of CSP is recommended in stable patients over laparotomy. Laparoscopic resection has been described as follows: creation of a bladder flap, identification of the prior hysterotomy and CSP, resection of the CSP (typically with an elliptical incision to also remove the scar tissue), and suture repair of the defect. This approach is similar to isthmocele (uterine niche) repair.

The Society of OB/GYN of Canada's EP treatment guidelines suggest physicians consider hysteroscopy for type 1 CSPs and consider laparoscopy for type 2 CSPs. The two types are designated as follows (134):

- *Type 1*: Implantation occurs on the hysterotomy scar with growth into the endometrial cavity. This is more likely to result in a viable birth; however, it is believed to have an increased risk of uterine rupture and/or abnormal placentation with potential for massive hemorrhage.
- *Type 2*: Implantation occurs within the hysterotomy scar or niche with growth into the scar and toward the bladder or abdominal cavity. This is more likely to result in rupture and associated hemorrhage.

11.18 Cervical Ectopic Pregnancy

In cervical pregnancies the embryo implants in the cervical tissue of the endocervical canal. These pregnancies account for less the 1% of all EPs (1). IVF is associated with a 2% risk for cervical pregnancy (144). Previous uterine curettage is also associated with increased risk of cervical pregnancy due to intrauterine adhesions, as well as induced abortion, uterine fibroids, and IUD presence (145). The most common clinical presentation is vaginal bleeding, which can be painless and profuse (146). Speculum examination may reveal a bulging and hyperemic cervix. The cervix may be closed or open, and occasionally blue or purple pregnancy tissue at the external os may be present. Bimanual examination should be avoided to prevent hemorrhage. The sonographic criteria for cervical pregnancies include the following:

- Gestational sac or placental tissue visualized within the cervix
- Cardiac motion noted below the level of the internal os
- No intrauterine pregnancy
- Hourglass uterine shape with ballooned cervical canal
- No movement of the sac with pressure from transvaginal probe (no "sliding sign" that is typically seen with incomplete abortions)
- Closed internal os (147)

As cervical pregnancies are rare, no established treatment options have been described. Methotrexate treatment, systemic and local, has been successful, with or without additional curettage (148, 149). Uterine artery embolization was also reported as effective treatment (150, 151).

Evidence for surgical treatment currently is entirely based on case reports and small case series. Surgical treatment is often necessary in patients that have failed or have contraindications to medical management or those who experience hemorrhage. It can also be considered in those who have significant pain. Surgical interventions reported include dilation and suction curettage and hysteroscopic resection. Hysteroscopic resection has been described using primarily resectoscope, with few cases of use of suction morcellators (152). Many reports utilize pretreatment with intramuscular or intragestational sac methotrexate, cervical Foley balloon placement (153), uterine artery embolization, or laparoscopic uterine artery ligation (152). Some surgeons describe placing stay sutures over the lateral cervix to ligate cervical branches of the uterine artery and potentially reduce bleeding (154). Intracervical vasopressin injection is another useful adjunct.

11.19 Ovarian Ectopic Pregnancy

Ovarian pregnancies comprise 1%–3% of EPs. No identifiable risk factors have been reported for ovarian EPs (145). A history of pelvic infection, infertility, or tubal disease is not associated with ovarian pregnancies. The clinical presentation of ovarian EPs is similar to that of tubal EPs. Typical ultrasound findings are a cystic ovarian mass that may be difficult to differentiate from other ovarian cysts or tubal EPs. The diagnosis is usually pathologic, based on Spielberg's criteria (155): the tube is intact, distinctly separate from the ovary, the gestational sac must occupy the normal anatomical location of the ovary, the gestational sac must be connected to the uterus by the uteroovarian ligament, and ovarian tissue must be demonstrated in the wall of the gestational sac. Systemic methotrexate treatment can be successful in ovarian pregnancies (156–158).

Surgical management should be performed in those who fail or have contraindications to medical management and those with concern for rupture or internal hemorrhage. Laparoscopic resection of the ectopic pregnancy (ovarian wedge resection, partial oophorectomy) is preferred to complete oophorectomy when feasible (109, 159). Care should be taken to remove as little healthy ovarian cortex as possible. The approach can be aided by injection of dilute vasopressin into the ovary and temporary occlusion of the ovarian blood supply to reduce surgical blood loss. As in all ovarian surgery, if future fertility is desired, the use of electrocautery should be limited given its negative effect on ovarian reserve (160). For ovarian hemostasis after resection, suture closure can be utilized to reduce the risk of continued bleeding and hematoma formation.

11.20 Abdominal Pregnancies

Abdominal pregnancies are a rare form of EPs, accounting for less than 1% of ectopic pregnancies (1, 161). Abdominal pregnancies can be primary, resulting from implantation of a blastocyst in the abdominal cavity, or secondary, resulting from a transition of a blastocyst that was initially located elsewhere (for example, a ruptured tubal ectopic pregnancy) (162). Abdominal pregnancy common locations include the posterior cul-de-sac, followed by the mesosalpinx, the omentum, the bowel and its mesentery, and the peritoneum of the pelvis and abdominal walls, including the anterior cul-de-sac (161). Other locations reported include the retroperitoneal space, liver, spleen, appendix, and lung (145). There are no established risk factors for abdominal pregnancies due to their rarity. A history of prior tubal surgery and EP were present in 50% and 39% of cases in a systematic review of 28 case reports (163). The natural history of abdominal pregnancy depends on gestational age at diagnosis, divided to early (≤ 20 weeks) and late (> 20 weeks). Early diagnosis is associated with similar outcomes as tubal EPs, whereas late diagnosis is associated with high mortality rate of up to 18%, 80% risk of blood transfusion, and 72% fetal mortality (145, 164). Clinical presentation can be either asymptomatic, nonspecific pregnancy symptoms, or hemodynamic instability due to intra-abdominal hemorrhage (165). Clinical findings may include fetal malpresentation, fetal growth restriction, palpable fetal parts, oligohydramnios, high serum alpha fetoprotein (AFP), and low serum unconjugated estriol (uE3) levels (165–170). Ultrasound findings include may include an empty uterus and a gestational sac outside the uterus, absence of myometrium between the fetus and the maternal abdominal wall or urinary bladder, and placenta outside of the uterine cavity (171). MRI can help to identify placental location, which may be difficult to localize with ultrasound (172). Because of the high complication rate, abdominal pregnancies should be terminated as soon as the diagnosis is confirmed (161, 173). However, expectant management of late abdominal pregnancies has been described (145, 174). These cases are typically admitted upon diagnosis and monitored similarly to patients with placenta accreta spectrum disorders.

In early abdominal pregnancies methotrexate has been used, although there is not enough data to determine efficacy (109). Often, surgery is utilized given the risks of hemorrhage and organ damage in abdominal ectopic pregnancy. Surgical interventions vary widely based on the location of implantation of the abdominal ectopic pregnancy. In cases of implantation outside of the pelvis, consultation with other surgical specialists is often required and encouraged. Surgical resection can be performed via laparoscopy or laparotomy depending on location and surgeon expertise. If surgery is to be undertaken, care should be taken to remove the pregnancy with minimal damage to underlying organs and tissues. In some case reports, the placenta has been left in situ after the umbilical cord was ligated and either treated expectantly or with methotrexate (175, 176). Certainly, the risk of hemorrhage with removal of the placenta should be considered depending on the location of implantation. Preoperative embolization of any vessels feeding the pregnancy can be considered (175).

11.21 Heterotopic Pregnancies

Heterotopic pregnancies are defined as a combination of an intrauterine pregnancy and a concurrent ectopic pregnancy. The incidence of heterotopic pregnancies has been increasing with the emergence of assisted reproductive therapies, from 1/30,000 pregnancies four decades ago, to 0.2% among women undergoing IVF between 2005 and 2018 (177, 178). Multiple embryo transfer during IVF is associated with increased heterotopic pregnancy risk (179). The ectopic pregnancy is usually located in the fallopian tube. Clinical manifestations are similar to those in threatened abortion or tubal EPs (177). Diagnosis is challenging because of the presence of an intrauterine pregnancy, and a high index of suspicion is important among women who conceived after IVF and/or experience vaginal bleeding or abdominal pain (180). Early diagnosis is key as women with heterotopic pregnancies are at higher risk for requiring blood transfusions compared with women with EPs (181). Transvaginal ultrasound is the mainstay of nonsurgical diagnosis, with reported sensitivity and specificity of 92% and 100%, respectively (182, 183). In heterotopic pregnancies with desired intrauterine pregnancy, methotrexate use is contraindicated (184). Nonsurgical treatments include transvaginal aspiration of the gestational sac, with or without direct injection of potassium chloride or hyperosmolar glucose (185–189). Low-dose methotrexate injection to the ectopic gestational sac with successful term delivery of the intrauterine pregnancy has also been described (190).

Surgical resection of the ectopic pregnancy can also be completed for the ectopic gestation in cases of heterotopic pregnancy depending on the location. If the intrauterine pregnancy is desired, care should be taken during surgical treatment to prevent disruption of the pregnancy within the endometrium, the blood flow to the uterus, and the corpus luteum prior to 10 weeks of gestation (191). If the corpus luteum is disrupted prior

to 10 weeks, progesterone supplementation is recommended. In all desired heterotopic pregnancies, the intrauterine pregnancy should be followed closely after resolution of the ectopic pregnancy. In cases of undesired pregnancy, a dilation and suction curettage for pregnancy termination can concurrently be completed at the time of surgical resection of the ectopic pregnancy (109).

11.22 Emergent and Life-Threatening Scenarios

Massive hemorrhage secondary to ectopic pregnancy remains the leading cause of maternal death in North America (18, 192). Pregnant individuals who are hemodynamically unstable or those with a physical exam concerning for an acute abdomen should have ruptured ectopic pregnancy as a leading differential. These patients should have expedited evaluation and surgical intervention to determine potential location of the pregnancy when feasible. Imaging should initially include a point-of-care ultrasound (POCUS) with or without a transvaginal ultrasound, as the addition of POCUS is useful in expediting identification of rupture and reducing time to operative room (193, 194).

Patients with ruptured or bleeding EPs typically require emergent surgery. Sometimes, laparoscopy is feasible. However, laparotomy is appropriate for unstable patients with significant intrabdominal bleeding and cases where laparoscopic visualization is limited due to hemorrhage. Preoperative resuscitation during evaluation and in route to the OR is helpful in these cases. As in all cases of suspected hemorrhage, establishing intravenous (IV) access via multiple large bore (18 gauge) peripheral IVs is immediately recommended. While placing multiple lines, labs can be drawn and should include a complete blood count, metabolic panel, β-hCG, and a type and screen (T&S). The blood bank should be notified of the potential need for uncrossmatched blood products in the interim. Crossmatched blood is preferable, especially in patients who desire future pregnancy, therefore early preparation is key. Early volume resuscitation with IV fluids is often helpful. A lactate level, prothrombin time, partial thromboplastin time, and fibrinogen level may also be helpful to obtain but should not delay transfer to the operating room. Along with hemorrhage shock, disseminated intravascular coagulation (DIC) can occur and treatment teams should be ready to provide additional blood products, including cryoprecipitate, as necessary. Often, these cases are managed in conjunction with emergency medicine specialists, anesthesiologists, and obstetrician gynecologists.

In emergencies, checklists have been found useful to expedite care and reduce errors (195). However, no validated emergency checklists specific to ruptured ectopic pregnancy were found in the literature. Preparation and forward thinking to facilitate efficient surgery and control of blood loss has the potential to alter outcomes. Treatment teams should be ready to initiate massive transfusion protocols to prevent hemorrhagic shock. Surgeons should consider methods to control bleeding intraoperatively. Tranexamic acid (TXA) inhibits the fibrinolytic pathway to stabilize clot formation and promote hemostasis. Evidence exists in the trauma and obstetric literature for TXA use in hemorrhage, however limited data exists in ruptured EP (196). Nevertheless, TXA should be considered to reduce morbidity in ruptured EP. Depending on the ectopic location, uterotonics may be useful adjuncts for hemostasis. Injection of dilute vasopressin should be utilized as indicated. Electrosurgery and/or suture ligation of the bleeding ectopic bed as well as ligation of blood supply should be considered and used as indicated.

11.23 Conclusion

Patients without an identified intrauterine pregnancy and positive β-hCG require careful follow-up to determine diagnosis of viable intrauterine pregnancy, nonviable intrauterine pregnancy, or ectopic pregnancy. If EP is diagnosed, medical and surgical options exist in stable patients. Treatment of stable patients should be initiated promptly after consideration and discussion of the individual clinical scenario, with consideration taken for location of EP, imaging findings, β-hCG levels, future pregnancy plans, and other clinical and patient characteristics. Unstable patients require urgent surgery with thoughtful consideration of both prevention of blood loss and resuscitation. For nontubal ectopic pregnancy, additional research is needed to continue to build evidence for standardized treatment guidelines for these EPs.

Key Points

- Patients without an identified intrauterine pregnancy and positive β-hCG require careful follow-up to determine diagnosis of viable intrauterine pregnancy, nonviable intrauterine pregnancy, or ectopic pregnancy.
- Treatment of patients should be initiated promptly after consideration and discussion of the individual clinical scenario, with consideration taken for location of EP, imaging findings, β-hCG levels, future pregnancy plans, and other clinical and patient characteristics.
- When abdominal surgery is required, ample evidence exists to establish laparoscopic management as the superior approach over laparotomy.

References

1. Bouyer J et al. Sites of ectopic pregnancy: a 10 year population-based study of 1800 cases. *Hum Reprod*. 2002;17(12):3224–3230.
2. Creanga AA et al. Trends in ectopic pregnancy mortality in the United States: 1980–2007. *Obstet Gynecol*. 2011; 117(4):837–843.
3. Cantwell R et al. Saving mothers' lives: reviewing maternal deaths to make motherhood safer: 2006–2008. The eighth report of the confidential enquiries into maternal deaths in the United Kingdom. *BJOG*. 2011;118(Suppl 1):1–203.
4. Berg CJ et al. Pregnancy-related mortality in the United States, 1998 to 2005. *Obstet Gynecol*. 2010;116(6):1302–1309.
5. Farquhar CM. Ectopic pregnancy. *Lancet*. 2005;366(9485): 583–591.
6. Sivalingam VN et al. Diagnosis and management of ectopic pregnancy. *J Fam Plann Reprod Health Care*. 2011;37(4):231–240.
7. ACOG practice bulletin 193: tubal ectopic pregnancy. *Obstet Gynecol*.2018;131(3):e91–e103.
8. CDC. Ectopic pregnancy – United States, 1990–1992. *MMWR Morb Mortal Wkly Rep*. 1995;44(3):46–48.
9. Mann LM et al. Trends in ectopic pregnancy diagnoses in United States emergency departments, 2006–2013. *Matern Child Health J*. 2020;24(2):213–221.

10. Cheng LY et al. Ectopic pregnancy following in vitro fertilization with embryo transfer: a single-center experience during 15 years. *Taiwan J Obstet Gynecol*. 2015;54(5):541–545.
11. Du T et al. Comparison of ectopic pregnancy risk among transfers of embryos vitrified on day 3, day 5, and day 6. *Fertil Steril*. 2017;108(1):108–116.e1.
12. Van Den Eeden SK et al. Ectopic pregnancy rate and treatment utilization in a large managed care organization. *Obstet Gynecol*. 2005;105(5 Pt 1):1052–1057.
13. Stulberg DB et al. Ectopic pregnancy rates and racial disparities in the Medicaid population, 2004–2008. *Fertil Steril*. 2014;102(6):1671–1676.
14. Barnhart KT et al. Risk factors for ectopic pregnancy in women with symptomatic first-trimester pregnancies. *Fertil Steril*. 2006;86(1):36–43.
15. Li C et al. Risk factors for ectopic pregnancy: a multi-center case-control study. *BMC Pregnancy Childbirth*. 2015;15:187.
16. Bouyer J et al. Risk factors for ectopic pregnancy: a comprehensive analysis based on a large case-control, population-based study in France. *Am J Epidemiol*. 2003;157(3):185–194.
17. Berenson A et al. Bacteriologic findings with ectopic pregnancy. *J Reprod Med*. 1991;36(2):118–120.
18. Marion LL et al. Ectopic pregnancy: history, incidence, epidemiology, and risk factors. *Clin Obstet Gynecol*. 2012;55(2):376–386.
19. Refaat B et al. Ectopic pregnancy secondary to in vitro fertilisation-embryo transfer: pathogenic mechanisms and management strategies. *Reprod Biol Endocrinol*. 2015;13:30.
20. Terres W et al. Bleifeld W. [Myocardial resting ischemia after intravenous infusion of a thromboxane-receptor antagonist]. *Dtsch Med Wochenschr*. 1987;112(36):1397.
21. Li C et al. Contraceptive use and the risk of ectopic pregnancy: a multi-center case-control study. *PLoS One*. 2014;9(12):e115031.
22. Saraiya M et al. Cigarette smoking as a risk factor for ectopic pregnancy. *Am J Obstet Gynecol*. 1998;178(3):493–498.
23. Yong PJ et al. Endometriosis and ectopic pregnancy: a meta-analysis. *J Minim Invasive Gynecol*. 2020;27(2):352–361.e2.
24. Peterson HB et al. The risk of pregnancy after tubal sterilization: findings from the U.S. collaborative review of sterilization. *Am J Obstet Gynecol*. 1996;174(4):1161–1168; discussion 1168–1170.
25. Alataş E et al. Laparoscopic management of a primary ectopic ovarian pregnancy and vaginal douching as a possible cause. *Arch Gynecol Obstet*. 2008;277(4):363–365.
26. Kutluay L et al. Tubal histopathology in ectopic pregnancies. *Eur J Obstet Gynecol Reprod Biol*. 1994;57(2):91–4.
27. Majmudar B et al. Salpingitis isthmica nodosa: a high-risk factor for tubal pregnancy. *Obstet Gynecol*. 1983;62(1):73–8.
28. Attar E. Endocrinology of ectopic pregnancy. *Obstet Gynecol Clin North Am*. 2004;31(4):779–794.
29. Alkatout I et al. Clinical diagnosis and treatment of ectopic pregnancy. *Obstet Gynecol Surv*. 2013;68(8):571–581.
30. Berek JS, ed. *Berek & Novak's Gynecology*, 16th edn. Wolters-Kluwer; 2019.
31. Barnhart KT et al. Clinical factors affecting the accuracy of ultrasonography in symptomatic first-trimester pregnancy. *Obstet Gynecol*. 2011;117(2 Pt 1):299–306.
32. Dogra V et al. First trimester bleeding evaluation. *Ultrasound Q*. 2005;21(2):69–85; quiz 149–150, 153–154.
33. Richardson A et al. Accuracy of first-trimester ultrasound in diagnosis of tubal ectopic pregnancy in the absence of an obvious extrauterine embryo: systematic review and meta-analysis. *Ultrasound Obstet Gynecol*. 2016;47(1):28–37.
34. Rottem S et al. Criteria for transvaginal sonographic diagnosis of ectopic pregnancy. *J Clin Ultrasound*. 1990;18(4):274–279.
35. Fleischer AC et al. Ectopic pregnancy: features at transvaginal sonography. *Radiology*. 1990;174(2):375–378.
36. Barnhart K et al. Pregnancy of unknown location: a consensus statement of nomenclature, definitions, and outcome. *Fertil Steril*. 2011;95(3):857–866.
37. Barnhart KT. Early pregnancy failure: beware of the pitfalls of modern management. *Fertil Steril*. 2012;98(5):1061–1065.
38. Daya S. Human chorionic gonadotropin increase in normal early pregnancy. *Am J Obstet Gynecol*. 1987;156(2):286–290.
39. Morse CB et al. Performance of human chorionic gonadotropin curves in women at risk for ectopic pregnancy: exceptions to the rules. *Fertil Steril*. 2012;97(1):101–106.e2.
40. Barnhart KT et al. Symptomatic patients with an early viable intrauterine pregnancy: HCG curves redefined. *Obstet Gynecol*. 2004;104(1):50–55.
41. Barnhart K et al. Decline of serum human chorionic gonadotropin and spontaneous complete abortion: defining the normal curve. *Obstet Gynecol*. 2004;104(5 Pt 1):975–981.
42. Barnhart KT et al. Differences in serum human chorionic gonadotropin rise in early pregnancy by race and value at presentation. *Obstet Gynecol*. 2016;128(3):504–511.
43. Silva C et al. Human chorionic gonadotropin profile for women with ectopic pregnancy. *Obstet Gynecol*. 2006;107(3): 605–610.
44. Butts SF et al. Predicting the decline in human chorionic gonadotropin in a resolving pregnancy of unknown location. *Obstet Gynecol*. 2013;122(2 Pt 1):337–343.
45. Cameron KE et al. Following declining human chorionic gonadotropin values in pregnancies of unknown location: when is it safe to stop? *Fertil Steril*. 2016;105(4):953–957.
46. Rausch ME et al. Serum biomarkers for detecting ectopic pregnancy. *Clin Obstet Gynecol*. 2012;55(2):418–423.
47. Stovall TG et al. Improved sensitivity and specificity of a single measurement of serum progesterone over serial quantitative beta-human chorionic gonadotrophin in screening for ectopic pregnancy. *Hum Reprod*. 1992;7(5):723–725.
48. Mol BW et al. The accuracy of single serum progesterone measurement in the diagnosis of ectopic pregnancy: a meta-analysis. *Hum Reprod*. 1998;13(11):3220–3227.
49. McCord ML et al. Single serum progesterone as a screen for ectopic pregnancy: exchanging specificity and sensitivity to obtain optimal test performance. *Fertil Steril*. 1996;66(4):513–516.
50. Condous G et al. Pregnancies of unknown location: consensus statement. *Ultrasound Obstet Gynecol*. 2006;28(2):121–122.
51. Bignardi T et al. Viability of intrauterine pregnancy in women with pregnancy of unknown location: prediction using human chorionic gonadotropin ratio vs. progesterone. *Ultrasound Obstet Gynecol*. 2010;35(6):656–661.
52. Kirk E et al. The practical application of a mathematical model to predict the outcome of pregnancies of unknown location. *Ultrasound Obstet Gynecol*. 2006;27(3):311–315.
53. Condous G et al. Prediction of ectopic pregnancy in women with a pregnancy of unknown location. *Ultrasound Obstet Gynecol*. 2007;29(6):680–687.
54. Kirk E et al. Rationalizing the follow-up of pregnancies of unknown location. *Hum Reprod*. 2007;22(6):1744–1750.
55. Banerjee S et al. Expectant management of early pregnancies of unknown location: a prospective evaluation of methods to predict spontaneous resolution of pregnancy. *BJOG*. 2001;108(2):158–163.
56. Banerjee S et al. The expectant management of women with early pregnancy of unknown location. *Ultrasound Obstet Gynecol*. 1999;14(4):231–236.
57. Braffman BH et al. Emergency department screening for ectopic pregnancy: a prospective US study. *Radiology*. 1994;190(3): 797–802.
58. Connolly A et al. Reevaluation of discriminatory and threshold levels for serum β-hCG in early pregnancy. *Obstet Gynecol*. 2013;121(1):65–70.
59. Flynn AN et al. Prioritizing desiredness in pregnancy of unknown location: an algorithm for patient-centered care. *Obstet Gynecol*. 2020;136(5):1001–1005.
60. van Mello NM et al. Methotrexate or expectant management in women with an ectopic pregnancy or pregnancy of unknown location and low serum hCG concentrations? A randomized comparison. *Hum Reprod*. 2013;28(1):60–67.
61. Barnhart KT et al. Effect of an active vs expectant management strategy on successful resolution of pregnancy among patients with a persisting pregnancy of unknown location: The ACT or NOT randomized clinical trial. *JAMA*. 2021;326(5): 390–400.

62. Barnhart KT et al. Usefulness of pipelle endometrial biopsy in the diagnosis of women at risk for ectopic pregnancy. *Am J Obstet Gynecol*. 2003;188(4):906–909.
63. Ries A et al. Use of the endometrial pipelle in the diagnosis of early abnormal gestations. *Fertil Steril*. 2000;74(3):593–595.
64. Rivera V et al. Change in quantitative human chorionic gonadotropin after manual vacuum aspiration in women with pregnancy of unknown location. *Am J Obstet Gynecol*. 2009;200(5):e56–e59.
65. Bleyer WA. The clinical pharmacology of methotrexate: new applications of an old drug. *Cancer*. 1978;41(1):36–51.
66. St Clair JT et al. Methotrexate in abdominal pregnancy. *JAMA*. Apr 21 1969;208(3):529–531.
67. Tanaka T et al. Treatment of interstitial ectopic pregnancy with methotrexate: report of a successful case. *Fertil Steril*. 1982;37(6):851–852.
68. Hajenius PJ et al. Interventions for tubal ectopic pregnancy. *Cochrane Database Syst Rev*. 2007;2007(1):CD000324.
69. Mol F et al. Current evidence on surgery, systemic methotrexate and expectant management in the treatment of tubal ectopic pregnancy: a systematic review and meta-analysis. *Hum Reprod Update*. 2008;14(4):309–319.
70. ASRM. Medical treatment of ectopic pregnancy: a committee opinion. *Fertil Steril*. 2013;100(3):638–644.
71. Lipscomb GH et al. Oral methotrexate for treatment of ectopic pregnancy. *Am J Obstet Gynecol*. 2002;186(6):1192–1195.
72. Stovall TG et al. Single-dose methotrexate: an expanded clinical trial. *Am J Obstet Gynecol*. 1993;168(6 Pt 1):1759–1762; discussion 1762–1765.
73. Barnhart K et al. Use of "2-dose" regimen of methotrexate to treat ectopic pregnancy. *Fertil Steril*. 2007;87(2):250–256.
74. Rodi IA et al. The medical treatment of unruptured ectopic pregnancy with methotrexate and citrovorum rescue: preliminary experience. *Fertil Steril*. 1986;46(5):811–813.
75. Barnhart KT et al. The medical management of ectopic pregnancy: a meta-analysis comparing "single dose" and "multidose" regimens. *Obstet Gynecol*. 2003;101(4):778–784.
76. Lipscomb GH et al. Analysis of three hundred fifteen ectopic pregnancies treated with single-dose methotrexate. *Am J Obstet Gynecol*. 1998;178(6):1354–1358.
77. Wang X et al. Conception, early pregnancy loss, and time to clinical pregnancy: a population-based prospective study. *Fertil Steril*. 2003;79(3):577–584.
78. Alur-Gupta S et al. Two-dose versus single-dose methotrexate for treatment of ectopic pregnancy: a meta-analysis. *Am J Obstet Gynecol*. 2019;221(2):95–108.e2.
79. Lipscomb GH et al. Comparison of multidose and single-dose methotrexate protocols for the treatment of ectopic pregnancy. *Am J Obstet Gynecol*. 2005;192(6):1844–1847; discussion 1847–1848.
80. Pisarska MD et al. Ectopic pregnancy. *Lancet*. 1998;351 (9109):1115–1120.
81. Menon S et al. Establishing a human chorionic gonadotropin cutoff to guide methotrexate treatment of ectopic pregnancy: a systematic review. *Fertil Steril*. 2007;87(3):481–484.
82. Dasari P et al. Life-threatening complications following multidose methotrexate for medical management of ectopic pregnancy. *BMJ Case Rep*. 2012:bcr0320126023.
83. Xiao C et al. Non-surgical management of tubal ectopic pregnancy: a systematic review and meta-analysis. *Med*. 2021;100(50):e27851.
84. Horne AW et al. Combination of gefitinib and methotrexate to treat tubal ectopic pregnancy (GEM3): a multicentre, randomised, double-blind, placebo-controlled trial. *Lancet*. 2023;401(10377):655–663.
85. Natale A et al. Pre- and post-treatment patterns of human chorionic gonadotropin for early detection of persistence after a single dose of methotrexate for ectopic pregnancy. *Eur J Obstet Gynecol Reprod Biol*. 2004;117(1):87–92.
86. Mashiach R et al. Significant increase in serum hCG levels following methotrexate therapy is associated with lower treatment success rates in ectopic pregnancy patients. *Eur J Obstet Gynecol Reprod Biol*. 2018;231:188–191.
87. Atri M et al. Ectopic pregnancy: evolution after treatment with transvaginal methotrexate. *Radiology*. 1992;185(3): 749–753.
88. Brown DL et al. Transvaginal sonography for diagnosing ectopic pregnancy: positivity criteria and performance characteristics. *J Ultrasound Med*. 1994;13(4):259–266.
89. Brown DL et al. Serial endovaginal sonography of ectopic pregnancies treated with methotrexate. *Obstet Gynecol*. 1991;77(3):406–409.
90. Fauconnier A et al. Ultrasound assessment of haemoperitoneum in ectopic pregnancy: derivation of a prediction model. *World J Emerg Surg*. 2007;2:23.
91. Svirsky R et al. The safety of conception occurring shortly after methotrexate treatment of an ectopic pregnancy. *Reprod Toxicol*. 2009;27(1):85–87.
92. Hackmon R et al. Effect of methotrexate treatment of ectopic pregnancy on subsequent pregnancy. *Can Fam Physician*. 2011;57(1):37–39.
93. Oriol B et al. Systemic methotrexate to treat ectopic pregnancy does not affect ovarian reserve. *Fertil Steril*. 2008;90(5):1579–1582.
94. Ohannessian A et al. Ovarian responsiveness in women receiving fertility treatment after methotrexate for ectopic pregnancy: a systematic review and meta-analysis. *Hum Reprod*. 2014;29(9):1949–1956.
95. Korhonen J et al. Serum human chorionic gonadotropin dynamics during spontaneous resolution of ectopic pregnancy. *Fertil Steril*. 1994;61(4):632–636.
96. Elson J et al. Expectant management of tubal ectopic pregnancy: prediction of successful outcome using decision tree analysis. *Ultrasound Obstet Gynecol*. 2004;23(6):552–556.
97. Colombo GE et al. Efficacy and safety of expectant management in the treatment of tubal ectopic pregnancy: a systematic review and meta-analysis. *Hum Reprod Open*. 2020;2020(4):hoaa044.
98. Craig LB et al. Expectant management of ectopic pregnancy. *Clin Obstet Gynecol*. 2012;55(2):461–470.
99. Webster K et al. Ectopic pregnancy and miscarriage: diagnosis and initial management: summary of updated NICE guidance. *BMJ*. 2019;367:16283.
100. Zohav E et al. Reproductive outcome after expectant management of ectopic pregnancy. *Eur J Obstet Gynecol Reprod Biol*. 1996;66(1):1–2.
101. Rantala M et al. Tubal patency and fertility outcome after expectant management of ectopic pregnancy. *Fertil Steril*. 1997;68(6):1043–1046.
102. Helmy S et al. Fertility outcomes following expectant management of tubal ectopic pregnancy. *Ultrasound Obstet Gynecol*. 2007;30(7):988–993.
103. Strobelt N et al. Fertility after ectopic pregnancy. Effects of surgery and expectant management. *J Reprod Med*. 2000;45(10):803–807.
104. Lundorff P et al. Laparoscopic surgery in ectopic pregnancy. A randomized trial versus laparotomy. *Acta Obstet Gynecol Scand*. 1991;70(4–5):343–348.
105. Vermesh M et al. Management of unruptured ectopic gestation by linear salpingostomy: a prospective, randomized clinical trial of laparoscopy versus laparotomy. *Obstet Gynecol*. 1989;73(3 Pt 1):400–404.
106. Cheng X et al. Comparison of the fertility outcome of salpingotomy and salpingectomy in women with tubal pregnancy: a systematic review and meta-analysis. *PLoS One*. 2016;11(3):e0152343.
107. Mol F et al. Salpingotomy versus salpingectomy in women with tubal pregnancy (ESEP study): an open-label, multicentre, randomised controlled trial. *Lancet*. 2014;383(9927): 1483–1489.
108. Fernandez H et al. Fertility after ectopic pregnancy: the DEMETER randomized trial. *Hum Reprod*. 2013;28(5):1247–1253.
109. Po L et al. Guideline no. 414: management of pregnancy of unknown location and tubal and nontubal ectopic pregnancies. *J Obstet Gynaecol Can*. 2021;43(5):614–630.e1.

110. Song T et al. Laparoscopic tube-preserving surgical procedures for ectopic tubal pregnancy. *Obstet Gynecol Sci*. 2016;59(6):512–518.
111. Morse AN et al. Optimal use of peri-operative human chorionic gonadotrophin concentrations to identify persistent ectopic pregnancy after laparoscopic salpingostomy: a retrospective cohort study. *Reprod Biomed Online*. 2018;36(3):361–368.
112. Ben-David A et al. Nonsurgical management of interstitial pregnancies: feasibility and predictors of treatment failure. *J Minim Invasive Gynecol*. 2020;27(3):625–632.
113. Moawad NS et al. Current diagnosis and treatment of interstitial pregnancy. *Am J Obstet Gynecol*. 2010;202(1):15–29.
114. MacRae R et al. Diagnosis and laparoscopic management of 11 consecutive cases of cornual ectopic pregnancy. *Arch Gynecol Obstet*. 2009;280(1):59–64.
115. Densley A et al. Angular and interstitial ectopic pregnancies: a clarification of terms and literature review. *Curr Probl Diagn Radiol*. 2023;52(2):84–88.
116. Lau S et al. Conservative medical and surgical management of interstitial ectopic pregnancy. *Fertil Steril*. 1999;72(2):207–215.
117. Tarim E et al. Angular pregnancy. *J Obstet Gynaecol Res*. 2004;30(5):377–379.
118. Ackerman TE et al. Interstitial line: sonographic finding in interstitial (cornual) ectopic pregnancy. *Radiology*. 1993;189(1):83–7.
119. Lewiss RE et al. The endomyometrial thickness measurement for abnormal implantation evaluation by pelvic sonography. *J Ultrasound Med*. 2014;33(7):1143–1146.
120. Bourdel N et al. [Interstitial pregnancy. Ultrasonographic diagnosis and contribution of MRI. A case report]. *Gynecol Obstet Fertil*. 2007;35(2):121–124.
121. Jermy K et al. The conservative management of interstitial pregnancy. *BJOG*. 2004;111(11):1283–1288.
122. Benifla JL et al. Alternative to surgery of treatment of unruptured interstitial pregnancy: 15 cases of medical treatment. *Eur J Obstet Gynecol Reprod Biol*. 1996;70(2):151–156.
123. Kim MJ et al. Therapeutic outcomes of methotrexate injection in unruptured interstitial pregnancy. *Obstet Gynecol Sci*. 2017;60(6):571–578.
124. Choi YS et al. Laparoscopic cornuotomy using a temporary tourniquet suture and diluted vasopressin injection in interstitial pregnancy. *Fertil Steril*. 2009;91(5):1933–1937.
125. Moon HS et al. New simple endoscopic operations for interstitial pregnancies. *Am J Obstet Gynecol*. 2000;182(1 Pt 1): 114–121.
126. Lee MH et al. Comparison of laparoscopic cornual resection and cornuotomy for interstitial pregnancy. *J Minim Invasive Gynecol*. 2017;24(3):397–401.
127. Pramayadi CT et al. Successful procedure in conservative management of interstitial (cornual) ectopic pregnancy. *Gynecol Minim Invasive Ther*. 2018;7(4):172–174.
128. Liao CY et al. Cornual wedge resection for interstitial pregnancy and postoperative outcome. *Aust N Z J Obstet Gynaecol*. 2017;57(3):342–345.
129. Rotas MA et al. Cesarean scar ectopic pregnancies: etiology, diagnosis, and management. *Obstet Gynecol*. 2006;107(6):1373–1381.
130. Ko JK et al. Caesarean scar pregnancy: a 10-year experience. *Aust N Z J Obstet Gynaecol*. 2015;55(1):64–9.
131. Calì G et al. Outcome of Cesarean scar pregnancy managed expectantly: systematic review and meta-analysis. *Ultrasound Obstet Gynecol*. 2018;51(2):169–175.
132. Timor-Tritsch IE et al. Recurrent Cesarean scar pregnancy: case series and literature review. *Ultrasound Obstet Gynecol*. 2021;58(1):121–126.
133. Lee CL et al. Laparoscopic management of an ectopic pregnancy in a previous Caesarean section scar. *Hum Reprod*. 1999;14(5):1234–1236.
134. Vial Y et al. Pregnancy in a cesarean scar. *Ultrasound Obstet Gynecol*. 2000;16(6):592–593.
135. Gonzalez N et al. Cesarean scar pregnancy: a systematic review. *J Minim Invasive Gynecol*. 2017;24(5):731–738.
136. Riaz RM et al. Cesarean scar ectopic pregnancy: imaging features, current treatment options, and clinical outcomes. *Abdom Imaging*. 2015;40(7):2589–2599.
137. Timor-Tritsch IE et al. Cesarean scar pregnancy is a precursor of morbidly adherent placenta. *Ultrasound Obstet Gynecol*. 2014;44(3):346–353.
138. Timor-Tritsch IE et al. Cesarean scar pregnancy and early placenta accreta share common histology. *Ultrasound Obstet Gynecol*. 2014;43(4):383–395.
139. Jauniaux E et al. New insights into the etiopathology of placenta accreta spectrum. *Am J Obstet Gynecol*. 2022;227(3):384–391.
140. Timor-Tritsch IE et al. Cesarean scar pregnancy: diagnosis and pathogenesis. *Obstet Gynecol Clin North Am*. 2019;46(4):797–811.
141. Zosmer N et al. Natural history of early first-trimester pregnancies implanted in Cesarean scars. *Ultrasound Obstet Gynecol*. 2015;46(3):367–375.
142. Miller R et al. Society for Maternal-Fetal Medicine (SMFM) Consult Series #49: Cesarean scar pregnancy. *Am J Obstet Gynecol*. 2020;222(5):B2–B14.
143. Maheux-Lacroix S et al. Cesarean scar pregnancies: a systematic review of treatment options. *J Minim Invasive Gynecol*. 2017;24(6):915–925.
144. Matorras R et al. Cervical pregnancy in assisted reproduction: an analysis of risk factors in 91,067 ongoing pregnancies. *Reprod Biomed Online*. 2020;40(3):355–361.
145. Fylstra DL. Ectopic pregnancy not within the (distal) fallopian tube: etiology, diagnosis, and treatment. *Am J Obstet Gynecol*. 2012;206(4):289–299.
146. Vela G et al. Cervical pregnancy: the importance of early diagnosis and treatment. *J Minim Invasive Gynecol*. 2007;14(4):481–484.
147. Kung FT et al. Differential diagnosis of suspected cervical pregnancy and conservative treatment with the combination of laparoscopy-assisted uterine artery ligation and hysteroscopic endocervical resection. *Fertil Steril*. 2004;81(6):1642–1649.
148. Hung TH et al. Prognostic factors for an unsatisfactory primary methotrexate treatment of cervical pregnancy: a quantitative review. *Hum Reprod*. 1998;13(9):2636–2642.
149. Hwang JH et al. Classification and management of cervical ectopic pregnancies: experience at a single institution. *J Reprod Med*. 2010;55(11–12):469–476.
150. Hansch E et al. Pelvic arterial embolization for control of obstetric hemorrhage: a five-year experience. *Am J Obstet Gynecol*. 1999;180(6 Pt 1):1454–1460.
151. Tang PP et al. [Diagnosis and treatment of cervical ectopic pregnancy]. *Zhongguo Yi Xue Ke Xue Yuan Xue Bao*. 2010;32(5):497–500.
152. Di Lorenzo G et al. Hysteroscopic treatment of cervical pregnancy: a scoping review of the literature. *J Minim Invasive Gynecol*. 2022;29(3):345–354.e1.
153. Sherer DM et al. Viable cervical pregnancy managed with systemic Methotrexate, uterine artery embolization, and local tamponade with inflated Foley catheter balloon. *Am J Perinatol*. 2003;20(5):263–267.
154. Ash S et al. Hysteroscopic resection of a cervical ectopic pregnancy. *Fertil Steril*. 1996;66(5):842–844.
155. Spigelberg O. Casusistik der ovarial schwangerschaft. *Arch Gynecol*. 1878;13:73.
156. Habbu J et al. Ovarian pregnancy successfully treated with methotrexate. *J Obstet Gynaecol*. 2006;26(6):587–588.
157. Papillon-Smith J et al. Ovarian pregnancy. *J Obstet Gynaecol Can*. 2016;38(1):1–2.
158. Alalade AO et al. Evidence-based management of non-tubal ectopic pregnancies. *J Obstet Gynaecol*. 2017;37(8):982–991.
159. Joseph RJ et al. Ovarian ectopic pregnancy: aetiology, diagnosis, and challenges in surgical management. *J Obstet Gynaecol*. 2012;32(5):472–474.

160. Pergialiotis V et al. The effect of bipolar electrocoagulation during ovarian cystectomy on ovarian reserve: a systematic review. *Am J Obstet Gynecol*.2015;213(5):620–628.
161. Shaw SW et al. Management of primary abdominal pregnancy: twelve years of experience in a medical centre. *Acta Obstet Gynecol Scand*. 2007;86(9):1058–1062.
162. Rohilla M et al. Advanced abdominal pregnancy: a search for consensus. Review of literature along with case report. *Arch Gynecol Obstet*. 2018;298(1):1–8.
163. Yoder N et al. Abdominal ectopic pregnancy after in vitro fertilization and single embryo transfer: a case report and systematic review. *Reprod Biol Endocrinol*. 2016;14(1):69.
164. Nkusu Nunyalulendho D et al. Advanced abdominal pregnancy: case report and review of 163 cases reported since 1946. *Rural Remote Health*. 2008;8(4):1087.
165. Huang K et al. Advanced abdominal pregnancy: an increasingly challenging clinical concern for obstetricians. *Int J Clin Exp Pathol*. 2014;7(9):5461–5472.
166. Cartwright PS et al. Advanced abdominal pregnancy associated with fetal pulmonary hypoplasia: report of a case. *Am J Obstet Gynecol*. 1986;155(2):396–397.
167. Tromans PM et al. Abdominal pregnancy associated with extremely elevated serum alpha-fetoprotein. Case report. *Br J Obstet Gynaecol*. 1984;91(3):296–298.
168. Audain L et al. Cocaine use as a risk factor for abdominal pregnancy. *J Natl Med Assoc*. 1998;90(5):277–283.
169. Worley KC et al. Advanced extrauterine pregnancy: diagnostic and therapeutic challenges. *Am J Obstet Gynecol*. 2008;198(3):297.e1–297.e7.
170. Bombard AT et al. Early detection of abdominal pregnancy by maternal serum AFP+ screening. *Prenat Diagn*. 1994 Dec;14(12):1155–1157.
171. Allibone GW et al. The sonographic features of intra-abdominal pregnancy. *J Clin Ultrasound*. 1981;9(7):383–387.
172. Lockhat F et al. The value of magnetic resonance imaging in the diagnosis and management of extra-uterine abdominal pregnancy. *Clin Radiol*. 2006;61(3):264–269.
173. Martin JN et al. Abdominal pregnancy: current concepts of management. *Obstet Gynecol*. 1988;71(4):549–557.
174. Marcellin L et al. Conservative management of an advanced abdominal pregnancy at 22 weeks. *AJP Rep*. 2014;4(1):55–60.
175. Demendi C et al. Successful operative management of an intact second trimester abdominal pregnancy with additional preoperative selective catheter embolization and postoperative methotrexate therapy. *Med Sci Monit*. 2011;17(5):CS53–CS55.
176. Eisner SM et al. Rare ectopic pregnancies – a literature review for the period 2007–2019 on locations outside the uterus and fallopian tubes. *Geburtshilfe Frauenheilkd*. 2020;80(7):686–701.
177. Reece EA et al. Combined intrauterine and extrauterine gestations: a review. *Am J Obstet Gynecol*. 1983 Jun 1;146(3):323–330.
178. Li X et al. Heterotopic interstitial pregnancy: early ultrasound diagnosis of 179 cases after in vitro fertilization-embryo transfer. *J Ultrasound Med*. Apr 2023;42(4):915–922.
179. Tummon IS et al. Transferring more embryos increases risk of heterotopic pregnancy. *Fertil Steril*. 1994 Jun;61(6):1065–1067.
180. Liu M et al. Risk factors and early predictors for heterotopic pregnancy after in vitro fertilization. *PLoS One*. 2015;10(10): e0139146.
181. Soriano D et al. Diagnosis and treatment of heterotopic pregnancy compared with ectopic pregnancy. *J Am Assoc Gynecol Laparosc*. 2002;9(3):352–358.
182. Li XH et al. Value of transvaginal sonography in diagnosing heterotopic pregnancy after in-vitro fertilization with embryo transfer. *Ultrasound Obstet Gynecol*. 2013;41(5):563–569.
183. Kirk E et al. Diagnosing ectopic pregnancy and current concepts in the management of pregnancy of unknown location. *Hum Reprod Update*. 2014;20(2):250–261.
184. Louis-Sylvestre C et al. The role of laparoscopy in the diagnosis and management of heterotopic pregnancies. *Hum Reprod*. 1997;12(5):1100–1102.
185. Barrenetxea G et al. Carbonero K. Heterotopic pregnancy: two cases and a comparative review. *Fertil Steril*. 2007;87(2):417. e9–417.e15.
186. Eom JM et al. Surgical and obstetric outcomes of laparoscopic management for women with heterotopic pregnancy. *J Obstet Gynaecol Res*. 2013;39(12):1580–1586.
187. Wang M et al. Nonsurgical management of live tubal ectopic pregnancy by ultrasound-guided local injection and systemic methotrexate. *J Minim Invasive Gynecol*. 2014;21(4):642–649.
188. Chen D et al. Heterotopic cervical pregnancy successfully treated with transvaginal ultrasound-guided aspiration and cervical-stay sutures. *Fertil Steril*. 2001;75(5):1030–1033.
189. Hsieh BC et al. Heterotopic Caesarean scar pregnancy combined with intrauterine pregnancy successfully treated with embryo aspiration for selective embryo reduction: case report. *Hum Reprod*. 2004;19(2):285–287.
190. Sijanovic S et al. Methotrexate in local treatment of cervical heterotopic pregnancy with successful perinatal outcome: case report. *J Obstet Gynaecol Res*. 2011;37(9):1241–1245.
191. Shah D et al. Luteal insufficiency in first trimester. *Indian J Endocrinol Metab*. 2013;17(1):44–49.
192. Creanga AA et al. Pregnancy-related mortality in the United States, 2011–2013. *Obstet Gynecol*. 2017;130(2):366–373.
193. Stone BS et al. Impact of point-of-care ultrasound on treatment time for ectopic pregnancy. *Am J Emerg Med*. 2021;49:226–232.
194. Urquhart S et al. Comparing time to diagnosis and treatment of patients with ruptured ectopic pregnancy based on type of ultrasound performed: a retrospective inquiry. *J Emerg Med*. 2022;62(2):200–206.
195. Hearns S. Checklists in emergency medicine. *Emerg Med J*. Sep 2018;35(9):530–531.
196. Bouthors AS et al. The role of tranexamic acid in the management of postpartum haemorrhage. *Best Pract Res Clin Anaesthesiol*. 2022;36(3–4):411–426.

12 EVALUATION OF WOMEN AND ADOLESCENT GIRLS WITH ABNORMAL UTERINE BLEEDING (AUB) IN THE REPRODUCTIVE YEARS

Malcolm G. Munro

Abnormal uterine bleeding (AUB) in the reproductive years encompasses a variety of symptoms in nonpregnant girls and women. These symptoms have been codified in the International Federation of Gynecology and Obstetrics (FIGO's) AUB System 1 and comprise abnormalities in menstrual frequency, regularity, duration, flow volume, and bleeding between periods (1). Whereas chronic AUB in the reproductive years describes those with symptoms affecting most of the menstrual experience in the previous 6 months, women may also experience the acute onset of AUB, which is essentially acute heavy menstrual bleeding (HMB). The definition of acute AUB adopted by FIGO is "An episode of heavy uterine bleeding, unrelated to pregnancy, which, in the opinion of the clinician, is severe enough to require urgent or emergent interventions" (2). Postmenopausal bleeding is also a symptom (not a diagnosis) that occurs in women following the permanent cessation of ovarian function.

Abnormal uterine bleeding in the reproductive years frequently has an adverse impact on a girl's or woman's quality of life and can result in economic challenges secondary to the costs of treatment, the need for excess menstrual pads and tampons, and work absenteeism and presenteeism that can lead to loss of income and even job security (3–5). Frequently added to these cyclically experienced symptoms are the daily symptoms related to iron deficiency (ID), and its extreme manifestation, iron deficiency anemia (IDA), a highly prevalent situation in women and girls with HMB. Those with ID frequently have compromised physical and cognitive function and often enter pregnancy in a condition that can adversely affect fetal growth and development, including long-lasting adverse impacts on neurodevelopment (6). Whereas many sources report the prevalence to be a few percent, or affecting up to 30% in their lifetime, it is apparent from direct surveys of women that the prevalence of one AUB symptom, heavy menstrual bleeding, may be present at any given time in as many as 50% of reproductive-aged girls and women (7–9). The impact of AUB on healthcare resources is massive; a 2007 estimate suggested that the US cost from all sources (direct and indirect) could be more than $37 billion (10), an amount that is, no doubt, much greater now more than 17 years later.

Related research, education, clinical evaluation, and patient counseling were previously impaired by inconsistently used terminologies and the absence of a classification of potential causes of AUB. Consequently, the Fédération Internationale de Gynécologie et d'Obstétrique (International Federation of Gynecology and Obstetrics), or "FIGO," has developed two systems: one for standardization of nomenclature and description of symptoms (Figure 12.1) and a second for classification of potential causes of AUB in reproductive-aged women (Figure 12.2) (1, 11) endorsed by the American College of Obstetricians and Gynecologists (ACOG) (12) and other national organizations. The nomenclature system (System 1) was the product of a structured consensus development process involving a wide variety of stakeholders, including national specialty and subspecialty organizations, journal editors, and recognized experts. The system is designed around four core parameters (cycle length, cycle predictability or regularity, period duration, and the perceived flow volume). It comprises terms that can be unambiguously translated into many languages while retaining a consistent meaning (13, 14). By producing FIGO System 1, the poorly defined terms have been abandoned, including dysfunctional uterine bleeding (also known by the initialism DUB), menorrhagia, hypermenorrhea, metrorrhagia, menometrorrhagia, polymenorrhea, oligomenorrhea, and a host of others. The consensus group recommended that the term amenorrhea be retained as it was thought to be unambiguous and consistently used by clinicians and educators and in the published literature.

FIGO's AUB System 2, the classification of causes of nongestational AUB in the reproductive years (Figure 12.2), currently comprises nine categories of disorders that are ordered according to the acronym "PALM-COEIN" (palm-koin): polyp; adenomyosis; leiomyoma; malignancy and hyperplasia; coagulopathy; ovulatory disorders; endometrial dysfunction; iatrogenic; and not otherwise classified. The PALM group are definable structural abnormalities, while the COEI categories reflect disorders unrelated to uterine structure, including coagulopathies, endometrial causes, and ovulatory disorders. The "N" category is reserved for conditions that are "not otherwise classified" currently, including the cesarean scar defect, sometimes referred to as the "niche" or "isthmocele." It is essential to recognize that polyps, adenomyosis, and leiomyomas frequently do not cause symptoms, so coagulopathies, ovulatory disorders, and endometrial dysfunction may be the causes of AUB, even when such structural abnormalities are identified.

See further Table 12.1.

12.1 Physiology of Menstruation

Knowledge of menstrual physiology is critical to understanding the pathogenesis of AUB as well as the investigational rationale and options for management. An important concept is that there are both systemic and local components to menstrual physiology; the local elements are somewhat unique to the endometrium as it is the only human tissue designed to bleed physiologically. Systemically, the endocrinologic interplay amongst the hypothalamus, pituitary, and ovary typically culminates in ovulation 10 to 24 days after the first day of the menstrual period, and absent pregnancy, the onset of the next period about 14 days later. While the length of this menstrual cycle ranges from 24 to 38 days, it is generally predictable in a given individual and, at least between the ages of 18 and 45, varies typically by less than 7–9 days.

The systematic stimulation provided, initially by estradiol alone, and, following ovulation, estradiol in combination with progesterone, prepares the endometrium both for embryo attachment, envelopment, and sustenance and, should pregnancy not occur, for an orderly and relatively hemostatic sloughing of the superficial or "functionalis" layer, the menstrual period. That process is initiated by the "demise" of the corpus

DOI: 10.1201/9781003312109-12

Parameter	Normal	Abnormal	☑
Frequency	Absent (no bleeding) = amenorrhea		☐
	Infrequent (>38 days)		☐
	Normal (≥24 and ≤38 days)		☐
	Infrequent (<24 days)		☐
Duration	Normal (≤8 days)		☐
	Prolonged (>8 days)		☐
Regularity	Normal or "Regular" (shortest to longest cycle variation: ≤7-9 days)*		☐
	Irregular (shortest to longest cycle variation: ≥10 days)		☐
Flow Volume (patient determined)	Light		☐
	Normal		☐
	Heavy		☐

Intermenstrual Bleeding (IMB) Bleeding between cyclically regular onset of menses	None		☐
	Random		☐
	Cyclic (Predictable)	Early Cycle	☐
		Mid Cycle	☐
		Late Cycle	☐

Unscheduled Bleeding on Progestin ± Estrogen Gonadal Steroids (birth control pills, rings, patches or injections)	Not Applicable (not on gonadal steroid medication)	☐
	None (on gonadal steroid medication)	☐
	Present	☐

© Malcolm G. Munro MD

FIGURE 12.1 FIGO AUB System 1. Defining normal and abnormal uterine bleeding in the reproductive years. (By courtesy of Malcolm G. Munro.) *The population-based studies that collectively comprise the database from which the 5th to 95th percentiles suggest that the normal regularity range is ± 2–20 days. However, these likely include a proportion of women with ovulatory disorders. A preliminary assessment of the data suggests that ≤ 4 days is a more accurate representation of the upper limit of normal for ovulatory women. Consequently, this table is constructed to guide the clinician to use ± 4 days to distinguish women who are consistently ovulatory from those who may have irregular, infrequent, or absent ovulation. **Original analysis suggested that the 5th–95th percentile was 4.5–8.0 days. However, reanalysis suggested that there were a wide range and no known clinical relevance to menses lasting less than 4 days.

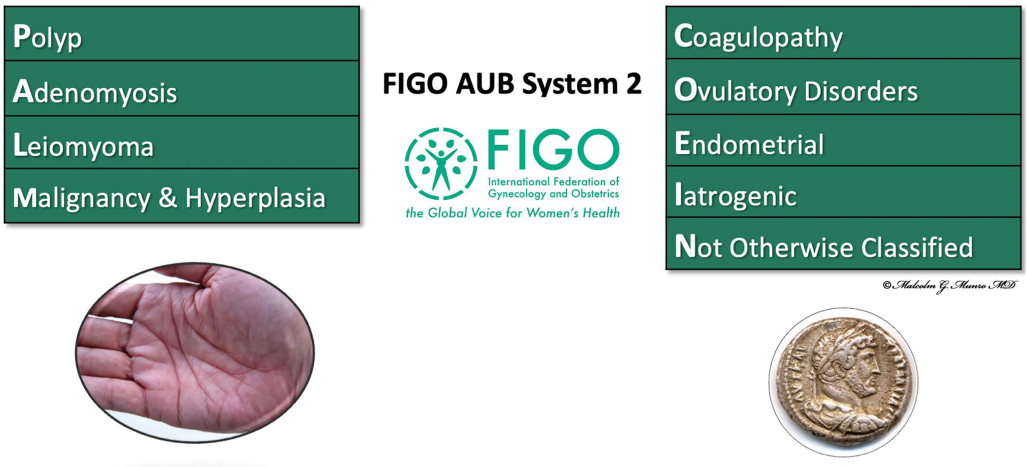


FIGURE 12.2 FIGO AUB System 2. The PALM-COEIN System for classification of causes of AUB in the reproductive years with the leiomyoma subclassification system (by courtesy of Malcolm G. Munro). The basic system (top) categorizes potential structural causes polyps ("P"), adenomyosis ("A"), leiomyomas ("L"), and malignancy and hyperplasia ("M") using the column on the left. On the right are the trio of coagulopathies ("C"), ovulatory disorders ("O"), and endometrial causes ("E"), as well as iatrogenic ("I") and those entities that are not otherwise classified ("N").

TABLE 12.1 FIGO System 1: Defining and Describing Normal and Abnormal Uterine Bleeding in the Reproductive Years

Clinical Dimensions of Menstruation and Menstrual Cycle	Descriptive Terms	Normal Limits (5th–95th percentile)[+]
Frequency of menses (days)	Frequent	< 24
	Normal	24–38
	Infrequent	> 38
	Absent	No bleeding
Regularity: Variation in days (shortest to longest cycle) over a 12-month period (days)	Regular	≤ 7–9 days*
	Irregular	> 7–9 days*
Duration of flow (days)	Prolonged	> 8
	Normal	Up to 8**
Volume of monthly blood loss (woman's perception/volume mL)	Heavy [see Other Descriptors, below]	> 80 mL
	Normal	5–80 mL
	Light	< 5 mL
Other Descriptors		
Heavy menstrual bleeding (HMB)	Self-defined by the patient as some combination of prolonged and heavy volume "Heavy menstrual bleeding (HMB) is defined as excessive menstrual blood loss which interferes with a woman's physical, social, emotional and/or material quality of life. It can occur alone or in combination with other symptoms" (1)	
Intermenstrual bleeding (IMB)	Bleeding that occurs between regular menses	

[+] Data are based primarily on data from large epidemiologic studies (2–4).

[*] The population-based studies that collectively comprise the database from which the 5th to 95th percentiles suggest that the normal regularity range is ± 2–20 days. However, these likely include a proportion of women with ovulatory disorders. Preliminary assessment of the data suggests that cycle variation of ≤ 7–9 days is a more accurate representation of the upper limit of normal for ovulatory women. Consequently, this table is constructed to guide the clinician to use 7–9 days, depending on age, to distinguish women who are consistently ovulatory from those who may have irregular, infrequent, or absent ovulation. For those aged 26–41 the range should be 7 days or less, while for those 18–25 or 42–46 the variation is up to 9 days. In part due to the frequency of ovulatory disorders available data do not define "normal" for those postmenarcheal adolescents under 18 or for premenopausal women 47 and up.

[**] Original analysis suggested that the 5th–95th percentile was 4.5–8.0 days. However, reanalysis suggested that there were a wide range and no known clinical relevance to menses lasting less than 4 days.

1. Hyams LL. Adenomyosis; its conservative surgical treatment (hysteroplasty) in young women. *New York State Journal of Medicine*. 1952;52(22):2778–2784.
2. Hallberg L, Hogdahl AM, Nilsson L, Rybo G. Menstrual blood loss-a population study. Variation at different ages and attempts to define normality. *Acta obstetricia et gynecologica Scandinavica*. 1966;45(3):320–351.
3. Treloar AE, Boynton RE, Behn BG, Brown BW. Variation of the human menstrual cycle through reproductive life. *Int J Fertil*. 1967;12(1 Pt 2):77–126.
4. Snowden R, Christian B. Patterns and Perceptions of Menstruation, A World Health Organization International Collaborative Study. London: Croom Helm; 1983.

luteum – withdrawal of systemic estradiol and progesterone – and then a sequence of events that include endometrial vascular spasm, secondary to thromboxane, endothelin (ET)-1, and prostaglandin (PG) F2α, and proteolytic activity related to the local release of matrix metalloproteinase (MMP) enzymes. Together, these molecular expressions culminate in the bleeding and the sloughing of the functionalis. Once the superficial sloughing occurs, the basilar endometrium relies upon the vasoconstrictors (ET-1, PG-F2α) and a balance of other expressions, such as plasminogen activator and its inhibitor, to maintain hemostasis and ultimately facilitate the process of regeneration and repair of the functionalis (Figure 12.3). Menstruation is normally over by the eighth day and is usually complete in 3 to 5 days.

The p account is only a summary of endometrial physiology; the reader is encouraged to delve into more extensive descriptions of endometrial physiology (15, 16). Such knowledge will facilitate understanding the various pharmacologic interventions that exist or are on the horizon. It can inform the development and implementation of surgical approaches to uterine disorders that optimally preserve endometrial function.

12.2 Pathogenesis of Chronic AUB

Chronic AUB occurs only in nonpregnant reproductive-aged girls and women and has been defined as any abnormality of frequency, regularity, duration, or volume of menstruation that has been present for most of the previous 6 months (11). It may also include intermenstrual bleeding and unplanned bleeding associated with using intrauterine devices or pharmaceutical agents that affect gonadal steroid expression or function. The causes of chronic AUB may be related to any one or a combination of the structural and nonstructural reasons defined by FIGO's System 2, the PALM-COEIN System (Figure 12.2) (11).

12.2.1 Polyps (AUB-P)

Endometrial polyps comprise hyperplastic projections of endometrium-like glands and stroma that can be found in up to 33% of women with AUB. Many such polyps are asymptomatic (12% to 36%); when symptoms occur, they generally manifest with intermenstrual bleeding, and available evidence suggests that about a quarter resolve spontaneously within a year (17–19). It is important for the clinician to realize that when symptoms such as HMB are present, they are unlikely to be related to polyps. Premalignant or malignant polyps are uncommon, particularly in the reproductive years, with the majority of the 1%–2% lesions that are malignant found in those with postmenopausal bleeding (20, 21). The challenge for the clinician is to determine whether the endometrial polyp is likely to contribute to the bleeding, a process that requires integration of a carefully taken history with the appearance of the polyp, or polyps, particularly with respect to friability. Hysteroscopically directed removal of polyps is safe, generally

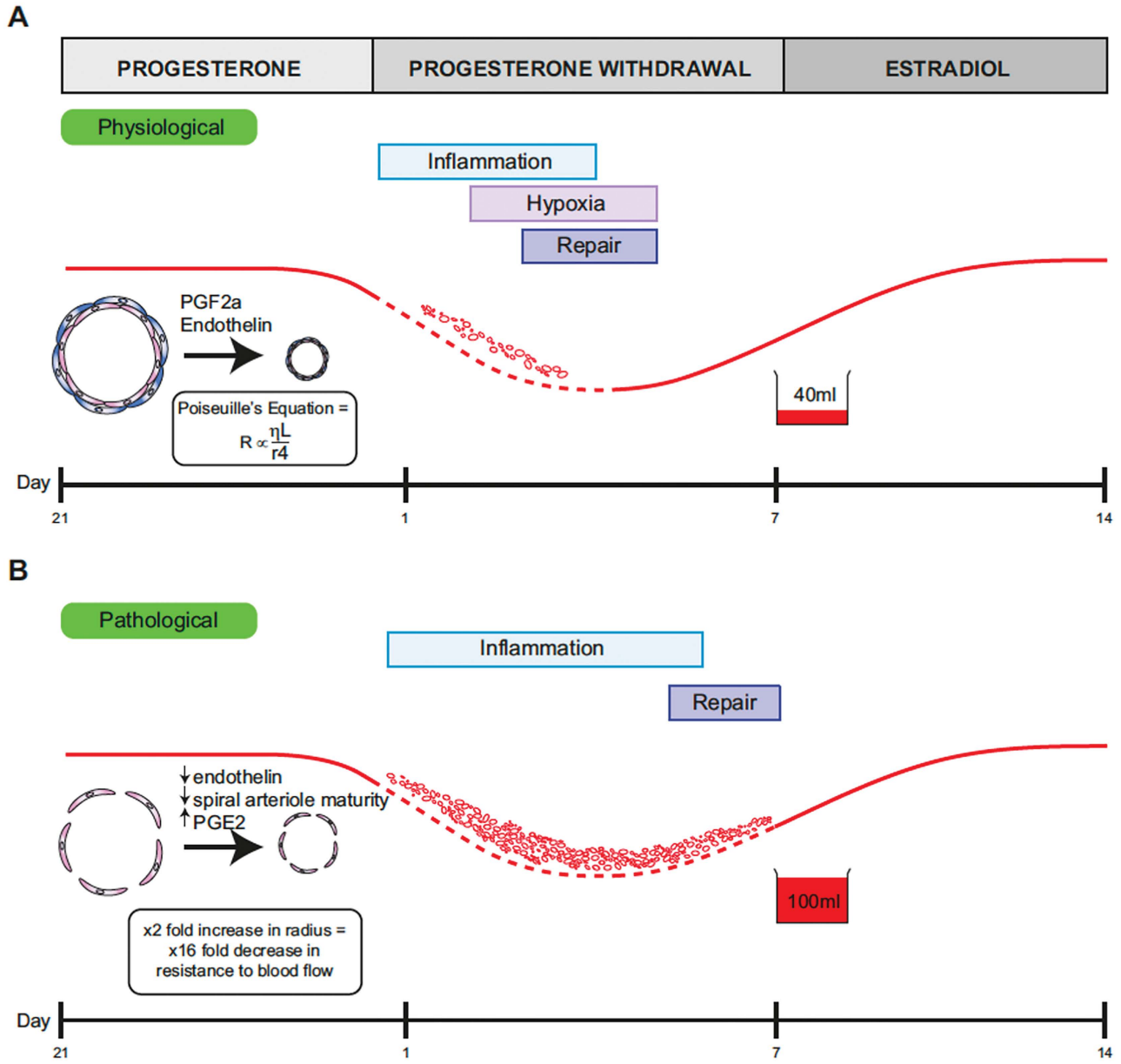


FIGURE 12.3 Normal endometrial hemostasis and the pathogenesis of AUB-E. (From Ref. 15 under Creative Commons Attribution license.) The top (A) characterizes the endometrium from an archetypical day 21 of one cycle to day 14 of the next cycle. Progesterone is responsible for the endometrial production of PG-F2α and endothelin-1, which, following progesterone withdrawal, are responsible for the vasoconstriction necessary for hemostasis and to set the stage for vascular clot formation. Note Poiseuille's equation where vessel resistance (R) is directly proportional to the length (L) of the vessel and the viscosity (η) of the blood and inversely proportional to the radius of the vessel to the fourth power (r^4). The local environment is hypoxic and involved with inflammation but repairs under the influence of estradiol without loss of function. The bottom panel (B) covers the same time frame but demonstrates the aberrant processes thought to be involved with AUB-E. The vessels are immature, and there are subnormal expressions of ET-1 and PG-F2α that result in reduced vasoconstriction that may also prevent the normal physiological hypoxic environment that is thought necessary for normal endometrial repair.

effective, and relatively inexpensive, especially if performed in an office environment under no or local anesthesia.

12.2.2 Adenomyosis (AUB-A)

Adenomyosis is an enigmatic disorder characterized histologically by the presence of endometrium-like glands and stroma within the myometrium, either diffusely or focally, generally with surrounding myometrial hyperplasia and hypertrophy. Historically, and generally based on hysterectomy for diagnosis, adenomyosis was perceived to be a disorder of women in the late reproductive years, but evidence obtained from imaging studies has demonstrated that it can be found frequently in younger girls and women, including those under the age of 18 (22–24). Imaging with transvaginal ultrasound or

MRI can be used to diagnose the disorder with approximately 80% sensitivity and specificity (25, 26). Several distinct features suggest the presence of adenomyosis on MRI and ultrasound, a circumstance that allows the description of a variety of phenotypes (see further Chapter 15). These have been recently categorized as either "direct," reflecting the observation of findings associated with endometrial glands and stroma, or "indirect," the features such as diffuse myometrial enlargement that are seen to be the result of adenomyosis (27).

Evidence of the presence or absence of adenomyosis on imaging studies expressed in a binary fashion (yes/no) is inadequate to determine whether the adenomyosis is likely to contribute to the symptom of HMB. Evidence from the United Kingdom suggests that, unless there are at least two adenomyosis features, it is unlikely that the disorder contributes to HMB (22). This evidence may help to explain the difficulty in linking the prevalence or absence of adenomyosis in hysterectomy specimens found in approximately 25%–65% of cases, to any individual or set of symptoms, including chronic AUB (28–31). Clinicians should carefully consider these issues when presented with an individual with AUB in general and HMB in particular before ascribing their symptoms to adenomyosis.

12.2.3 Leiomyomas (AUB-L)

Leiomyomas are frequent and often perplexing findings encountered when evaluating women with acute or chronic AUB symptoms. These benign tumors of the myometrium are widespread; ultrasound-based population studies of "normal" women demonstrate a prevalence of 40%–60% by age 35 and 70%–80% by age 50, with the highest prevalence in black women (32). Because the overwhelming majority of leiomyomas are asymptomatic, the clinician can be challenged when determining when identified lesions likely contribute to AUB symptoms and when a causal relationship is unlikely. The high prevalence of uterine leiomyomas, in combination with their putative relationship to AUB, infertility, and recurrent pregnancy loss, was a principal reason for the development of FIGO's leiomyoma classification system (Figure 12.4).

While it is possible that leiomyomas may contribute to AUB due to structural factors in the overlying endometrium, increased uterine vascularity, and venous ectasia, the most relevant mechanisms whereby leiomyomas contribute to AUB is by the tumor's molecular expressions interfering with the processes involved in local hemostasis (see AUB-E). These generally include alterations in vasoconstrictor activity by endothelin-1 (33) and PG-F2α (34), and TGF-β3 interference with BMP-2 activity with resultant reductions in plasminogen activator inhibitor, thrombomodulin, and antithrombin III (35). Such a mechanism requires the leiomyoma to be in proximity to the endometrium, generally in direct contact, a hypothesis that would reduce the population of leiomyomas responsible for HMB to those that are submucous in location – Types 0, 1, 2, 2–5, and perhaps 3 and 3–5 lesions (Figure 12.4). Published evidence shows that submucous leiomyomas can potentially negatively impact at least some of the required mechanisms for endometrial hemostasis that are brought into play following the

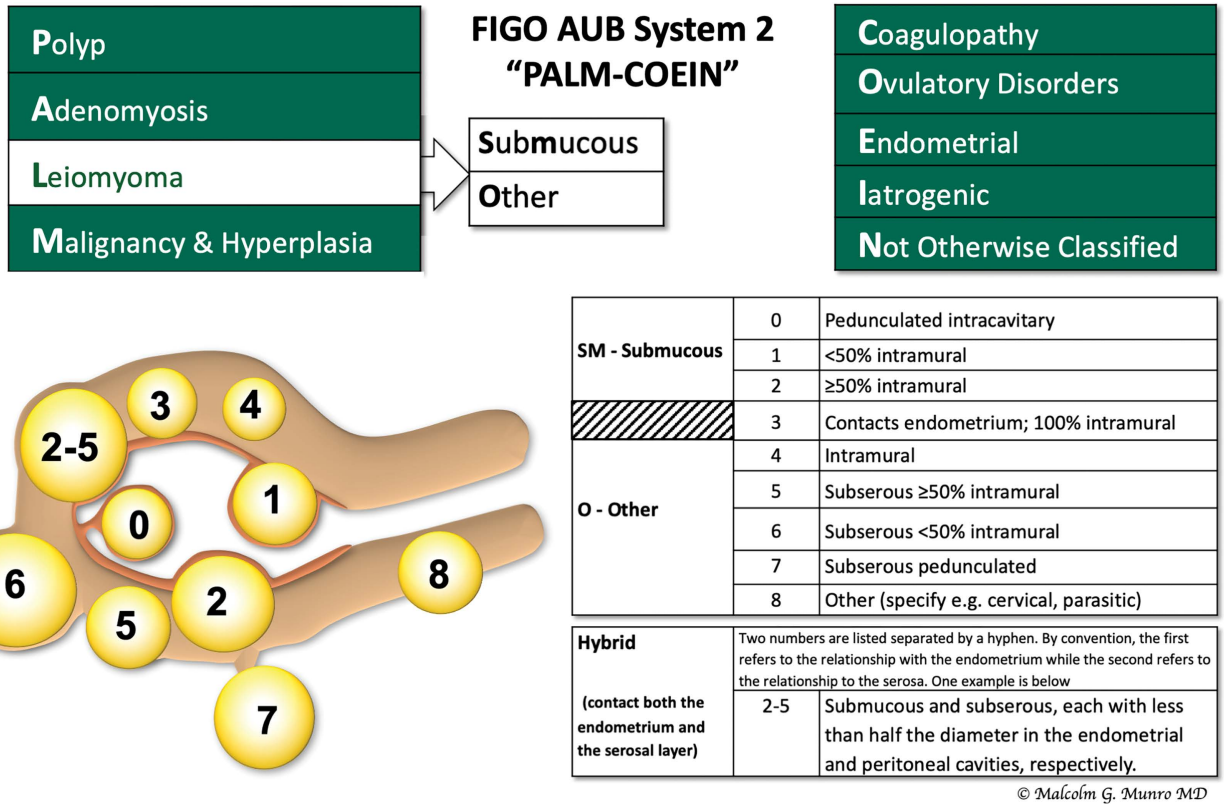


FIGURE 12.4 The FIGO leiomyoma classification system (by courtesy of Malcolm G. Munro). Leiomyomas have a simple subclassification system (submucous [sm] or "other" [o]) and a detailed classification based on the previously published Wamsteker system. Optimal classification requires one or a combination of ultrasound, contrast ultrasound, MRI, and hysteroscopy.

initiation of menses (35). As a result of these issues, women with chronic AUB who have at least one Type 0, 1, 2, 2–5, 3, and 3–5 leiomyoma are categorized in the FIGO system as having AUB-L_{SM} where "SM" stands for submucous, those with Type 4–8 lesions are designated AUB-L_O where "O" stands for "other" or "outside" the endometrial cavity (36). Indeed, those with AUB-L_O likely have another explanation for their AUB symptoms.

12.2.4 Malignancy or Hyperplasia (AUB-M)

Premalignant changes in the endometrium and Type 1 endometrial adenocarcinoma typically, but not always, occur in the context of unopposed systemic estrogens, which in premenopausal women is commonly associated with chronic anovulation and obesity. In addition to the existing WHO system for categorizing endometrial hyperplasia (37), other proposed systems are now designed to improve reproducibility (38, 39). It seems clear that there should be a unified system, but for now, the system in use should be the one selected by the clinician based, at least in part, on what is used by local pathologists and oncologists. For endometrial cancer, the FIGO systems for staging and grading endometrial carcinoma (40, 41) should be used.

12.2.5 Coagulopathies (AUB-C)

Systemic disorders of hemostasis, also called coagulopathies, are surprisingly common findings in patients with the AUB symptom of HMB. The mechanisms underlying these causes of chronic AUB are deficiencies in the tissue factor or contact activation pathways impairing hemostasis once menstruation begins. When such abnormalities are found on laboratory assessment, the patient is categorized as having AUB-C (1). Of adolescents who describe persistently heavy flow requiring admission to hospital, or those with HMB resulting in IDA, about 20% will be found to have a coagulopathy, the most common of which is von Willebrand disease (vWD) (42, 43). A systematic review of studies of women and girls of all ages with HMB demonstrated that 13% had vWD (44). If additional tests are ordered, particularly those designed to detect platelet dysfunction, abnormalities can be found in up to 47%, again, in women and girls of all ages (45). The clinical significance of all these findings is in question. Still, the evidence underlines the need to consider coagulopathies, regardless of age, in all women with the symptom of HMB.

Von Willebrand disease is, by far, the most common inherited coagulopathy. There are three recognized vWD variants, with 60%–80% having Type 1, a mild and commonly overlooked form that can only be diagnosed when the clinician requests specific testing for von Willebrand factor (vWF) levels (43, 46). Type 2 vWD is a quantitative deficiency that typically manifests with easy bruising or the symptom HMB frequently without impaired clotting function and vWF levels that are 10%–45% of normal. Von Willebrand disease in its most severe form is characterized as Type 3 that manifests with HMB and severe bleeding from even mild injury along with extremely low levels of vWF. Individuals affected with Type 3 vWD generally present in childhood or at the time of menarche when the menstrual volume is prolonged and excessively heavy (47).

12.2.6 Ovulatory Disorders (AUB-O)

Ovulatory disorders are defined in the FIGO classification system as any alterations in normal ovulatory function in nonpregnant women in the usual reproductive years (48, 49). Affected women and reproductive-aged girls are described as having AUB-O. The recently published FIGO classification of ovulatory disorders recognizes four basic categories that can be remembered by the acronym "HyPO-P," which stands for the hypothalamus (Hy), pituitary (P), and ovary (O), and polycystic ovarian syndrome (P) (Figure 12.5) (50). Each of the HyPO categories has a list of genetic, autoimmune, iatrogenic, neoplastic, functional, inflammatory, and other specific causes that may contribute to ovulatory dysfunction. It is also apparent that ovulatory disorders occupy a spectrum that ranges from occasional delayed or absent ovulation to chronic anovulation. This spectrum is, in part, responsible for the variable impact on menstruation, which can range from amenorrhea to isolated episodes of delayed menses that may be associated with an episode of acute HMB requiring emergent management. Of course, most with chronic anovulation may have irregular onset and varying bleeding volumes with long durations between periods (51). For adolescent girls under the age of 18 (52), and those over the age of 45 in their late reproductive years, disordered ovulation is common, leading many to suggest that it is a variation of normal (53). Unfortunately, such an approach tends to "normalize" what may be a disruptive experience for the perimenopausal woman or adolescent girl. This experience can generally be successfully and safely managed with nonsurgical interventions.

For many if not most women, a specific cause of infrequent or absent ovulation is frequently not identified, although factors such as psychological stress, eating disorders, low body weight, obesity, and excessive exercise are suggested as causes that ultimately manifest via the hypothalamus (54). There are also pituitary causes or contributors such as prolactinomas (55) or hypothyroidism that, via increased levels of thyrotropin-releasing hormone, also stimulate the pituitary production of prolactin, each interfering with the pituitary's role in normal ovulatory function (56). The ovary may independently adversely impact ovulatory function via various disorders ranging from autoimmune disease to androgen-secreting tumors. A recently defined ovulatory disorder of ovarian origin is the "luteal out-of-phase" (LOOP) event (57, 58). While women experiencing this disorder continue to ovulate, they variably experience premature follicular development in the luteal phase, associated high circulating levels of estradiol, low early follicular levels of inhibin B, low luteal levels of progesterone, and resulting very heavy menstrual flow (58).

Polycystic ovarian syndrome is a separate category because it is the world's most common endocrine disorder affecting reproductive-aged women (59). The disorder is actually a systemic metabolic disorder frequently associated with hyperandrogenemia, insulin resistance, increased risks of cardiovascular disease, and some malignancies, in addition to variable impacts on ovulatory function (53, 59).

Several commonly prescribed medications may also interfere with ovulatory function, including tricyclic antidepressants, phenothiazines, and other pharmaceutical agents that impact dopamine metabolism resulting in hyperprolactinemia (60).

12.2.7 Endometrial Disorders (AUB-E)

The process of endometrial sloughing and menstruation starts with corpus luteum involution, withdrawal of systemic progesterone, and the subsequent release of the molecular expressions such as ET-1 and PG-F2α necessary for both the initiation of menstruation and attaining hemostasis (15). The existence of one or more disorders of these local hemostatic mechanisms can result in HMB in an ovulating woman in the absence of, or unrelated to, coagulopathies or structural abnormalities of the uterus (Figure 12.3). Such disorders are categorized in FIGO System 2 as AUB-E (15).

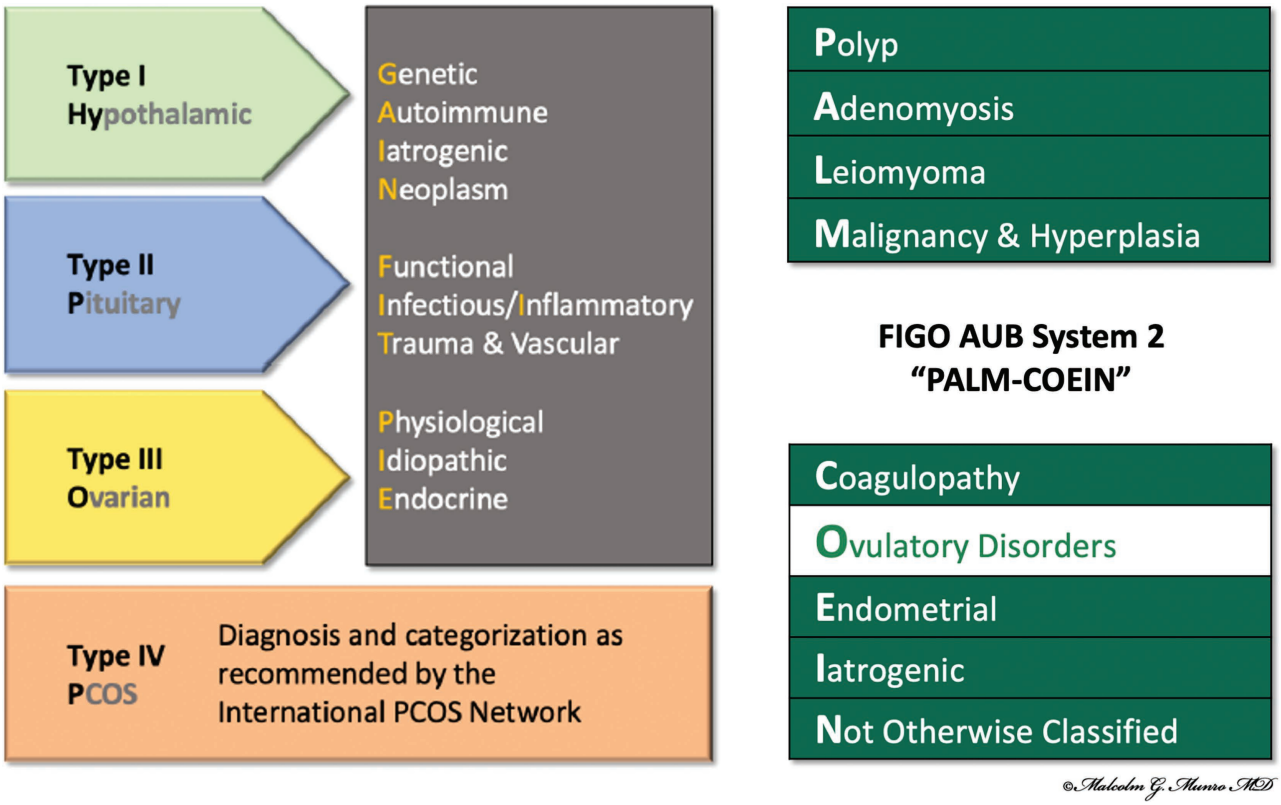


FIGURE 12.5 The HyPO-P FIGO ovulatory disorders classification system (by courtesy of Malcolm G. Munro). The system is the product of a rigorous Delphi consensus development process involving a global set of professional and lay stakeholders. The HyPO component comprises the three anatomic components of the hypothalamic, pituitary, and ovarian axis, while the second P is the polycystic ovarian syndrome. Each of the HyPO elements comprises a variety of entities that can be categorized via the "GAIN-FIT-PIE" mnemonic.

Although there is a lack of molecular data from large-scale population studies, it is likely that AUB-E is far more common than generally appreciated and may comprise the majority of the clinically normalized cases of HMB that are only identified through direct surveys of women (7–9). This entity is generally what was meant by some with the use of terms such as "menorrhagia," "essential menorrhagia," "idiopathic menorrhagia," and "ovulatory dysfunctional uterine bleeding" that have been discarded by a well-constructed consensus development process (13, 14). It is apparent that women with the symptom of HMB, consistent with AUB-E, have one or a combination of disordered local levels of vasoconstrictors such as ET-1 (61) and PG-F2α (62), excess plasminogen activator (63), and elevated local production of vasodilators, such as PGE_2 and prostacyclin (PGI_2) (15, 64, 65) (Figure 12.3). Although this evidence has been available for more than 30 years, there are, unfortunately, no laboratory tests available to clinicians. It is also important to realize that AUB-E may be the cause of HMB in ovulatory women with structural lesions likely to be asymptomatic such as Type 4 through 8 leiomyomas or adenomyosis based on a single ultrasound feature (66).

There may exist other primary endometrial disorders that could contribute either to HMB or intermenstrual bleeding (IMB). Investigators have proposed a number of potential mechanisms including inflammatory disorders and disturbances in the molecular mechanisms of endometrial repair (15, 67). However, as yet, there are no available and consistent data that would allow for meaningful characterization of such mechanisms.

12.2.8 Iatrogenic Bleeding (AUB-I)

Selected systemic or local medical therapy and intrauterine systems primarily designed for contraception have the potential to cause or contribute to iatrogenic AUB and are collectively called AUB-I. Pharmacological causes of AUB-I include those agents that directly affect the endometrium, the systemic control of ovulation, or normal blood coagulation mechanisms. Estrogens, progestins, and androgens, used either alone or in combination, can prevent ovulation and directly affect the endometrium. The impact of gonadal steroid use on a woman's uterine bleeding experience depends on the route, dose, and timing of administration. While the cyclical administration of progestins, with or without estrogens, is expected to manifest in predictably scheduled withdrawal bleeding, continuous progestin use is generally designed to result in amenorrhea. Unscheduled or random bleeding (breakthrough bleeding) commonly occurs with continuous progestins and is thought to be related to impaired absorption of the agent, coexistent ovarian estradiol production, or irregular systemic levels of gonadal steroids secondary to poor compliance.

Intrauterine medical devices, often called "intrauterine systems" (IUS) are either "inert" with no pharmacologically active component or "medicated" as they continuously release a therapeutic agent that is almost always a progestin and typically levonorgestrel. While those IUS that are wrapped with copper or a copper alloy generally are considered "inert," their metal component can genuinely result in unique effects on endometrial physiology. Such intrauterine systems have been associated with HMB and IMB that are thought to occur secondary to changes in the local (endometrial) levels of prostaglandins and inflammatory cells (68–70). The systems that continuously secrete levonorgestrel into the endometrial environment (LNG-IUS) create complex changes in local endometrial morphology, histopathology, and pharmacology that profoundly affect the volume and other aspects of menstrual bleeding (71). At least for ovulatory women, the volume of menstrual flow typically dramatically decreases, and for some, there is intermenstrual spotting or light bleeding that, in the majority of instances, resolves spontaneously by about 6 months (72).

12.2.9 Not Otherwise Classified (AUB-N)

Abnormal uterine bleeding may be associated with several conditions or abnormalities that are either rare, a questionable contributor to AUB, or otherwise not assigned to one of the other categories. Arteriovenous malformation (AVM) is an example of a relatively rare condition characterized by a localized collection of abnormally connected arteries and veins. In the uterus, these lesions are either congenital or acquired, particularly after uterine curettage, and have been associated with episodes of acute and excessively heavy bleeding (73). The diagnosis can be made with color Doppler transvaginal ultrasound or contrast-enhanced MRI (74, 75).

A diagnosis currently included in this category is known by various names isthmocele, niche, or cesarean scar defect, descriptive of the variably characterized gap frequently left in the lower uterine segment or upper cervix following cesarean section. A recently published systematic review has demonstrated a relationship between AUB and typical features, including dark spotting, typically in the postmenstrual follicular phase of the cycle (76). As a result, FIGO is considering modifications in System 2 to take into account the observation of this relationship. Of course, as with other structural anomalies, the presence of AUB and a C-scar defect does not necessarily mean that the relationship is one of cause and effect.

12.3 Acute Nongestational Uterine Bleeding

As defined previously, acute HMB, unrelated to pregnancy, is that which, in the opinion of the clinician, requires urgent or emergent medical intervention (11). As discussed previously, inherited bleeding disorders are relatively common in adolescent girls and women, and acute HMB at menarche is a common presentation in those affected with such disorders (77, 78). In the later reproductive years, women with acute HMB often have underlying structural causes or contributors to chronic AUB and/or experience concomitant ovulatory disorders (AUB-O) or AUB-E. Despite its apparent frequency and clinical impact, there has been relatively little research regarding this clinical situation's pathogenesis, and evidence-based management guidance has generally been lacking.

12.3.1 Clinical Evaluation

Acute HMB ranges in severity from modestly excessive bleeding to that associated with hypovolemic shock. If a patient is hemodynamically unstable, the initial efforts should be focused on establishing appropriate intravenous lines, administration of isotonic fluids, obtaining blood samples for laboratory testing, and, if appropriate, cross-matching of blood. The clinician's responsibility is to get an adequate initial history and perform a pelvic evaluation to confirm that the bleeding originates from the uterus. Ideally, once stabilized, pelvic imaging should be performed to evaluate the uterus before implementing medical or surgical approaches designed to stop or control the hemorrhage.

The search for a congenital or acquired bleeding disorder (coagulopathy) is initiated by reviewing the personal, medical, and family history. A lifelong history of HMB, or any history of postpartum bleeding, excessive bleeding with surgical or dental procedures, frequent bruising, and a family history of these symptoms are components of a screening tool that has 90% sensitivity to detect these relatively common disorders (79) (Table 12.1). The presence of an arteriovenous malformation, an uncommon but frequently overlooked cause of acute HMB, might be suggested if there is a history of curettage for the termination of pregnancy or post-pregnancy bleeding (80).

The laboratory assessment should include a complete blood count, ABO blood type, and a urinary (or serum) assay for pregnancy. When coagulopathy is suspected, several nonspecific assays should be considered, including fibrinogen, prothrombin time (PT), and activated partial thromboplastin time (PTT). For those with a positive screening history, von Willebrand disease should be considered, and assays for von Willebrand factor, factor VIII, and ristocetin cofactor should be obtained (81, 82). For those women using anticoagulants, INR and other appropriate measures of coagulation function should be measured. If a disorder of systemic hemostasis is known or suspected, consultation with a specialist in hematology is generally appropriate.

The HMB may impair the performance of both histological evaluations of the endometrium and sonographic and hysteroscopic imaging of the endometrial cavity because of the influence of intrauterine blood and clot. Consequently, it may be necessary to repeat these steps, as appropriate, later in the clinical course.

12.4 Evaluation of Women with Chronic AUB in the Reproductive Years

It is recommended that an individual with abnormal vaginal bleeding be evaluated using a structured approach that incorporates both FIGO Systems 1 and 2, the latter the PALM-COEIN system. Such an approach is summarized in Figure 12.6.

12.4.1 The Structured History

Since girls and women may not be sure about the source of vaginal bleeding, it is incumbent on the clinician to confirm that the bleeding is or is likely emanating from the uterus by evaluating for other sources of blood loss. In addition, it is essential to evaluate for pregnancy using suitable urine or blood testing for β-hCG.

Once it is determined that the reproductive-aged patient has AUB, it is important to apply FIGO System 1 initially to

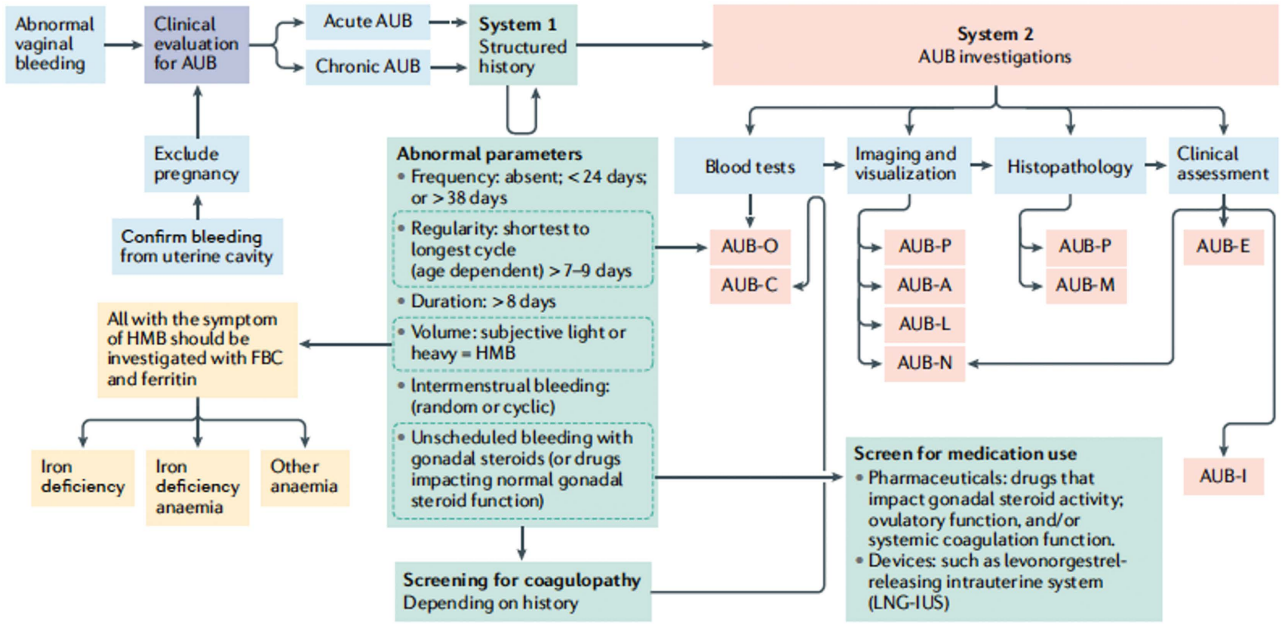


FIGURE 12.6 The approach to evaluation of nonpregnant women and girls with AUB. (From Ref. 16 with permission.) The pathway starts in the top left, where abnormal vaginal bleeding is presented to the clinician, who must perform a physical examination and exclude pregnancy before concluding that indeed the individual has AUB. Whether or not the individual has acute or chronic AUB, the evaluation process starts with FIGO AUB System 1 to define and categorize the nature of the symptoms, a critical component of the ultimate determination of causation. For those known or suspected to have the symptom of heavy menstrual bleeding, it is essential that a complete (full) blood count be obtained, as well as a measurement of ferritin, the latter to evaluate the patient for iron deficiency. An essential component of assessing those with HMB is screening for the presence of a bleeding disorder (coagulopathy) by using a validated structured history. Those who screen positive should be investigated with appropriate laboratory investigations. This is also a time to determine if the individual is using medications that may alter the nature of menstrual bleeding, including those that may affect ovulatory function, and, if HMB is present, the use of anticoagulants. To identify individuals with AUB-P, -A, -L, or -N, imaging is critical, while histopathology is the only recognized method of determining the presence of atypical endometrial hyperplasia/endometrial intraepithelial neoplasia or malignancy. AUB-E is diagnosed when AUB, generally HMB, is present absent any other abnormality or when structural abnormalities are not thought to contribute to the bleeding. Regardless of the presumptions of causation, if multiple abnormalities are identified, all are listed, e.g., AUB-A, -L, -O.

determine the ovulatory status; the predictable onset of menstrual bleeding with a consistent cycle length of 24 to 38 days is highly correlated with ovulation (83). Irregularity of the menstrual cycle length greater than 7 days between the ages of 26 and 41, or 9 days for those 18–25 or 42–45, suggests the presence of an ovulatory disorder. While there is no lower boundary for the duration of the menstrual period, the upper limit is 8 days, after which the periods are deemed "prolonged." The patient determines the volume of bleeding; FIGO and NICE define heavy menstrual bleeding as "volume" sufficient to interfere with a woman's physical, social, emotional, and/or material quality of life (1, 84).

It may be necessary to ask additional questions to provide better insight into the menstrual experience, including the simultaneous use of tampons and pads, the passage of large clots, the need for "accommodations" that include the use of towels to protect upholstery, the desire to wear black and baggy clothing, and the need for extra protection at night to prevent spill onto bedsheets (85). Women with HMB are frequently iron deficient, so it is essential to inquire about fatiguability, reduced cognitive function ("brain fog"), and changes in exercise tolerance.

Bleeding between menstrual periods of regular cyclical onset is termed intermenstrual bleeding. When randomly experienced, such bleeding typically reflects the presence of a focal lesion such as a polyp, while cyclical IMB is often associated with hormonal causes with the exception of the early cycle, when it may be reflective of a cesarean scar defect (76).

Because of their relatively high prevalence, screening women with HMB for bleeding disorders (coagulopathies) is essential, a process that is facilitated using the validated questionnaire discussed previously (Table 12.1). Those who screen positive require evaluation with appropriate laboratory assessments, preferably under the guidance of a hematologist.

When the structured menstrual history suggests the presence of AUB-O based upon infrequent or irregular menses, the clinician should attempt to identify potential endocrinological causes of ovulatory dysfunction, such as hyperandrogenism, hyperprolactinemia, and thyroid dysfunction. However, it is also essential to identify other possible mechanisms that

include psychological stress, excessive exercise, eating disorders, weight change, and nonprescription drugs such as opiates or prescription pharmacological agents, each of which can alter dopamine metabolism. Dopamine physiology can also be altered by using prescribed medications, including tricyclic antidepressants and other norepinephrine and dopamine reuptake inhibitors.

12.4.2 Physical Examination

For women with the symptom of HMB, iron deficiency may be such that the individual is anemic with physical manifestations that include, in addition to an overall pale complexion, conjunctival pallor, tongue depapillation, and the presence of koilonychia – horizontal lines and depressions in the fingernails (86). For those who have apparent AUB-O based upon irregular and/or infrequent menses, low or high body weight should be noted, if present, and features known to be associated with hypothyroidism, hyperandrogenism, and hyperprolactinemia should be sought. The visual and manual pelvic examination is performed initially to evaluate for pathology that could explain bleeding, particularly IMB, that the patient perceives as being from the uterus. Consequently, the clinician evaluates the vulva, vagina, exocervix, perineum, periurethral, and perianal regions looking for friable lesions. A manual examination is essential to assess the uterus for flexion, version, size, irregularity, and tenderness – an adnexal examination should be performed as well. It should be noted that the physical examination, while necessary, is not very useful at determining the cause of AUB – the palpable leiomyomas may have nothing to do with the symptom, while the submucous fibroid causing HMB is typically not palpable.

12.4.3 Laboratory Assessment

The specifics of laboratory assessment for women with chronic AUB can vary according to the results of the structured history. It is essential to recognize that ID precedes the development of anemia. It can cause symptoms like reduced cognitive function and impairment of physical function as well as the vaguely defined but generally recognizable symptom of "brain fog" (87–89). While regular assessment of iron status by measurement of ferritin and, potentially, transferrin saturation (TSAT) is important for all women in their reproductive years; such evaluation, in combination with complete blood count (CBC), is essential with those with known or suspected HMB. While there is controversy about the lower limit of normal for ferritin, with the WHO claiming it to be 15 μg/L, it seems clear that the lower limit should be no less than 30 μg/L in individuals without comorbidities (89). Because ferritin may be elevated in those with chronic inflammatory conditions, a fasting TSAT can be used to detect the ID that otherwise may be missed (normal ≥ 20%) (90).

For those who screen "positive" for the potential presence of coagulopathy, several laboratory investigations are in order, selected, and performed, preferably in association with a hematologist or internist with experience in the diagnosis of bleeding disorders. Analyses that should be considered include prothrombin time (PT), activated partial thromboplastin time (APTT), vWF antigen, ristocetin cofactor, and factor VIII (FVIII). Those individuals who test positive are categorized as having AUB-C.

Women with irregular menstrual bleeding typically have an ovulatory disorder and can be categorized as AUB-O. If there is doubt about the presence of AUB-O, serum progesterone can be obtained in what is suspected to be the luteal phase, but such an assessment may not reflect the chronic state as it samples only one cycle. If AUB-O is present, several potential causes can be detected with laboratory evaluation. These include hypothyroidism, hyperandrogenemia, and various causes of hyperprolactinemia. Consequently, and, in part, depending on the history and the physical findings, measurement of serum thyroid function, prolactin, and/or testosterone may be considered.

12.4.4 Imaging

Bimanual examination of the uterus is inadequate for detecting the structural causes of AUB in the reproductive years. Endometrial polyps and cesarean scars cannot be felt, the diagnosis of adenomyosis may be suggested but not confirmed, and while the palpable fibroid may not explain the bleeding, the responsible leiomyoma may not be palpable. Uterine imaging, properly performed and interpreted, is an essential component of the complete evaluation. Details on gynecological imaging can be found elsewhere in this book (Chapter 9).

12.4.4.1 Transvaginal Ultrasound

Transvaginal ultrasound (TVUS) should be used liberally in the evaluation of both the endometrium and the myometrium, and the use of fluid contrast (sonohysterography) should be part of the diagnostic armamentarium of any clinician specializing in uterine and adnexal disorders (see further Chapter 9). This means that, while there is an essential role for the radiologist and their storage system, the clinician should be adept at performing transvaginal ultrasound-based evaluations and intimately familiar with the interpretation of other imaging technologies, including MR imaging (MRI). Indeed, there is evidence that a well-trained gynecologist may be more accurate at identifying the features of adenomyosis than a radiologist (91). While two-dimensional (2D) ultrasound is widely available, three-dimensional (3D) TVUS is becoming increasingly available and, in some instances, can serve to replace MRI. This may have particular application in the diagnosis and characterization of Müllerian anomalies, while for adenomyosis, the available evidence is less clear.

The overall uterine dimensions should be identified and measured to capture the sagittal length of the corpus and cervix, the anteroposterior dimensions, and, if possible, a coronal view of the corpus to allow determination of the transverse diameter. While during this process, obvious leiomyomas or adenomyosis might be seen, attention could be directed to the evaluation of the endometrial echo complex (EEC), often trivialized as the "endometrial stripe" that provides far more information than a simple metric from one endomyometrial junction to the other. From the perspective of AUB, focal endometrial thickening may suggest the presence of an endometrial polyp, and submucous leiomyomas may be suggested if the tumor is seen to be in contact with the endometrium. In such cases, it may be categorized as submucous. In addition to indirect features such as globular enlargement, asymmetrical myometrial thickening, fan-shaped shading, and an indistinct myometrial junction, direct features suggestive of adenomyosis, such as myometrial cysts, echogenic islands, and echogenic subendometrial lines and buds may be identified by careful evaluation of the myometrium (27).

12.4.4.2 Sonohysterography

Sonohysterography using gel or normal saline is a highly useful diagnostic procedure that is easily performed in an office setting and one that can be combined with endometrial biopsy if appropriate (see further Chapter 9). The instillation of saline or gel into the endometrial cavity can be accomplished with several devices and techniques, including insemination catheters, specially designed SHG catheters, and even endometrial biopsy cannulas if the proximal end is fitted with a Luer adaptor. A transvaginal ultrasound is performed once the endometrial cavity is catheterized or injected with gel (92, 93). The technique will generally demonstrate or confirm the presence of endometrial polyps and allow better discrimination amongst FIGO Type 0, 1, 2, 2–5, 3, and 3–5 leiomyomas, including characterization of their diameters, number, and, if applicable, relationship with the uterine serosa. Sonohysteroscopy may also confirm the presence and allow the characterization of cesarean scar defects. If an endometrial biopsy catheter or cannula is used (excepting the pipelle), it is relatively easy to sample the endometrium under direct visualization with no deterioration in the quality of the specimen, at least with the use of saline (94).

12.4.4.3 Elastography

Both ultrasound and, more recently, MRI have been used to quantify tissue biomechanical properties via a technique called elastography, which can be seen to quantify the process of palpation by determining the stiffness of an organ or tissue (95, 96). The gynecologic disorder where elastography appears to offer the greatest promise is adenomyosis, where it has been shown that lesional stiffness may correlate with the nature and severity of symptoms, including menstrual blood loss (97). As a result, this technique may serve as an adjunct to imaging studies by providing another dimension for assessment that may have future value as a way to monitor response to therapy (98). The concept of elastography measures tissue's response to mechanical excitation. Strain elastography is based on the pressure exerted by the ultrasound probe and the resulting mechanical deformation of the tissue. The shear wave technique involves measuring the response to an acoustic wave induced by the transducer. The stiffness of tissue is depicted on a display using a color-based "heat map" of the target organ. The elastography technology is increasingly included as a standard or optional feature of ultrasound machines in clinical use.

12.4.4.4 Magnetic Resonance Imaging

In several instances, TVUS and abdominal ultrasound are inadequate for evaluating the uterus in women with AUB in the reproductive years. In such cases, magnetic resonance imaging can be effective. For example, MRI may be superior to ultrasound for the diagnosis of adenomyosis when the uterus is quite large, typically the case when leiomyomas are also present (99). Radiological identification of diffuse adenomyosis by MRI can also be based on the identification of direct and indirect features. Globular enlargement and asymmetrical thickening of the corpus are examples of indirect features, while the presence of myometrial cysts or T2-weighted signal-intense foci is generally accepted as direct evidence of adenomyosis. The junctional zone (JZ) of the uterus is primarily an MRI-defined T2 hypointense region of the myometrium that roughly corresponds to the inner myometrium. Thickening of the JZ beyond a predetermined amount, usually over 11 mm, has been associated with the presence of adenomyosis. However, evolving evidence suggests that the finding of a thicker JZ may in itself be relatively nonspecific for adenomyosis. Instead, the relationship between the JZ and the endometrium – distinct or irregular, or poorly defined – appears to be a more accurate predictor of the presence of adenomyosis (100).

12.4.4.5 Hysteroscopy

Hysteroscopy is another office-based tool for evaluating women with AUB with high sensitivity and specificity for detecting polyps and leiomyomas (101). One limitation of diagnostic hysteroscopy is the inability to precisely determine the extent of myometrial involvement of a Type 1 or 2 leiomyoma. The performance of simultaneous hysteroscopy and abdominal ultrasound-based contrast sonography can often be helpful in this regard, although it is of limited value in women with high BMI and/or a severely retroverted and retroflexed uterus. More on hysteroscopy for diagnosis can be found in Chapter 27.

12.4.4.6 Notation

The FIGO systems for the diagnosis and evaluation of AUB in the reproductive years were designed to provide support for teaching and clinical care and structure for basic, translational, clinical, and epidemiological investigators. For investigators, the approach should help standardize research populations to improve the fidelity and generalizability of results and facilitate the performance of meaningful systematic reviews and meta-analyses. Because there frequently are multiple potential causes or contributors to AUB symptoms, FIGO System 2 (PALM-COEIN) and classification subsystems (currently leiomyomas and ovulatory disorders) can be used to document accordingly. The notation system described in Figure 12.7 is suggested, particularly when more than one cause or contributor to AUB symptoms is known or suspected.

12.5 Conclusion

Abnormal uterine bleeding can be acute or chronic and may be found associated with any one or combination of the entities described in FIGO's AUB System 2, the PALM-COEIN system. It is essential to understand that while structural abnormalities such as polyps, adenomyosis, and leiomyomas may be present, they may not be the cause of the bleeding, while functional abnormalities such as coagulopathies (AUB-C), ovulatory dysfunction (AUB-O), and primary endometrial disorders (AUB-E) may be the actual cause of the symptoms experienced by the patient. Appropriate investigation requires some combination of a structured history, a physical examination, and a selected set of laboratory and imaging studies that together provide the information necessary for synthesizing both a diagnosis and a menu of therapeutic options for consideration by the patient. At the forefront, current and future desires regarding pregnancy will be critically important factors in the decision-making processes. In most instances, effective medical therapies exist, but should they fail, be poorly tolerated, or be inappropriate for the clinical situation, there are several alternatives to hysterectomy that have been demonstrated effective.

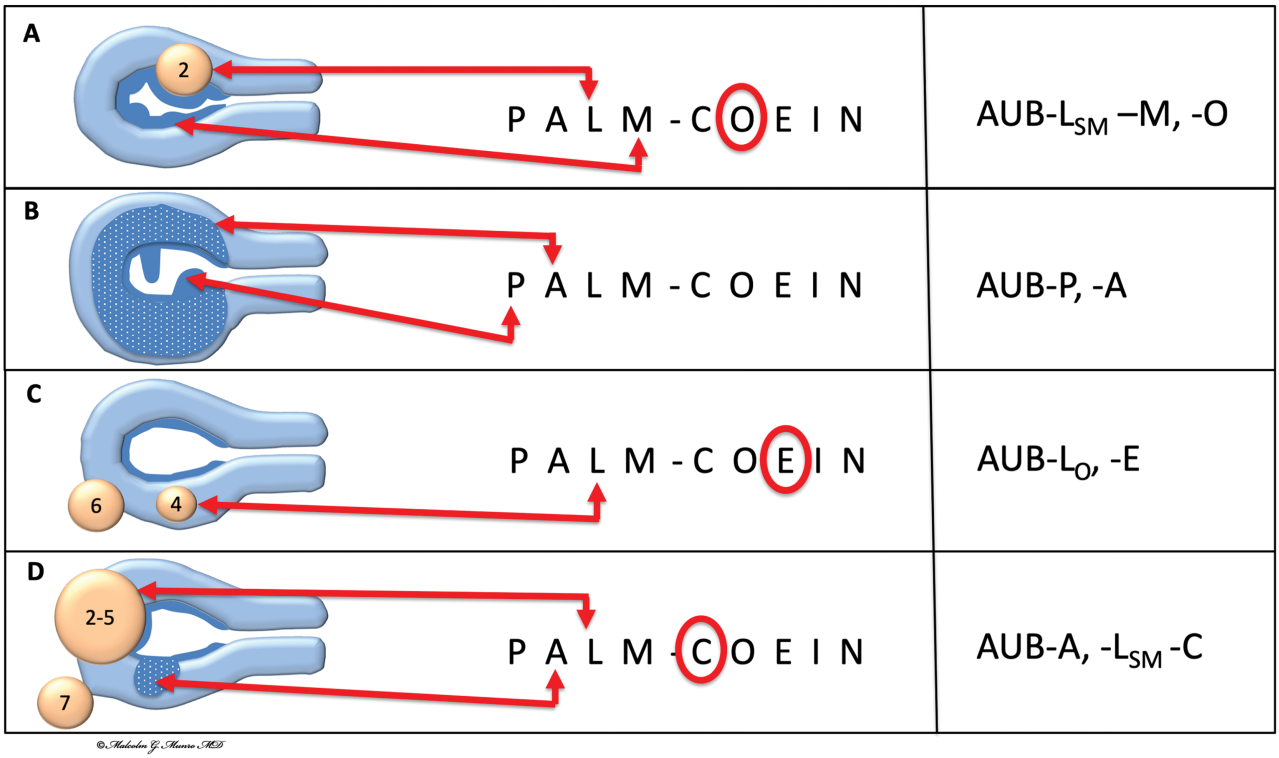


FIGURE 12.7 FIGO System 2 when there are multiple findings (by courtesy of Malcolm G. Munro). Depictions of the outcomes of clinical evaluation where multiple potential causes or contributors to AUB are identified. The sagittal images in the left panels depict what might be seen with sonohysterography with a dilated endometrial cavity. The structural findings (PALM) based on imaging or histopathology are denoted with arrows, while the nonstructural contributors (COEI) are circled. The suggested notation is found in the panels on the right. (A) The submucous leiomyoma is identified in a woman with long-term irregular menses suggesting an ovulatory disorder (FIGO AUB System 1), and an endometrial biopsy demonstrated endometrial intraepithelial neoplasia. (B) The patient with both HMB and random intermenstrual bleeding (FIGO AUB System 1) is found to have both an endometrial polyp (P) and sonographic evidence of diffuse adenomyosis. (C) The patient had long-term HMB (FIGO System 1), did not have a coagulopathy, and was found to have Types 4 and 6 leiomyomas not likely to contribute to the AUB. Such individuals are thought to have AUB-E. (D) An individual with lifelong HMB that was increasing in severity (FIGO AUB System 1) and was found to have a Type 2–5 leiomyoma, evidence of focal adenomyosis, and with appropriate testing Type 1 von Willebrand disease.

References

1. Munro MG et al. The two FIGO systems for normal and abnormal uterine bleeding symptoms and classification of causes of abnormal uterine bleeding in the reproductive years: 2018 revisions. FIGO Committee on Menstrual Disorders. *Int Journal Gynaecol Obstet*. 2018;143(3):393–408.
2. Munro MG et al. FIGO classification system (PALM-COEIN) for causes of abnormal uterine bleeding in nongravid women of reproductive age. FIGO Working Group on Menstrual Disorders. *Int J Gynaecol Obstet*. 2011;113(1):3–13.
3. Cote I et al. Work loss associated with increased menstrual loss in the United States. *Obstet Gynecol*. 2002;100(4):683–687.
4. Frick KD et al. Financial and quality-of-life burden of dysfunctional uterine bleeding among women agreeing to obtain surgical treatment. *Womens Health Issues*. 2009;19(1):70–78.
5. Schoep ME et al. Productivity loss due to menstruation-related symptoms: a nationwide cross-sectional survey among 32 748 women. *BMJ Open*. 2019;9(6):e026186.
6. Georgieff MK. Iron deficiency in pregnancy. *Am J Obstet Gynecol*. 2020;223(4):516–524.
7. Fraser IS et al. Prevalence of heavy menstrual bleeding and experiences of affected women in a European patient survey. *Int J Gynaecol Obstet*. 2015;128(3):196–200.
8. Schoep ME et al. The impact of menstrual symptoms on everyday life: a survey among 42,879 women. *Am J Obstet Gynecol*. 2019;220(6):569 e1- e7.
9. Henry C et al. Barriers to seeking consultation for abnormal uterine bleeding: systematic review of qualitative research. *BMC Womens Health*. 2020;20(1):123.
10. Liu Z et al. A systematic review evaluating health-related quality of life, work impairment, and health-care costs and utilization in abnormal uterine bleeding. *Value Health*. 2007;10(3):183–194.
11. Munro MG et al. The FIGO classification system ("PALM-COEIN") for causes of abnormal uterine bleeding in non-gravid women in the reproductive years, including guidelines for clinical investigation. *Int J Gynaecol Obstet*. 2011;113(1):3–13.
12. Practice bulletin 128: diagnosis of abnormal uterine bleeding in reproductive-aged women. *Obstet Gynecol*. 2012;120(1):197–206.
13. Fraser IS et al. A process designed to lead to international agreement on terminologies and definitions used to describe abnormalities of menstrual bleeding. *Fertil Steril*. 2007;87(3):466–476.

14. Fraser IS et al. Can we achieve international agreement on terminologies and definitions used to describe abnormalities of menstrual bleeding? *Hum Reprod*. 2007;22(3):635–643.
15. Critchley HOD et al. Physiology of the endometrium and regulation of menstruation. *Physiol Rev*. 2020;100(3):1149–1179.
16. Jain V et al. Uterine bleeding: how understanding endometrial physiology underpins menstrual health. *Nat Rev Endocrinol*. 2022;18(5):290–308.
17. Savelli L et al. Histopathologic features and risk factors for benignity, hyperplasia, and cancer in endometrial polyps. *Am J Obstet Gynecol*. 2003;188:927–931.
18. Lieng M et al. Prevalence, 1-year regression rate, and clinical significance of asymptomatic endometrial polyps: cross-sectional study. *J Minim Invasive Gynecol*. 2009;16(4):465–471.
19. Lieng M et al. Clinical effectiveness of transcervical polyp resection in women with endometrial polyps: randomized controlled trial. *J Minim Invasive Gynecol*. 2010;17(3): 351–357.
20. Anastasiadis PG et al. Endometrial polyps: prevalence, detection, and malignant potential in women with abnormal uterine bleeding. *Eur J Gynaecol Oncol*. 2000;21(2):180–183.
21. Shushan A et al. How often are endometrial polyps malignant? *Gynecol Obstet Invest*. 2004;58(4):212–215.
22. Naftalin J et al. Association between ultrasound features of adenomyosis and severity of menstrual pain. *Ultrasound Obstet Gynecol*. 2016;47(6):779–783.
23. Pinzauti S et al. Adenomyosis by transvaginal ultrasonographic features in nulligravid women without endometriosis aged 18–30 years: correlation with symptoms. *Ultrasound Obstet Gynecol*. 2015;46:730–736.
24. Exacoustos C et al. Ultrasound findings of adenomyosis in adolescents: type and grade of the disease. *J Minim Invasive Gynecol*. 2022;29(2):291–299 e1.
25. Champaneria R et al. Ultrasound scan and magnetic resonance imaging for the diagnosis of adenomyosis: systematic review comparing test accuracy. *Acta Obstet Gynecol Scand*. 2010;89(11):1374–1384.
26. Maheshwari A et al. Adenomyosis and subfertility: a systematic review of prevalence, diagnosis, treatment and fertility outcomes. *Hum Reprod Update*. 2012;18:374–392.
27. Harmsen MJ et al. Consensus on revised definitions of Morphological Uterus Sonographic Assessment (MUSA) features of adenomyosis: results of modified Delphi procedure. *Ultrasound Obstet Gynecol*. 2022;60(1):118–131.
28. Molitor JJ. Adenomyosis: a clinical and pathological appraisal. *Am J Obstet Gynecol*. 1971;110(2):275–284.
29. Bird CC et al. The elusive adenomyosis of the uterus – revisited. *Am J Obstet Gynecol*. 1972;112(5):583–593.
30. Seidman JD et al. Pathologic findings from the Maryland Women's Health Study: practice patterns in the diagnosis of adenomyosis. *Int J Gynecol Pathol*. 1996;15(3):217–221.
31. Weiss G et al. Adenomyosis a variant, not a disease? Evidence from hysterectomized menopausal women in the Study of Women's Health Across the Nation (SWAN). *Fertil Steril*. 2009;91(1):201–206.
32. Day Baird D et al. High cumulative incidence of uterine leiomyoma in black and white women: ultrasound evidence. *Am J Obstet Gynecol*. 2003;188(1):100–107.
33. Pekonen F et al. Differential expression of mRNAs for endothelin-related proteins in human endometrium, myometrium and leiomyoma. *Mol Cell Endocrinol*. 1994;103(1–2):165–170.
34. Miura S et al. Differential infiltration of macrophages and prostaglandin production by different uterine leiomyomas. *Hum Reprod*. 2006;21(10):2545–2554.
35. Sinclair DC et al. Leiomyoma simultaneously impair endometrial BMP-2-mediated decidualization and anticoagulant expression through secretion of TGF-beta3. *J Clin Endocrinol Metab*. 2011;96(2):412–421.
36. Munro MG et al. FIGO classification system (PALM-COEIN) for causes of abnormal uterine bleeding in nongravid women of reproductive age. *Int J Gynaecol Obstet*. 2011;113(1):3–13.
37. Tavassoli FA et al. *World Health Organization Classification of Tumors: Pathology and Genetics of Tumours of the Breast and Female Genital Organs*. Lyon: IARC Press; 2003.
38. Mutter GL. Endometrial intraepithelial neoplasia (EIN): will it bring order to chaos? The Endometrial Collaborative Group. *Gynecol Oncol*. 2000;76(3):287–290.
39. Bergeron C et al. A multicentric European study testing the reproducibility of the WHO classification of endometrial hyperplasia with a proposal of a simplified working classification for biopsy and curettage specimens. *Amer J Surg Pathol*. 1999;23(9):1102–1108.
40. Creasman WT et al. Carcinoma of the corpus uteri. FIGO 6th Annual Report on the Results of Treatment in Gynecological Cancer. *Int J Gynaecol Obstet*. 2006;95(Suppl 1):S105–S143.
41. Creasman W. Revised FIGO staging for carcinoma of the endometrium. *Int J Gynaecol Obstetrics*. 2009;105(2):109.
42. James AH et al. Evaluation and management of acute menorrhagia in women with and without underlying bleeding disorders: consensus from an international expert panel. *Eur J Obstet Gynecol Reprod Biol*. 2011;158:124–134.
43. Kouides PA et al. Hemostasis and menstruation: appropriate investigation for underlying disorders of hemostasis in women with excessive menstrual bleeding. *Fertil Steril*. 2005;84(5):1345–1351.
44. Shankar M et al. von Willebrand disease in women with menorrhagia: a systematic review. *BJOG*. 2004;111(7):734–740.
45. Bouchard P et al. Selective progesterone receptor modulators in reproductive medicine: pharmacology, clinical efficacy and safety. *Fertil Steril*. 2011;96(5):1175–1189.
46. Lukes AS et al. Disorders of hemostasis and excessive menstrual bleeding: prevalence and clinical impact. *Fertil Steril*. 2005;84(5):1338–1344.
47. Kadir RA et al. Variations in coagulation factors in women: effects of age, ethnicity, menstrual cycle and combined oral contraceptive. *Thromb Haemost*. 1999;82(5):1456–1461.
48. Munro MG et al. The FIGO ovulatory disorders classification system. *Int J Gynaecol Obstet*. 2022;159(1):1–20.
49. Munro MG et al. The FIGO ovulatory disorders classification systemdagger. *Hum Reprod*. 2022;37(10):2446–2464.
50. Munro MG et al. The FIGO ovulatory disorders classification system. *Fertil Steril*. 2022;118(4):768–786.
51. Widholm O et al. A statistical analysis of the menstrual patterns of 8,000 Finnish girls and their mothers. *Acta Obstetric Gynecol Scand Suppl*. 1971;14(Suppl 14):1–36.
52. Rosenfield RL. Clinical review: adolescent anovulation: maturational mechanisms and implications. *The J Clin Endocrin Metabol*. 2013;98(9):3572–3583.
53. Hickey M et al. Abnormal uterine bleeding: a focus on polycystic ovary syndrome. *Women's Health*. 2009;5(3):313–324.
54. Warren MP et al. The effects of intense exercise on the female reproductive system. *J Endocrin*. 2001;170(1):3–11.
55. Lee DY et al. Prevalence of hyperprolactinemia in adolescents and young women with menstruation-related problems. *Am J Obstet Gynecol*. 2012;206(3):213 e1–213 e5.
56. Krassas GE. Thyroid disease and female reproduction. *Fertil Steril*. 2000;74(6):1063–1070.
57. Robertson DM et al. Interrelationships between ovarian and pituitary hormones in ovulatory menstrual cycles across reproductive age. *J Clin Endocrin Metabol*. 2009;94(1):138–144.
58. Hale GE et al. Atypical estradiol secretion and ovulation patterns caused by luteal out-of-phase (LOOP) events underlying irregular ovulatory menstrual cycles in the menopausal transition. *Menopause*. 2009;16(1):50–59.
59. Goodman NF et al. American Association of Clinical Endocrinologists, American College of Endocrinology, and Androgen Excess and PCOS Society disease state clinical review: guide to the best practices in the evaluation and treatment of polycystic ovary syndrome – part 2. *Endocr Pract*. 2015;21(12):1415–1426.
60. O'Keane V. Antipsychotic-induced hyperprolactinaemia, hypogonadism and osteoporosis in the treatment of schizophrenia. *J Psychopharmacol*. 2008;22(2 Suppl):70–75.

61. Salamonsen LA et al. Endometrial endothelin: regulator of uterine bleeding and endometrial repair. *Clin Exp Pharmacol Physiol*. 1999;26(2):154–157.
62. Jensen DV et al. Prostaglandins in the menstrual cycle of women. A review. *Dan Med Bull*. 1987;34(3):178–182.
63. Gleeson NC. Cyclic changes in endometrial tissue plasminogen activator and plasminogen activator inhibitor type 1 in women with normal menstruation and essential menorrhagia. *Am J Obstet Gynecol*. 1994;171(1):178–183.
64. Smith SK et al. A role for prostacyclin (PGi2) in excessive menstrual bleeding. *Lancet*. 1981;1(8219):522–524.
65. Smith SK et al. Prostaglandin synthesis in the endometrium of women with ovular dysfunctional uterine bleeding. *Br J Obstet Gynaecol*. 1981;88(4):434–442.
66. Naftalin J et al. Is adenomyosis associated with menorrhagia? *Hum Reprod*. 2014;29(3):473–479.
67. Jain V et al. Contemporary evaluation of women and girls with abnormal uterine bleeding: FIGO systems 1 and 2. *Int J Gynaecol Obstet*. 2023;162(Suppl 2):29–42.
68. Sheppard BL et al. The effects of intrauterine contraceptive devices on the ultrastructure of the endometrium in relation to bleeding complications. *Am J Obstet Gynecol*. 1983;146(7):829–839.
69. Sheppard BL. Endometrial morphological changes in IUD users: a review. *Contraception*. 1987;36(1):1–10.
70. Mishell DR. Intrauterine devices: mechanisms of action, safety, and efficacy. *Contraception*. 1998;58(3 Suppl):45S–53S; quiz 70S.
71. Guttinger A et al. Endometrial effects of intrauterine levonorgestrel. *Contraception*. 2007;75(6 Suppl):S93–S98.
72. Jensen JT et al. Subject and clinician experience with the levonorgestrel-releasing intrauterine system. *Contraception*. 2008;77(1):22–29.
73. Kim TH et al. Presenting features of women with uterine arteriovenous malformations. *Fertil Steril*. 2010;94(6):2330 e7–2330 e10.
74. Yoon DJ et al. A systematic review of acquired uterine arteriovenous malformations: pathophysiology, diagnosis, and transcatheter treatment. *AJP Rep*. 2016;6(1):e6–e14.
75. Giurazza F et al. Uterine arteriovenous malformations. *Semin Ultrasound CT MR*. 2021;42(1):37–45.
76. Murji A et al. Cesarean scar defects and abnormal uterine bleeding: a systematic review and meta-analysis. *Fertil Steril*. 2022;118(4):758–766.
77. Claessens EA et al. Acute adolescent menorrhagia. *Am J Obstet Gynecol*. 1981;139(3):277–280.
78. Falcone T et al. Dysfunctional uterine bleeding in adolescents. *J Reprod Med*. 1994;39(10):761–764.
79. Kadir RA et al. Frequency of inherited bleeding disorders in women with menorrhagia. *Lancet*. 1998;351(9101):485–489.
80. Peitsidis P et al. Uterine arteriovenous malformations induced after diagnostic curettage: a systematic review. *Arch Gynecol Obstet*. 2011;284(5):1137–1151.
81. Lusher JM. Screening and diagnosis of coagulation disorders. *Am J Obstet Gynecol*. 1996;175(3 Pt 2):778–783.
82. Timor-Tritsch IE et al. Ultrasound diagnosis and management of acquired uterine enhanced myometrial vascularity/arteriovenous malformations. *Am J Obstet Gynecol*. 2016;214(6):731 e1–731 e10.
83. Malcolm CE et al. Does anovulation exist in eumenorrheic women? *Obstet Gynecol*. 2003;102(2):317–318.
84. National Institute for Health and Clinical Evidence (NICE Guideline). *Heavy Menstrual Bleeding*. London: RCOG Press; 2007. PMID: 2193886.
85. Fraser IS et al. A preliminary study of factors influencing perception of menstrual blood loss volume. *Am J Obstet Gynecol*. 1984;149(7):788–793.
86. Auerbach M et al. How we diagnose and treat iron deficiency anemia. *Am J Hematol*. 2016;91(1):31–38.
87. Coad J et al. Iron deficiency and iron deficiency anemia in women. *Scand J Clin Lab Invest Suppl*. 2014;244:82–89; discussion 9.
88. Dugan C et al. The misogyny of iron deficiency. *Anaesthesia*. 2021;76(Suppl 4):56–62.
89. Garcia-Casal MN et al. Serum or plasma ferritin concentration as an index of iron deficiency and overload. *Cochrane Database Syst Rev*. 2021;5(5):CD011817.
90. Lopez A et al. Iron deficiency anaemia. *Lancet*. 2016;387(10021):907–916.
91. Tamhane N et al. Association between preoperative adenomyosis detection rate during pelvic ultrasonography and the specialty of the reading physician. *J Minim Invasive Gynecol*. 2020;27(2):504–509.
92. Dueholm M et al. Transvaginal sonography combined with saline contrast sonohysterography in evaluating the uterine cavity in premenopausal patients with abnormal uterine bleeding. *Ultrasound Obstet Gynecol*. 2001;18(1):54–61.
93. Bij de Vaate AJ et al. Gel instillation sonohysterography (GIS) and saline contrast sonohysterography (SCSH): comparison of two diagnostic techniques. *Ultrasound Obstet Gynecol*. 2010;35(4):486–489.
94. Vroom AJ et al. The effects of Saline Infusion Sonography on the histological quality of endometrial sampling in women with postmenopausal bleeding. *BMC Womens Health*. 2023;23(1):46.
95. Sigrist RMS et al. Ultrasound elastography: review of techniques and clinical applications. *Theranostics*. 2017;7(5):1303–1329.
96. Mariappan YK et al. Magnetic resonance elastography: a review. *Clin Anat*. 2010;23(5):497–511.
97. Huang Q et al. How does the extent of fibrosis in adenomyosis lesions contribute to heavy menstrual bleeding? *Reprod Med Biol*. 2022;21(1):e12442.
98. Guo SW et al. In search of an imaging classification of adenomyosis: a role for elastography? *J Clin Med*. 2022;12(1).
99. Dueholm M et al. Transvaginal ultrasound or MRI for diagnosis of adenomyosis. *Curr Opin Obstet Gynecol*. 2007;19(6):505–512.
100. Tellum T et al. Diagnosing adenomyosis with MRI: a prospective study revisiting the junctional zone thickness cutoff of 12 mm as a diagnostic marker. *Eur Radiol*. 2019;29(12):6971–6981.
101. van Dongen H et al. Diagnostic hysteroscopy in abnormal uterine bleeding: a systematic review and meta-analysis. *BJOG*. 2007;114(6):664–675.

13 UTERINE LEIOMYOMA

Pathophysiology, Symptomatology, and Evaluation

Radmila Sparić, Mladen Anđić, and Andrea Tinelli

13.1 Introduction

Uterine leiomyoma or fibroid, one of the most common gynecological disorders, is a benign monoclonal neoplasm of the myometrium that affects more than 70% of women of reproductive age (1–3). Even though uterine leiomyomas are benign pelvic tumors, they are a common cause of significant morbidity and gynecologic and reproductive dysfunction and include pelvic and/or abdominal pain, menorrhagia, infertility, recurrent miscarriage, and preterm labor (1, 4, 5).

It has been reported that uterine leiomyomas and associated symptoms influence the quality of life, leading to a reduction in the quality of life of affected women, especially in women who belong to racial minorities and women with lower income (6, 7). In addition, it has been estimated that the annual economic cost associated with uterine leiomyoma in the United States is about $34.4 billion annually. It includes direct and indirect management costs (surgery, hospital admissions, outpatient visits), as well as medications, lost work-hour costs, and costs of obstetric complications caused by uterine leiomyomas (8).

Although uterine leiomyoma significantly affects health, economic status, and social well-being, to date there are no long-term or noninvasive management options for these benign neoplasms. There is a lack of knowledge about the molecular mechanisms involved in the pathogenesis and development of uterine leiomyomas (1). However, the possible molecular mechanisms involved in the development of uterine leiomyoma have been detected. It has been presumed, based on epidemiological, clinical, and experimental evidence, that ovarian steroid hormones such as estradiol and progesterone play a role in the development of uterine leiomyoma (9). Both steroid hormones induce the production of mitogenic stimuli from leiomyoma cells to the undifferentiated cells and support the growth of uterine leiomyoma. Estradiol increases the leiomyoma's sensitivity to progesterone, and progesterone leads to the further development and proliferation of uterine leiomyoma cells (9). This is supported by the evidence that selective estrogen receptor modulators as well as selective progesterone modulators inhibit fibroid growth and lead to the apoptosis of the uterine leiomyoma cells (9–11).

However, the sex steroid hormone-related signal mechanisms are not only the only factors involved in the progression of pathogenesis and uterine leiomyoma. Many genetic, epigenetic, autocrine, and paracrine factors contribute to the appearance and progression of these neoplasms. One of the potential causes of uterine leiomyoma is hormonal exposure in early development which leads to developmental reprogramming via epigenetic changes, which results in the onset and/or progression of uterine leiomyoma (12). Moreover, one of the causes of uterine leiomyoma onset is the persistence of the driver mutations, which lead to the clonal expansion of the leiomyoma cells from the single transformed myometrial stem cell (12). The animal models of uterine leiomyomas support findings that aberrations in the menstrual cycle, genetic mutations, and dysregulation of some signaling pathways play a role in uterine leiomyoma pathogenesis, but none of the possible pathological mechanisms is definitive (13).

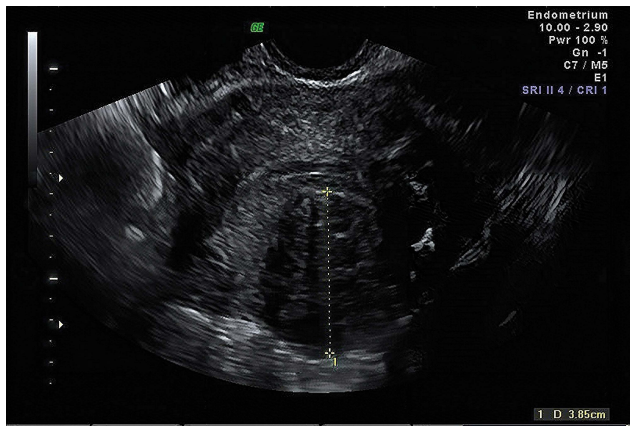


FIGURE 13.1 Ultrasound image of an intramural uterine leiomyoma.

There is significant morbidity related to uterine leiomyoma, with a wide spectrum of symptoms usually linked to heavy or prolonged menstrual bleeding and consequently iron-deficiency anemia (5). If the uterus is enlarged, the typical symptomatology of leiomyoma is pain, abdominal distension, gastrointestinal symptoms (diarrhea, constipation), and urinary symptoms (such as urinary retention, urinary frequency, and nocturia) (5). Independent of a woman's age, parity, and desire to become pregnant, there are anticipated, medicinal, and surgical alternatives to hysterectomy to treat symptomatic uterine leiomyoma (14).

The interindividual diversity in the size, localization, and number of uterine leiomyomas and many symptoms represent problems in its diagnosis (Figure 13.1). The symptoms linked to uterine leiomyomas are not specific and are common in other gynecological diseases, as well as ovulatory dysfunctions, endometrial polyps, and endometriosis (15). This is the reason many women affected with uterine leiomyoma are undiagnosed (Figure 13.2).

13.2 Pathogeneses

The findings from epidemiological studies and results observed from animal models report that the risk factors for uterine leiomyoma are age, race, body mass index, sex hormones, reproductive factors, and comorbidities such as obesity, diabetes, and hypertension (15). It is observed that age is a significant factor for the pathogenesis of uterine leiomyoma, and it is assumed that the incidence of uterine leiomyoma increases as women age and achieves its peak around 50 years. Uterine leiomyoma does not occur before puberty and its incidence decreases in menopause (16, 17).

DOI: 10.1201/9781003312109-13

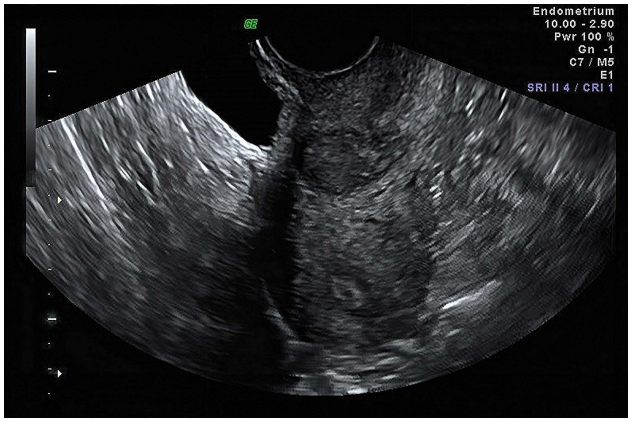


FIGURE 13.2 Ultrasound image of a cervical uterine leiomyoma.

The number of fibroids as well as the rate of hospitalization also increase with age, with a peak of 62.7 per 10,000 among women 45–49 years old (16, 18). There are observed racial disparities in the incidence of uterine leiomyoma. The incidence of uterine leiomyoma during reproductive years in black women is about 50% and about 25% in white women. The observed lifetime risk for uterine leiomyoma by age 50 is about 70% in white women and more than 80% for black women (19). In addition, there are clinical differences in uterine leiomyoma between black and white women. In black women, uterine leiomyomas are diagnosed at an earlier age and are often larger and more numerous, leading to more severe symptoms compared with other racial groups (20). It is reported that African American women diagnosed with uterine leiomyoma are 2.4 times more likely to have a hysterectomy and 6.8 times to undergo uterus-sparing myomectomy (21). According to the results observed in the US population-based study of incidence, trends, and prevalence of uterine leiomyoma in the period 2005–2014, the incidence rates were the highest in women aged 45–49 years (240.3 per 10,000 woman-years in 2014) and in the population of black women across all years. A significant decline in the incidence rates of uterine leiomyoma was observed during the 10-year study interval, from 139.4 per 10,000 woman-years in 2005 to 101.4 in 2014. The highest prevalence of uterine leiomyoma was observed in black women (18.5%), which was higher than the prevalence of uterine leiomyoma reported for other racial/ethnic groups (22). The racial disparity in the incidence and clinical characteristics of uterine leiomyoma could be the consequence of the polymorphisms of the genes related to the sex hormone biosynthesis and/or metabolism (16).

Some studies revealed a protective effect of pregnancy on the development of uterine leiomyoma (16, 23, 24). It has been presumed that elevations and declines in the estrogen and progesterone level during early pregnancy and the postpartum period can cause a dramatic effect on uterine leiomyoma growth (16).

Although the link between high parity and a lower prevalence of uterine leiomyoma could be overestimated because the condition itself is a risk factor for infertility or subfertility, the epidemiological studies have shown that women whose last childbirth occurred 5 or more years ago have a two- to threefold higher risk of developing uterine leiomyoma compared with those who gave birth more recently, in both black and white populations (20, 25). Some studies revealed that a nearly age of menarche and late menopause are risk factors for the development of uterine leiomyoma (16, 26, 27). Moreover, environmental and lifestyle factors that are potentially modifiable and linked to uterine leiomyoma include diet, alcohol and caffeine consumption, and physical activity (15). It has been observed that soya intake possibly leads to a higher incidence of uterine leiomyoma (28, 29). Also, a higher intake of dietary fat, meat, and fish is linked with a higher incidence of uterine leiomyoma (30–32). A diet that includes fruit and vegetables is associated with a decreased risk for uterine leiomyoma development (33, 34). Alcohol and coffee intake increases the risk of uterine leiomyoma developing, but there are conflicting results observed for dairy products and their association with uterine leiomyoma incidence (29, 35–37). It was observed in the experimental models of uterine leiomyoma that the extracts of some fruit and natural compounds such as lycopene, quercetin, resveratrol, and curcumin isolated from vegetables and fruits have antiproliferative effects, decreasing proliferation and increasing the apoptosis of uterine leiomyoma cells (38–40).

However, although the epidemiological and animal studies cannot identify the key risk factors and pathological mechanisms involved in the onset and development of uterine leiomyoma, they refer to the potential molecular mechanisms involved. In recent years progress has been made in the understanding of the pathobiology of uterine leiomyoma. The current point of view is that the stem cell population from which uterine leiomyoma develops differs from the stem cells from which normal myometrial tissue originates (41).

The steroid sex hormones estradiol and progesterone are traditionally considered the main molecular basis of uterine leiomyoma onset and development, although the true functional role of the steroid sex hormones is still unclear (12, 42–44). Early menarche is linked to a higher risk for uterine leiomyoma onset, due to longer exposure to estradiol and progesterone (2, 12). It has also been observed that the risk of uterine leiomyoma onset is higher in nulliparous women, while a lower risk is associated with increased parity (2, 13). This paradoxical association could be explained by the remodeling of the myometrium during pregnancy, rendering it less susceptible to the actions of the different factors involved in uterine leiomyoma development (10, 13, 45). Also, ischemia of uterine leiomyoma during delivery and postpartum remodeling of the myometrium leads to a reduction in leiomyoma volume after gestation (12, 46).

As previously observed, estrogen signal transduction leads to a higher expression of progesterone receptors and sensitivity to progesterone in uterine leiomyoma cells (12). Progesterone regulates multiple genes and promotes the proliferation and survival of uterine leiomyoma cells and the production of extracellular matrix. Progesterone induces the expression of genes involved in proliferation, such as genes from the BCL-2 family, and modulates signaling pathways, such as AKT andMEK1/2 Rho/Rock pathways, which are involved in the promotion of uterine leiomyoma cells (12, 47–49). Not only does progesterone contribute to the proliferation of uterine leiomyoma cells, but estradiol also increases production of growth factors, mainly PDGF, via modulation of the MAPK-PKC pathway, and leads to higher proliferation (12, 50). Estradiol also modulates the Wnt/β-catenin signaling pathway and induces proliferation (51).

Although ovarian sex steroid hormones are key regulators of uterine leiomyoma development, genetic and epigenetic factors, as well as molecular mechanisms and signaling pathways,

also contribute to its development. First, uterine leiomyoma cells have a genetic background that refers to the results of family-based association studies and interracial and interpopulation disparities in the prevalence of uterine leiomyoma (12, 52, 53). Current genome-wide association studies (GWAS) have identified the specific genetic variants which possibly predispose women to the onset of uterine leiomyoma cells (53, 54). It has been observed that variants in some genes are not just associated with uterine leiomyoma susceptibility, but also with their size. These genes include *ODFC3, BET1L, RIC8A, SIRT3, SLK, OBFC1, TNRC6B, FASN* and *HMGA2* (12, 55, 56). Also, two groups of genes are involved in uterine leiomyoma onset. The first group includes genes whose product is involved in the regulation of genome stability, such as TERT, TERC, OBFC1, TP53, and ATM, and the second group includes genes which have a role in the development of genitourinary systems, such as WNT4, WT1, SALL1, MED12, ESR1, GREB1, FOXO1, DMRT1 and uterine stem cell marker antigen CD44 (57).

The mutation in the MED-12 gene is the most common genetic mutation in uterine leiomyoma cells, observed in more than 70% of uterine leiomyoma specimens (58, 59). MED12 is the regulator of RNA polymerase II-mediated transcription, which controls precise transcription regulation via binding with CKD8 – the catalytic core of RNA polymerase II (60). In cases of the mutations of MED12, there is an altered interaction of the MED12–CDK8 complex and consequently altered regulation of transcription of different genes which leads to tumorigenesis in uterine leiomyoma cells (61).

Recent studies suggest a role for polymorphisms in genes involved in DNA repair mechanisms, such as the Xeroderma pigmentosum complementation group genes, in uterine leiomyoma development (62). There are observed chromosomal rearrangements in about 40%–50% of uterine leiomyomas – the most common is the translocation between 12 and 14 chromosomes, and 6 and 10 chromosomes, as well as trisomy of the chromosome 12 and the deletion in the chromosomes 3 and 7, with the structural aberrations in the candidate genes (63).

Nevertheless, not just genetic but also epigenetic factors influence the pathogenesis of uterine leiomyomas (64). The small micro-ribonucleic acids are a group of non-coding single-stranded ribonucleic acids with about 22 nucleotides that regulate gene expression (64). The different expressions of these molecules lead to the different expressions of their target genes, some of which are involved in uterine leiomyoma cell proliferation (65). Abnormal levels of methylation and/or acetylation of some genes are crucial in tumorigenesis, emphasizing the epigenetic role in uterine leiomyoma pathobiology (66). Extracellular matrix components have a significant role in uterine leiomyoma pathobiology, especially taking into account that such components are reservoirs of the different signal molecules and growth factors (67). It is presumed that several signaling pathways are crucial in uterine leiomyoma pathogenesis, such as Wnt/β-catenin, TGFβ, PI3K/AKT/mTOR, etc. (68–70). It is important to emphasize that none of the pathological mechanisms potentially involved in uterine leiomyoma development can fully explain its pathogenesis, but each provides novel insight its underlying biology and potential therapeutic options.

13.3 Histological Studies

Histological studies of fibroid tissues from patients treated with progesterone showed more cellular growth than did those from patients not treated with progesterone (71). Fibroids are benign (noncancerous) neoplasms, affecting 20% to 30% of women of childbearing age (72). This type of tumor is uncommonly found in other parts of the body. Indman et al. reported that calcification of the fibroid was due to the deposition of calcium (73).

The first to describe leiomyomas was Matthew Baille in 1793. Leiomyomas consists mainly of smooth muscle cells containing different amounts of fibrous tissue. During its growth, myoma determines compression on the surrounding structures (myometrium and endometrium), causing the progressive formation of a sort of pseudocapsule, rich in collagen fibers, neurofibers, and blood vessels. Occasionally the continuous surface of the pseudocapsule is interrupted by bridges of collagen fibers and vessels that anchor the myoma to the myometrium. This causes the formation of a clear cleavage plane between the myoma and the pseudocapsule and between the pseudocapsule and the surrounding myometrium. This pseudocapsule causes a displacement action (which is not destructive) on the myometrium; however, the integrity and contractility of the uterine structure are maintained. The following are histological variants of uterine fibroids:

1. Leiomyoma with red degeneration (characterized by coagulation necrosis, often associated with pregnancy or oral contraceptive use)
2. Apoplectic leiomyoma
3. Leiomyoma with hydropic degeneration (mimicking the myxoid leiomyosarcoma)
4. Leiomyoma with lymphoid infiltration (mimicking lymphoma)
5. Cellular leiomyoma (a benign tumor that increases cellularity, but not coagulative necrosis, atypia, or an excessive number of mitotic figures: the differential diagnosis includes leiomyosarcoma)
6. Atypical, bizarre, or pleomorphic leiomyoma (includes atypical cellular elements, but not coagulation necrosis or mitotic activity)
7. Mitotically active leiomyoma (tumors that are 5 to 10 × HPF mitosis, but an absence of coagulation necrosis and cytologic atypia)
8. Leiomyolipoma, epithelioid leiomyoma, parasitic leiomyoma with skeletal differentiation, and intravenous leiomyomatosis (with growth in the lumen of the uterine or pelvic veins, proceeding up to the vena cava and right atrium; distant metastases are exceptionally rare and long-term survival is excellent)
9. Benign metastasizing leiomyoma (benign tumor that has characteristics typical of leiomyoma, but an absence of coagulation necrosis, increased mitotic activity, and significant atypia), accompanied by pulmonary nodules, enlarged lymph nodes, etc., which have the same characteristics of the original leiomyoma and probably represent metastases

The extrauterine nodules may show some characteristics of leiomyosarcoma or smooth muscle tumors of uncertain or indeterminate malignant potential (STUMP). The interval between hysterectomy and the occurrence of pulmonary nodules is about 15 years. The clinical course is more indolent, and survival is about 10 years following the excision of these "metastatic" nodules. The neoplasms mentioned earlier should be called leiomyomas or metastasizing low-grade leiomyosarcomas, mimicking leiomyomas. Their histological characterization depends on whether we want to define them based on

morphology (leiomyomas) or according to their behavior (in this case, leiomyosarcomas).

In surgical pathology, there is an unsolved problem regarding the differentiation of uterine leiomyoma. When using the traditional criteria of classification of Kempson, such as mitosis, atypia, coagulative necrosis, etc., to surgical pathology, these aspects are not enough to predict the prognosis of these tumors, when they are used alone or in combination. According to that, some pathologists suggest that uterine leiomyoma must be called smooth muscle tumors based on the phenotypic and genotypic data in correlation to their prognosis and recommended treatment.

Also, it is still not well understood if uterine leiomyosarcoma develops from the malignant transformation of uterine leiomyoma or if they are the consequences of the transformation of the normal myometrium via uterine leiomyoma. Current genetic and molecular evidence suggests that uterine leiomyosarcomas develop independently and that there are differences in genetic mutations, as well as in the expression of enzymes, proteins, and microRNAs, between uterine leiomyosarcoma and uterine leiomyoma. These differences represent potential molecular markers for the differential diagnosis between uterine leiomyoma and uterine leiomyosarcoma, including MED12, HMGA2, TOP2A, CHI3L1, MELK, PRC1, TOP2A, TPX2, DFF40, DFF45, the BCL-2 gene, miRNAs (miR-1246 and miR-191–5p), STMN1, MKI67micro RNA, and the let-7 family of microRNAs (74). Interestingly, the same histologic studies revealed rare examples of uterine leiomyosarcoma progressing from uterine leiomyoma (75).

13.4 Symptomatology of Uterine Leiomyoma

Uterine leiomyomas are rarely linked to mortality, but their symptomatology may lead to an impairment in quality of life (76). The symptomatology of uterine leiomyoma includes abnormal uterine bleeding, pain, and gastrointestinal and urinary symptoms; uterine leiomyoma can also be asymptomatic. The symptoms of uterine leiomyomas mostly depend on their location (5). For example, submucosal leiomyomas have more effect on abnormal menstrual bleeding and, in the case of submucosal uterine leiomyomas, small leiomyomas could protrude into the uterine cavity and lead to menstrual irregularities (5). On the other hand, the characteristic of the subserosal uterine leiomyoma is slow growth, and there is a long period before onset of symptoms such as back, pelvic, or leg pressure and/or abdominal and pelvic pain (5).

The link between uterine leiomyoma and abnormal uterine bleeding is not fully understood. It is paradoxical that many women affected by uterine leiomyoma have normal menstrual bleeding, yet the condition is highly prevalent among women diagnosed with abnormal uterine bleeding (77). It is also clear that in women with abnormal uterine bleeding, other etiological factors for abnormal uterine bleeding must be considered (78).

Puri et al. (79) conducted a retrospective study to determine the relationship between submucosal uterine leiomyomas and heavy menstrual bleeding and anemia. They observed significantly lower hemoglobin and a higher risk of anemia in patients with hysteroscopically diagnosed submucosal uterine leiomyomas. However, the ultrasound diagnostic of submucosal uterine leiomyoma does not find a statistically significant association between uterine leiomyoma and hemoglobin levels or risk of anemia. This finding could explain the inconsistent results in the literature regarding the relationship between uterine leiomyoma and abnormal uterine bleeding.

Fuldeore et al. (80) estimated the prevalence of different symptoms in women affected by uterine leiomyoma in the United States and compared its prevalence in women without uterine leiomyoma. They observed a statistically higher prevalence of heavy menstrual bleeding (16.7% vs 7.7%), a higher prevalence of severe spotting/bleeding between periods, and a higher prevalence of severe pelvic pressure in women with uterine leiomyoma, compared to the control group (without leiomyoma). In a group of women with uterine leiomyoma, authors observed the prevalence of typical symptoms such as heavy menstrual bleeding, the passage of clots, spotting/bleeding between periods, constipation/bloating/diarrhea, and pelvic pressure: 56.4%, 32.3%, 26.4%, 25.8%, and 20.4%, respectively (Figure 13.3).

The enlargement of uterine leiomyoma leads to the outgrowing of their blood supply, which leads to the apoptosis of uterine leiomyoma cells and degeneration (81). Also, the torsion of the pedunculated fibroid could manifest as acute pelvic pain (82). Uterine leiomyoma can also causes symptoms such as dyspareunia, as well as urological manifestations including incontinence, overactive bladder symptoms, and incomplete bladder emptying. These symptoms could be explained by the compression of the bladder (Figure 13.4) and other pelvic organs by

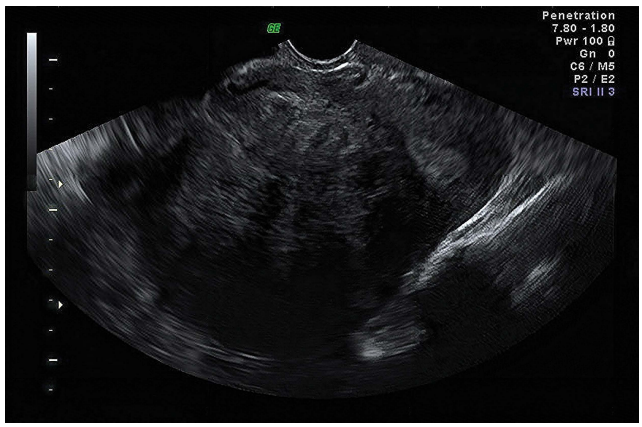


FIGURE 13.3 Ultrasound image of a uterine leiomyoma localized in the posterior uterine wall.

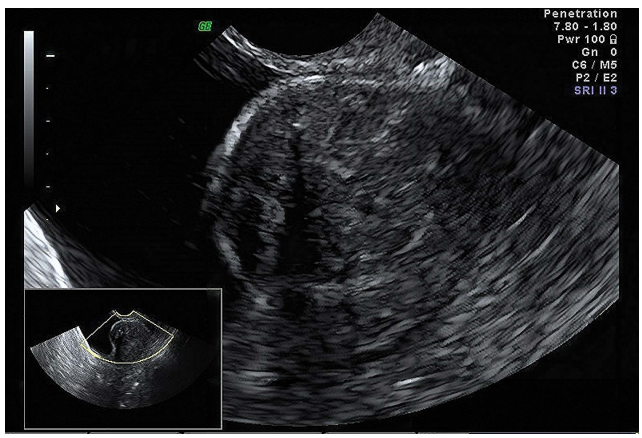


FIGURE 13.4 Ultrasound image of a uterine leiomyoma localized in a sub-vesical space.

the uterine leiomyoma and/or uterus (83). There are described cases of acute urinary retention caused by uterine leiomyoma (84, 85). It has been reported that acute urinary retention can occur when a uterine leiomyoma leads to the superior and anterior rotation of the uterine cervix, which causes bladder-neck or urethral compression (86). Uterine leiomyoma could also lead to obstructive uropathy with unilateral or bilateral hydronephrosis. Some lower urinary tract symptoms (LUTS), such as nocturia, urinary urgency, urinary frequency, and/or urinary incontinence, could also be caused by uterine leiomyoma.

One of the symptoms of uterine leiomyoma that affects quality of life is impaired sexual function. The barriers to sexual function in female patients with leiomyoma include pelvic pain, dyspareunia, orgasmic disorders, decreased vaginal lubrication, decreased libido, irritative or obstructive bladder symptoms, and urinary incontinence. Sexual dysfunction in women diagnosed with uterine leiomyoma is usually caused by the pain and discomfort caused by the repetitive contact between uterine leiomyoma and the vaginal wall. Unfortunately, in this case, there is no treatment for dyspareunia except for surgical management of the uterine leiomyoma. Other urological symptoms of uterine leiomyoma that are rarely reported include hematuria, renal failure, and vesicouterine fistula (87–91).

Uterine leiomyomas not only cause urological symptoms but can also cause defecatory symptoms such as obstructed defecation (92). In terms of reproduction, uterine leiomyomas are linked to infertility and miscarriage. Although results are inconsistent, there is general agreement that submucosal uterine leiomyoma decreases fertility and that intramural uterine leiomyoma > 4 cm has a negative influence on fertility. On the other hand, subserosal myomas have little or no effect on fertility (Figure 13.5). Even though the mechanisms of the negative influence of uterine leiomyoma on fertility are not still clear, some theories include the alteration of local anatomical location and the cavity distortion by the uterine leiomyoma (Figure 13.6), molecular and functional changes of the myometrium and endometrium, and endocrine and paracrine molecular mechanisms. All of these mechanisms could impair gamete transport, reduce the likelihood of embryo implantation, and disrupt the creation of an environment needed for pregnancy (93). The presence of uterine leiomyoma could increase the risk of some adverse pregnancy outcomes such as spontaneous miscarriage, especially in infertile women with multiple submucosal lesions. Women with uterine leiomyoma also have an increased risk of placenta previa, placental abruption, and fetal malpresentation (94) (Figure 13.7).

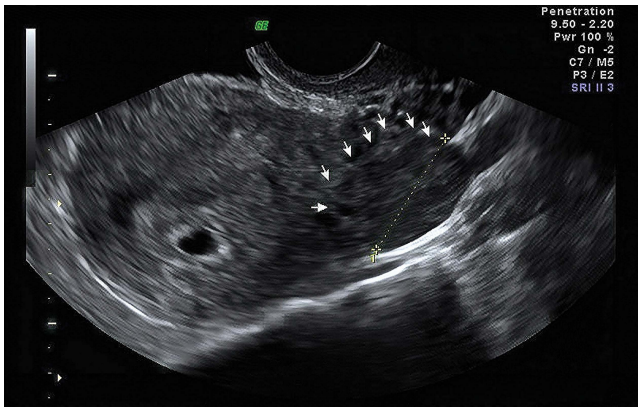


FIGURE 13.5 Ultrasound image of a uterine leiomyoma in a 6-week-old pregnancy.

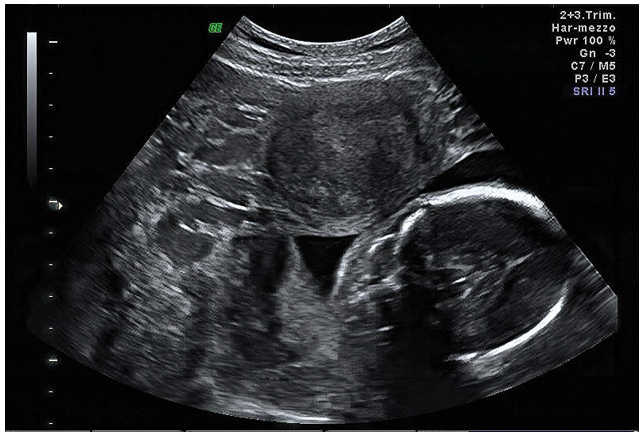


FIGURE 13.6 Ultrasound image of a uterine leiomyoma in a 23-week-old pregnancy.

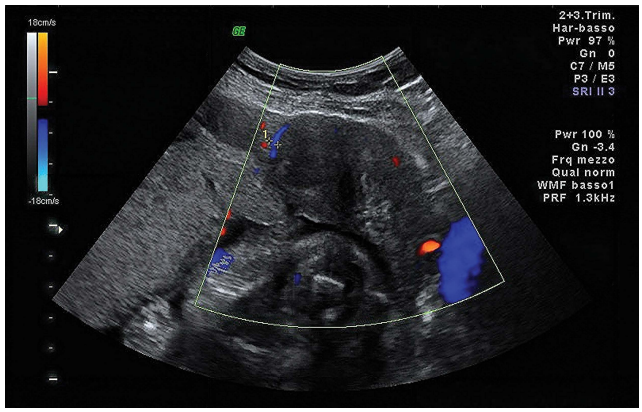


FIGURE 13.7 Ultrasound image of a uterine leiomyoma in a 26-week-old pregnancy.

13.5 Evaluation of Uterine Leiomyoma

It has been reported that the diagnosis of uterine leiomyoma is complicated by their diversity in size and location, as well as by nonspecific symptoms that are commonly observed in other gynecological diseases (5). According to the location of the uterine leiomyomas relative to the endometrium (submucosal surface) and the serosal surface, the International Federation of Gynecology and Obstetrics (FIGO) proposed its classification system primary for the cause of abnormal uterine bleeding (5).

Traditionally, uterine leiomyomas have been classified a submucosal, intramural, subserosal, or cervical, depending on their location within the uterus. Intramural uterine leiomyomas are leiomyomas located in the uterine wall and are the most common type of uterine leiomyoma. If not large, this leiomyoma could be asymptomatic. Typically, intramural leiomyomas begin as small nodules in the uterine wall of the uterus but can grow in size, causing elongation and distortion of the uterine cavity. On the other hand, subserosal uterine leiomyomas are located beneath the peritoneum of the uterus and can reach large dimensions over time. The subserosal leiomyoma

can grow in a papillary manner and be transformed into a pedunculated uterine leiomyoma. Submucosal uterine leiomyomas are located in the muscle beneath the endometrium of the uterus and lead to the distortion of the uterine cavity. The uterine leiomyoma could be located in the wall of the uterine cervix and also be found in the uterine ligaments (round ligament, broad ligament, uterosacral ligament).

Although this traditional classification was used for a long period, it often leads to suboptimal management (95). For example, a 100% intramural uterine leiomyoma in contact with endometrium could be misclassified as a submucosal uterine leiomyoma and treated with hysteroscopic resection (95).

The FIGO classification system is developed for uniformly and consistently describing and classifying uterine leiomyomas and is aimed to facilitate communication between medical professionals as well as clinical care and research. Accurate classification of uterine leiomyoma leads to the best treatment plan for all women diagnosed with the condition through hysteroscopy, laparoscopy/laparotomy, or pharmacological treatment (96), using the FIGO classification (96). The FIGO classification system is used not only in the pretreatment of uterine leiomyoma but also in posttreatment follow-up for assessing the treatment response, monitoring changes in the overall tumor, and detecting recurrent lesions (96). According to the FIGO classification system, uterine leiomyoma types include submucosal uterine leiomyoma which includes Type 0 (pedunculated intracavitary), Type 1 (≥ 50% submucosal), Type 2 (< 50% submucosal), and uterine leiomyoma without submucosal components that include Type 3 (100% intramural uterine leiomyoma with endometrial contact), Type 4 (100% intramural uterine leiomyoma with no endometrial contact), Type 5 (≥ 50% uterine leiomyoma with subserosal component), Type 6 (< 50% intramural uterine leiomyoma with subserosal component), Type 7 (pedunculated subserosal uterine leiomyoma), and Type 8 (non-myometrial location, such as cervical, broad ligament, and parasitic uterine leiomyoma), and hybrid uterine leiomyoma with both submucosal and subserosal components (96).

Submucosal fibroids (FIGO 0, FIGO 1, and FIGO 2) are located beneath the uterus mucosal lining. They are usually associated with menorrhagia and/or dysmenorrhea, infertility, and pregnancy loss (97). Depending on their size they could be treated with hysteroscopic leiomyoma resection and/or medical treatment. Hysterectomy is an option in the case of symptomatic women who do not desire pregnancy (98). The treatment for the FIGO 1 uterine leiomyoma (≥ 50% submucosal and < 50% intramural) and FIGO 2 fibroids (< 50% submucosal and ≥ 50% intramural) is usually hysteroscopic myomectomy, with special emphasis on differentiating between FIGO 1 and FIGO 2 uterine leiomyomas (98).

All uterine leiomyomas that lack a submucosal component are classified as "other" (FIGO 3–8). This class of uterine leiomyoma includes intramural and subserosal types, as well as those located in extrauterine regions such as the cervix and broad ligament. These leiomyomas are associated with bulk-related symptoms and may cause urological and/or gastrointestinal manifestations. Treatment options for this class of uterine leiomyoma are myomectomy, hysterectomy, radiofrequency ablation, uterine artery embolization, and pharmacological management. Taking into account that the FIGO 3 uterine leiomyoma is 100% intramural and contacts the endometrium without distortion of the endometrial cavity, careful laparoscopic or open resection of FIGO 3 uterine leiomyoma to prevent injury of the endometrium is necessary (99). On the other hand, FIGO 4 uterine leiomyomas are 100% intramural without contact with endometrium or serosa. The different management options are proposed for the FIGO 2 – hysteroscopic resection and FIGO 3 and FIGO 4 uterine leiomyoma – laparoscopy or open myomectomy, make the accurate diagnosis and differentiating of FIGO 2 uterine leiomyoma from FIGO 3 and FIGO 4 types of uterine leiomyoma a key point in the preoperative period.

The subserosal uterine leiomyomas are classified into FIGO 5, FIGO 6, and FIGO 7 types depending on their intramural extent. FIGO 5 are uterine leiomyomas with ≥ 50% intramural and < 50% subserosal components while the uterine leiomyomas with < 50% intramural and ≥ 50% subserosal components are classified as FIGO 6. The pedunculated subserosal uterine leiomyomas without intramural components are classified as FIGO 7. Subserosal uterine leiomyomas are often asymptomatic, but when they enlarge, they can cause a wide spectrum of symptoms depending on their contact with other structures in the pelvis. Twisting and detaching are the risks in the case of the FIGO 7 uterine leiomyoma. An extrauterine leiomyoma that is usually localized to the cervix, broad ligament, or pelvis is classified as FIGO 8. A uterine leiomyoma that extends from the submucosa to the serosa is classified as a hybrid uterine leiomyoma and is assigned two numbers – the first number characterizes the relationship of the uterine leiomyoma and endometrium and the second number describes its relationship with serosa (95).

Although the palpation of a firm multilobular uterus or firm masses extending from the uterus is associated with the presence of uterine leiomyomas, in contemporary clinical practice, ultrasonography is usually used for the diagnosis of uterine leiomyomas (5). It has been observed that the sensitivity and specificity of transvaginal ultrasonography in the diagnosis of uterine leiomyomas were 90% and 87%, respectively, while the sensitivity and specificity of sonohysterography were 100% and 98%, respectively (5, 100, 101). In the ultrasound examination, uterine leiomyomas usually present as well-defined solid concentric, hypoechoic masses with a wide spectrum of acoustic shadowing. Depending on the calcification and/or presence of fibrous tissue, uterine leiomyoma could have different echogenicity, but the most common present as hypoechogenic or echogenic. The calcifications are present as echogenic foci with shadowing. In case of necrosis, uterine leiomyomas are present with anechogenic components. When they are located in the lower uterine segment like the cervix, uterine leiomyoma could obstruct the uterine canal. Also, when the uterine leiomyomas are small and are echogenic to the myometrial tissue, the only ultrasound sign for their diagnosis is a bulge in the uterine contour (102).

Differential diagnosis is important in the diagnosis and management of uterine leiomyomas. The most common misdiagnosis pathologies with uterine leiomyoma are adenomyosis, endometrial polyps, and solid tumor of the adnexa. Adenomyosis is often misdiagnosed as uterine intramural leiomyoma and vice versa because there is a lack of significant ultrasonographic and clinical signs for the adenomyosis diagnosis. However, some ultrasound signs suggest the presence of adenomyosis such as globular uterine enlargement without the presence of leiomyomata, heterogeneous echo texture, obscured endometrial/myometrial border, cystic anechoic spaces or lakes in the myometrium, uterine wall thickening, subendometrial echoic linear striations and thickening of the transition zone (103).

Adnexal masses could be misdiagnosed with subserosal uterine leiomyomas, especially when the subserosal uterine

leiomyomas are pedunculated or with predominantly extrauterine components. Sometimes ovarian tumors such as Brenner tumors and fibroadenomas could have large fibrous components with ultrasonographic as well as magnetic resonance imaging characteristics similar to uterine leiomyoma, and the diagnosis is not possible before surgery (102).

Doppler ultrasonography, which shows blood flow, arterial supply, and circumferential vascularity of the uterine leiomyoma, is another useful tool in the diagnosis of the condition. Intrauterine benign masses, as well as submucosal intrauterine leiomyomas and endometrial polyps, could be also misdiagnosed. Taking into account that the echogenicity of uterine leiomyoma, which could be hypoechogenic, isoechogenic, hyperechogenic, or of mixed echogenicity, could be misdiagnosed with homogeneous hyperechogenic intracavitary mass such as an endometrial polyp. In this case, color Doppler is an especially useful method for the differential diagnosis of submucosal uterine leiomyoma and endometrial polyp, and this is based on the vascularization of these lesions. Multiple circular vascularity is characteristic of the submucosal uterine leiomyoma, while a single feeding artery is characteristic of the endometrial polyp. Complementary to the ultrasound method for the differential diagnosis of the uterine submucosal leiomyoma and the endometrial polyp is elastography, which visualizes the different stiffness of endometrial polyps and submucosal leiomyomas. Furthermore, transvaginal ultrasonography can be combined with saline instillation into the uterine cavity aimed at differential submucosal uterine leiomyomas and endometrial polyps (102).

Unfortunately, uterine leiomyosarcoma is the pathology in which a misdiagnosis as uterine leiomyoma has the worst outcomes. The clinical symptoms of malignant leiomyosarcoma and benign leiomyoma are similar. There is no pelvic imaging technique or other diagnostic tool that can differentiate with enough accuracy and reliability between uterine leiomyoma and uterine leiomyosarcoma. In both pathologies, there are mixed echogenic and poor echogenic components and central necrosis, and color Doppler shows irregular vessel distribution with low impedance to flow and high peak systolic velocity (102).

Hysteroscopy is the diagnostic tool for differentiation of the intracavitary uterine leiomyoma and large endometrial polyps (104). As mentioned before, ultrasonography with saline infusion and diagnostic hysteroscopy are usually complementary examinations, when hysteroscopy myomectomy is considered. Hysteroscopy could be used not only for the diagnosis of uterine leiomyoma but also for endometrial biopsy, in case of irregular bleeding or for a patient at risk for endometrial hyperplasia (105).

Another diagnostic tool for uterine leiomyoma is magnetic resonance imaging (MRI), whose sensitivity and specificity are close to 100%. Magnetic resonance imaging is usually required in cases where ultrasonography is not advised (women with larger body habitus or who do not tolerate transvaginal probe or installation of contrast media), as the precise information MRI can provide is useful for the complex procedure of uterine leiomyoma management, where an enlarged uterus extends outside the pelvis or when precise identification of uterine leiomyoma for infertility management is required (5, 106). In T1 and T2 magnetic resonance imaging scans, uterine leiomyomas are present as areas of low or intermediate signal with sharp margins (107, 108). MRI could suggest a diagnosis of uterine leiomyosarcoma; even though there is no preoperative test for an accurate diagnosis of uterine leiomyosarcoma, this diagnostic tool has become a more common preoperative diagnostic imaging method, taking into account that uterine leiomyosarcoma has an incidence estimated round 1/1500 in women aged < 40 years and 1/1100 in women aged 40–44 (109).

FIGURE 13.8 A laparotomic myomectomy of a huge uterine leiomyoma.

There is a limitation to the use of computer tomography (CT) scan in the diagnosis of uterine leiomyoma because of the similar attenuation characteristics between uterine leiomyomas and healthy myometrium. On the other hand, in the cases of calcified or necrotic uterine leiomyoma, CT scan gives a better presentation of uterine leiomyoma than ultrasonography or MRI does. In this case, the uterine leiomyoma is present as a soft tissue density area with central or peripheral calcification (110).

Further diagnosis of uterine leiomyoma implies the histological evaluation of the specimen (Figure 13.8) and estimation of their malignant potential and differential diagnosis with uterine leiomyosarcoma and other gynecological diseases (5).

References

1. Yang Q et al. Comprehensive review of uterine fibroids: developmental origin, pathogenesis, and treatment. *Endocr Rev*. 2022;43:678–719.
2. Wise LA et al. Epidemiology of uterine fibroids: from menarche to menopause. *Clin Obstet Gynecol*. 2016;59:2–24.
3. Al-Hendy A et al. Uterine fibroids: burden and unmet medical need. *Semin Reprod Med*. 2017;35:473–480.
4. Jayes FL et al. Evidence of biomechanical and collagen heterogeneity in uterine fibroids. *PLoS One*. 2019;14:e0215646.
5. Stewart EA et al. Uterine fibroids. *Nat Rev Dis Primers*. 2016;2:16043.
6. Marsh EE et al. Burden, prevalence, and treatment of uterine fibroids: a survey of U.S. women. *J Womens Health*. 2018;27:1359–1367.
7. Hervé F et al. Impact of uterine fibroids on quality of life: a national cross-sectional survey. *Eur J ObstetGynecolReprod Biol*. 2018;229:32–37.

8. Cardozo ER et al. The estimated annual cost of uterine leiomyomata in the United States. *Am J Obstet Gynecol*. 2012;206:211.e1–211.e9.
9. Reis FM et al. Hormones and pathogenesis of uterine fibroids. *Best Pract Res Clin ObstetGynaecol*. 2016;34:13–24.
10. Puchar A et al. Ulipristal acetate for uterine fibroid-related symptoms. *Drugs Today*. 2015;51:661–667.
11. Baggio S et al. Influence of ulipristal acetate therapy on uterine fibroid-related symptoms and on uterine and fibroid volumes and vascularity indices assessed by ultrasound. *J Ultrasound Med*. 2018;37:2215–2223.
12. Machado-Lopez A et al. Molecular and cellular insights into the development of uterine fibroids. *Int J Mol Sci*. 2021;22:8483.
13. Commandeur AE et al. Epidemiological and genetic clues for molecular mechanisms involved in uterine leiomyoma development and growth. *Hum Reprod Update*. 2015;21:593–615.
14. Giuliani E et al. Epidemiology and management of uterine fibroids. *Int J Gynaecol Obstet*. 2020;49:3–9.
15. Sparic R et al. Epidemiology of uterine myomas: a review. *Int J FertilSteril*. 2016;9:424–435.
16. Pavone D et al. Epidemiology and Risk Factors of Uterine Fibroids. *Best Pract Res Clin Obstet Gynaecol*. 2018;46:3–11.
17. Marshall LM et al. Variation in the incidence of uterine leiomyoma among premenopausal women by age and race. *Obstet Gynecol*. 1997;90(6):967–973.
18. Whiteman MK et al. Inpatient hospitalization for gynecologic disorders in the United States. *Am J Obstet Gynecol*. 2010;202:541.e1–541.e6.
19. Baird DD et al. High cumulative incidence of uterine leiomyoma in black and white women: ultrasound evidence. Am J *Obstet Gynecol*. 2003;188:100–107.
20. Wise LA et al. Reproductive factors, hormonal contraception, and risk of uterine leiomyomata in African-American women: a prospective study. *Am J Epidemiol*. 2004;159:113–123.
21. Wechter ME et al. Leiomyoma-related hospitalization and surgery: prevalence and predicted growth based on population trends. *Am J Obstet Gynecol*. 2011;205:492.e1–492.e5.
22. Yu O et al. A US population-based study of uterine fibroid diagnosis incidence, trends, and prevalence: 2005 through 2014. *Am J Obstet Gynecol*. 2018;219:591.e1–591.e8.
23. Chen CR et al. Risk factors for uterine fibroids among women undergoing tubal sterilization. *Am J Epidemiol*. 2001;153:20–26.
24. Sato F et al. Familial aggregation of uterine myomas in Japanese women. *J Epidemiol*. 2002;12:249–253.
25. Terry KL et al. Reproductive characteristics and risk of uterine leiomyomata. *Fertil Steril*. 2010;94(7):2703–2707.
26. Marshall LM et al. A prospective study of reproductive factors and oral contraceptive use in relation to the risk of uterine leiomyomata. *Fertil Steril*. 1998;70:432–439.
27. Templeman C et al. Risk factors for surgically removed fibroids in a large cohort of teachers. *Fertil Steril*. 2009;92:1436–1446.
28. Shen Y et al. Environmental exposure and risk of uterine leiomyoma: an epidemiologic survey. *Eur Rev Med Pharmacol Sci*. 2013;17:3249–3256.
29. Gao M et al. Frequent milk and soybean consumption are high risks for uterine leiomyoma: a prospective cohort study. *Medicine*. 2018;97:e12009.
30. He Y et al. Associations between uterine fibroids and lifestyles including diet, physical activity and stress: a case-control study in China. *Asia Pac J Clin Nutr*. 2013;22:109–117.
31. Nagata C et al. Association of intakes of fat, dietary fibre, soya isoflavones and alcohol with uterine fibroids in Japanese women. *Br J Nutr*. 2009;101:1427–1431.
32. Lambertino A et al. Uterine leiomyomata in a cohort of Great Lakes sport fish consumers. *Environ Res*. 2011;111:565–572.
33. Wise LA et al. Intake of fruit, vegetables, and carotenoids in relation to risk of uterine leiomyomata. *Am J Clin Nutr*. 2011;94:1620–1631.
34. Shen Y et al. Vegetarian diet and reduced uterine fibroids risk: a case-control study in Nanjing, China. *J Obstet Gynaecol Res*. 2016;42:87–94.
35. Wise LA et al. Risk of uterine leiomyomata in relation to tobacco, alcohol and caffeine consumption in the Black Women's Health Study. *Hum Reprod*. 2004;19:1746–1754.
36. Wise LA et al. A prospective study of dairy intake and risk of uterine leiomyomata. *Am J Epidemiol*. 2010;171:221–232.
37. Malik M et al. Curcumin, a nutritional supplement with antineoplastic activity, enhances leiomyoma cell apoptosis and decreases fibronectin expression. *Fertil Steril*. 2009;91(5 Suppl):2177–2184.
38. Greco S et al. Quercetin and indole-3-carbinol inhibit extracellular matrix expression in human primary uterine leiomyoma cells. *Reprod Biomed Online*. 2020;40:593–602.
39. Sahin K et al. Dietary tomato powder supplementation in the prevention of leiomyoma of the oviduct in the Japanese quail. *Nutr Cancer*. 2007;59:70–75.
40. Ho Y et al. Resveratrol inhibits human leiomyoma cell proliferation via crosstalk between integrin αvβ3 and IGF-1R. *Food Chem Toxicol*. 2018;120:346–355.
41. Elkafas H et al. Origin of uterine fibroids: conversion of myometrial stem cells to tumor-initiating cells. *Semin Reprod Med*. 2017;35:481–486.
42. Lethaby A et al. Fibroids (uterine myomatosis, leiomyomas). *BMJ Clin Evid*. 2015;2015:0814.
43. Deng L et al. Selective estrogen receptor modulators (SERMs) for uterine leiomyomas. *Cochrane Database Syst Rev*. 2012;10:CD005287.
44. Sangkomkamhang US et al. Progestogens or progestogen-releasing intrauterine systems for uterine fibroids (other than preoperative medical therapy). *Cochrane Database Syst Rev*. 2020;11:CD008994.
45. Ciavattini A et al. Uterine fibroids: pathogenesis and interactions with endometrium and endomyometrial junction. *Obstet Gynecol Int*. 2013;2013:173184.
46. Mitro SD et al. Natural history of fibroids in pregnancy: National Institute of Child Health and Human Development Fetal Growth Studies – Singletons cohort. *Fertil Steril*. 2022;118:656–665.
47. Zhang L et al. Progesterone receptor antagonist provides palliative effects for uterine leiomyoma through a Bcl-2/Beclin1-dependent mechanism. *Biosci Rep*. 2019;39:BSR20190094.
48. Hoekstra AV et al. Progestins activate the AKT pathway in leiomyoma cells and promote survival. *J Clin Endocrinol Metab*. 2009;94:1768–1774.
49. Cordeiro Mitchell CN et al. Mechanical stiffness augments ligand-dependent progesterone receptor B activation via MEK 1/2 and Rho/ROCK-dependent signaling pathways in uterine fibroid cells. *Fertil Steril*. 2021;116:255–265.
50. Luo N et al. Estrogen-mediated activation of fibroblasts and its effects on the fibroid cell proliferation. *Transl Res*. 2014;163:232–241.
51. Zhou W et al. LncRNA APTR promotes uterine leiomyoma cell proliferation by targeting ERα to activate the Wnt/β-catenin pathway. *Front Oncol*. 2021;11:536346.
52. Bray MJ et al. Estimating uterine fibroid SNP-based heritability in European American women with imaging-confirmed fibroids. *Hum Hered*. 2019;84:73–81.
53. Wise LA et al. African ancestry and genetic risk for uterine leiomyomata. *Am J Epidemiol*. 2012;176:1159–1168.
54. Bondagji NS et al. Replication of GWAS loci revealed the moderate effect of TNRC6B locus on susceptibility of Saudi women to develop uterine leiomyomas. *J Obstet Gynaecol Res*. 2017;43:330–338.
55. Aissani B et al. Evaluation of GWAS candidate susceptibility loci for uterine leiomyoma in the multi-ethnic NIEHS uterine fibroid study. *Front Genet*. 2015;6:241.
56. Gallagher CS et al. Genetic association studies in uterine fibroids: risk alleles presage the path to personalized therapies. *Semin Reprod Med*. 2016;34:235–241.
57. Välimäki N et al. Genetic predisposition to uterine leiomyoma is determined by loci for genitourinary development and genome stability. *Elife*. 2018;7:e37110.
58. Firdaus R et al. Multiple mutations in exon-2 of med-12 identified in uterine leiomyomata. *J Reprod Infertil*. 2021;22:201–209.

59. Ajabnoor GMA et al. Expanded somatic mutation spectrum of MED12 gene in uterine leiomyomas of Saudi Arabian women. *Front Genet*. 2018;9:552.
60. Klatt F et al. A precisely positioned MED12 activation helix stimulates CDK8 kinase activity. *Proc Natl Acad Sci USA*. 2020;117:2894–2905.
61. Park M al. Oncogenic exon 2 mutations in mediator subunit MED12 disrupt allosteric activation of cyclin C-CDK8/19. *J Biol Chem*. 2018;293:4870–4882.
62. Liu ZQ et al. Polymorphisms in XPC gene and risk of uterine leiomyoma in reproductive women. *Pathol Oncol Res*. 2020;26:1459–1464.
63. Vergara D et al. Genetics and genomics of uterine myomas. In: Tinelli A et al., eds. *Uterine Myoma, Myomectomy and Minimally Invasive Treatments*. Cham: Springer Publisher; 2015:12–25.
64. Ciebiera M et al. The role of miRNA and related pathways in pathophysiology of uterine fibroids - from bench to bedside. *Int J Mol Sci*. 2020;21:3016.
65. Zhao W et al. Effects of miRNA-199a-5p on cell proliferation and apoptosis of uterine leiomyoma by targeting MED12. *Open Med*. 2022;17:151–159.
66. Yang Q et al. The mechanism and function of epigenetics in uterine leiomyoma development. *Reprod Sci*. 2016;23:163–175.
67. Islam MS et al. Extracellular matrix in uterine leiomyoma pathogenesis: a potential target for future therapeutics. *Hum Reprod Update*. 2018;24:59–85.
68. El Sabeh M et al. Wnt/β-catenin signaling pathway in uterine leiomyoma: role in tumor biology and targeting opportunities. *Mol Cell Biochem*. 2021;476:3513–3536.
69. Zannotti A et al. Macrophages and immune responses in uterine fibroids. *Cells*. 2021;10:982.
70. Wang C et al. Insulin-like growth factor-1 promotes human uterine leiomyoma cells proliferation via PI3K/AKT/mTOR pathway. *Cells Tissues Organs*. 2023;212:194–202.
71. Memarzadeh M. Benign disorder of the uterine corpus. In: Decherney AH et al., eds. *Current Obstetric and Gynaecologic Diagnosis and Treatment*, 9th edn. New York: McGraw Hill; 2003:693–707.
72. Cooper NP et al. Fibroids in pregnancy – common but poorly understood. *Obstet Gynecol Surv*. 2005;60(2):132–138.
73. Indman PD. Hysteroscopic treatment of submucous myomas. *Clin Obstet Gynecol*. 2006;49(4):811–820.
74. Sparić R et al. Molecular insights in uterine leiomyosarcoma: a systematic review. *Int J Mol Sci*. 2022;23(17):9728.
75. Robboy SJ et al. Pathology and pathophysiology of uterine smooth-muscle tumors. *Environ Health Perspect*. 2000;108(Suppl 5):779–784.
76. Parker WH. Etiology, symptomatology, and diagnosis of uterine myomas. *Fertil Steril*. 2007;87:725–736.
77. Whitaker L et al. Abnormal uterine bleeding. *Best Pract Res Clin Obstet Gynaecol*. 2016;34:54–65.
78. Gerema U et al. Abnormal uterine bleeding and associated factors among reproductive age women in Jimma town, Oromia Region, Southwest Ethiopia. *Womens Health*. 2022;18:17455057221077577.
79. Puri K et al. Submucosal fibroids and the relation to heavy menstrual bleeding and anemia. *Am J Obstet Gynecol*. 2014;210:38.e1–38.e7.
80. Fuldeore MJ et al. Patient-reported prevalence and symptomatic burden of uterine fibroids among women in the United States: findings from a cross-sectional survey analysis. *Int J Womens Health*. 2017;9:403–411.
81. Murase E et al. Uterine leiomyomas: histopathologic features, MR imaging findings, differential diagnosis, and treatment. *Radiographics*. 1999;19:1179–1197.
82. Lai YL et al. Torsion of pedunculated subserous uterine leiomyoma: a rare complication of a common disease. *Taiwan J Obstet Gynecol*. 2018;57:300–303.
83. Dagur G et al. Urological complications of uterine leiomyoma: a review of literature. *Int Urol Nephrol*. 2016;48:941–948.
84. Andrada AO et al. Pelvic plexus compression due to a uterine leiomyoma in a woman with acute urinary retention: a new hypothesis. *Int Urogynecol J*. 2014;25:429–431.
85. Bidziński M et al. Ostre zatrzymanie odpływu moczu spowodowane mięśniakiem szyjki macicy – opis przypadku i przegląd literatury [Acute urinary retention due to cervical myoma – a case report and a review of the literature]. *Ginekol Pol*. 2015;86:77–79.
86. Yazdany T et al. Urinary retention and voiding dysfunction in women with uterine leiomyoma: a case series. *J Reprod Med*. 2012;57:384–389.
87. Parker-Autry C et al. Lower urinary tract symptoms in patients with uterine fibroids: association with fibroid location and uterine volume. *Female Pelvic Med Reconstr Surg*. 2011;17:91–96.
88. Yildiz F et al. A rare cause of difficulty with sexual intercourse: large retroperitoneal leiomyoma. *J Sex Med*. 2009;6:3221–3223.
89. Bettez M et al. Early versus delayed repair of vesicouterine fistula. *Can Urol Assoc J*. 2011;5:E52–E55.
90. Fletcher HM et al. Renal impairment as a complication of uterine fibroids: a retrospective hospital-based study. *J Obstet Gynaecol*. 2013;33:394–398.
91. Price N et al. Delayed presentation of vesicouterine fistula 12 months after uterine artery embolisation for uterine fibroids. *J Obstet Gynaecol*. 2007;27:205–207.
92. Dancz CE et al. The relationship between uterine leiomyomata and pelvic floor symptoms. *Int Urogynecol J*. 2014;25:241–248.
93. Zepiridis LI et al. Infertility and uterine fibroids. *Best Pract Res Clin Obstet Gynaecol*. 2016;34:66–73.
94. Coutinho LM et al. Uterine fibroids and pregnancy: how do they affect each other? *Reprod Sci*. 2022;29:2145–2151.
95. Gomez E et al. MRI-based pictorial review of the FIGO classification system for uterine fibroids. *Abdom Radiol*. 2021;46:2146–2155.
96. Munro MG et al. FIGO Working Group on Menstrual Disorders. FIGO classification system (PALM-COEIN) for causes of abnormal uterine bleeding in nongravid women of reproductive age. *Int J Gynaecol Obstet*. 2011;113:3–13.
97. Wada Y et al. Characteristics of submucosal leiomyomas that could cause severe hemorrhage with relugolix: an observational study. *BMC Womens Health*. 2023;23:110.
98. American Association of Gynecologic Laparoscopists, Advancing Minimally Invasive Gynecology Worldwide. AAGL practice report: practice guidelines for the diagnosis and management of submucous leiomyomas. *J Minim Invasive Gynecol*. 2012;19:152–171.
99. Tanos V et al. Prevention and management of complications in laparoscopic myomectomy. *Biomed Res Int*. 2018:8250952.
100. Cicinelli E et al. Transabdominal sonohysterography, transvaginal sonography, and hysteroscopy in the evaluation of submucous myomas. *Obstet Gynecol*. 1995;85:42–47.
101. Becker E Jr et al. The added value of transvaginal sonohysterography over transvaginal sonography alone in women with known or suspected leiomyoma. *J Ultrasound Med*. 2002;21:237–247.
102. Woźniak et al. Ultrasonography of uterine leiomyomas. *Prz Menopauzalny*. 2017;16(4):113–117.
103. Sakhel K et al. Sonography of adenomyosis. *J Ultrasound Med*. 2012;31:805–808.
104. Parazzini F et al. Pregnancy outcome and uterine fibroids. *Best Pract Res Clin Obstet Gynaecol*. 2016;34:74–84.
105. Donnez J et al. Uterine fibroid management: from the present to the future. *Hum Reprod Update*. 2016;22:665–686.
106. Dudiak CM et al. Uterine leiomyomas in the infertile patient: preoperative localization with MR imaging versus US and hysterosalpingography. *Radiology*. 1988;167:627–630.
107. Bolan C et al. MR imaging of atypical fibroids. *Abdom Radiol*. 2016;41:2332–2349.
108. Jondal DE et al. Uterine fibroids: correlations between MRI appearance and stiffness via magnetic resonance elastography. *Abdom Radiol*. 2018;43:1456–1463.
109. Wright JD et al. Uterine pathology in women undergoing minimally invasive hysterectomy using morcellation. *JAMA*. 2014;312:1253–1255.
110. Gross BH et al. Computed tomography of gynecologic diseases. *AJR*. 1983;141:765–773.

14 ADENOMYOSIS

From Pathophysiology to Symptomatology and Evaluation

Giovanni Pecorella, Roberta Montefrancesco, and Andrea Tinelli

Abbreviations

AUB	Abnormal uterine bleeding
COMT	Catechol-O-methyltransferase
HMB	Heavy menstrual bleeding
JZ	Junctional zone
LIF	Leukemia inhibitory factor
LNG-IUS	Levonorgestrel intrauterine system
MRI	Magnetic resonance imaging
MRKH	Mayer–Rokitansky–Küster–Hauser syndrome
MMPs	Metalloproteinases
TIAR	Tissue injury and repair mechanism
TUS	Transvaginal ultrasound
US	Ultrasound

14.1 Introduction to Adenomyosis

Adenomyosis is still a complex clinical condition to understand and treat, in women of fertility age, showing patients suffering for enlarged uterus, abnormal uterine bleeding (AUB), pelvic pain, dyspareunia, and infertility (1). Epidemiologic studies show a large variation concerning the prevalence, from 10% to 57% of the female population (2), since the diagnostic is often just post-hysterectomy, not defined by the age of onset (3).

A huge epidemiological study was led by the Department of Gynecology and Obstetrics of the University of Milan. They led a pathological examination of every patient who underwent a hysterectomy in the years 1990–1992, with a special focus on adenomyosis, to establish prevalence data (4). Of the pool of 1334 analyzed patients, adenomyosis was diagnosed in 332 (25%). To macroscopic inspection, the adenomyotic nodules are recognized as fibrotic (Figure 14.1) or elastic (Figure 14.2) or hard nodule (Figure 14.3) in the uterine myometrium (5) (Figure 14.4). To deeply understand the pathology, knowledge of embryology is necessary (6).

The female genital system derives from Müllerian ducts (7) and originates from mesoderm, primordial germ cells, mesenchyme, and coelomic epithelium (8). The Müllerian ducts spring out from coelomic epithelium and develop the upper two-thirds of the vagina, the cervix-uteri, uterus, and both salpinx (7, 8). The myometrium splits into two different layers of different embryological origin, an inner part called subendometrial myometrium or stratum subvascular and the outer part, stratum vascular and supravascular (9).

The inner part is formed from endometrium, the junctional zone (JZ), positioned between endometrium and myometrium and stratum sub vascular, as a layer of myometrium. These layers form the so-called archimetra, or old uterus, present in most vertebrates (10). The outer two layers of myometrium form the "neometra." Archimetra originates from Müllerian ducts, neometra from non-Müllerian ducts. Adenomyosis is a pathology of the archimetra (6).

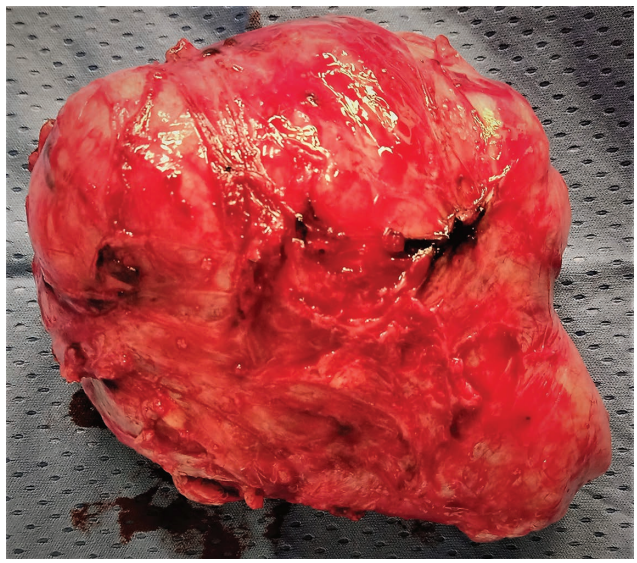


FIGURE 14.1 Intraoperative macroscopic image of an adenomyoma fibrotic nodule.

FIGURE 14.2 Intraoperative macroscopic image of an adenomyoma elastic nodule.

DOI: 10.1201/9781003312109-14

FIGURE 14.3 Intraoperative macroscopic image of a large adenomyoma hard nodule.

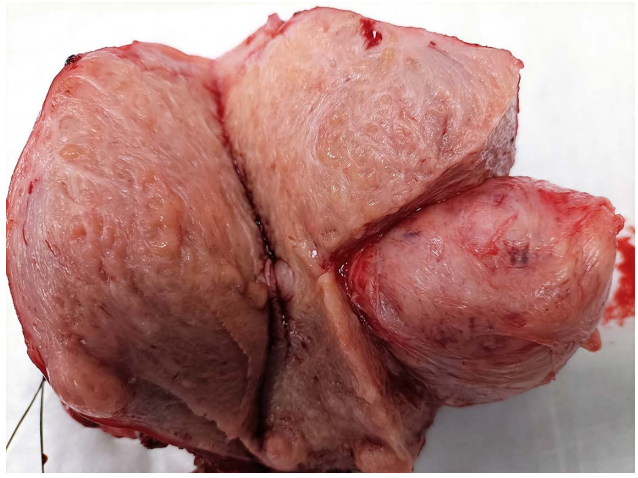


FIGURE 14.4 Intraoperative macroscopic image of a uterus with diffuse adenomyosis and adenoma nodule within it.

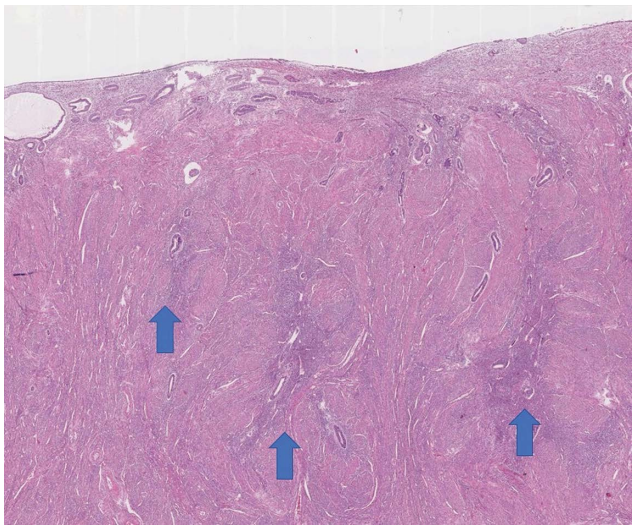


FIGURE 14.5 At microscopic higher magnification, it can be seen that the foci of adenomyosis (blue arrows) consist of non-neoplastic endometrial glands and stroma, which penetrate deep into the myometrium (at least one low power field from the endomyometrial junction).

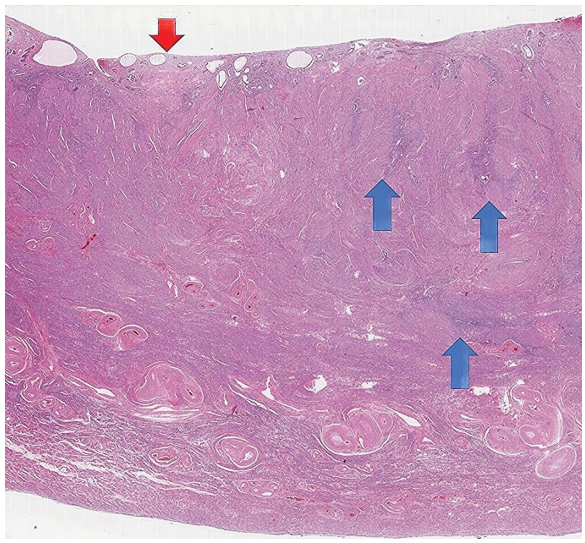


FIGURE 14.6 A full-thickness microscopic section of the uterus showing normal endometrium (red arrow) and foci of adenomyosis deep in the myometrium (blue arrows). Even at low magnification it is possible to notice how the foci of adenomyosis appear basophilic (in contrast to eosinophilic myometrium) due to the presence of endometrial stroma.

From the anatomopathological point of view, adenomyosis is characterized by endometrial cells within the smooth muscle of the myometrium, at a depth of at least 2.5 mm and often surrounded by hyperplastic smooth muscle (11) (Figure 14.5).

Endometrial epithelial cells and stromal fibroblasts could be abnormally detected in the myometrial layer (Figure 14.6), leading to hyperplasia and hypertrophy of surrounding smooth muscle cells (Figure 14.7). They are organized in nodules with a poorly defined boundary in a healthy uterus (Figure 14.8) (12, 13).

14.2 Pathophysiology of Adenomyosis

For many years, adenomyosis was defined as a histopathological diagnosis after hysterectomy in perimenopausal women (Figure 14.9) scheduled to surgery for heavy menstrual bleeding (HMB) or pelvic pain (14–16). This complex pathological entity is often confused with the endometriosis and both are often described as a single pathological entity. In other words, the major features of the two diseases (ectopic endometrium) are the same, but their locations are different.

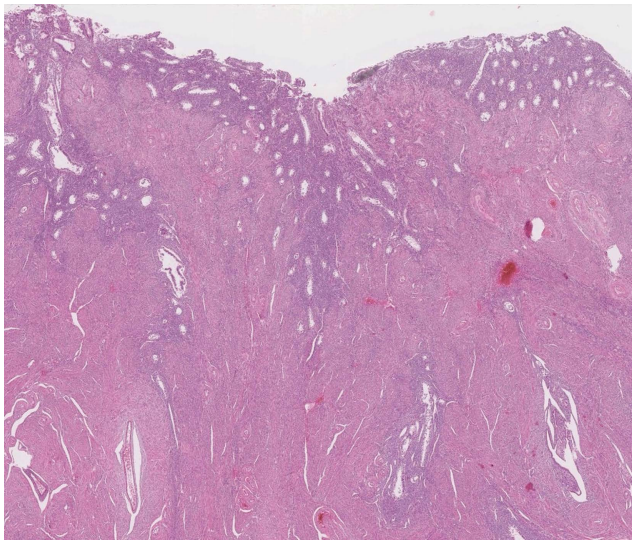


FIGURE 14.7 A full-thickness microscopic section of the uterus showing glandular tissue present in adenomyosis, generally of basalis or proliferative endometrium type, but one-fourth is functional (as shown in the figure). It is important to remember that foci of adenomyosis can be subject to any type of modification, both benign and malignant, that normal endometrium can undergo.

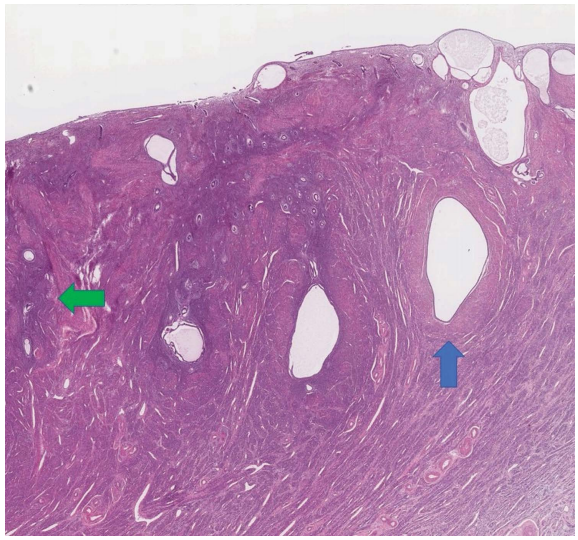


FIGURE 14.8 At microscopic higher magnification, it can be seen that the proportion between stoma and glands in the foci of adenomyosis may be more in favor of the glands (stroma poor adenomyosis, blue arrow) or of the stroma (gland poor adenomyosis, green arrow).

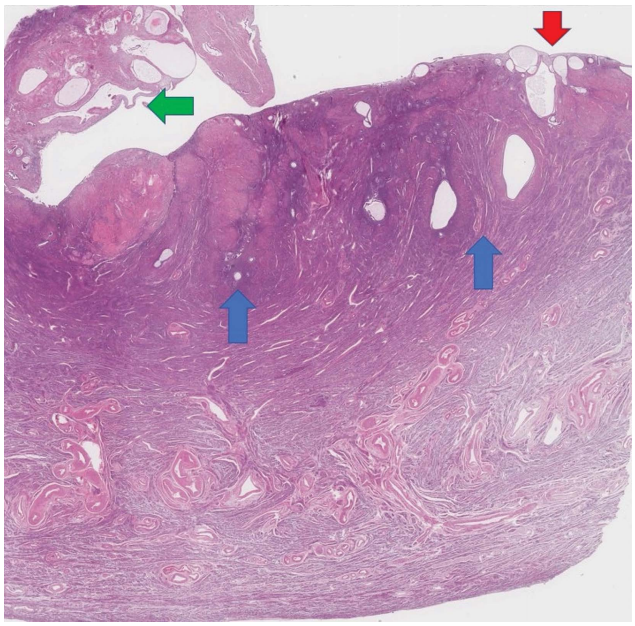


FIGURE 14.9 A full-thickness image of the uterus, showing an atrophic endometrium (red arrow) of a menopausal woman and foci of adenomyosis (blue arrows), with a cystic appearance. In the upper left corner (green arrow) there is also an atrophic endometrial polyp.

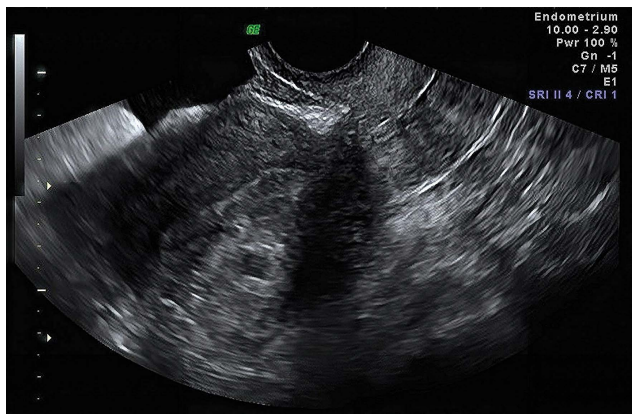


FIGURE 14.10 The term "internal endometriosis" can be encompassed in this transvaginal ultrasound scan of uterus with posterior body wall completely affected by adenomyosis.

As such, adenomyosis used to be called "endometriosis interna" (Figure 14.10), presumably due to such a similarity (9). The two entities share similar pathophysiology, clinical and therapeutic aspects, and diagnostic features (9), and both are influenced by estrogens on growth and regression (17). Adenomyosis seems to be associated with a history of curettage (18), termination of pregnancy (11), and caesarian delivery (19, 20). A retrospective study analyzing a large pool of patients showed no direct association between race and adenomyosis (21, 22). The age of menarche also shows no association with adenomyosis in the literature (4, 18, 23), instead a cycle with a length of ≤ 24 days showed an increase of 46% compared with women with a cycle of 28 days (21). Pregnancy and delivery are generally recognized as risk factors (4, 18, 23, 24).

The damage caused from the trophoblast implantation and the delivery (mainly cesarean sections) are seen as a rupture of

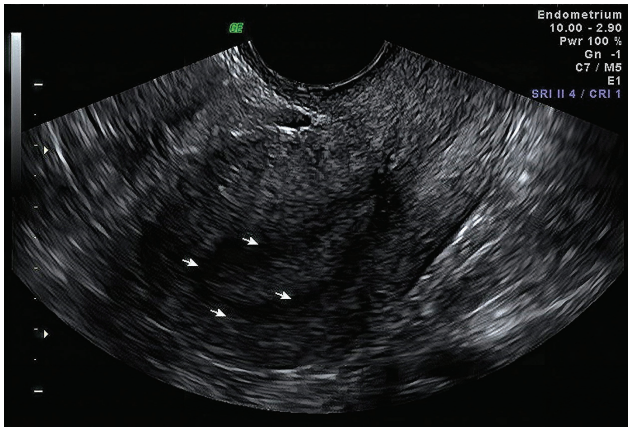


FIGURE 14.11 Transvaginal ultrasound image of a uterus taken in longitudinal section of a JZ, highlighted by white arrows. Generally, a JZ thickness of greater than 12 mm is the most widely accepted criterion in establishing the presence of adenomyosis. This threshold was derived after several studies that correlated the measurement of the JZ with the histologic diagnosis of adenomyosis.

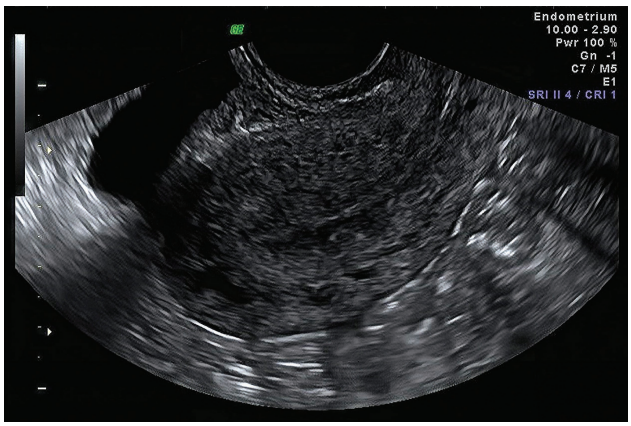


FIGURE 14.12 Ultrasound transvaginal scan of a uterus with diffuse adenomyosis.

the physiological integrity of the JZ (Figure 14.11), and that is why it's considered a risk factor (25, 26). High-risk pregnancies are characterized by complications that arise during the 9th–12th week, corresponding to the implantation window (26). Adenomyosis diagnostics are enhanced by the improvement in imaging instruments such as transvaginal ultrasound (TUS) (Figure 14.12) and magnetic resonance imaging (MRI) (Figure 14.13).

Thus, adenomyosis diagnosis remains challenging because of the difficulty in connecting the imaging and the histopathology to identify the pathogenesis, the different phenotypes, and the best option for treatment (14). Adenomyosis pathophysiology is still unclear, but the two more accredited theories in the literature are endometrial invagination as a consequence of activation of the tissue injury and repair mechanism (TIAR) and stem cell metaplasia (25). There are a few etiopathogenic theories, but none is considered definitive.

In detail, the decreased expression of hydroxysteroid dehydrogenase type 2 (17-b HSD2) (antiestrogenic enzyme) has been

FIGURE 14.13 Radiological image of nuclear MRI in T2 which highlights a uterus with wall asymmetry due to the prevalence of the posterior one (anterior wall of 17 mm and posterior wall of 24 mm), with blurred appearance of the junctional line on the posterior wall with contiguous area of blurred myometrial hypo intensity for a non-secretory adenomyosis. The invagination theory is based on the fact that **E2 estrogen levels** are the main protagonists in the pathogenesis of the disease. Estrogens levels in women with a diagnosed adenomyosis are significantly higher because of a dual mechanism – a reduction of catabolism and increased production (27).

shown in adenomiotic patients (28). Studies report that gene polymorphism causes the increased production of estrogen due to an increase of aromatization through cytochrome P450–1B1 (CYP1B1) 432 C/G and cyclooxygenase-2 (COX-2) 1195 G/A and a decrease of breakdown in the eutopic and ectopic endometrium (catechol-O-methyltransferase [COMT] 158 G/A) (27, 29, 30).

Moreover, the aromatase cytochrome P450 involved in steroidogenesis is not present in the normal endometrium but is in women with adenomyosis (31). The adenomyotic patients seems to have a lower immunoreactivity for isoform B of the progesteron receptor (PR-B); this receptor normally thwarts estrogen-related proliferation, and that mechanism seems not to work properly in such patients (32, 33). This explains why in the estrogen-dependent phase of the menstrual cycle, the endometrium grows abnormally in women with this mutation (33).

Moreover, stress caused by high levels of estrogen, may may lead to elevated oxytocin-mediated uterine activity; as a consequence, altered endometrial proliferation and tissue damage, primarily in the JZ, have been observed. A recent study shows a higher presence of myofibroblast in the endometrial-myometrial JZ in uteri with adenomyosis, as evidence of chronic tissue microtrauma (34). A consequence of this microtrauma is the triggering of an estrogen-dependent reparation process, tissue injury and repair (TIAR) (35).

The TIAR system can be activated following tissue trauma anywhere in the body (25). The microtrauma, caused from

oxytocin activity, activates a local inflammatory cascade. Everything starts with the local production of interleukin-1 that induces activation of COX-2, which consequently produces prostaglandin E2.

The inflammatory cascade leads, through a positive feedback mechanism, to a chronic cellular reshaping in the JZ, resulting in a constant disruption of the muscular tissue in the myometrial wall (25). The spaces (or lacunae) formed within the myometrium appear to be filled by the thickened endometrium, leading to an invagination of the basal endometrial layer into the myometrium (25).

This theory, suggesting that microscopic lesions and their defective repair lead to adenomyosis-like healing, may be supported by the observation that macroscopic uterine injuries can predispose certain women to develop adenomyosis (cesarean delivery, multiparity, and uterine surgery) (18, 19, 21, 24). On the other hand, Hoo et al. led a study that again speaks to the invasion theory and introduces metaplastic etiology.

They analyzed adenomyosis in patients with Mayer–Rokitansky–Küster–Hauser syndrome (MRKH) (36). This syndrome is characterized by congenital aplasia of the uterus and the upper part (2/3) of the vagina in women showing normal development of secondary sexual characteristics (37).

To explain the occurrence of adenomyosis in patients without a functional endometrium – where invagination cannot take place – another well-established theory comes into play, attributing the genesis of adenomyosis to metaplasia of pluripotent Müllerian stem cells (1, 38–40). The Müllerian ducts are embryonal structures that will develop to form some of the female structures (salpinx, higher tract of the vagina and uterus) (41). This theory is based on the idea that some of these embryonal cells remain in the myometric wall, leading to the production of ectopic endometrium in the myometrium (40).

In addition to the theory that stem cells migrate from the endometrium to the myometrium, another suggests that adenomyosis could be triggered from endometrial mesenchymal stem cells (eMSCs) trough retrograde mestruation (1). eMSCs are an integrating part of menstrual blood (42, 43).

Chapron et al. proposed a new theory that supports the high concurrence of posterior adenomyosis foci, or the inside-out theory (44). This theory is based on the fact that adult endometrial cell (or stem cells) could infiltrate the uterine serosa and reach the myometrium constituting the adenomyosis lesion (44).

14.2.1 Symptomatology of Adenomyosis

The main symptom of adenomyosis is pelvic and abdominal pain, associated with dysmenorrhea and dyspareunia (1, 14, 16, 45). Menorrhagia, infertility, and sterility are the second line of symptoms and are among the most represented. Following those is a feeling of swelling, which is an infrequent symptom but also reported by patients (45). On the other hand, what is reported in the literature is somewhat strange: up to 30% of patients are completely asymptomatic (16). The main challenge in making a diagnosis based on symptoms is that adenomyosis is often associated with endometriosis or other causes of pelvic pain (45).

14.3 Pain

Concerning abdominal and pelvic pain, the literature shows that pelvic pain is the most frequent symptom in adenomyosis, from 50% to 93.4% among patients (46, 47). Another interesting result is that the pain level is directly proportional to the extent of adenomyosis in the uterus (48, 49). As mentioned earlier, adenomyosis and endometriosis are frequently associated. Depending on the location of the lesions, two sorts of pelvic pain can be distinguished: somatic (if the lesions are located mainly on the peritoneum or pelvic wall) and visceral (from the uterus, bladder, or intestine). Somatic pain is sharp and localized. Adenomyotic pain (from uterus) is visceral, dull, and spasm-like (50). While pelvic pain in deep endometriosis well established, the lack of nerve fibers in the uterus (51) makes the origin of pain in adenomyosis matter of debate (45). The main argument is that histopathological examination shows the absence of an innervation in the endometrium and myometrium JZ in healthy patients. Thus, some studies demonstrated the presence of nerve fibers in the functional layer of patients with symptomatic adenomyosis (52).

14.4 Bleeding

Adenomyosis integrates part of the FIGO classification for causes of abnormal uterine bleeding (AUB): the PALM-COEIN classification (53) (Figure 14.14). An increase of the menstrual blood loss is shown to be up to 22% in adenomyotic patients (54). McCausland et al. (55) tried to quantify the blood loss according to the quantity and the size of the clot needed. The

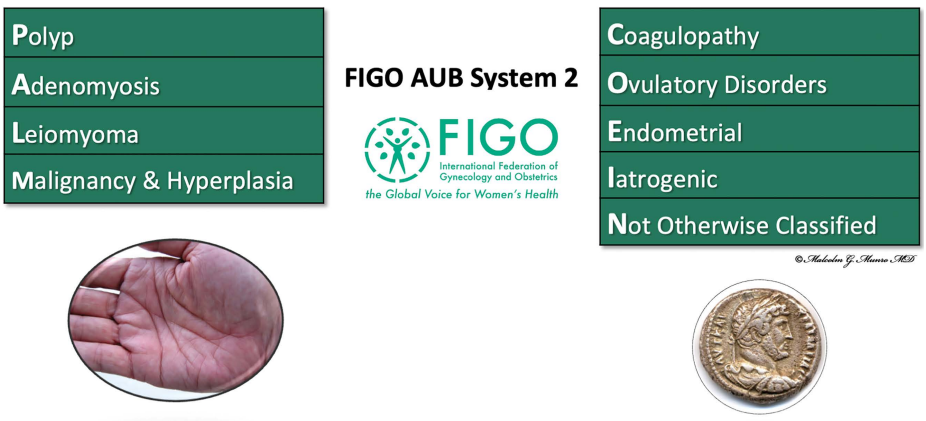


FIGURE 14.14 The PALM-COEIN classification as an integrating part of the FIGO classification for causes of abnormal uterine bleeding (AUB).

scientific community finds a direct correlation between menorrhagia and depth of endometrial penetration (55).

14.5 Infertility/Reduced Fertility Mechanism

The mechanism that leads an adenomyotic patient to be infertile is not scientifically proven. The goal of this section is to understand if an adenomyosis-induced anatomy/physiological alteration can cause infertility.

14.6 Anatomical Alterations

It is reasonable to understand that the location of a lesion could mechanically hinder implantation. An adenomyoma could cause an obstruction of the tubal ostia, presenting an obstacle for sperm migration and the journey of the embryo (56–58).

14.7 Altered Uterine Contractility

Studies have reported that the adenomyosis extension is directly proportional hyper/dysperistalsis rate (59). Kissler et al. compared 41 infertile subjects with endometriosis and among them 35 with additional adenomyosis. This abstract analyzed the uterus mobility through T2-weighed MRI (Figure 14.15). Among the six women without adenomyosis, only two (33%) showed dysperistalsis or hyperperistalsis, compared with 14 of 24 (58%) in the focal adenomyosis group and 10 of 11 (91%) in the diffuse adenomyosis group (59). This study was led using 99m-Tc-labeled microalbumin aggregates, placed into the posterior vaginal fornix and gamma camera that shoot at regular intervals a photogram to demonstrate the migration of the fluid. In fertile patients a unidirectional flow towards the dominant follicle is seen. Adenomyotic patients showed a blockage

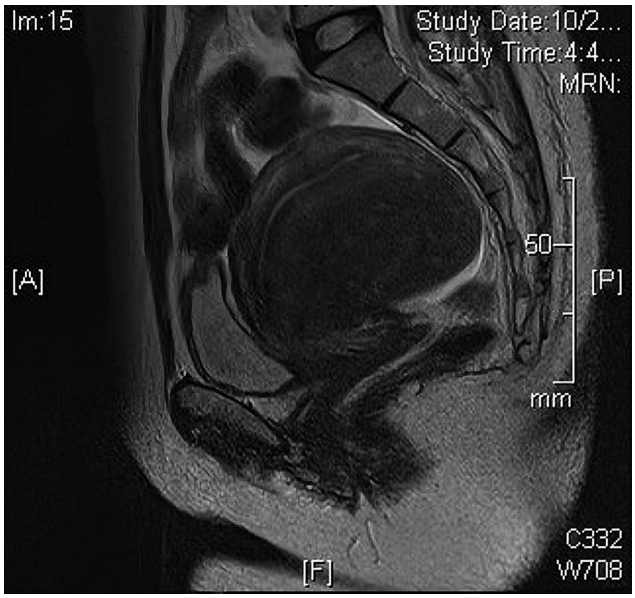


FIGURE 14.15 Radiological image of nuclear MRI in T2, which highlights a uterus with a large adenomyoma of the posterior wall.

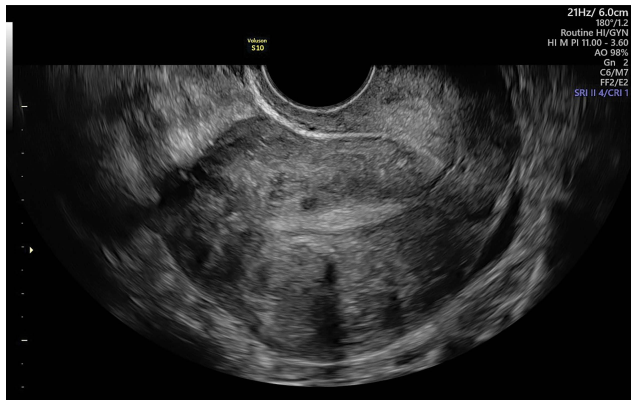


FIGURE 14.16 Transvaginal scan of an enlarged uterus demonstrating a slight decrease in uterine echogenicity and calcified leiomyoma with shadowing on the fundus.

of fluid in the uterus in 70% of cases, contralateral flow in 22%, and ipsilateral flow in only 8% (56, 59). As we reported, the adenomyosis affects myometrium showing cytological alteration.

The smooth muscle cells are hypertrophic and hyperplastic, leading to altered uterine peristalsis that may disrupt the transport of gametes between the uterus and the fallopian tubes. Consequently, adenomyotic uteri show a lack of nerve fibers in the endometrial–myometrial junction, resulting in impaired uterine contractility (51).

14.7.1 Imaging of Adenomyosis

The first case report of adenomyosis was dated 1949, reporting the first approach of diagnostic imaging by X-ray. The hysterosalpingography was of great help in showing the presence of intrauterine pathology, such as adenomyosis (60, 61). Nowadays it is largely abandoned to diagnose adenomyosis. Since the 1980s, research has increasingly focused on transabdominal ultrasound as a diagnostic tool (62).

A retrospective study listed the ultrasonographic features common in patients after histological confirmation on uterus, after hysterectomy. The most common feature is surely uterine enlargement: 90% of imaging showed a slight decrease in uterine echogenicity, and 10% showed a calcified leiomyoma with shadowing (Figure 14.16) (62). A 1994 study compared the transvaginal ultrasound (TUS) vs MRI to detect adenomyosis (63). Study results showed the MRI diagnostic specificity and sensibility in 15 of 17 patients, compared to 9 of 17 by TUS examination (63).

Another study showed that TUS showed 89% sensitivity and 89% specificity compared to MRI sensitivity of 86% and specificity of 86% (64). Summarizing, TUS could be considered for feasibility, safety, availability, and lower cost compared to MRI, as preferred instrumental diagnosis for adenomyosis (Figure 14.17). In case of absence of ultrasound findings, the MRI could be decisive for a diagnosis of adenomyosis (65).

14.8 Ultrasound and Adenomyosis Diagnosis

The front line of the adenomyosis diagnosis is TUS (15). In literature an adenomyosis prevalence in the population that

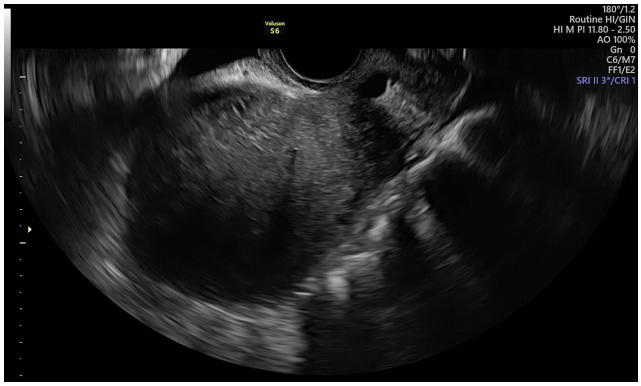


FIGURE 14.17 Transvaginal scan of uterus with adenomyosis.

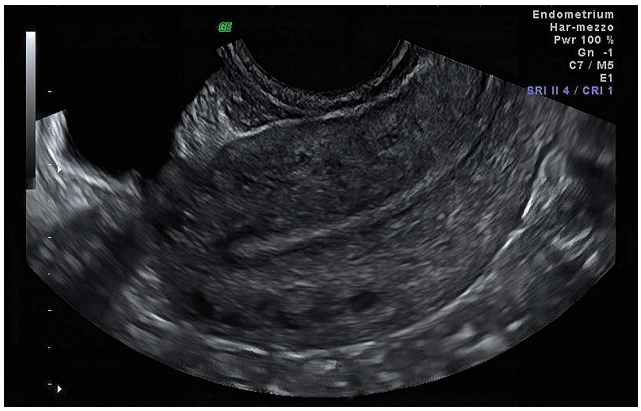


FIGURE 14.18 Transvaginal scan of uterus with adenomyosis in which the JZ between the endometrium and myometrium is clearly visible.

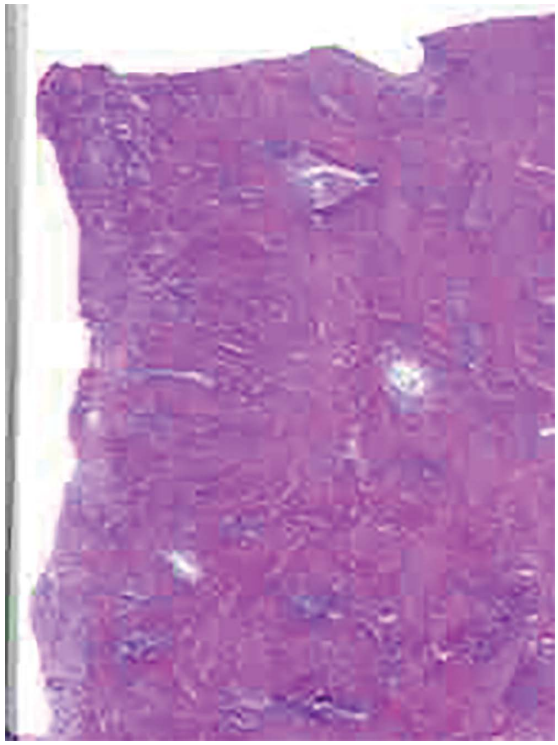


FIGURE 14.19 Histological image of a section of the uterus with adenomyosis. A pluri-nodular enlargement of the wall without perilesional contours is observed. The muscle fibers of the myometrium end up assuming a random pattern betraying the normal architectural texture of the myometrium.

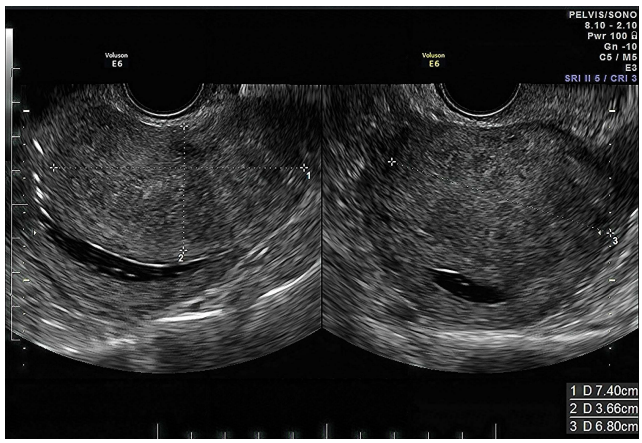


FIGURE 14.20 Transvaginal ultrasound scan demonstrating a globular uterine configuration, for a voluminous adenoma approximately 7 cm in diameter.

can oscillate between 5% and 70% is reported (66). This broad variable range is due to the most important features necessary for adenomyosis diagnosis, a high-quality ultrasound machine and a high level of physician skill (67).

Myometrial ultrasonography can be differentiated in three different layers: internal, composed of the circular and longitudinal muscle fiber (archimetra), intermediate, and extern. The intermediate layer is the most detectable in TUS because of its higher echogenicity; it is separated from the outer layer by the arcuate venous and arterial plexus (66).

The inner layer is sonographically hypoechoic, but detection through MRI is relatively straightforward, appearing as a low-signal-intensity band – also known as the JZ. The JZ is the area we have to focus on for adenomyosis diagnosis (66) and is the layer between the endometrium and the myometrium (Figure 14.18), that could be described after the appearance of MRI and histological examination (Figure 14.19).

Histologically, this layer is formed from smooth muscle fibers surrounded by a few extracellular matrixes. A 12 mm hypertrophy and hyperplasia of this layer, surrounded by little extracellular matrix, is what distinguishes adenomyosis (10).

Embryologically, the JZ originates from the paramesonephric ducts, whereas the remaining myometrium derives from the mesenchyme (10). Concerning the TUS features of adenomyosis reported in the literature, it is surely to assess globular uterine configuration (Figure 14.20), myometrial anterior-posterior asymmetry, heterogeneous myometrial echotexture as "venetian blind" (Figure 14.21), poor definition of the JZ (Figure 14.22), and intramyometral cysts (Figure 14.23) (65).

An Italian research group performed a prospective study showing general ultrasonic features as adenomyotic uteri, after confirmation by uterine histopathological examination. The

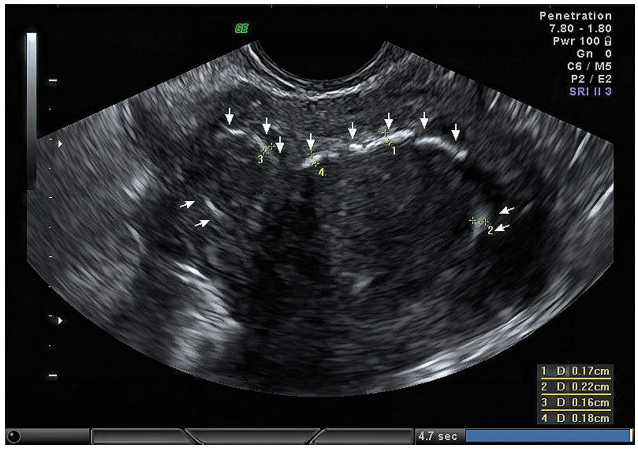


FIGURE 14.21 Transvaginal ultrasound scan demonstrating extensive and diffuse fibrotic thickening of the outer margins of the adenoma, irregularly occupying most of the uterine volume. This thickening is not pseudocapsule as it is nonvascular and excessively thick.

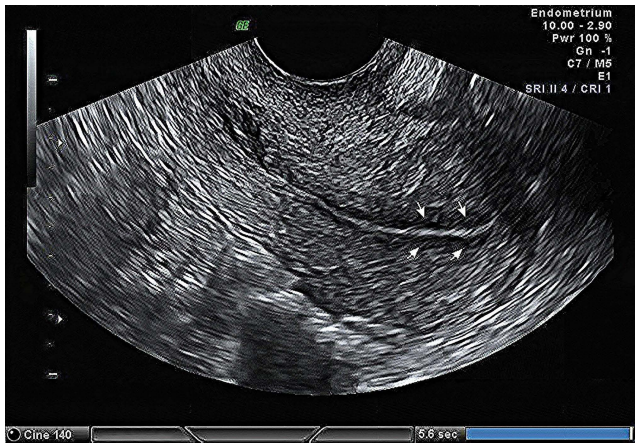


FIGURE 14.22 Transvaginal ultrasound scan showing irregular JZ (with arrows).

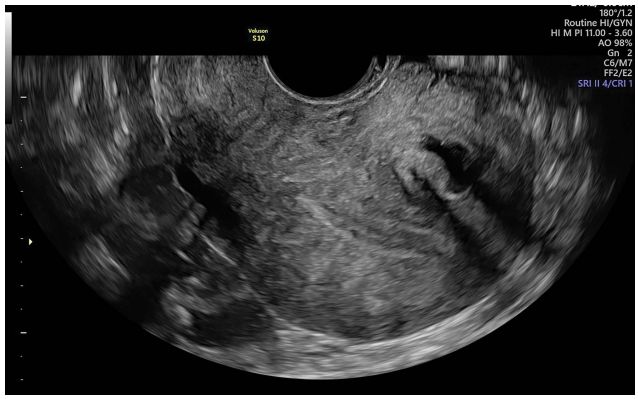


FIGURE 14.23 Transvaginal ultrasound scan demonstrating intramyometral cysts of the posterior wall of the uterine body.

FIGURE 14.24 Transvaginal ultrasound scan showing a heterogeneous myometrium structure of the uterine body.

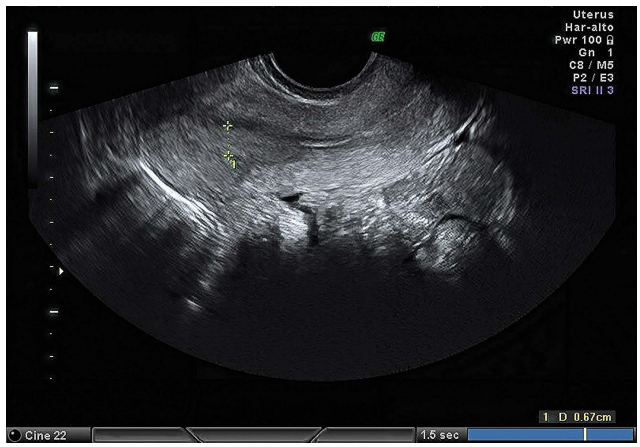


FIGURE 14.25 Transvaginal ultrasound scan detecting an adenomyoma, with completely different echogenicity from the surrounding myometrium, below the JZ of the uterine body.

typical US features were heterogeneous myometrium structure (Figure 14.24), asymmetry of the uterine walls, and difficulty in delimiting the endometrial-myometrial junctional area (64). The study group represented uteri from a curved corpus uterus backwards, where the fundus uteri was in front of the posterior pelvic compartmented and the cervix was direct facing the urinary bladder (68).

An important and simple ultrasonic parameter that improves the TUS detection rate is the question mark sign (68). It is characterized by backward flexion of the uterine fundus toward the posterior pelvic compartment, with the cervix directed anteriorly toward the urinary bladder.

This sign shows a specificity and sensitivity of 92% and 75%, respectively, detected on 18 of 24 patients with histological adenomyosis (75%) and on two of 26 of women without the question mark sign (7.6%) (68). On the other hand, adenomyomas are easier to detect because of the mass effect in uterus (Figure 14.25). It is more difficult, however, to distinguish between adenomyomas and fibroids.

Fibroids can be distinguished from adenomyomas by the typical shape, elliptical rather than globular, the lack of calcification (Figure 14.26), and edge shadowing (64, 69). Eco-Doppler can surely help gynecologists in the sonographic diagnosis of

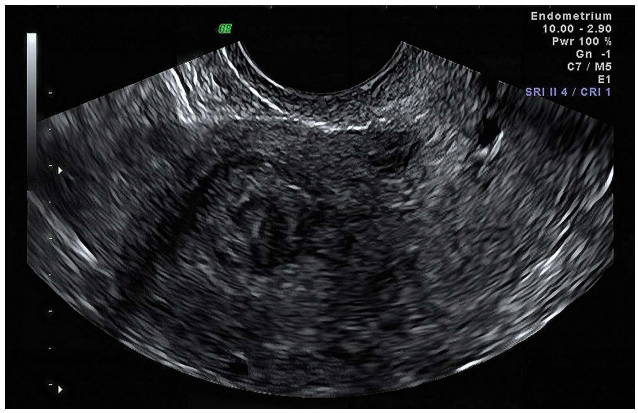


FIGURE 14.26 Transvaginal ultrasound scan showing an anterior myoma of the uterine body.

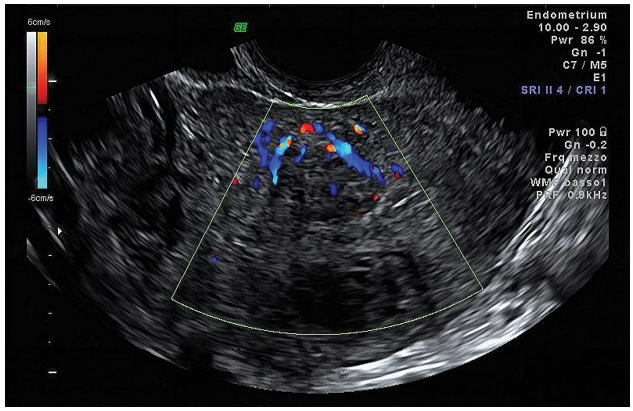


FIGURE 14.27 Transvaginal ultrasound scan showing a myoma of the uterine body with an overlying ring of fire.

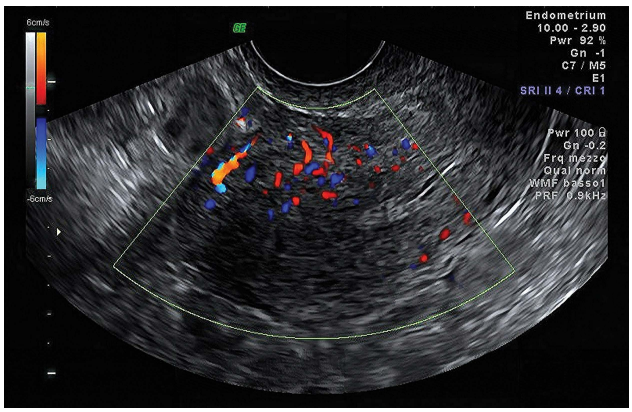


FIGURE 14.28 Transvaginal ultrasound scan showing a fundal adenomyoma; the vessels are not influenced by the presence of this lesion.

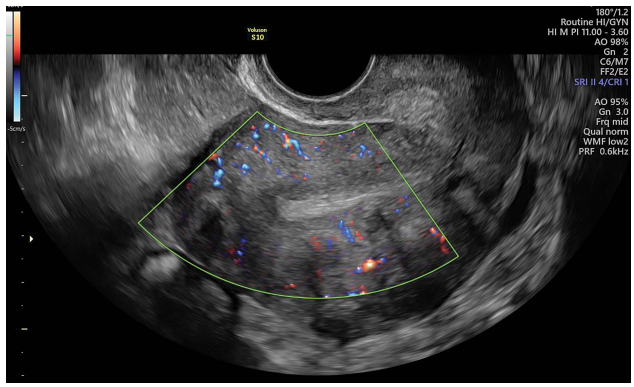


FIGURE 14.29 Longitudinal section of transvaginal ultrasound of a uterus with diffuse adenomyotic nodules, with color Doppler echo: Flows are perpendicular to uterine axis.

adenomyosis, as the course of the vessels is different in fibroids and adenomyosis.

Fibroids are typically surrounded by vessels as "a ring of fire" (Figure 14.27) and a few of them enter the mass. In a uterus with adenomyomas, the vessels are not influenced by the presence of this lesion (Figure 14.28), and flows are normally perpendicular to the uterine axis (Figure 14.29) (70).

Concerning US bias in adenomyosis diagnosis, the posterior US uterine evaluation needs adequate analysis (61). Coronal uterine reconstructions could be added to conventional imaging in the sagittal and transverse planes, favoring the complete endometrial-myometrial planes imaging, fundus included (61). Nevertheless, 3D ultrasound is helpful both during live examination and retrospectively, as postprocessing with volume-contrast can better visualize the JZ (61).

14.9 MRI and Adenomyosis Diagnosis

The gold standard to diagnose adenomyosis is the MRI (65), as largely reported in the literature (12, 71, 72). MRI is an accurate and noninvasive tool for the adenomyosis diagnosis, basing on high sensitivity (77%) and specificity (89%) (72). The T2-weighted sequences are those that allow the best evaluation of the uterine anatomy. On T2-weighted sequences, the uterus physiologically presents three distinct areas, with different signal intensity:

- Endometrium, with high signal intensity since it is made up of glands.
- Myometrium, which is characterized by an intermediate signal intensity, as it is made up of a less crowded cellular component than in the junctional area.
- JZ, which constitutes the innermost part of the myometrium and shows low signal intensity due to the high concentration of smooth muscle cells, compared to the more peripheral layer.

The JZ constitutes a unique entity from a morphological and functional point of view compared to the other layers of the uterus. The excellent contrast resolution of MRI allows the identification of morphological changes related to adenomyosis (73). The most common MRI findings concern the JZ, usually thicker than 12 mm, besides the maximum JZ/total myometrium ratio greater than 40% and the difference between maximum and minimum thickness of the JZ of more

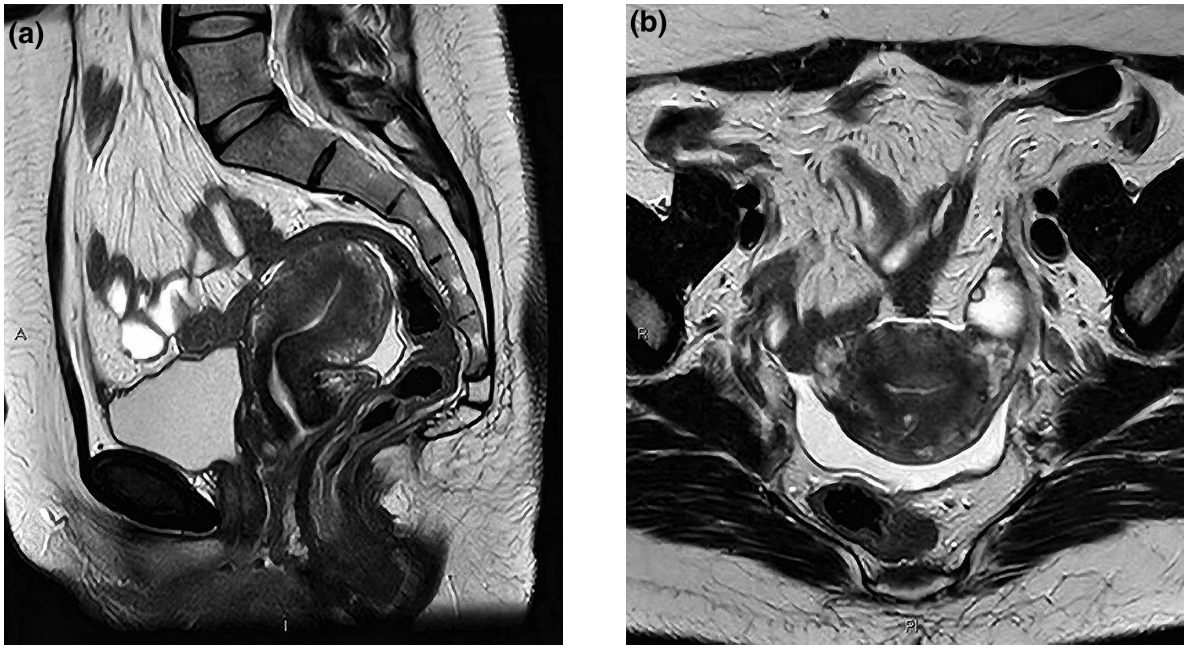


FIGURE 14.30 (a) MRI scan of the uterus with inhomogeneous myometrial signal intensity and thickened, fuzzy appearance of the JZ (12 mm) for non-secretory adenomyosis. (b) In T2-weighted axial scan, evidence of free fluid in the Douglas pouch.

than 5 mm (Figure 14.30) (74). The MRI images should always be evaluated by focusing on the menstrual phase of the woman. Physiological myometrium contraction could also be a source of misdiagnosis (74). T2-weighted MRI scans are guide images for diagnosing adenomyosis, because they focus and better analyze the uterine anatomy (Figure 14.31) (75). T1-weighted sequences help for diagnosis, since they are evidenced by high-signal intensity foci, representing intra-myometrial hemorrhage (Figure 14.32) (75). Gadolinium contrast enhancement could be useful in cases of diagnostic uncertainty regarding the nature of the nodules. A study classified lesions into four categories based on their location (74):

- *Internal adenomyosis*: The lesions are located in the JZ, but the rest of the normal muscular structures are intact outside.
- *External adenomyosis*: The lesion is in the outer side of myometrium, the normal muscular structures are located among the adenomyotic lesion, and the JZ is normal.
- *Intramural adenomyosis*: The lesion is shown within the myometrium, preserving the JZ and the serosa.
- *Whole wand adenomyosis*: The lesion invades the endometrium, myometrium, and serosa.

The main feature of internal adenomyosis on MRI scan is the thickening of the JZ. A joint layer thickness < 8 mm is considered normal. The finding of JZ thickening > 12 mm is one of the main MRI findings to establish the diagnosis of adenomyosis. Adenomyosis usually presents as a well-demarcated area, hypointense on T2-weighted sequences. In T2-weighted

FIGURE 14.31 T2-weighted sagittal scan, which highlights an enlarged uterus with wall asymmetry due to the prevalence of the posterior one (anterior wall 17 mm, posterior wall 33 mm) with uneven signal intensity due to diffuse adenomyosis with little glandular-cystic component.

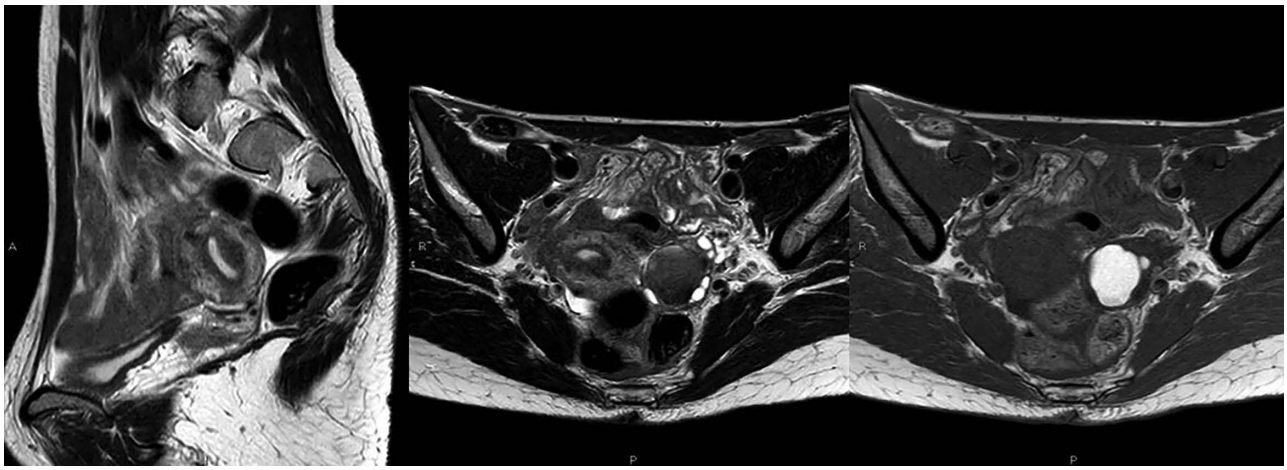


FIGURE 14.32 T2-weighted sagittal and coronal scans of the pelvis in a patient suffering from adenomyosis, which highlights an area of non-secreting adenomyosis in the right lateral fundic region with a diameter of 11 mm. The left ovary is enlarged, with an endometriotic cyst 35 mm in diameter, with hyperintense blood content, on T1-weighted axial sequences.

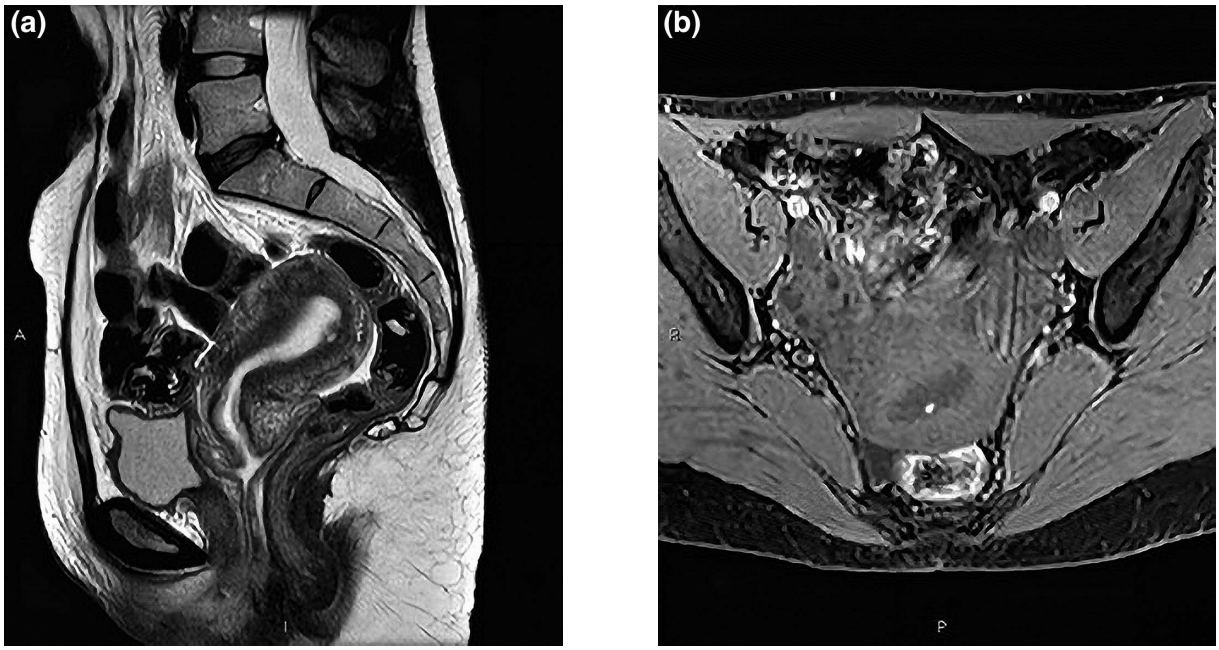


FIGURE 14.33 A T2-weighted MRI sagittal scan and a T1-weighted THRIVE (T_1 High-Resolution Isotropic Volume Examination) axial scan were performed. (a) Uterus with uneven myometrial signal intensity particularly at the level of the posterior wall where an area of submucous gland-cystic adenomyosis with a diameter of 13 mm is observed; (b) hyperintense bleeding spot in the T1-weighted THRIVE sequence.

sequences, even millimeter areas of signal hyperintensity can be demonstrated to refer to ectopic endometrium or to minute cysts; some of these sometimes show hemorrhagic-like signal, which appears as hyperintensity on fat-suppressed T1 sequences (Figure 14.33). The presence of submucosal microcysts is pathognomonic for adenomyosis, representing the main direct sign (73, 76).

Bazot et al. concluded that the finding of JZ thickness > 12 mm, a JZ thickness to myometrial thickness ratio > 40%, and the presence of an intra-myometrial high signal-intensity spot showed the highest power for predicting adenomyosis (76).

External adenomyosis arises in the outer myometrium or may invade from outside the uterus, disrupting the serosa but not affecting the JZ (Figure 14.34). Generally, it is associated with deep endometriosis, which probably represents the progenitor of this subtype of adenomyosis. The posterior myometrium is the most frequent location of externa adenomyosis, in line with the high frequency of posterior deep endometriosis (76).

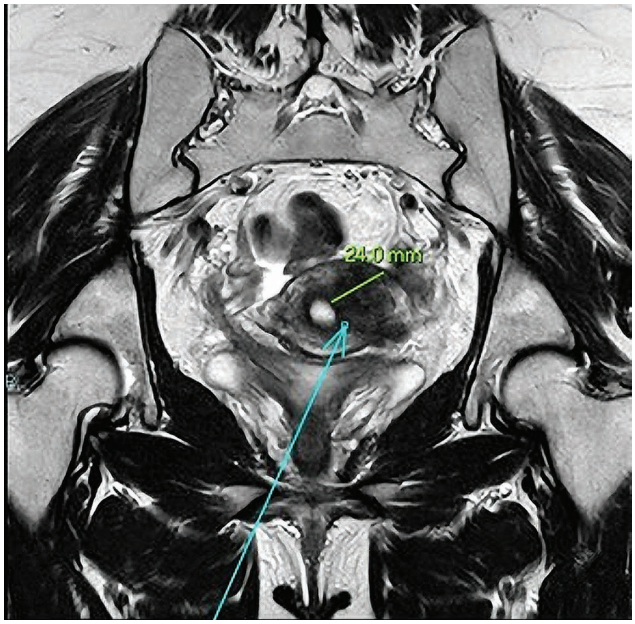


FIGURE 14.34 A T2-weighted MRI coronal scan showing a uterus with inhomogeneous myometrial signal intensity in the left lateral area, where there is an area of adenomyosis with a diameter of 24 mm with associated thickened and blurred appearance of the junctional line (and an adenomyosis plaque; blue arrow); note the thickening of the uterine serosa and the fibrotic adherent striae reaching the parietal pelvic peritoneum.

On MRI findings, external adenomyosis is diagnosed as an ill-defined subserosal posterior or anterior myometrial mass, giving a hypointense signal on T2-weighted MRI (Figure 14.35).

This bulky irregular thickening of the subserosal myometrium appears hypointense on T2-weighted sequences (77). In some cases, small internal cysts (2–9 mm in diameter), as hyperintense elements on T2 sequences, can be identified; if blood is present inside the cyst, it appears hyperintense on T1 with and without fat saturation, due to the presence of hemoglobin degradation products (Figure 14.36).

If this condition is not associated with internal adenomyosis, the junctional line is unaffected (76).

Nonetheless, literature shows different classification concerning the anatomic localization and the infiltration of endometriosis lesions. In 2020, Kobayashi et al. proposed their MRI classification of adenomyosis that brings all together the previously used classifications (72). This classification is mainly based on the correlation between MRI findings and other clinically relevant parameters.

The classification is based on five main categories:

1. The *affected area*, classified into internal myometrium (internal adenomyosis; the inner one-third of the uterine wall) and external myometrium (external adenomyosis)
2. The *pattern*, indicated as diffuse or focal adenomyosis
3. The *size*, further categorized into three volumes (< 1/3, < 2/3, or > 2/3 of the uterine wall)
4. The *location* (anterior, posterior, left-lateral, right-lateral, or fundal)
5. The *presence of concomitant pathologies* (none, peritoneal endometriosis, ovarian endometrioma, deep infiltrating endometriosis, uterine fibroids, or others)

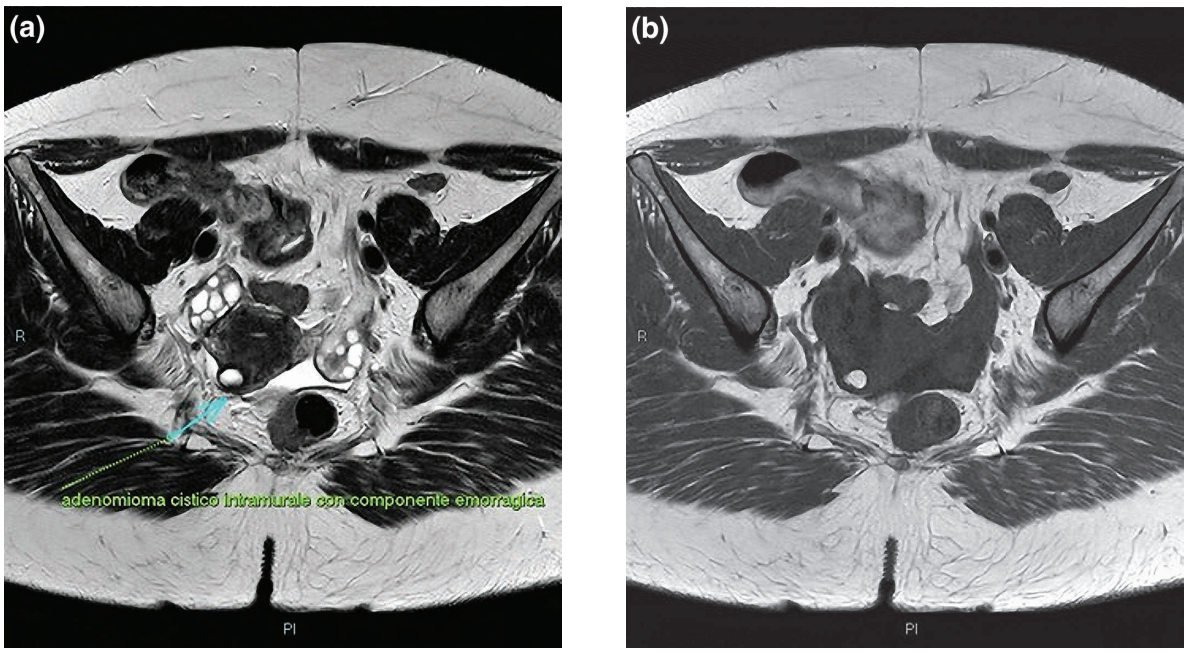


FIGURE 14.35 T1- and T2-weighted MRI scans of the pelvis with adenomyosis. Inhomogeneous myometrium with thickening and fuzzy appearance of the junctional line due to adenomyosis. (a) An intramural/subserous cystic adenoma of the right posterolateral wall, with an intranodular hemorrhagic component clearly appreciable in the T1-weighted sequence (blue arrow). (b) The adenomyoma rests on the mesorectal fascia, which appears thickened.

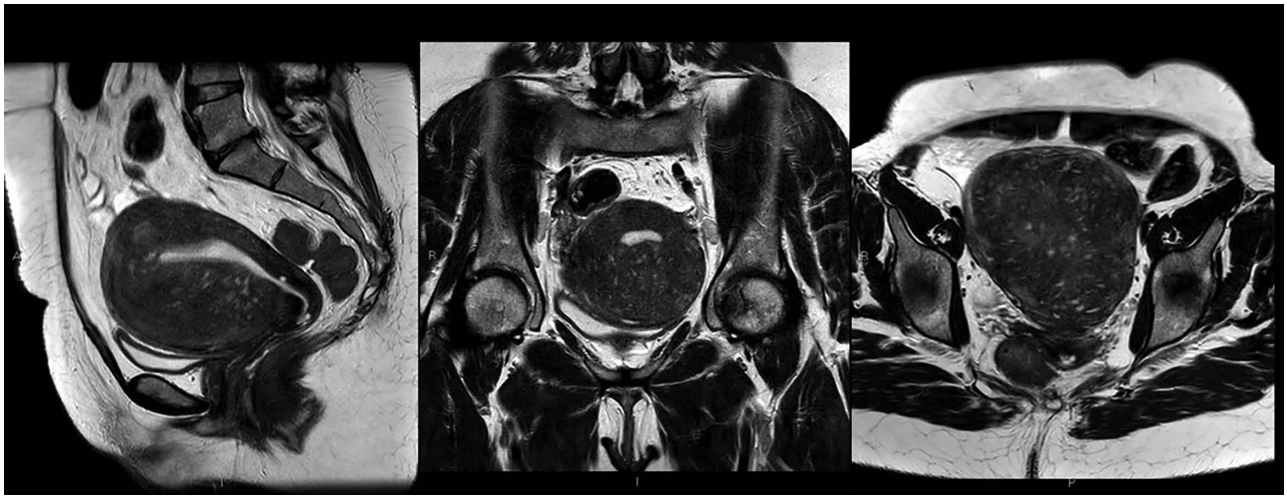


FIGURE 14.36 T2-weighted MRI sagittal, coronal, and axial scans of uterus with adenomyosis. Enlarged uterus with marked thickening of the anterior wall and disappearance of the myometrial–junctional border; presence of multiple myometrial cystic glandular ectasias, some blood-based as seen on the T1-weighted THRIVE sequence.

FIGURE 14.37 Sagittal scan of T2-weighted MRI of uterus with adenomyoma. Enlarged uterus, with fundus reaching to the umbilical region, characterized by diffuse fibrosis and adenomyosis, poor secretion, and voluminous adenomyoma.

The adenomyoma appears, on MRI imaging, as a heterogeneous lesion contained within the wall of the myometrium and which does not involve either the JZ or the uterine serosa.

On T2-weighted sequences, adenomyoma appears as an hypointense mass with well-defined margins showing small internal cystic components with high signal intensity or hemorrhagic cystic components greater than 5 mm, hyperintense on T1-weighted sequences (Figure 14.37).

The MRI provides an accurate assessment of their location (intramural, submucosal, or subserosal) and their number and allows the identification of other associated conditions such as internal adenomyosis and leiomyomas (76, 77).

FIGURE 14.38 Intraoperative finding of adenomyoma; it is possible to highlight the bluish cystic endometriotic nodules scattered in the context of the mass.

According to the Kobayashi classification, adenomyoma (Figure 14.38) represents a subgroup of focal adenomyosis, different from diffuse adenomyosis (Figure 14.39) (72, 74).

14.10 TUS vs MRI in Adenomyosis Diagnosis

Literature reports comparative studies comparing the two instrumental methods, TUS vs MRI, concerning sensibility and sensitivity. The TUS had a pooled sensitivity of 72% (95% CI: 65%–79%), specificity of 81% (95% CI: 77%–85%), positive likelihood ratio of 3.7 (95% CI: 2.1–6.4), and negative likelihood ratio of 0.3 (95% CI: 0.1–0.5). MRI showed a pooled sensitivity of 77% (95% CI: 67%–85%), specificity of 89% (95% CI: 84%–92%),

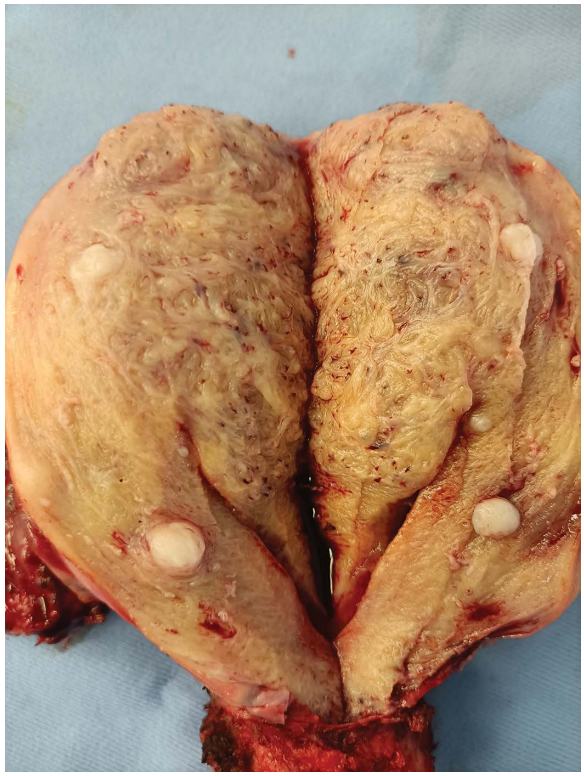


FIGURE 14.39 Intraoperative finding of uterus with diffuse adenomyosis.

FIGURE 14.40 Intraoperative section of a uterus with adenomyosis mixed with diffuse fibrosis; it highlights many hemorrhagic spots within the myometrium.

positive likelihood ratio of 6.5 (95% CI: 4.5–9.3), and negative likelihood ratio of 0.2 (95% CI: 0.1–0.4) (78). Leaving the numbers aside, it could deduct that a correct adenomyosis diagnosis should be reached easier by MRI (78). It is understandable that, because of its high cost and limited availability, MRI cannot be used as a screening method. The sequence should be that, in clinical suspicion of adenomyosis, the TUS is performed first, and then, if the results of the scans are still not clear, MRI should come to aid (Figure 14.40).

14.11 Conclusion

Adenomyosis is a much more frequent pathology that is complex to study and analyze accurately with dedicated diagnostic equipment. It is necessary to have skill and dedication, as well as extensive experience, in order to perform a precise diagnosis and preserve the womb, if the patient is in the reproductive period and would like to become, eventually, pregnant. The instrumental means currently available for precise diagnostics are currently available, but it is necessary to integrate them and use them in the best possible way, with dedicated software and with extensive knowledge of the literature. In this way it is possible to drastically reduce the diagnostic evaluation times and increase the accuracy.

14.12 Acknowledgments

We express sincere thanks to these two colleagues who contributed to the finalization of the chapter, with their anatomic-pathological support: Dr Enrico Prosperi, from Division of Pathology, Città di Castello Hospital, Italy, and Dr. Med. Christa Flechtenmacher, from General Pathology and Pathological Anatomy, University Hospital Heidelberg, Germany.

Key Points

- Adenomyosis is still a complex clinical condition to understand and treat, in women of fertility age, showing patients suffering for enlarged uterus, abnormal uterine bleeding (AUB), pelvic pain, dyspareunia, and infertility.
- The female genital system derives from Müllerian ducts originates from mesoderm, primordial germ cells, mesenchyme, and coelomic epithelium. Archimetra originates from Müllerian ducts and neometra from non-Müllerian ducts. Adenomyosis is a pathology of the archimetra.
- Adenomyosis pathophysiology is still unclear, but the two more accredited theories in the literature are endometrial invagination as a consequence of activation of the tissue injury and repair mechanism (TIAR) and stem cells metaplasia.
- The main symptom of adenomyosis is pelvic and abdominal pain, associated with dysmenorrhea and dyspareunia. Menorrhagia, infertility, and sterility are the second line of symptoms and are among the most represented, while 30% of the patients are completely asymptomatic.
- Transvaginal ultrasound can be considered the preferred diagnostic method for adenomyosis due to its feasibility, safety, availability, and lower cost compared with MRI. In the absence of ultrasound findings, MRI could be decisive for diagnosing adenomyosis.
- The location of the lesion could cause a mechanical hindrance for implantation. An adenomyoma could cause an obstruction of the tubal ostia, an obstacle for sperm migration, and an obstacle for the embryo migration into the uterine cavity.
- Concerning the ultrasonographic features of adenomyosis reported in the literature, it is important

to assess the globular uterine configuration, anterior–posterior myometrial asymmetry, heterogeneous myometrial echotexture ("venetian blind" appearance), poor definition of the JZ, and the presence of intramyometral cysts.

- Among the proposed MRI classifications, the one most used is based on the adenomyosis localization: *internal adenomyosis*: the lesions are located in the JZ, but the rest of the normal muscular structures are intact outside; *external adenomyosis*: the lesion is in the outer side of myometrium, the normal muscular structures are located among the adenomyotic lesion and the JZ, and the JZ is normal; *intramural adenomyosis*: the lesion is shown within the myometrium, preserving the JZ and the serosa; and *whole wand adenomyosis*: the lesion invades endometrium, myometrium, and serosa.
- Because of its higher costs and limited availability, MRI cannot be a routine screening method. The sequence should be, in clinical suspicion of adenomyosis, the transvaginal ultrasound exam and then, if the results are still not clear and further aid is needed, MRI evaluation.

References

1. Zhai J et al. Adenomyosis: mechanisms and pathogenesis. *Semin Reprod Med*. 2020;38(2–03):129–143.
2. Vercellini P et al. Adenomyosis: epidemiological factors. *Best Pract Res Clin Obstet Gynaecol*. 2006;20(4):465–477.
3. Upson K et al. Epidemiology of adenomyosis. *Semin Reprod Med*. 2020;38(2–3):89–107.
4. Vercellini P et al. Adenomyosis at hysterectomy: a study on frequency distribution and patient characteristics. *Hum Reprod*. 1995;10(5):1160–1162.
5. Kishi Y et al. Phenotypic characterization of adenomyosis occurring at the inner and outer myometrium. *PLoS One*. 2017;12(12):e0189522.
6. Maruyama S et al. Relationship between adenomyosis and endometriosis: different phenotypes of a single disease? *Eur J Obstet Gynecol Reprod Biol*. 2020;253:191–197.
7. Kurita T. Normal and abnormal epithelial differentiation in the female reproductive tract. *Differentiation*. 2011;82(3):117–126.
8. Moncada-Madrazo M et al. *Embryology, Uterus* [Internet]. StatPearls. Treasure Island, FL: StatPearls Publishing; 2022.
9. Guo S-W. The pathogenesis of adenomyosis vis-à-vis endometriosis. *J Clin Med*. 2020;9(2):485.
10. Tanos V et al. Junctional zone endometrium morphological characteristics and functionality: review of the literature. *Gynecol Obstet Invest*. 2020;85(2):107–117.
11. Levgur M et al. Adenomyosis: symptoms, histology, and pregnancy terminations. *Obstet Gynecol*. 2000;95(5):688–691.
12. Bazot M et al. Ultrasonography compared with magnetic resonance imaging for the diagnosis of adenomyosis: correlation with histopathology. *Hum Reprod*. 2001;16(11):2427–2433.
13. Bourdon M et al. Adenomyosis: an update regarding its diagnosis and clinical features. *J Gynecol Obstet Hum Reprod*. 2021;50(10):102228.
14. Vannuccini S et al. Recent advances in understanding and managing adenomyosis. *F1000Res*. 2019;8.
15. Van den Bosch T et al. Ultrasound diagnosis of endometriosis and adenomyosis: state of the art. *Best Pract Res Clin Obstet Gynaecol*. 2018;51:16–24.
16. Peric H et al. The symptomatology of adenomyosis. *Best Pract Res Clin Obstet Gynaecol*. 2006;20(4):547–555.
17. Kitawaki J. Adenomyosis: the pathophysiology of an oestrogen-dependent disease. *Best Practice Res Clin Obstet Gynaecol*. 2006;20(4):493–502.
18. Parazzini F et al. Risk factors for adenomyosis. *Hum Reprod*. 1997;12(6):1275–1279.
19. Riggs JC et al. Cesarean section as a risk factor for the development of adenomyosis uteri. *J Reprod Med*. 2014;59(1–2):20–24.
20. Harris WJ et al. Prior cesarean section. A risk factor for adenomyosis? *J Reprod Med*. 1985;30(3):173–175.
21. Templeman C et al. Adenomyosis and endometriosis in the California Teachers Study. *Fertil Steril*. 2008;90(2):415–424.
22. Jean-Baptiste H et al. Characteristics associated with postoperative diagnosis of adenomyosis or combined adenomyosis with fibroids. *Int J Gynaecol Obstet*. 2013;122(2):112–114.
23. Parazzini F et al. Determinants of adenomyosis in women who underwent hysterectomy for benign gynecological conditions: results from a prospective multicentric study in Italy. *Eur J Obstet Gynecol Reprod Biol*. 2009;143(2):103–106.
24. Taran FA et al. Understanding adenomyosis: a case control study. *Fertil Steril*. 2010;94(4):1223–1228.
25. García-Solares J et al. Pathogenesis of uterine adenomyosis: invagination or metaplasia? *Fertil Steril*. 2018;109(3):371–379.
26. Opara EI et al. The interpretation and clinical application of the word 'parity': a survey. *BJOG*. 2007;114(10):1295–1297.
27. Rižner TL. The important roles of steroid sulfatase and sulfotransferases in gynecological diseases. *Front Pharmacol*. 2016;7:30.
28. Kitawaki J et al. Progesterone induction of 17beta-hydroxysteroid dehydrogenase type 2 during the secretory phase occurs in the endometrium of estrogen-dependent benign diseases but not in normal endometrium. *J Clin Endocrinol Metab*. 2000;85(9):3292–3296.
29. Wang Y et al. Genetic variation in COX-2–1195 and the risk of endometriosis and adenomyosis. *Clin Exp Obstet Gynecol*. 2015;42(2):168–172.
30. Tong X et al. COMT 158G/A and CYP1B1 432C/G polymorphisms increase the risk of endometriosis and adenomyosis: a meta-analysis. *Eur J Obstet Gynecol Reprod Biol*. 2014;179:17–21.
31. Kitawaki J et al. Expression of aromatase cytochrome P450 protein and messenger ribonucleic acid in human endometriotic and adenomyotic tissues but not in normal endometrium. *Biol Reprod*. 1997;57(3):514–519.
32. Mehasseb MK et al. Estrogen and progesterone receptor isoform distribution through the menstrual cycle in uteri with and without adenomyosis. *Fertil Steril*. 2011;95(7):2228–2235, 35.e1.
33. Jichan N et al. Promoter hypermethylation of progesterone receptor isoform B (PR-B) in adenomyosis and its rectification by a histone deacetylase inhibitor and a demethylation agent. *Reprod Sci*. 2010;17(11):995–1005.
34. Ibrahim MG et al. Myofibroblasts are evidence of chronic tissue microtrauma at the endometrial-myometrial junctional zone in uteri with adenomyosis. *Reprod Sci*. 2017;24(10):1410–1418.
35. Leyendecker G et al. A new concept of endometriosis and adenomyosis: tissue injury and repair (TIAR). *Horm Mol Biol Clin Investig*. 2011;5(2):125–142.
36. Hoo PS et al. Rare case of leiomyoma and adenomyosis in Mayer-Rokitansky-Kuster-Hauser syndrome. *Case Rep Obstet Gynecol*. 2016;2016:3725043.
37. Morcel K et al. Mayer–Rokitansky–Küster–Hauser (MRKH) syndrome. *Orphanet J Rare Dis*. 2007;2:13.
38. Vannuccini S et al. Pathogenesis of adenomyosis: an update on molecular mechanisms. *Reprod Biomed Online*. 2017;35(5):592–601.
39. Gargett CE. Uterine stem cells: what is the evidence? *Hum Reprod Update*. 2007;13(1):87–101.
40. Ferenczy A. Pathophysiology of adenomyosis. *Hum Reprod Update*. 1998;4(4):312–322.
41. Ostrer H. Sexual differentiation. *Semin Reprod Med*. 2000;18(1):41–49.
42. Musina RA et al. Endometrial mesenchymal stem cells isolated from the menstrual blood. *Bull Exp Biol Med*. 2008;145(4):539–543.

43. Gargett CE et al. Adult stem cells in the endometrium. *Mol Hum Reprod*. 2010;16(11):818–834.
44. Chapron C et al. Relationship between the magnetic resonance imaging appearance of adenomyosis and endometriosis phenotypes. *Hum Reprod*. 2017;32(7):1393–1401.
45. Gordts S et al. Symptoms and classification of uterine adenomyosis, including the place of hysteroscopy in diagnosis. *Fertil Steril*. 2018;109(3):380–388.e1.
46. Leyendecker G et al. Adenomyosis and endometriosis. Re-visiting their association and further insights into the mechanisms of auto-traumatisation. An MRI study. *Arch Gynecol Obstet*. 2015;291(4):917–932.
47. Pinzauti S et al. Transvaginal sonographic features of diffuse adenomyosis in 18–30-year-old nulligravid women without endometriosis: association with symptoms. Ultrasound *Obstet Gynecol*. 2015;46(6):730–736.
48. Taran FA et al. Clinical characteristics indicating adenomyosis at the time of hysterectomy: a retrospective study in 291 patients. *Arch Gynecol Obstet*. 2012;285(6):1571–1576.
49. Kissler S et al. Duration of dysmenorrhoea and extent of adenomyosis visualised by magnetic resonance imaging. *Eur J Obstet Gynecol Reprod Biol*. 2008;137(2):204–209.
50. Gruber TM et al. Pathogenesis of endometriosis: the origin of pain and subfertility. *Cells*. 2021;10(6).
51. Quinn M. Uterine innervation in adenomyosis. *J Obstet Gynaecol*. 2007;27(3):287–291.
52. Zhang X et al. Innervation of endometrium and myometrium in women with painful adenomyosis and uterine fibroids. *Fertil Steril*. 2010;94(2):730–737.
53. Munro MG et al. The FIGO classification of causes of abnormal uterine bleeding in the reproductive years. *Fertil Steril*. 2011;95(7):2204–2208, 8.e1–8.e3.
54. Naftalin J et al. Is adenomyosis associated with menorrhagia? *Hum Reprod*. 2014;29(3):473–479.
55. McCausland AM. Hysteroscopic myometrial biopsy: its use in diagnosing adenomyosis and its clinical application. *Am J Obstet Gynecol*. 1992;166(6 Pt 1):1619–1626; discussion 26–28.
56. Soave I et al. Treatment options and reproductive outcome for adenomyosis-associated infertility. *Curr Med Res Opin*. 2018;34(5):839–849.
57. Farhi J et al. Effect of uterine leiomyomata on the results of in-vitro fertilization treatment. *Hum Reprod*. 1995;10(10):2576–2578.
58. Stovall DW et al. Uterine leiomyomas reduce the efficacy of assisted reproduction cycles: results of a matched follow-up study. *Hum Reprod*. 1998;13(1):192–197.
59. Kissler S et al. Uterotubal transport disorder in adenomyosis and endometriosis – a cause for infertility. *BJOG*. 2006;113(8):902–908.
60. Goldberger MA et al. Roentgen diagnosis of adenomyosis uteri. *Am J Obstet Gynecol*. 1949;57(3):563–568.
61. Cunningham RK et al. Adenomyosis: A sonographic diagnosis. *Radiographics*. 2018;38(5):1576–1589.
62. Bohlman ME et al. Sonographic findings in adenomyosis of the uterus. *AJR*. 1987;148(4):765–766.
63. Ascher SM et al. Adenomyosis: prospective comparison of MR imaging and transvaginal sonography. *Radiology*. 1994;190(3):803–806.
64. Reinhold C et al. Diffuse adenomyosis: comparison of endovaginal US and MR imaging with histopathologic correlation. *Radiology*. 1996;199(1):151–158.
65. Puente JM et al. Adenomyosis in infertile women: prevalence and the role of 3D ultrasound as a marker of severity of the disease. *Reprod Biol Endocrinol*. 2016;14:60.
66. Dueholm M. Transvaginal ultrasound for diagnosis of adenomyosis: a review. *Best Practice & Research Clinical Obstetrics & Gynaecology*. 2006;20(4):569–582.
67. Exacoustos C et al. Ultrasound imaging for ovarian and deep infiltrating endometriosis. *Semin Reprod Med*. 2017;35(1):5–24.
68. Di Donato N et al. Question mark form of uterus: a simple sonographic sign associated with the presence of adenomyosis. *Ultrasound Obstet Gynecol*. 2015;46(1):126–127.
69. Andres MP et al. Transvaginal ultrasound for the diagnosis of adenomyosis: systematic review and meta-analysis. *J Minim Invasive Gynecol*. 2018;25(2):257–264.
70. Chiang CH et al. Tumor vascular pattern and blood flow impedance in the differential diagnosis of leiomyoma and adenomyosis by color Doppler sonography. *J Assist Reprod Genet*. 1999; 16(5):268–275.
71. Tamai K et al. Spectrum of MR features in adenomyosis. *Best Pract Res Clin Obstet Gynaecol*. 2006;20(4):583–602.
72. Kobayashi H et al. A classification proposal for adenomyosis based on magnetic resonance imaging. *Gynecol Obstet Invest*. 2020;85(2):118–126.
73. Novellas S et al. MRI characteristics of the uterine junctional zone: from normal to the diagnosis of adenomyosis. *AJR*. 2011;196(5):1206–1213.
74. Kobayashi H et al. Relationship between magnetic resonance imaging-based classification of adenomyosis and disease severity. *J Obstet Gynaecol Res*. 2021;47(7):2251–2260.
75. Agostinho L et al. MRI for adenomyosis: a pictorial review. *Insights Imaging*. 2017;8(6):549–556.
76. Bazot M et al. Role of transvaginal sonography and magnetic resonance imaging in the diagnosis of uterine adenomyosis. *Fertil Steril*. 2018;109(3):389–397.
77. Celli V et al. MRI and adenomyosis: what can radiologists evaluate? *Int J Environ Res Public Health*. 2022;19(10):5840.
78. Gong C et al. Evaluation of high intensity focused ultrasound treatment for different types of adenomyosis based on magnetic resonance imaging classification. *Int J Hypertherm*. 2022;39(1):530–538.
79. Champaneria R, Abedin P, Daniels J, Balogun M, Khan KS. Ultrasound scan and magnetic resonance imaging for the diagnosis of adenomyosis: systematic review comparing test accuracy. *Acta Obstet Gynecol Scand*. 2010;89(11):1374–1384.

15 LAPAROSCOPIC AND ROBOTIC MYOMECTOMY

Shan Biscette and Nita Desai*

15.1 Introduction

Uterine leiomyomas are benign fibromuscular tumors of the myometrium, known by several names, including "leiomyoma," "myoma," or more commonly "fibroid," affecting women of reproductive age, occurring in 70%–80% of women by menopause (1, 2). The prevalence is likely underestimated due to the asymptomatic and insidious nature of this neoplasm. Symptoms can be divided into three predominant categories: reproductive dysfunction, menstrual abnormalities, and mass effects (3). Prevalence varies across racial groups and is highest among African Americans (1). Studies indicate several risk factors for leiomyoma development, including demographic characteristics, reproductive and disease status, and environmental and dietary conditions. Leiomyomata have an extensive impact on healthcare costs worldwide, with annual direct and indirect costs estimated as high as $34.4 billion in the United States (4–6).

15.2 Patient Presentation

Clinical manifestations vary and depend on the location, size, and number of leiomyomas within the uterine body. Although most women with leiomyomas are asymptomatic, approximately 30% will present with abnormal uterine bleeding (AUB), anemia, pelvic pain and heaviness, bowel and/or urinary dysfunction, subfertility, and pregnancy-related complications (4).

15.3 FIGO Classification

Anatomic location of uterine leiomyomas can play a major role in symptomatology. The International Federation of Gynecology and Obstetrics (FIGO) classification system, established in 2011, outlined a system to describe uterine leiomyoma location in relation to the endometrial and serosal surfaces (7). Large leiomyomas may compress surrounding structures, leading to urinary, bowel and/or vascular sequelae of impaired renal function, constipation and tenesmus, and venous thromboembolism, respectively (8, 9). Leiomyomas are typically characterized as submucosal, intramural, subserosal, and pedunculated lesions as depicted in Figure 13.4.

15.4 Fertility

Fibroids may be the sole cause of infertility in 2%–3% of women and have been implicated in recurrent pregnancy loss (4, 10). Several studies indicate that compared to women without leiomyomas, those with leiomyomas are more likely to be infertile (11–13). Many studies evaluating the impact of leiomyomas on fertility are limited by their observational nature, heterogeneity, and small sample sizes. More research is needed to better understand how the different characteristics of leiomyomas negatively impact infertility in patients undergoing artificial reproductive techniques (ART) or natural conception.

15.5 Diagnosis/Imaging

Initial evaluation begins with a thorough history and physical exam, with consideration of additional laboratory evaluation, based on individual patient circumstances. Pelvic exam accuracy is often limited by body habitus or intolerance of pelvic exams. Imaging, therefore, is paramount in precisely assessing and diagnosing uterine leiomyomas, including size, number, and location of leiomyomas, in order to provide an individualized plan of care.

Pelvic ultrasound is the most commonly utilized imaging modality due to ease of access and use, and lack of ionizing radiation (11). It is both less invasive and less costly compared to other imaging modalities and is recommended as a first-line method of imaging in AUB, and by extension leiomyomas (11, 14).

Computerized tomography (CT) is less useful for the diagnosis of leiomyomas (3). In cases where ultrasound findings are ambiguous, magnetic resonance imaging (MRI) may be implemented to provide additional information, with a specificity of 100%, accuracy of 97%, and sensitivity of 86%–92% (10). MRI is also beneficial in differentiating between uterine leiomyomas and other uterine pathology, such as adenomyosis/adenomyomas, which may be difficult to distinguish by pelvic ultrasound. MRI helps to evaluate the type, number, size, and location of leiomyomas, which is essential in counseling regarding treatment options, as well as the appropriate approach to myomectomy. In our practice, we order MRI for all patients desiring myomectomy to thoroughly evaluate the relationship between the leiomyomata, the serosa, and the endometrium. MRI may also be helpful in assessing the volume of normal myometrium, which, in cases of high leiomyoma burden, may help determine if myomectomy is a feasible treatment plan.

15.6 Management

Management of uterine leiomyomas is driven by symptoms as well as a patient's desire to preserve fertility, with numerous medical, procedural, and surgical options. This chapter will focus on leiomyoma removal via myomectomy.

15.7 Surgical Approaches to Myomectomy

15.7.1 Approach

The optimal surgical approach to myomectomy is subject to several variable factors, including but not limited to surgeon experience/preference, uterine size and mobility, myoma number and location, OR time and/or access, and available surgical assistants, among others. Specifically, robotic access may be limited at certain institutions. This chapter will discuss the similarities and differences between laparoscopic (LSC) and robotic-assisted laparoscopic (RAL) techniques. Although the number of myomas removed can affect perioperative and postoperative outcomes, the surgical approach does not (15). There are no significant differences in rate of blood transfusion, conversion to laparotomy, wound infection, VTE, ileus,

* Both authors contributed equally to this chapter.

DOI: 10.1201/9781003312109-15

or readmission between laparoscopic and robotic approaches. Additionally, length of stay and number of myomas removed are also similar across both approaches (16). While there may always be certain indications for laparotomic approach, we always promote a minimally invasive (MIS) option, when applicable and safely executable.

An MIS myomectomy can be viewed in three parts: enucleation of leiomyoma(s), uterine repair/reconstruction, and finally, extraction of leiomyoma(s) from the abdomen.

15.7.2 Uterine Manipulator

A uterine manipulator should be considered for two primary reasons. The manipulator will allow for steady maneuvering during both leiomyoma removal and reconstruction particularly with posterior myoma(s). Furthermore, with a uterine manipulator in place, chromopertubation can easily be performed to identify the borders of the endometrial cavity, prior to complete myoma enucleation, to prevent inadvertent perforation into the endometrial cavity. Subsequently, chromopertubation can also help direct repair, should a perforation be diagnosed.

15.7.3 Trocar Placement

Trocar placement should be individualized to optimize both myoma enucleation and hysterotomy closure. Surgeon flexibility in placement is necessary, particularly with larger and/or irregularly shaped leiomyomata.

15.7.4 Laparoscopic Port Placement

An LSC approach to myomectomy typically employs four ports: a camera port, two additional working ports, and a port for the assistant. Depending on the patient's surgical history and surgeon's practice, a Palmer's point entry will allow for a panoramic assessment of the pelvis to allow for additional port placement. Accessory trocars can then be placed at the umbilicus and at the right and left lateral quadrants, typically at the level of and parallel to the umbilicus. In a patient with no prior pelvic surgery and low to normal BMI, the umbilicus is often the initial entry point for many surgeons. The laparoscopic approach allows for use of smaller 5 mm accessory ports; however, there can be a need for larger 10–12 mm ports to allow for use of larger grasping instruments, such as a 10 mm tenaculum, as well as for suturing. Ultimately, this approach allows for significant flexibility in port size depending on the surgeon's preference and planned extraction technique (Figure 15.1).

15.7.5 Robotic Trocar Placement

After entering the abdomen, based on anatomy, an "M" configuration can be used for trocar placement. This "M" configuration uses five ports (camera plus four arms; Figure 15.2), optimizing spacing between the two lateral ports, thereby decreasing arm collision and enhancing triangulation. We recommend using all robotic trocars to maximize port-hopping capabilities. When not in use with a robotic arm, either the right or left upper quadrant ports can function as the accessory port site for the bedside assistant. While the camera and arms may port-hop during the myoma enucleation, we recommend the umbilicus serve as the ultimate landing point for the camera during myometrial repair. In doing so, the traditional configuration of a central camera with lateral arms for suturing is achieved. Often, with large uteri/myoma, it is tempting to consider a supraumbilical camera port placement. However, while helpful at the start of the case, it can prove difficult to visualize and work in the pelvis, as the case progresses. Using four robotic arms plus the camera, combined with port-hopping, allows for adequate uterine/myoma mobilization, and ultimately the umbilicus can be used for myoma extraction at the end of the procedure.

Similar to LSC, the two lateral ports are typically placed at the level of, and parallel to, the umbilicus, along the anterior axillary line. Specific to RAL, further lateral placement, beyond the anterior axillary line, is not beneficial, as it can lead to collision of these arms with the anterior superior iliac spine. Typically these ports do not need to be placed superior to the

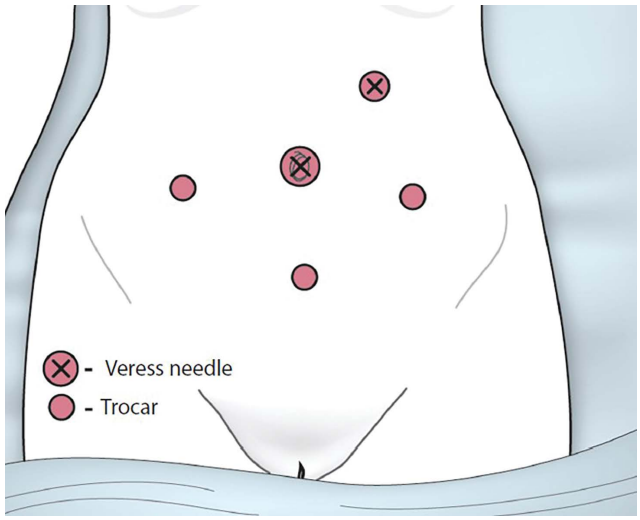


FIGURE 15.1 Laparoscopic port placement. (From Lang TG et al. Creation of Pneumoperitoneum and Trocar Insertion Techniques In: Pasic RP et al. *Practical Manual of Minimally Invasive Gynecologic and Robotic Surgery: A Clinical Cook Book*, 3rd edn. Boca Raton, FL: CRC Press; 2018:43–54, with permission.)

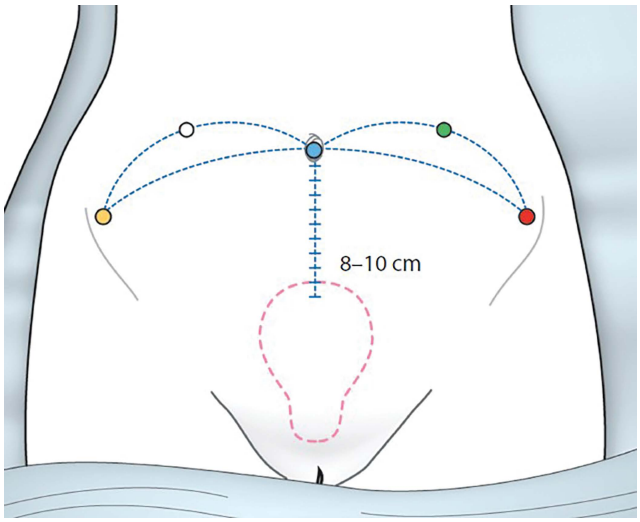


FIGURE 15.2 The "M" configuration for trocar placement (From Sasaki Ket al. Robotics. In: Pasic RP et al. *Practical Manual of Minimally Invasive Gynecologic and Robotic Surgery: A Clinical Cook Book*, 3rd edn. Boca Raton, FL: CRC Press; 2018: 303–310, with permission).

level of the umbilicus, as their lateral placement allows for significant control and mobilization of the uterus/myoma. The two upper quadrant ports are subject to more flexibility with placement, either more superior or inferior, depending on the patient's habitus and uterine/myoma dimensions. Additional ports should be utilized as needed, regardless of approach. In RAL, for multiport systems, port size can range from 8 to 12 mm. We recommend using all 8 mm trocars, as an 8 mm trocar can easily accommodate larger needle sizes for suturing. However, in LSC, the range of port size varies from 5 to 15 mm, and the surgeon will need to decide if upsizing is required to accommodate suture passage.

15.7.6 Instrumentation

Instrument choice is similar across both approaches. Typically, the surgeon will require three primary instruments, not including the camera; an instrument with cutting/electrosurgical capabilities, as well as one to two graspers. A scissor, with monopolar energy, is a common choice for opening the serosa. However, the second and third instrument choices are variable among surgeons. LSC myomectomy allows for use of any electrosurgical, ultrasonic, and/or plasmacautery instrumentation, whereas the RAL approach is limited by the instruments and energy available to that particular system. Regardless of instrument choice or surgical approach, an ideal configuration allows the surgeon to use two energy sources simultaneously, one in each hand, to actively manage any blood loss, while still maintaining a working grasper. We strongly advocate for a third – and perhaps most important – instrument in both approaches, the tenaculum. The tenaculum allows the surgeon to apply traction on the myoma, allowing for increased mobility and subsequent visualization. In cases of posterior myoma, where rolling the entire uterus towards the bladder is necessary, the tenaculum can provide excellent support during myoma removal, as well as uterine stabilization during repair. From either an LSC or RAL standpoint, the surgeon is still free to use their scissors and grasper, while the tenaculum, which is placed in one of the lateral ports, can provide continuous support and traction.

A 30-degree camera is similarly advantageous across both approaches, especially in cases of multiple and large leiomyomas, as this can assist with visualization around these often distorted uteri. There are no large head-to-head studies comparing these different modalities, and ultimately instrument choice is often based on surgeon preference, cost to the institution, and access.

15.8 Reducing Blood Loss

15.8.1 Preoperative Management

Prevention of intraoperative blood loss, a primary sequela of myomectomy, begins prior to myoma enucleation. There are multiple studies which support the administration of rectal misoprostol, for uterotonic benefits. Misoprostol, a prostaglandin E1 analogue, binds uterine smooth muscle cells and induces myometrial contractions, thereby reducing the amount of bleeding by restricting vascular support and blood flow to leiomyomas (17). It was reported that intraoperative blood loss was lower and postoperative hemoglobin higher in recipients of preoperative (800 μg rectal) misoprostol (18). Also, preoperative use of misoprostol was associated with less blood loss, less decrease in hemoglobin, and fewer cases needing blood transfusion (18). Vaginal misoprostol recipients were reported to experience lower levels of blood loss and hemoglobin decrease (17).

Preoperative tranexamic acid (TXA) has also been used to prevent intraoperative blood loss. TXA is a synthetic derivative of lysine that exerts anti-fibrinolytic effects by inhibiting the interaction of plasminogen with formed plasmin and fibrin (19). In recent years, TXA has gained widespread use in a multitude of surgical specialties including orthopedic, cardiothoracic, general, gynecologic, and obstetric procedures (20). Routine preoperative use in myomectomy is questionable as multiple studies have reported inconsistent outcomes (20–22). Given these contradictory findings, routine preoperative use of TXA remains controversial as multiple trials have failed to routinely demonstrate reliable reduction of blood loss. As such, use of this medication is dependent on surgeon experience and preference.

15.8.2 Intraoperative Management

The most widely used medication for intraoperative blood loss prevention is vasopressin. Vasopressin is a synthetic antidiuretic hormone analog that causes increased uterine smooth muscle contraction through mobilization of intracellular calcium, essentially acting as a hormonal tourniquet to reduce blood loss in surgery (23, 24). Dilutions of vasopressin can vary, ranging from 20 units/30 mL normal saline (NS) to 20 units/400 mL NS. These concentration variations revealed no differences in blood loss for MIS myomectomy (25). As such, no standard dosing exists. We recommend using a dilute solution of 20 units/100 mL, up to 100 cc, to optimize vasoconstrictive benefits, while mitigating systemic complications associated with myometrial vasopressin use. These complications are rare, but can include hypotension and vasoconstriction as well as severe complications, such as sudden cardiac arrest with bradycardia, pulmonary edema, and myocardial infarction (25).

It is important to note the vasoconstrictive effect of vasopressin lasts for approximately 10–35 minutes (26). This relatively short half-life must be taken into account when strategizing myoma removal, especially in cases of high myoma burden. For myomectomy requiring multiple incisions, we recommend injecting the vasopressin solution under the serosa of the initial site of myoma removal. Depending on the size of the myoma, 5–20 mL may be used. Additional solution may be injected as needed, particularly when moving to a different site.

The concomitant use of pre-incision misoprostol, combined with intraoperative vasopressin, has been proven to be effective in reducing intraoperative blood loss for both abdominal and MIS myomectomy, alike. Vasopressin plus misoprostol ranked first in reducing blood loss during open myomectomy (27). The additive effect of misoprostol to vasopressin has been shown to significantly reduce intraoperative blood loss and the postoperative drop in hemoglobin in women undergoing laparoscopic myomectomy (28). However, no standard dosing exists.

Uterine artery ligation, both temporary and permanent, has been shown to decrease blood loss in myomectomy; although permanent occlusion with respect to long-term data concerning fertility and perinatal outcomes is needed. Temporary uterine artery ligation remains a fair option to mitigate blood loss, with data showing a decrease by half in intraoperative blood loss, as compared to cases performed without this intervention (29). This specific intervention requires the surgeon to have both comfort and efficiency with retroperitoneal dissection and identification of the bilateral uterine arteries and

application of suture, clips, or clamps, to the uterine artery, which would then be released at the end of the procedure. This anatomic knowledge and experience are the rate limiting factors in commonplace implementation of this technique.

15.8.3 Myoma Enucleation

High myoma burden can limit both visibility and mobility, so regardless of LSC or RAL approach, we recommend strategizing myoma removal. This outcome is achieved by determining which myomas allow for optimal progression of surgery.

For example, while anterior and fundal myomas are typically easy to visualize, posterior myomas are not. Posterior myoma(s) require rolling of the uterus towards the bladder and/or laterally for adequate visualization. If myomas present both anteriorly and posteriorly, then removal of the anterior myoma(s) first will naturally allow for better visualization of posterior myoma(s) by increasing the mobility of the uterus in the direction of the bladder. In another example, should a large fundal myoma obscure visualization of the remainder of the uterus, this should be removed first. The use of a 30-degree camera and tenaculum are paramount in optimizing visualization. With high myoma burden, reassessment after removal may point to changes in instrument placement to optimize completion of the procedure.

Similar for both approaches, fewer myometrial incisions are always recommended to decrease the risk of future dehiscence. The prevalence of uterine rupture after myomectomy, regardless of approach, is less than 1%, and there is also no significant difference between MIS and laparotomic approaches (30). The overall rate of uterine rupture after myomectomy is low and further studies are needed to make more distinct recommendations. That said, the gestalt of using fewer incisions, while prioritizing the extraction of the highest number of myomas and minimizing injury to myometrium and fallopian tubes, remains at the forefront of myomectomy. Additionally, unless there is significant bleeding, we recommend holding closure of incisions until all myoma(s) are removed. This allows for endometrial cavity assessment at a singular time and minimizes the number of instrument changes.

15.8.4 Suture

Presently, there is a plethora of data showing barbed suture has comparable outcomes to non-barbed suture as it pertains to integrity of closure and reproductive outcomes (31–33). Given this overwhelming data, these authors recommended using barbed suture due to ease of use and notably faster closure times, as compared to non-barbed suture (32). Other sutures, including polyglactin (Vicryl) may be used. There are no studies available comparing the use of different sutures with regard to strength of the uterine wound.

The following are tactics for efficiency:

- Pass multiple sutures one a single pass.
- Park these sutures in a visible but nonobstructive site, such as the obliterated umbilical artery.
- Remove needles in succession, as each suture is used.
- Use the longest suture you can manage to minimize the number of sutures used and time to wait for new suture.

The number of layers required for adequate closure of the myometrium and serosa is still highly debated. If the size of the needle can reapproximate the depth of the myometrium in a single layer, then a single-layer closure may be employed. If the depth of the myometrial defect is significant, or if the endometrial cavity is entered, then multiple layers are required for adequate tissue approximation (34). This difference in layers of suture closure is dependent on the depth of the defect and will vary for each individual. Given this difference, there is paucity in data directly comparing single versus multilayer closure. Some studies evaluating pregnancy outcomes with single-layer closure reveal a low risk of uterine rupture (35), whereas others show a higher risk of rupture with single-layer closure (30). Given these discrepancies, surgeon experience weighs heavily onto this decision. We recommend placing as many layers as necessary to achieve myometrial approximation without leaving any defects and avoiding tissue strangulation. The serosa is ideally approximated using either barbed or monofilament suture, in an inverted manner, commonly known as a "baseball stitch." This technique inverts the serosal edges in an attempt to decrease adhesion formation, however there is no evidence to indicate that this is standard of care (36). The method of serosal closure is therefore a surgeon's preference.

15.8.5 Adhesion Prevention

Most patients undergoing myomectomy hope to achieve future fertility, and they will likely undergo cesarean section for delivery. Given the high likelihood of repeat surgery after myomectomy, adhesive barriers should be considered. Use of cellulose absorbable barriers, whether oxidized regenerated cellulose or carboxymethylcellulose powder adhesion barrier, have been shown to significantly lower the incidence of adhesions at second-look laparoscopy, without adding significant time to the length of the procedure (37). Anecdotally, we recommend using oxidized regenerated cellulose. This material, which is fabric-like in texture, is easily delivered through laparoscopic trocars, as compared to carboxymethylcellulose powder adhesion barrier, which can crack and break when delivered through laparoscopic trocars.

In recent years, hemostatic sealants, such as fibrin sealants and resorbable hydrogel, have been used for adhesion prevention in myomectomy. Initial studies are promising, as both fibrin sealants and resorbable hydrogel reportedly reduce adhesions at second-look surgery, as compared to the control groups (38, 39). These results were not statistically significant, and these promising results have not been reproduced in recent years. Additional studies are needed before routine use of these products is recommended.

15.8.6 Tissue Extraction

The use of any MIS approach for performing a myomectomy implies the need for tissue extraction. Prior to the US Food and Drug Association (FDA) recommendation against the use of power morcellation in 2014, most surgeons utilized various available devices to complete tissue extraction via power morcellation through an expanded laparoscopic or robotic port (40). The use of power morcellation has been attributed to dissemination of malignant and premalignant conditions, as well as parasitic myoma and disseminated peritoneal leiomyomatosis (41). Given these concerns, it has been restricted from use in the US market since 2014 (40).

In the years following the restriction on power morcellation, various techniques have been developed or rediscovered for tissue extraction after an MIS approach to myomectomy. In contrast to hysterectomy, LSC or RAL treatment for myomas rarely uses a vaginal approach for tissue extraction. The surgeon therefore has been tasked with consideration of

innovative approaches to tissue extraction to be able to offer a patient an MIS approach to myomectomy.

Techniques for tissue extraction after myomectomy vary based on the skill of the surgeon, patient body habitus, size of tissue specimen, and available equipment. In some institutions, surgeons still have access to the power morcellator but are restricted to use with a contained morcellation bag. In those instances the bag and morcellator can be placed via a 12–20 mm port to achieve the extraction.

Tissue extraction is commonly performed via an abdominal approach, i.e., manual morcellation via minilaparotomy. Manual morcellation can be performed by a contained system (in bag) or uncontained. The risk of uncontained morcellation includes spread of an undiagnosed malignancy with decreased survival, especially with leiomyosarcoma (40). These risks have been reported with morcellation of all types, including vaginal and minilaparotomy techniques (40). As such, contained manual morcellation is the primary practice. A study surveying methods of tissue extraction in MIS surgical treatment of uterine fibroids indicated that when minilaparotomy was performed, the median incision length was 3 cm. The most common location of tissue extraction is the umbilicus (68.8%), followed by suprapubic incisions (39.9%), extension of a lateral port site (9.8%), and supraumbilical incisions (2.2%) (42). Techniques involving minilaparotomy are significantly more cumbersome in patients with increased abdominal adiposity and may also involve more postoperative pain and morbidity. A larger suprapubic incision, regardless of BMI, may not result in the same desirable cosmesis as standard MIS incisions. Contained transvaginal extraction of fibroid specimens can also be performed safely and efficiently in most women undergoing MIS myomectomy. This technique represents a valuable MIS alternative to intracorporeal morcellation. The limitations of morcellation apply to both vaginal and minilaparotomy techniques and are specific to MIS approaches.

15.9 Conclusion

In conclusion, there are many methods in which gynecologists can provide MIS options to patients, while avoiding the morbidity of open surgery. Ultimately, the choice of surgical approach is a joint decision between the patient and surgeon. As there are more similarities than differences between the two techniques, with similar outcomes, either MIS approach can deliver the desired outcome.

References

1. Stewart EA et al. Epidemiology of uterine fibroids: a systematic review. *BJOG*. 2017;124(10):1501–1512.
2. Donnez J et al. Uterine fibroid management: from the present to the future. *Hum Reprod Update*. 2016;22(6):665–686.
3. Awiwi MO et al. Review of uterine fibroids: imaging of typical and atypical features, variants, and mimics with emphasis on workup and FIGO classification. *Abdom Radiol*. 2022;47(7):2468–2485.
4. Giuliani E et al. Epidemiology and management of uterine fibroids. *Int J Gynaecol Obstet*. 2020;149(1):3–9.
5. Cardozo ER et al. The estimated annual cost of uterine leiomyomata in the United States. *Am J Obstet Gynecol*. 2012;206(3):211 e1–211.e9.
6. Lou Z et al. Global, regional, and national time trends in incidence, prevalence, years lived with disability for uterine fibroids, 1990–2019: an age- period-cohort analysis for the global burden of disease 2019 study. *BMC Publ Health*. 2023;23:916.
7. Munro MG et al. FIGO classification system (PALM-COEIN) for causes of abnormal uterine bleeding in nongravid women of reproductive age. *Int J Gynaecol Obstet*. 2011;113(1):3–13.
8. Whitaker L et al. Abnormal uterine bleeding. *Best Pract Res Clin Obstet Gynaecol*. 2016;34:54–65.
9. Flyckt R et al. Minimally invasive myomectomy. *Clin Obstet Gynecol*. 2017;60(2):252–272.
10. Freytag D et al. Uterine fibroids and infertility. *Diagnostics*. 2021;11(8):1455.
11. Alkhrait S et al. Fibroids and fertility. *Obstet Gynecol Clin North Am*. 2023;50(4):663–675.
12. Somigliana E et al. Fibroids and natural fertility: a systematic review and meta-analysis. *Reprod Biomed Online*. 2021;43:100–110.
13. Rikhraj K et al. The impact of noncavity-distorting intramural fibroids on live birth rate in in vitro fertilization cycles: a systematic review and meta-analysis. *J Wom Health*. 2002;29(2):210–219.
14. Maheux-Lacroix S et al. Imaging for polyps and leiomyomas in women with abnormal uterine bleeding: a systematic review. *Obstet Gynecol*. 2016;128(6):1425–1436.
15. Shue S et al. Comparison of long term fertility outcomes after myomectomy: relationship with number of myomas removed. *J Minim Invasive Gynecol Surg*. 2018;25(6):1002–1008.
16. Leaf MC et al. Feasibility and perioperative outcomes of minimally invasive higher order myomectomy. *J Minim Invasive Gynecol*. 2024;31(10):870–874.
17. Güven CM et al. Evaluation of the effect of preoperative rectal misoprostol use on the postoperative outcomes of hysteroscopic myomectomy. *J Obstet Gynaecol Res*. 2023;49(8):2086–2092.
18. Khan QQ et al. Efficacy of preoperative misoprostol in reducing hemorrhage during abdominal myomectomy. *J Ayub Med Coll Abbottabad*. 2020;32(2):198–203.
19. Cai J et al. The many roles of tranexamic acid: an overview of the clinical indications for TXA in medical and surgical patients. *Eur J Haematol*. 2020;104:79–87.
20. Olaleye AA et al. Efficacy of tranexamic acid in reducing myomectomy-associated blood loss among patients with uterine myomas at federal teaching hospital Abakaliki: a randomized control trial. *Int J Reprod Med*. 2024(1):2794052.
21. Baradwan S et al. Prophylactic tranexamic acid during myomectomy: a systematic review and meta-analysis of randomized controlled trials. *Eur J Obstet Gynecol Reprod Biol*. 2022;276:82–91.
22. Opoku-Anane J et al. Intraoperative tranexamic acid to decrease blood loss during myomectomy: a randomized, double-blind, placebo-controlled trial. *Am J Obstet Gynecol*. 2020;223(3):413–e1.
23. Barbosa PA et al. How to minimize bleeding in laparoscopic myomectomy. *Curr Opin Obstet Gynecol*. 2021;33:255–261.
24. Lee EJ et al. Effect and safety of diluted vasopressin injection on bleeding during robot-assisted laparoscopic myomectomy: a protocol for a randomised controlled pilot trial. *BMJ Open*. 2022;12:e056145.
25. Cohen SL et al. Dilute versus concentrated vasopressin administration during laparoscopic myomectomy: a randomised controlled trial. *BJOG*. 2017;124(2):262–268.
26. Mitra JK et al. Vasopressin: its current role in anesthetic practice. *Indian J Crit Care Med*. 2011;15(2):71–77.
27. Samy A et al. Perioperative nonhormonal pharmacological interventions for bleeding reduction during open and minimally invasive myomectomy: a systematic review and network meta-analysis. *Fertil Steril*. 2020;113(1):224–233.
28. Srivastava S et al. Comparison of intramyometrial vasopressin plus rectal misoprostol with intramyometrial vasopressin alone to decrease blood loss during laparoscopic myomectomy: randomized clinical trial. *Eur J Obstet Gynecol*. 2018;228:279–283.
29. Hiratsuka D et al. The effect of temporary uterine artery ligation on laparoscopic myomectomy to reduce intraoperative blood loss: a retrospective case – control study. *Eur J Obstet Gynecol Reprod Biol: X*. 2022;15:100162.

30. Claeys J et al. The risk of uterine rupture after myomectomy: a systematic review of the literature and meta-analysis. *Gynecol Surg*. 2014;11:197–206.
31. Arena A et al. Comparison of fertility outcomes after laparoscopic myomectomy for barbed versus nonbarbed sutures. *Fertil Steril*. 2021;115(1):248–255.
32. Paul PG et al. Reproductive outcomes after laparoscopic myomectomy: conventional versus barbed suture. *J Minim Invasive Gynecol*. 2022;29(1):77–84.
33. Pepin K et al. Reproductive outcomes following use of barbed suture during laparoscopic myomectomy. *J Minim Invasive Gynecol*. 2020;27(7):1566–1572.
34. Dumitrașcu MC et al. Laparoscopic myomectomy – the importance of surgical techniques. *Frontiers Med*. 2023; 10:1158264.
35. Aksin S et al. Pregnancy outcomes of patients undergoing single-layer sutured laparoscopic myomectomy. *Int J Clin Practice*. 2021;75(11):e14870.
36. Faes T et al. Myomectomy: surgical techniques anno 2018. A systematic review. *Int J Surg Procedures*. 2018;1(3):112.
37. Raimondo D et al. Cellulose absorbable barrier for prevention of de-novo adhesion formation at the time of laparoscopic myomectomy: a systematic review and meta-analysis of randomized controlled trials. *Eur J Obstet Gynecol Reprod Biol*. 2020;245:107–113.
38. Mettler L et al. A safety and efficacy study of a resorbable hydrogel for reduction of post-operative adhesions following myomectomy. *Human Reprod*. 2008;23(5):1093–1100.
39. Angioli R et al. The use of novel hemostatic sealant (Tisseel®) in laparoscopic myomectomy: a case – control study. *Surg Endosc*. 2012;26:2046–2053.
40. Ricci S et al. Uterine leiomyosarcoma: epidemiology, contemporary treatment strategies and the impact of uterine morcellation. *Gynecol Oncol*. 2017;145(1):208–216.
41. Wright JD et al. Uterine pathology in women undergoing minimally invasive hysterectomy using morcellation. *JAMA*. 2014;312(12):1253–1255.
42. Kim R et al. Current methods of tissue extraction in minimally invasive surgical treatment of uterine fibroids. *JSLS*. 2022;26(3):e2022.00036.

16 LAPAROSCOPIC AND ROBOTIC-ASSISTED HYSTERECTOMY

Olanrewaju Dawodu, Briana Baxter, Natalia Parra, and Jin Hee Kim

16.1 Introduction

A minimally invasive approach to a hysterectomy, when feasible, is superior to open surgery due to a number of advantages and benefits including lower blood loss, fewer perioperative complications, less postoperative pain, shorter hospital stay, and a shorter recovery period. Hysterectomy approaches include abdominal, vaginal, laparoscopic, robotic, and vaginal natural orifice transluminal endoscopic surgery (vNOTES). Single incision laparoscopy is a subcategory within laparoscopic and robotic surgery. Subtypes of laparoscopic hysterectomy include total laparoscopic hysterectomy, laparoscopic supracervical hysterectomy, and laparoscopic-assisted vaginal hysterectomy (1, 2).

Given all the benefits of minimally invasive surgery, laparoscopic hysterectomy has become the most common approach to hysterectomy, with a trend toward same-day discharge as an outpatient procedure (3, 4).

16.2 Preoperative Preparation

16.2.1 Patient Selection

The indications for benign hysterectomy include but are not limited to uterine leiomyomas, abnormal uterine bleeding, endometriosis, adenomyosis, pelvic pain, and uterine prolapse (5). After a careful history and physical examination are performed, treatment alternatives with risks and benefits are discussed. Feasibility of laparoscopic hysterectomy is based on a multitude of patient factors including uterine size/mobility/shape, vaginal access, and presence of extrauterine disease and surgical factors including medical and surgical history, surgeon training/experience, and preference of the informed patient. According to the American College of Obstetricians and Gynecologists (ACOG), laparoscopic hysterectomy is a preferable alternative to open abdominal hysterectomy for those patients in whom a vaginal hysterectomy is not indicated or feasible (6). Shared decision making and informed consent is obtained after discussing the risks, benefits, and alternatives. Included in the informed consent should be a discussion about opportunistic bilateral salpingectomy or elective salpingo-oophorectomy. If contained tissue extraction is anticipated, its use and the risk of possible disseminated cells should be discussed. The standard workup with laboratory and radiologic testing should be completed, including a recent pap test, endometrial biopsy if indicated, and appropriate imaging. If the patient is anemic, preoperative correction of anemia should be initiated with oral or intravenous iron and hormonal or nonhormonal medications to suppress menses.

16.2.2 Antibiotic Prophylaxis

To decrease the risk of surgical site infections (SSI), antibiotic prophylaxis is given to all patients undergoing laparoscopic and robotic hysterectomies. Antibiotic regimen is summarized in Table 16.1. SSI remain one of the most common

TABLE 16.1 Antibiotic Prophylaxis

	Regimen	Dose
ACOG recommended	Cefazolin OR	< 120 kg: 2 g IV
		≥ 120 kg: 3 g IV
	Cefoxitin or cefotetan	2 g IV
Based on additional studies	Above + metronidazole	500 mg IV
Alternative regimen	Ampicillin-sulbactam	3 g IV
Alternative regimen	Clindamycin OR	900 mg IV
	Vancomycin	15 mg/kg (not to exceed 2 g)
	PLUS one of the following:	
	Gentamicin OR	5 mg/kg IV
	Aztreonam OR	2 g IV
	Ciprofloxacin OR	400 mg IV
	Levofloxacin OR	500 mg IV
	Moxifloxacin	400 mg IV
Alternative regimen	Metronidazole	
	PLUS one of the following:	
	Gentatmicin OR	5 mg/kg IV
	Ciprofloxacin OR	400 mg IV
	Levofloxacin OR	500 mg IV
	Moxifloxacin	400 mg IV

(adapted from ref 49)

DOI: 10.1201/9781003312109-16

complications of surgical procedures in gynecology (7, 8). The incidence of SSI is estimated at 2%–5% for all surgeries and it complicates approximately 2%–3% of hysterectomies (9). It is a major source of morbidity, accounting for emergency room visits and longer hospitalization, and it is the most common reason for postoperative readmissions. The Centers for Disease Control (CDC) define SSI as an infection related to an operative procedure that occurs at or near the surgical incision within 30 days (9, 10). Infections can be categorized as superficial incisional, involving the skin and subcutaneous tissues, deep incisional involving the deeper soft tissues, such as the muscle or fascia, or organ/space involving any part of the anatomy other than the incised body layers.

Several patient characteristics have been identified as factors that can impact the risk of SSI. Obesity, for example, is associated with longer operating times, limited surgical visualization, decreased tissue oxygenation, and reduced antibiotic penetration and is considered a major risk factor for SSI (11, 12). Tobacco use is also known to increase the risk of SSI due to its negative effects on tissue perfusion and delayed wound healing. Hyperglycemia is another well-established risk factor, as it impairs wound healing and increases susceptibility to infections. Numerous studies have emphasized the importance of achieving adequate glucose control before and after surgery to minimize the risk of SSI (13–15).

Preoperative antibiotic prophylaxis is standard of care for all hysterectomies, with the preferred option being a single dose of β-lactam antibiotic, most commonly cefazolin 1–2 g IV with or without metronidazole (15). In one retrospective cohort study of 18,255 hysterectomies, the use of prophylactic cefazolin plus metronidazole resulted in a significantly lower SSI after hysterectomy compared with cefazolin or second-generation cephalosporin alone (16). Alternative prophylaxis for severe penicillin allergy can include clindamycin 600 mg IV plus gentamicin 1.5 mg/kg IV or metronidazole 500 mg IV plus gentamicin 1.5 mg/kg IV (17). Adjustment and redosing of antibiotics are recommended for certain scenarios such as morbidly obese patients, operative length > 3 hours, excessive blood loss (18).

16.3 Procedure

16.3.1 Laparoscopic Equipment Setup

Typical equipment for laparoscopic hysterectomy includes the standard laparoscopic equipment and an electrosurgical device of choice. Typically, monopolar and bipolar electrosurgical devices are utilized and/or is an advanced vessel sealing device or ultrasonic energy device.

16.3.2 Robotic Equipment Setup

The setup for the robotic surgical system, most commonly the da Vinci surgical system, includes a surgeon's console, a patient cart that holds the robotic arms, and a vision tower. It is recommended to have a dedicated robotic operating room to accommodate the size of the system's components and allow for flexible docking of the robot from various angles. The surgeon's console provides a three-dimensional view of the surgical site and controls the robotic arms. The vision cart houses essential electronic equipment, including the light source and video/image processing devices required for the endoscope used in robotic surgery. The patient cart which typically holds three to four arms should be sterilely draped prior to bringing it into the surgical field. It is necessary for surgeons to familiarize themselves with the manual of these devices to effectively operate and utilize them during robotic procedures.

16.3.3 Uterine Manipulator

Uterine manipulators are considered essential for improving exposure and the margin of safety during laparoscopic and robotic hysterectomies. The uterine manipulator can aid in with mobilization of the uterus as another hand during laparoscopy, in addition to assisting with the identification of the cervicovaginal junction at the time of colpotomy. These devices typically include an intrauterine cannula inserted to fit the length of the uterine cavity and a colpotomy cup that identifies the vaginal fornices and lateralizes the ureters, particularly with cephalad tension. Colpotomy cups come in different sizes ranging from 2.5 to 4.2 cm depending on the type of manipulator used. The appropriate cup size can be chosen after measuring cervical size with a cervical sizer or with visual estimation. Accurate determination of the colpotomy cup size is critical, if under- or oversized the delineation of safe surgical planes and degree of manipulation can be compromised. Uterine manipulators are usually placed before or in tandem with peritoneal entry. In situations where placement is difficult, insertion under laparoscopic visualization can reduce the risk of perforation, or intentional perforation under laparoscopic guidance can be considered in cases of patients with a history of a prior endometrial ablation.

Several uterine manipulators for hysterectomy have been designed, including both disposable and reusable systems. Device selection depends on surgeon preference and device availability. Although laparoscopic/robotic hysterectomy without the use of a uterine manipulator has been described, the decision to use a manipulator can be critical and should be tailored to the patient and pathology. The RUMI® II system and Advincula Arch® feature a reusable metal shaft and utilize similar disposable intrauterine tips and colpotomy cups. The RUMI® II handle comes off the main shaft at a 90-degree angle with the ability to adjust and lock the intrauterine tip for anteversion of the uterus at several angles. Other reusable systems available outside of the US include the Clermont–Ferrand, Hohl, Mangeshikar, and Donnez uterine manipulators. The Advincula Arch® has an ergonomic curved shape for easy manual manipulation. Disposable systems such as the VCare®Plus, Advincula Delineator®, and Fornisee® System are single use devices. Disposable systems may have the benefit of a preassembled design, but some can have a lighter-weight design which may impact manipulation in patients with a larger uterus or high body mass index with excess pelvic soft tissue. The disposable manipulators may offer an additional benefit in cases requiring staged colpotomy, as the tip can be retracted while maintaining the cup securely around the cervix.

The ALLY II Uterine Positioning System (UPS)™ is a table-mounted system that securely attaches to the RUMI II®, Arch®, and Delineator® manipulators. It provides stability and eliminates the need for a surgical assistant at the perineum. Additionally, it allows the primary surgeon to personally position the uterus and maintain adequate visualization without being limited by human fatigue or experiencing downward drifting.

16.3.4 Peritoneal Access

Peritoneal access in laparoscopic procedures can be achieved through various techniques, including closed and open entry methods. Closed entry can be performed using the Veress needle, direct trocar, or radially expanding access system, while

the open method known as the Hasson technique requires a surgical incision down to the peritoneum followed by the insertion of a blunt trocar under direct visualization. Most laparoscopic complications occur during abdominal entry, and numerous techniques have been developed to minimize this risk (19). However, there is no clear consensus on the optimal method of entry. A Cochrane analysis conducted in 2019 found no significant difference in rates of vascular or visceral injuries among the various laparoscopic entry techniques. Nevertheless, direct trocar entry was associated with a lower risk of failed entry compared to Veress needle entry (19). Ultimately, surgeons should adhere to their preferred and most commonly performed technique while also being well versed in various techniques to choose the entry method that offers the utmost safety and effectiveness.

Abdominal entry is commonly initiated at the umbilicus as this is the thinnest part of the abdominal wall due to the fusion of fascial layers. However, there are special situations where a different entry location may be beneficial at reducing risk. Surgeons should consider alternative sites or avoiding closed entry techniques in patients with prior midline abdominal incisions extending to the umbilicus, large umbilical hernias, or masses, or those with history of umbilical mesh placement. In such scenarios, the right or left upper quadrant (Palmer's point) are good alternatives. Raoul Palmer described this location as 3 cm below the left costal margin and the midclavicular line (20). For patients with known hepatosplenomegaly or gastric or pancreatic surgeries or cancers, alternative sites should be considered. Additionally, other techniques including ninth intercostal space, uterine fundus, and posterior vaginal fornix have been described (21). To further minimize entry-related injury, decompression of the stomach with orogastric or nasogastric tube and the bladder with a Foley catheter is recommended prior to entry.

16.3.5 Trocar Placement and Instrumentation

Once abdominal entry is confirmed, insufflation pressure is set high, such as to 20 mmHg to allow for maximum abdominal wall distension away from vital structures prior to trocar insertion. Subsequently, after all additional trocars are inserted, the pressure should ideally be reduced (e.g., 10–12 mmHg) for ventilation purposes. While there are variations in port placement in conventional versus robotic-assisted laparoscopy, the camera port is typically positioned at the umbilicus. In most hysterectomy cases involving larger uteri, the camera port can remain at the umbilicus or its upper edge, as the most cephalad area of surgical activity, such as the adnexa or lower uterine segment, is usually caudad to the umbilicus. In some cases, the trocar sites may need to be adjusted more cephalad depending on uterine pathology and size. Although it may seem that cephalad to the umbilicus may provide improved visualization of the pelvic structures and the surgical field in case of a large uterus, it also increases the distance from the lower uterine segment. As accessing the lower uterine segment and vessels is critical for the success of laparoscopic hysterectomy, our preferred approach is to insert the optical trocar at the umbilicus, even when operating on uteri greater than 20-week size. Port-hopping techniques can be utilized for both conventional and robotic hysterectomy. This approach, coupled with the use of a 30-degree scope, enhances visualization, and with the uterus pushed cephalad, much of its bulk can be kept away from the operative field. All secondary ports should be placed under direct visualization, noting the course of the inferior epigastric vessels and being sure to avoid injury to major blood vessels, bladder, and bowel.

In conventional laparoscopic cases, our standard practice involves utilizing a 30-degree scope for optimal visualization, although a 0-degree scope can also be used. Two additional trocars are placed in the right and left quadrants, which can be positioned at higher levels in accordance with the size of the uterus. In many instances, a fourth port becomes necessary or may be advisable for efficiency and can be positioned either ipsilaterally or in the suprapubic region. Ipsilateral or suprapubic port placement will depend on surgeon preference, particularly for laparoscopic suturing. A suprapubic port may offer some advantages when managing large uteri, as it circumvents uterine interference and allows effective access to both sides; however, there may be a learning curve for suprapubic laparoscopic suturing. Typically used are 5 mm trocars, but a 10 mm trocar may be needed if a 10 mm laparoscope or any another 10 mm device is used, or if several needle exchanges are anticipated during the case. In terms of electrosurgical instruments, typically an advanced bipolar energy or high-frequency ultrasound energy device can be used. Many of these tools combine cutting and sealing capabilities for vessels up to 7 mm in diameter, providing excellent precision during tissue dissection.

In robotic-assisted cases, the procedure begins similarly with peritoneal entry. Once pneumoperitoneum is established, a 5 mm optical trocar is inserted in the left upper quadrant under direct visualization. Confirmation of abdominal entry is followed by a thorough examination of the initial peritoneal access site to ensure no injury and the completion of an abdominal survey. This upper entry site serves as the assistant port and can be adjusted to the right upper quadrant, depending on the side that the robot patient side cart is docked. The utilization of the Airseal® insufflation system may play a vital role in maintaining a stable pneumoperitoneum and enabling continuous evacuation of surgical smoke. Next is the placement of the three or four robotic trocars, depending on the complexity of the case. An 8 or 12 mm robotic trocar is placed in the umbilicus to serve as the robotic camera port. While there are general guidelines for the lateral trocar sites to be 8–10 cm or a hand's breadth apart, individualized port placement based on pathology is recommended rather than relying solely on premeasured sites. The two most lateral ports are typically at the level of the umbilicus or slightly lower, in line with the anterior superior iliac spine or just slightly medial to it. This site corresponds to the curve of the dome of the abdominal wall when viewed internally. The more medial port is then placed a hand's breadth away from the adjacent ports and a few centimeters above the umbilicus, creating an M-shaped configuration. Care must be taken to avoid placing the medial robotic port close to the umbilicus, as it increases the chance of collision with the robotic camera when working on the contralateral side. During port insertion, care is taken to ensure the port is placed perpendicular to the skin and well seated against the fascia. This enables greater freedom of movement around the fulcrum, minimizes resistance during the surgical procedure, and prevents instrument collision from having ports too close to each other. Ports are inserted until the second black line is just visible above the peritoneum. Once all desired ports are appropriately positioned (Figure 16.1), the patient is placed in the minimum Trendelenburg position needed prior to docking.

The robotic system can be docked either in the center or on the side (Figure 16.2). In our practice, we prefer side cart docking as it frees the perineum for easy manipulation and tissue extraction and is user friendly to the operating room circulator. However, the choice of docking configuration can be adjusted based on the specific layout and space available in the

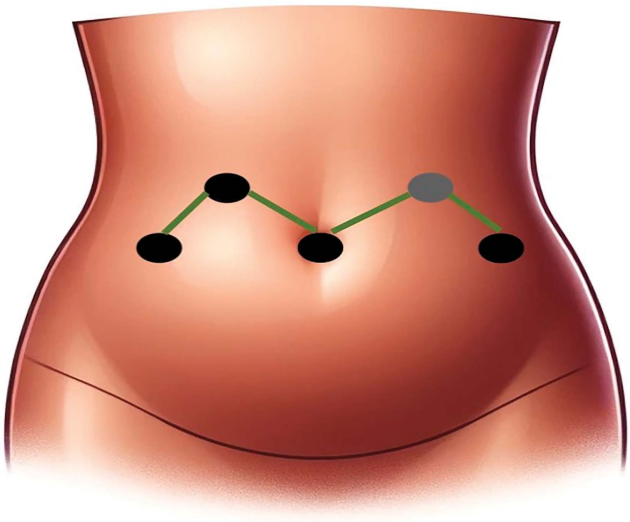


FIGURE 16.1 Port placement for the Xi system. Camera port is located at the umbilicus and remaining ports are placed creating an "M or rainbow" configuration. The assistant port (Airseal®) is at the left upper quadrant.

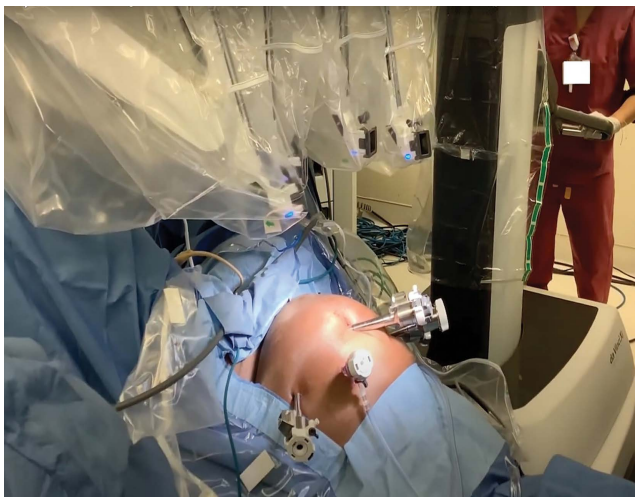


FIGURE 16.2 Side docking of the robotic cart driven by the OR circulator.

operating room. Each case begins with the long bipolar grasper on the left (arm 1), 30-degree robotic scope (arm 2), monopolar scissors (arm 3), and prograsp forceps (arm 4). There are a variety of endowristed bipolar cautery instruments, vessel sealers, and ultrasonic instruments, in addition to several graspers with different grip strengths.

16.3.6 The Adnexa

Evidence of distal fallopian tube being the origin of high-grade serous ovarian cancer has increased over the years. Patients are counseled on the American College of Obstetrics recommendation for opportunistic bilateral salpingectomy at the time of benign hysterectomy (22). This practice has not been shown to be associated with decreased ovarian reserve or confer any significant operative complications (23, 24). In contrast, the evidence on risks and benefits of elective oophorectomy continues to evolve. Following the Women's Health Initiative trial's concerns over hormone replacement therapy, there was a decline in rates of elective oophorectomy (25). This was further supported by Parker et al. in 2005, which showed increased mortality risk in patients who underwent oophorectomy before age 65 (26). More recently, Rush et al. reevaluated the Markov model and concluded that oophorectomy during hysterectomy for women aged 50 or older had a similar mortality rate at age 80 as hysterectomy with ovarian retention. However, for women aged 45–49, oophorectomy may increase mortality risk, which can however be mitigated with estrogen replacement therapy (27). These findings challenge previous assumptions and highlight the importance of individualized decision making.

The hysterectomy typically begins with identifying the ureter through the intact peritoneum as it courses caudad past the pelvic brim along the lateral pelvic sidewall. If ovarian preservation is planned, the fallopian tube can be dissected off the mesosalpinx and left attached at the cornua or freed from its uterine attachment if there is concern of impacted visualization caused by it dangling. While performing the salpingectomy, it is important to minimize thermal spread to the infundibulopelvic ligament as salpingectomy has been shown to increase risk of menopausal symptoms when compared to hysterectomy alone (28, 29). The utero-ovarian ligament is then coagulated and dissected proximally. This dissection is continued to the round ligament until the broad ligament is entered. Care should be taken to perform this dissection slightly away from the uterus to avoid bleeding from the uterine corpus.

If unable to visualize the ureter or in cases where oophorectomy is planned, the retroperitoneum is opened starting from the avascular triangle inferior to the round ligament, lateral to the infundibulopelvic (IP) ligament and medial to the external iliac vessels. The peritoneal incision is extended down to the pelvic brim parallel to the IP ligament. With the IP ligament displaced medially and areola tissue divided, the ureter is identified coursing in the medial leaf of the broad ligament. A peritoneal window can then be made well above the ureter, and the utero-ovarian or infundibulopelvic ligament (in cases of oophorectomy) can be isolated, coagulated, and dissected (Figure 16.3).

16.3.7 Broad Ligament

Following dissection of the adnexal pedicles and round ligament (Figure 16.4), the anterior and posterior leaves of the broad ligament are separated. In both conventional laparoscopic and robotic hysterectomies, if a fourth port is utilized, the proximal round ligament can be grasped and used to deviate the uterus to the contralateral side to create sufficient tension for effective dissection. However, in cases with large uteri, this maneuver may be challenging, and instead, the grasping instrument should be used to apply medial pressure on the uterus.

The dissection of the posterior leaf of the broad ligament proceeds towards the colpotomy cup, which exposes the uterine vessels and further lateralizes the ureter. Anteriorly, the broad ligament is dissected caudally and the vesicouterine peritoneum is incised at the level of the cup. To develop the bladder flap, the vesicouterine peritoneum is gently grasped and tented upwards exposing the areolar tissue between the bladder and the uterus. Using a combination of sharp and blunt dissection, the loose connective tissue is dissected, gradually moving the bladder caudally and identifying the pubocervical fascia.

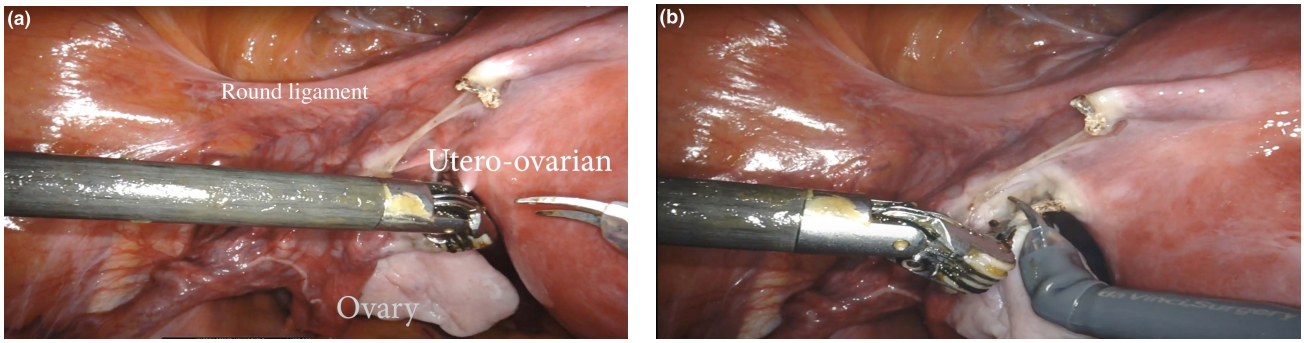


FIGURE 16.3 (a) Coagulation and (b) transection of the utero-ovarian ligament.

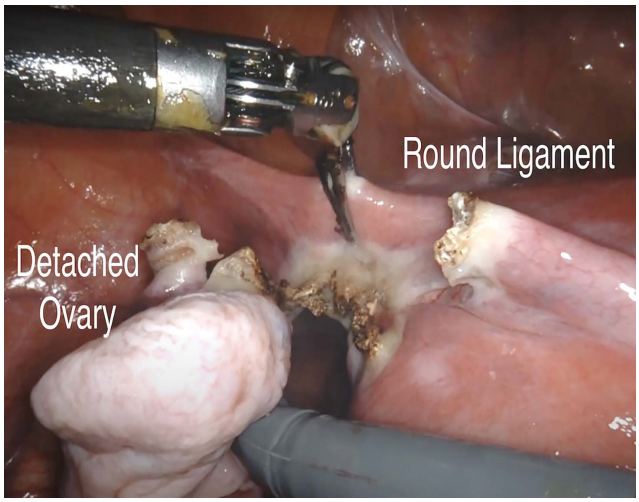


FIGURE 16.4 Coagulation and transection of the round ligament.

In cases of an obliterated anterior cul-de-sac, following identification of the uterine vessels posteriorly, a safe avascular space can be developed anteriorly by tunneling over the uterine artery and under the bladder on the lateral aspect of the colpotomy cup since the majority of bladder adhesions from cesarean sections tend to be in the midline. Bilateral securing of the uterine vessels is crucial for reducing bleeding, after which the adhesions can be carefully dissected using a lateral to medial approach. Additionally, backfilling the bladder with methylene blue solution may aid in identifying its margins during the dissection process.

16.3.8 Uterine Vessels

After dissecting the anterior and posterior peritoneum down to the colpotomy cup, the remaining areolar tissue surrounding the uterine vessels is dissected and cut. This step of skeletonizing is crucial to ensure precise coagulation and minimize thermal spread. Once the skeletonization is complete, a bipolar or advanced sealing device is positioned at a 90-degree angle at the level of the internal os, bouncing off the cervical cup, to coagulate and desiccate the uterine vessels (Figure 16.5). The vascular pedicle is then laterally mobilized below the level of the cup to facilitate colpotomy. Additionally, the proximal part of the pedicle should be coagulated up to the lateral wall of the uterus to minimize back bleeding.

16.3.9 Colpotomy and Cuff Closure

The colpotomy cup serves as a valuable tool in identifying the cervicovaginal junction and initiating the vaginal incision. The choice of electrosurgical instrument for this procedure may vary depending on the surgical approach. In conventional laparoscopic cases, monopolar (hook, spatula, or scissors) or ultrasound energy can be used. In robotic cases, monopolar shears are commonly utilized. When using high-frequency ultrasound energy, a metal colpotomy cup may need to be considered and additional care taken to prevent the risk of breaking off pieces that could potentially be lost in the peritoneal cavity.

To begin, upward traction on the uterus is provided by the manipulator, aiding in the visualization and accessibility of the cervicovaginal junction. Adequate pneumoperitoneum is maintained using a pneumo-occluder inserted with the manipulator to ensure optimal visualization and surgical conditions. The colpotomy can be initiated either anteriorly or posteriorly and is then carried out in a circumferential manner, taking care to follow the curve of the cup. This approach helps to avoid injury to the lateral vascular pedicles and the ureter. Both cut and coagulation functions of the electrosurgical instrument can be employed. However, it is important to minimize the dwell time to avoid excessive tissue thermal damage, devascularization, and necrosis, which could increase the risk of cuff dehiscence.

In cases where the uterus is exceptionally large, it can be difficult to elevate the uterus sufficiently to visualize the posterior cul-de-sac and complete colpotomy. To overcome this challenge, a staged colpotomy technique can be employed, specifically by separating the uterine corpus from the cervix, as in a supracervical hysterectomy (Figure 16.6a). To initiate, a supracervical incision is created at the level of the internal os anteriorly and laterally. The incision is then extended until the tip of the manipulator becomes visible (Figure 16.6b). Throughout this process, the colpotomy cup is maintained in its position. The balloon tip of the manipulator is deflated, and the shaft is slowly retracted until the deflated balloon tip can be introduced through the incision and into the abdominal cavity (Figure 16.6c). This allows for anteversion of the uterus, facilitating the completion of the supracervical hysterectomy. Special care should be taken to stabilize the uterine corpus to avoid auto-amputation and trauma to the

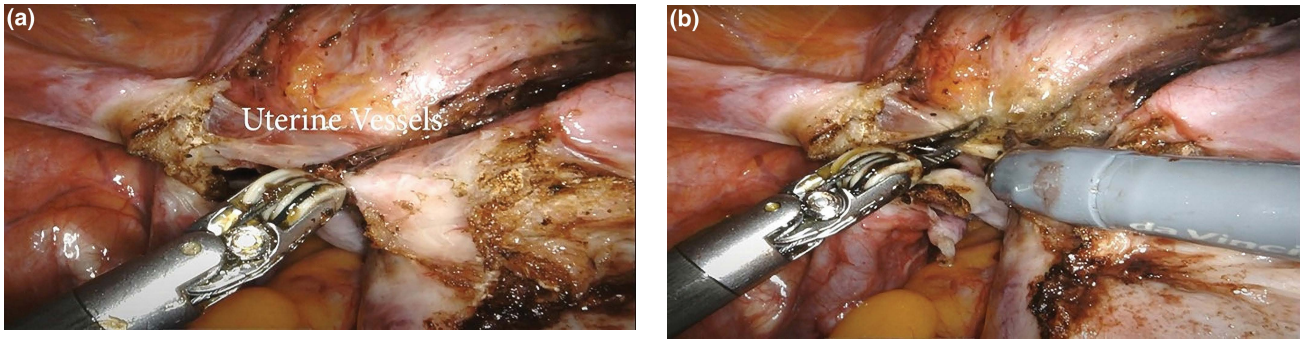


FIGURE 16.5 (a, b) Coagulation and dissection of the uterine vessels.

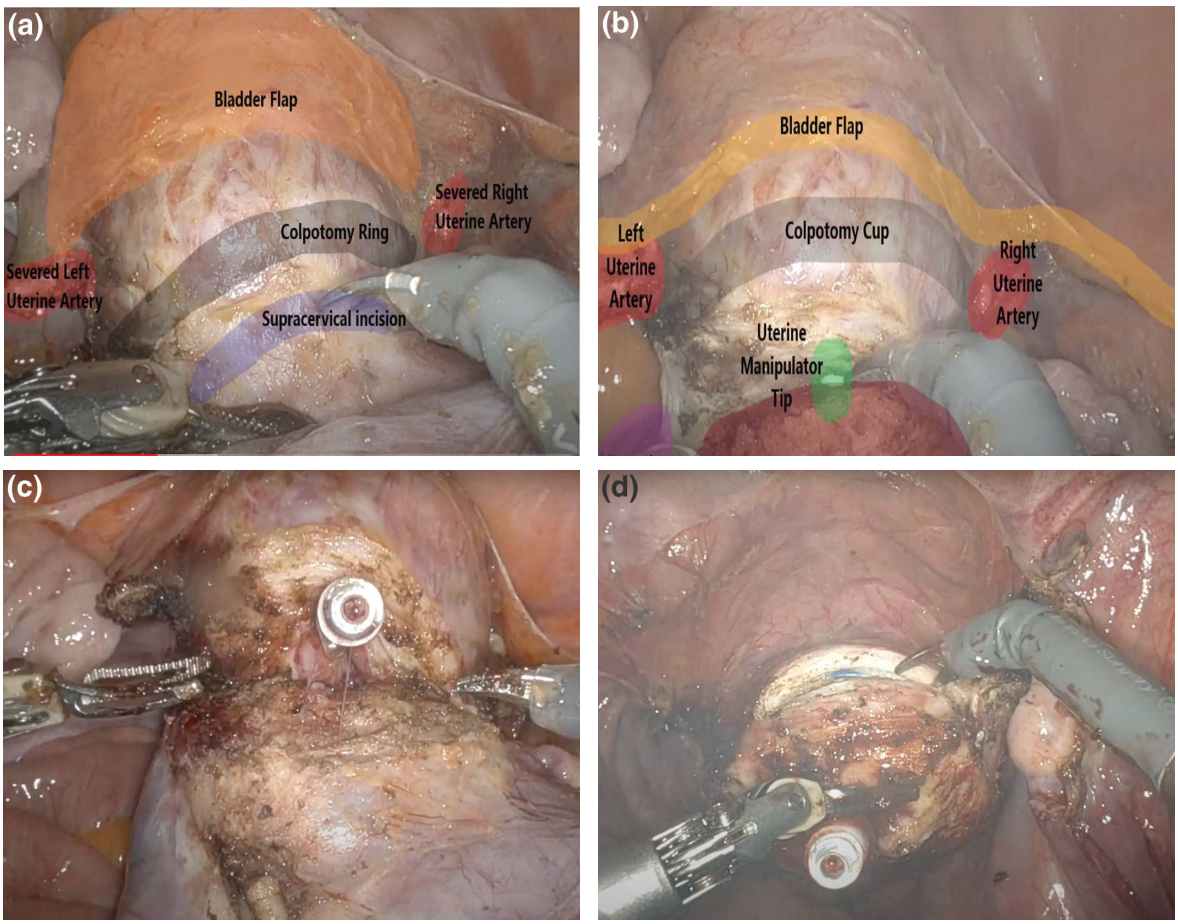


FIGURE 16.6 Staged colpotomy technique: (a) Initiate a supracervical incision; (b) extend incision until manipulator tip is visible; (c) deflate balloon tip, retract, and push into abdominal cavity; (d) perform a trachelectomy.

posterior peritoneum. Once the uterine corpus is amputated, the bulky specimen is allowed to fall into the upper abdomen, and trachelectomy is performed using the usual techniques (Figure 16.6d).

Once completely detached, the specimen is delivered via the vagina, when possible, either intact if small enough or via vaginal contained cold knife tissue extraction. If umbilical contained tissue extraction is opted, cuff closure is performed prior to contained tissue extraction. The pneumo-occluder or stuffed sterile glove is placed to maintain intraperitoneal pressure. Attention is then turned to the cuff closure, after dissecting the bladder off the vagina even further if needed. The vaginal cuff closure can be done via interrupted or running suture of an absorbable/delayed absorbable or barbed suture. In our practice, the vaginal cuff is closed in a continuous fashion in two layers using a 12-inch 2–0 or 0 V-loc-180 absorbable barbed suture on a GS-21 needle. To enhance apical support the cardinal and uterosacral ligaments should be incorporated into the angled closure. Additional apical support procedures can be considered if needed for

prolapse. Following closure, all vascular pedicles are irrigated and inspected to ensure adequate hemostasis. Additionally, a low-pressure check is performed by lowering the abdominal pressure to less than 8 mmHg, serving as an additional assessment for hemostasis.

16.3.10 Extraction and Morcellation

When the uterus is too large to be easily delivered through the vagina during a hysterectomy, tissue extraction is necessary. In 2014, the US Food and Drug Administration (FDA) issued a safety warning cautioning that uncontained power morcellation may be associated with the dissemination of malignant tissue within the peritoneal cavity, leading to the concern of upstaging the disease and compromising patient outcomes (30). Since then, the FDA issued an update to recommend performing laparoscopic morcellation for hysterectomy or myomectomy only in the presence of a tissue containment system, legally marketed in the US (31).

Contained tissue extraction can be performed either through the vagina or via minilaparotomy at the umbilicus or any other abdominal sites. The choice of morcellation technique depends on various factors, including the size of the uterus, surgeon preference, and patient characteristics, among others. Due to the potential risk of spreading undetected malignancies, including uterine sarcomas, the use of bag containment systems is strongly recommended to mitigate this risk. Currently, the Olympus Pneumoliner is an FDA-approved containment system that allows power morcellation.

Whether a transabdominal or a transvaginal contained tissue extraction method is used, there are several bag containment systems available. The appropriate-sized retrieval bag is selected based on uterine size, device availability, bag capacity and shape, and surgeon preference. Although several containment bag systems exist, they vary widely in size, shape, durability, and construction. The containment systems that are typically large enough to hold a large fibroid uterus include extraction systems that can hold 1500–6500 mL in volume (32).

For transabdominal contained tissue extraction, after closure of the vaginal cuff, the camera is moved from the umbilical port to a lateral port, and any remaining suture is removed under direct visualization through the umbilical port. At the bedside, the umbilical incision is extended to a suitable length to accommodate the chosen specimen extraction bag, typically 15–25 mm. Once the bag is introduced into the pelvis under direct visualization, the specimen is placed in the bag and the bag edge exteriorized. After the specimen containing bag is brought through the umbilical incision, the skin and fascia of the incision are extended to about 2.5 cm. To aid in visualization and access, an extra-small self-retaining retractor is inserted (Figure 16.7a). The specimen within the bag is then securely grasped with penetrating clamps (Figure 16.7b), and an 11-blade scalpel is used to create a reversed C-shaped incision on the bag, following the principles of the extracorporeal C-incision tissue extraction (ExCITE) technique. Once extraction is complete, the bag and self-retaining retractor are removed (Figure 16.7c) and the fascia and skin closed (Figure 16.7d).

16.4 Special Situations

16.4.1 Supracervical Hysterectomy

First described by Semm in 1991, laparoscopic supracervical hysterectomy (LSH) is characterized by amputation of the uterine corpus, leaving the cervix in situ. Supracervical hysterectomy is an option for patients desiring hysterectomy except for malignancy or precursors of malignancy of the uterus and cervix (33, 34). The risks and benefits of cervical

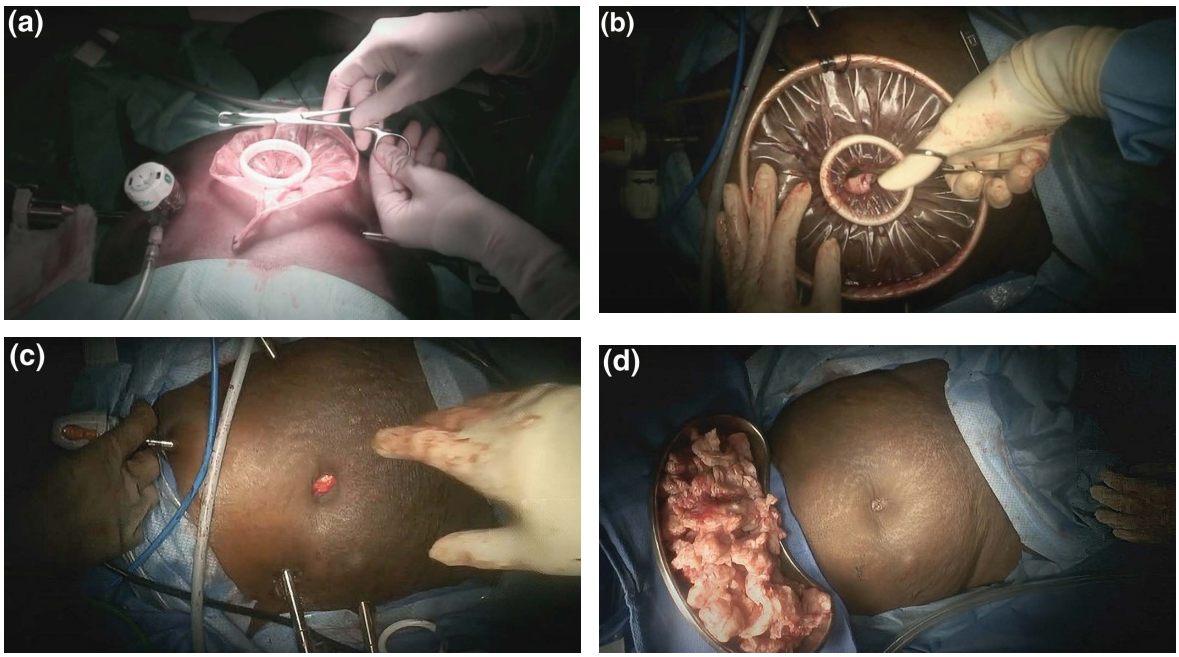


FIGURE 16.7 Umbilical contained cold knife tissue extraction. (a) An extra small self-containing retractor is inserted in the containment bag. (b) Grasp specimen with penetrating clamp to initiate extraction. (c) Remove bag and retractor when extraction completed. (d) After fascia and skin closure.

retention have long been a subject of debate amongst surgeons, specifically as it pertains to sexual satisfaction, prevention of pelvic organ prolapse, risk of urologic injury, and decreased operative time (35). However, a recent systematic review and meta-analysis concluded that there was no difference in sexual function after hysterectomy of any type (total or supracervical) or surgical route (vaginal, abdominal, or laparoscopic) (36). Moreover, cervical retention does not offer protection against the development or recurrence of pelvic organ prolapse. This remains true even when comparing total versus supracervical hysterectomy at the time of sacrocolpopexy, as studies have shown no significant difference in rates of prolapse recurrence (37, 38).

The decision to retain or remove the cervix during hysterectomy is primarily based on patient preference, as the only absolute contraindication for cervical retention is the presence of cervical or uterine malignancy or premalignant conditions. However, it is important to consider certain factors when discussing cervical retention with patients. Those with endometriosis or chronic pelvic pain may have a higher likelihood of requiring subsequent trachelectomy after supracervical hysterectomy (39). In addition, patients who choose cervical retention should be aware of the possibility of continued cyclic bleeding, although the volume is typically minimal and may not have significant clinical implications. Preoperative counseling should include reported incidence of bleeding, which ranges from 0% to 37%. Finally, regarding the risk of cervical malignancy, the incidence of cervical stump neoplasia in patients with previously normal pap smear results is less than 0.3%, and this risk can be further reduced to less than 0.1% with continued screening (35).

16.4.1.1 Surgical Technique

After the uterine vessels are secured, the uterine corpus is amputated at the level of the internal os, also termed the uterine isthmus. The procedure can be performed with or without the use of a uterine manipulator and with or without colpotomy cup (33, 40). However, in our experience the use of a uterine manipulator with a colpotomy cup increases the safety profile of the procedure by simplifying the dissection of the bladder and occlusion of the uterine vessels and clearly delineating the uterine isthmus. Amputation can be accomplished in a variety of ways, with the use of a laparoscopic cold knife and ultrasonic or monopolar instruments. Proprietary loop-style devices have been developed to more efficiently complete amputation, but these devices are disposable and can be costly (33).

Once amputation is complete and the uterine manipulator is removed, the endocervix is then either excised using a reverse cone technique or coagulated with electrosurgery to decrease the risk of postoperative cyclic bleeding (33). The final step in the procedure is retrieval of the uterine corpus. This can be achieved transabdominally or via posterior colpotomy using either mechanical or manual contained morcellation. Transcervical mechanical morcellation has also been described with the use of proprietary devices (33). In-bag specimen morcellation is always preferred over open morcellation. In our practice, the umbilical incision is extended to accommodate a specimen retrieval bag of the appropriate size. The specimen is then manually morcellated using the ExCITE technique as described earlier. There is no evidence to suggest that one morcellation technique is superior to another, however, since the 2014 FDA safety warning against laparoscopic power morcellators in surgery for fibroids, use of power morcellation is uncommon (33, 41, 42).

16.4.2 Trachelectomy

Trachelectomy is a surgical procedure that entails the removal of the cervix. It is commonly performed as a follow-up procedure after subtotal hysterectomy, as part of fertility-sparing surgical management for cervical cancer, and during the Manchester procedure when the cervix is amputated and uterosacral ligaments are used for suspension. For the purposes of this chapter, simple and radical trachelectomy for management of cervical cancer will not be discussed.

Trachelectomy is typically performed in cases of persistent or recurrent symptoms following supracervical hysterectomy, with an incidence ranging from 2% to 23%. In a retrospective analysis of 1140 patients who underwent excision of the retained cervix between 2010 and 2014, the most reported indications were leiomyoma (35.3%, 95% CI: 29.1%–41.5%), prolapse (13.6%, 95% CI: 9.1%–18.1%), bleeding (10.3%, 95% CI: 6.4%–11.3%), and endometriosis (6.2%, 95% CI: 3.0%–9.3%) (43). The incidence of cyclic vaginal bleeding following trachelectomy varies, ranging from 0% to 25%. Notably, patients experiencing persistent pain after laparoscopic supracervical hysterectomy often have underlying endometriosis.

Generally, trachelectomy can be performed vaginally, laparoscopically (conventional laparoscopy or robot assisted), or abdominally. However, reported complication rates are relatively high. In a retrospective study by McHale et al., the complication rate was as high as 38.1% (95% CI: 31.8%–44.5%), with the most common complication being bleeding requiring transfusion, occurring in 15.2% of cases (95% CI: 10.5%–20.0%) (44). It is worth noting that many cases in that cohort were performed abdominally, accounting for 88.5% (95% CI: 84.4%–92.7%) of the procedures. Studies have shown that vaginal approach is superior to abdominal approach, especially when the indication for surgery is prolapse (45). However, in patients with persistent pelvic pain or endometriosis, laparoscopic approach is recommended. Unfortunately, there is a paucity of data studying outcomes after laparoscopic or robotic trachelectomy. In a cohort of 40 patients undergoing laparoscopic trachelectomy with the use of a colpotomy cup, 94.59% had no intraoperative complications, 78.38% had mild to extensive adhesions requiring adhesiolysis, and 24% had no postoperative complications (46). Similarly, in a cohort of 11 patients undergoing robot-assisted laparoscopic trachelectomy with the use of a colpotomy cup, three complications were reported: one bladder injury repaired postoperatively, one ureteral injury necessitating stent placement, and one vaginal cuff hematoma (45).

16.4.2.1 Surgical Technique

After peritoneal access is obtained, trocar placement can be determined based on surgeons' preference. In our center, we consistently use a uterine/cervical manipulator with a colpotomy cup. The procedure typically begins with identification of the ureters bilaterally, followed by ureterolysis and adhesiolysis of bladder and intestinal adhesions to the cervical stump. Once the cervix is clear, the manipulator is placed under laparoscopic guidance. Once this is safely completed, the bladder is further mobilized away from the cervical stump prior to colpotomy. Colpotomy is then performed, cervical stump is removed vaginally, and the vaginal cuff is closed in two layers using barbed suture in our standard fashion.

16.5 Postoperative Recovery – See Chapter 5 and 55

1. Postoperative follow-up visits are typically scheduled as follows:
   a. *Two weeks after surgery*: Assess wound healing, pain control, and resumption of activities of daily living. This visit may be a telehealth visit if no physical issues are present.
   b. *Six to eight weeks after surgery*: Perform a vaginal cuff exam and determine if the patient is ready to discontinue pelvic rest and initiate heavy lifting.

16.6 Complications Unique to Hysterectomy

16.6.1 Wound Complications/SSI

Hysterectomies are generally classified as "clean-contaminated" procedures, indicating that the entry into the genital tract is performed in a controlled manner (8, 17). However, if there is an infection present at the time of surgery, it is considered a "contaminated" procedure, which can increase the risk of wound infection. The incidence of wound infection is generally lower in laparoscopic hysterectomies compared to abdominal hysterectomies (47). Wound infection can present with fever, pain at the incision site, induration, purulent drainage, or skin erythema. Treatment is recommended at the first suspicion and typically begins with a penicillin-based antibiotic.

Vaginal cuff cellulitis is a potential complication that can occur after a hysterectomy. The incidence ranges from 0%–8.3% (48). Symptoms can include fever, purulent vaginal discharge, or pelvic, abdominal, or low back pain. While cultures can confirm the presence of an infection, antibiotics should be initiated if there is clinical evidence of infection. Bacteria associated with vaginal cuff cellulitis are usually polymicrobial and thus broad-spectrum antibiotics are recommended, such as a broad-spectrum penicillin with β-lactam inhibitor or a later generation cephalosporin (47). One could also consider a multi-agent regimen if there is no improvement with the addition of metronidazole or clindamycin for anaerobic coverage. Bacterial vaginosis (BV) has also been posed as a risk factor for vaginal cuff cellulitis and abscesses with rates as high as 27% in the setting of untreated BV. Recent studies have explored the potential benefits of routine preoperative screening and treatment for BV or universal prophylaxis (16, 49, 50). While there is compelling evidence that universal prophylaxis for BV lowers the incidence of SSI, the recommendations from ACOG have not changed and continue to recommend cephazolin alone for surgical prophylaxis. However, based on the available evidence and the substantial decrease in SSI risk, many practitioners, including our practice, have chosen to routinely add metronidazole to cefazolin as part of the surgical prophylaxis regimen for hysterectomy.

16.6.2 Vaginal Cuff Dehiscence

Vaginal cuff dehiscence (VCD) is a partial or complete separation of the vaginal incision after total hysterectomy. It is a rare but potentially serious complication that may require urgent surgical repair. Due to its rare nature, incidence in the literature varies and ranges from 0.14% to 5.8% with multiple studies showing higher rates with laparoscopic hysterectomy compared to vaginal and abdominal hysterectomy (43, 51, 52). A few studies also report higher rates of VCD with robot-assisted laparoscopic hysterectomy compared to traditional hysterectomy, but these studies are all small cohorts (52). One recent large single-center study showed that VCD rates for RA-TLH were low, comparable to traditional laparoscopy, and the difference was not found to be significant.

The risk factors of VCD are not well defined but include anything that involves poor wound healing such as poorly controlled diabetes, presence of vaginal infection before or after surgery, and tobacco use. Mechanical factors such as early resumption of intercourse, trauma, and increased abdominal pressure with coughing, lifting, or straining are also risk factors for VCD. Electrosurgery has been posed as a risk factor given its increased use during laparoscopic and robotic surgery, but no significant association has been found.

VCD is a clinical diagnosis and, where suspected, should prompt physical examination. If VCD is found, abdominopelvic imaging can be used if there is a concern for pelvic abscess, hematoma, or bowel injury, but this should not delay surgical intervention. Once a VCD is diagnosed, management depends on the extent of dehiscence and whether there is bowel evisceration. If there is evidence of bowel evisceration but it can be reduced, the bowel should be gently returned to the abdomen and a moist vaginal packing placed. If the bowel cannot be reduced back into the abdomen, it should be covered with a moist towel and the patient should be taken to the operating room immediately. There are no set guidelines for VCD repair, and this should be guided by the surgeon's expertise and the clinical scenario. Various methods have been reported in the literature of closing a VCD including vaginal, laparoscopic/abdominal, combined approach, and healing by second intention (53). Regardless of approach, careful attention should be paid to bring healthy tissue edges together. Prevention of VCD includes mitigating risk factors already mentioned including treatment of vaginal infections, adequate glucose control, reduction in tobacco use, pelvic rest after surgery, and use of stool softener to avoid constipation and straining.

Other complications including port site hernia, and GI and GU complications are discussed in Chapter 50.

16.7 Conclusion

Laparoscopic and robotic hysterectomy is a type of minimally invasive approach with clinical benefits over laparotomy, including lower blood loss, fewer perioperative complications, less postoperative pain, shorter hospital stay, and a shorter recovery period. Hysterectomy approaches include abdominal, vaginal, laparoscopic, robotic, and vaginal natural orifice transluminal endoscopic surgery (vNOTES). Subtypes of laparoscopic hysterectomy include total laparoscopic hysterectomy, laparoscopic supracervical hysterectomy, and laparoscopic-assisted vaginal hysterectomy. Outpatient laparoscopic and robotic hysterectomy is a safe option with minimal complications. A vital part of successful surgery is adequate preoperative preparation with appropriate patient selection, informed consent, antibiotic prophylaxis, and thromboprophylaxis. Utilizing safe intraoperative techniques and postoperative care following the ERAS protocol can all contribute to improved perioperative outcome while lowering complications.

References

1. Pickett CM et al. Surgical approach to hysterectomy for benign gynaecological disease. *Cochrane Database Syst Rev*. 2023;8(8):CD003677.
2. Olive DL et al. The AAGL classification system for laparoscopic hysterectomy. Classification committee of the American Association of Gynecologic Laparoscopists. *J Am Assoc Gynecol Laparosc*. 2000;7(1):9–15.
3. Wright JD et al. Nationwide estimates of annual inpatient and outpatient hysterectomies performed in the United States. *Obstet Gynecol*. 2022;139(30):446.
4. Cohen SL et al. Outpatient hysterectomy volume in the United States. *Obstet Gynecol*. 2017;130(1):130.
5. Wright JD et al. Nationwide trends in the performance of inpatient hysterectomy in the United States. *Obstet Gynecol*. 2013;122(2 Pt 1):233–241.
6. ACOG Committee Opinion 701. *Choosing the route of hysterectomy for benign disease* [Internet]. 2017. Available at: www.acog.org/clinical/clinical-guidance/committee-opinion/articles/2017/06/choosing-the-route-of-hysterectomy-for-benign-disease.
7. Darouiche RO et al. Chlorhexidine – alcohol versus povidone – iodine for surgical-site antisepsis. *N Engl J Med*. 2010;362(1):18–26.
8. Lake AG et al. Surgical site infection after hysterectomy. *Am J Obstet Gynecol*. 2013;209(5):490. e1–490. e9.
9. CDC. *Surgical Site Infections (SSI)* [Internet]. 2023. Available at: www.cdc.gov/nhsn/opc/ssi/index.html (Accessed Jun 2023).
10. Colling KP et al. Abdominal hysterectomy: reduced risk of surgical site infection associated with robotic and laparoscopic technique. *Surg Infect*. 2015;16(5):498–503.
11. Young H et al. Sustained reduction in surgical site infection after abdominal hysterectomy. *Surg Infect*. 2013;14(5):460–463.
12. Steiner HL et al. Surgical-site infection in gynecologic surgery: pathophysiology and prevention. *Am J Obstet Gynecol*. 2017;217(2):121–128.
13. Ringel NE et al. Hysterectomy complications relative to HbA1c levels: identifying a threshold for surgical planning. *J Minim Invasive Gynecol*. 2021;28(10):1735–1742.e1.
14. Al-Niaimi AN et al. Intensive postoperative glucose control reduces the surgical site infection rates in gynecologic oncology patients. *Gynecol Oncol*. 2015;136(1):71–76.
15. Bratzler DW et al. Antimicrobial prophylaxis for surgery: an advisory statement from the National Surgical Infection Prevention Project. *Am J Surg*. 2005;189(4):395–404.
16. Till SR et al. Reducing surgical site infections after hysterectomy: metronidazole plus cefazolin compared with cephalosporin alone. *Am J Obstet Gynecol*. 2017;217(2):187.e1–187.e11.
17. Classen DC et al. The timing of prophylactic administration of antibiotics and the risk of surgical-wound infection. *N Engl J Med*. 1992;326(5):281–286.
18. Kahr HS et al. Venous thromboembolic complications for benign disease: a nationwide cohort study. *J Minim Invasive Gynecol*. 2018;25(4):715–723.
19. Ahmad G et al. Laparoscopic entry techniques. *Cochrane Database Syst Rev*. 2019;1(1):CD006583.
20. Palmer R. Safety in laparoscopy. *J Reprod Med*. 1974;13:1–5.
21. Agarwala N et al. Safe entry techniques during laparoscopy: left upper quadrant entry using the ninth intercostal space – a review of 918 procedures. *J Minim Invasive Gynecol*. 2005;12:55–61.
22. Hanley GE et al. Opportunistic salpingectomy for ovarian cancer prevention. *Gynecologic Oncol Res Pract*. 2015;2:1–9.
23. McAlpine JN et al. Opportunistic salpingectomy: uptake, risks, and complications of a regional initiative for ovarian cancer prevention. *Am J Obstet Gynecol*. 2014;210(5):471.e1–471.e11.
24. Findley AD et al. Short-term effects of salpingectomy during laparoscopic hysterectomy on ovarian reserve: a pilot randomized controlled trial. *Fertil Steril*. 2013;100(6):1704–1708.
25. Jacoby VL et al. The swinging pendulum: elective oophorectomy at the time of hysterectomy. *Obstet Gynecol*. 2022;139(5):721–723.
26. Parker WH et al. Ovarian conservation at the time of hysterectomy for benign disease. *Obstet Gynecol*. 2005;106(2):219–226.
27. Rush SK et al. A revised Markov model evaluating oophorectomy at the time of hysterectomy for benign indication: age 65 years revisited. *Obstet Gynecol*. 2022;139(5):735–744.
28. Collins E et al. Menopausal symptoms and surgical complications after opportunistic bilateral salpingectomy, a register-based cohort study. *Am J Obstet Gynecol*. 2019;220(1):85.e1–85.e10.
29. van Lieshout LAM et al. Hysterectomy with opportunistic salpingectomy versus hysterectomy alone. *Cochrane Database Syst Rev*. 2019;8(8):CD012858.
30. US Food and Drug Administration (FDA). *Laparoscopic uterine power morcellation in hysterectomy and myomectomy: FDA safety communication* [Internet]. 2014. Available at: http://wayback.archive-it.org/7993/20170722215731/www.fda.gov/MedicalDevices/Safety/AlertsandNotices/ucm393576.htm (Accessed May 2023).
31. US Food and Drug Administration (FDA). *UPDATE: perform only contained morcellation when laparoscopic power morcellation is appropriate: FDA safety communication* [Internet]. 2020. Available at: www.fda.gov/medical-devices/safety-communications/update-perform-only-contained-morcellation-when-laparoscopic-power-morcellation-appropriate-fda (Accessed May 2023).
32. Sia T et al. Laparoscopic specimen retrieval bags in gyn surgery: expert guidance on selection. *OBG Management*. 2020;32(10):36–44.
33. AAGL practice report: practice guidelines for laparoscopic subtotal/supracervical hysterectomy (LSH). *J Minim Invas Gynecol*. 2014;21(1):9–16.
34. Lee CL et al. Subtotal hysterectomy by natural orifice transluminal endoscopic surgery. *Gynecol Minim Invasive Ther*. 2017;6(4):195–198.
35. Nesbitt-Hawes EM et al. Laparoscopic subtotal hysterectomy: evidence and techniques. *J Minim Invasive Gynecol*. 2013;20(4):424–434.
36. Dedden SJ et al. Hysterectomy and sexual function: a systematic review and meta-analysis. *J Sexual Med*. 2023;20(4):447–466.
37. Kikuchi JY et al. Prolapse and mesh reoperations following sacrocolpopexy: comparing supracervical hysterectomy, total hysterectomy, and no hysterectomy. *Int Urogynecol J*. 2023;34(1):135–145.
38. Lethaby A et al. Total versus subtotal hysterectomy for benign gynaecological conditions. *Cochrane Database Syst Rev*. 2012;(4):CD004993.
39. Tsafrir Z et al. Risk factors for trachelectomy following supracervical hysterectomy. *Acta Obstet Gynecol Scand*. 2017;96(4):421–425.
40. Rock JA et al., eds. *Te Linde's Operative Gynecology*, 10th edn. Lippincott Williams & Wilkins; 2008:1–1449.
41. Lum DA et al. Impact of the 2014 food and drug administration warnings against power morcellation. *J Minim Invas Gynecol*. 2016;23(4):548–556.
42. Uterine morcellation for presumed leiomyomas: ACOG Committee opinion, number 822. *Obstet Gynecol*. 2021;137(3):e63–e74.
43. Brosens I et al. Bowel injury in gynecologic laparoscopy. *J Am Assoc Gynecol Laparosc*. 2003;10(1):9–13.
44. McHale MP et al. Outcomes of women undergoing excision of the retained cervix after supracervical hysterectomy. *Obstet Gynecol*. 2021;137(5):831–836.
45. Tsafrir Z et al. Robotic trachelectomy after supracervical hysterectomy for benign gynecologic disease. *JSLS*. 2016;20(3).
46. Dawood AS et al. Surgical outcomes of laparoscopic trachelectomy following supracervical hysterectomy: a multicenter study. *Obstet Gynecol Sci*. 2022;65(6):542–551.
47. Clarke-Pearson DL et al. Complications of hysterectomy. *Obstet Gynecol*. 2013;121(3):654.

48. Aarts JWM et al. Surgical approach to hysterectomy for benign gynaecological disease. *Cochrane Database Syst Rev*. 2015;2015(8):CD003677.
49. American College of Obstetricians and Gynecologists, prevention of infection after gynecologic procedures, ACOG practice bulletin no. 195. *Obstet Gynecol*. 2018;131:e172–e189.
50. McElligott KA et al. Preoperative screening strategies for bacterial vaginosis prior to elective hysterectomy: a cost comparison study. *Am J Obstet Gynecol*. 2011;205(5):500.e1–500.e7.
51. Llarena NC et al. Bowel injury in gynecologic laparoscopy: a systematic review. *Obstet Gynecol*. 2015;125(6): 1407–1417.
52. Hur HC et al. Vaginal cuff dehiscence after different modes of hysterectomy. *Obstet Gynecol*. 2011;118(4):794–801.
53. Ceccaroni M et al. Vaginal cuff dehiscence after hysterectomy: a multicenter retrospective study. *Eur J Obstet Gynecol Reprod Biol*. 2011;158(2):308–313.

17 ALTERNATIVE MANAGEMENT OF LEIOMYOMA (INCLUDING RF AND UAE)

Sarah Allen and Richard Guido

17.1 Introduction

Multiple uterine-sparing options exist for the treatment of bulk symptoms and abnormal uterine bleeding due to uterine fibroids. Historically, fibroid resection via myomectomy was the only available option for patients with symptomatic uterine fibroids desiring uterine preservation; however, alternative uterine-sparing options have rapidly expanded and proven to be effective and safe. Such techniques include radiofrequency ablation, uterine fibroid embolization, and imaging-guided focused ultrasound techniques. These techniques focus on destroying the leiomyoma, while preserving the surrounding uterine myometrium and endometrium. This chapter focuses on these ablative techniques for the management of uterine fibroids.

17.2 Overview of Procedures

17.2.1 Radiofrequency Ablation

Radiofrequency ablation (RFA) of uterine fibroids uses a monopolar electrosurgical circuit to transmit radiofrequency energy leading to thermal destruction of target tissue in the form of coagulative necrosis. Fibroids are heated to a target temperature which denatures the extracellular protein matrix, resulting in immediate softening of the myoma. Over time, additional protein fragments are resorbed, leading to further shrinkage. With this reduction in fibroid size and vascularity, patients experience improvements in bulk symptoms and heavy menstrual bleeding (1).

RFA includes both laparoscopic and transcervical approaches, both of which use ultrasonic guidance to target fibroids. The laparoscopic RFA system (the Acessa ProVu® system, Hologic, Marlborough, MA) was FDA approved in 2012 and the transcervical RFA system (the Sonata® system, Gynesonics, Redwood City, California) was FDA approved for use in 2018. The American College of Obstetrics and Gynecology (ACOG) recommends radiofrequency ablation via laparoscopic, transvaginal, or transcervical approach as uterine-preserving modalities for treating uterine fibroids, all of which are similarly effective (2).

Both laparoscopic radiofrequency ablation (lap-RFA) and transcervical radiofrequency ablation (T-RFA) are ambulatory procedures. The lap-RFA system (Figure 17.1) includes a

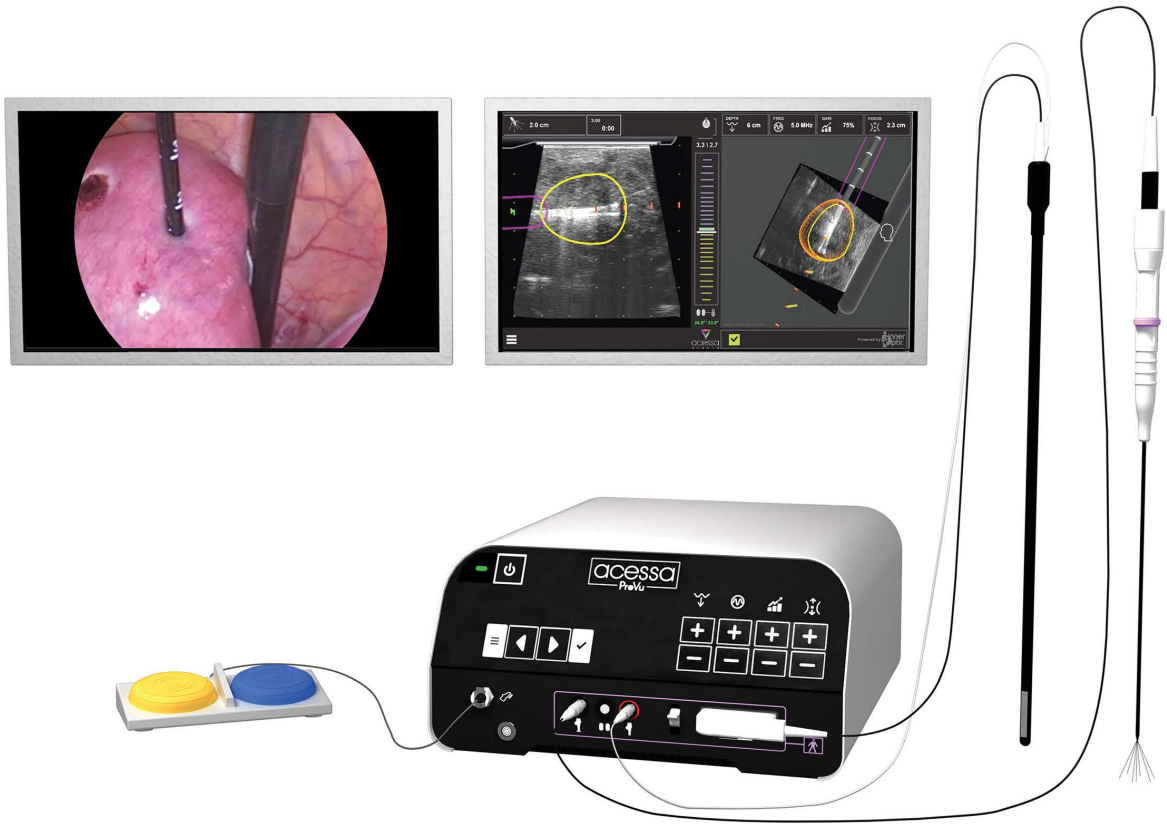


FIGURE 17.1 Components of the Acessa ProVu® system, including a laparoscopic ultrasound probe and RFA handpiece (right) with RF generator and foot pedals (bottom), intraoperative image of US probe and RF handpiece inserted into a target fibroid (top left) with real-time graphic overlay (top right). (Image of Acessa ProVu® system provided courtesy of Hologic, Inc. and affiliates, Marlborough, MA.)

DOI: 10.1201/9781003312109-17

laparoscopic ultrasound positioned cephalad to the uterine fundus, a radiofrequency ablation handpiece with deployable needle arrays and two adjacent video monitors for the laparoscopic and ultrasonic images with the ProVu 3D guidance (3). RFA is performed under general anesthesia with a mean procedure time of 73 minutes, time to discharge of 10.7 hours, return to work of 6.5 days, and return to normal activities of 9.0 days (4).

The T-RFA system configuration is similar to the lap-RFA but uses a combined radiofrequency and ultrasound handheld device (Figures 17.2 and 17.3). This allows for an ultrasound beam always within the plane of the needle electrode array (5). T-RFA can be performed under intravenous sedation or general anesthesia. The mean procedural time is 25 minutes, with a mean length of hospital stay of 2.5 hours and return to normal activities of 2 days (6–8).

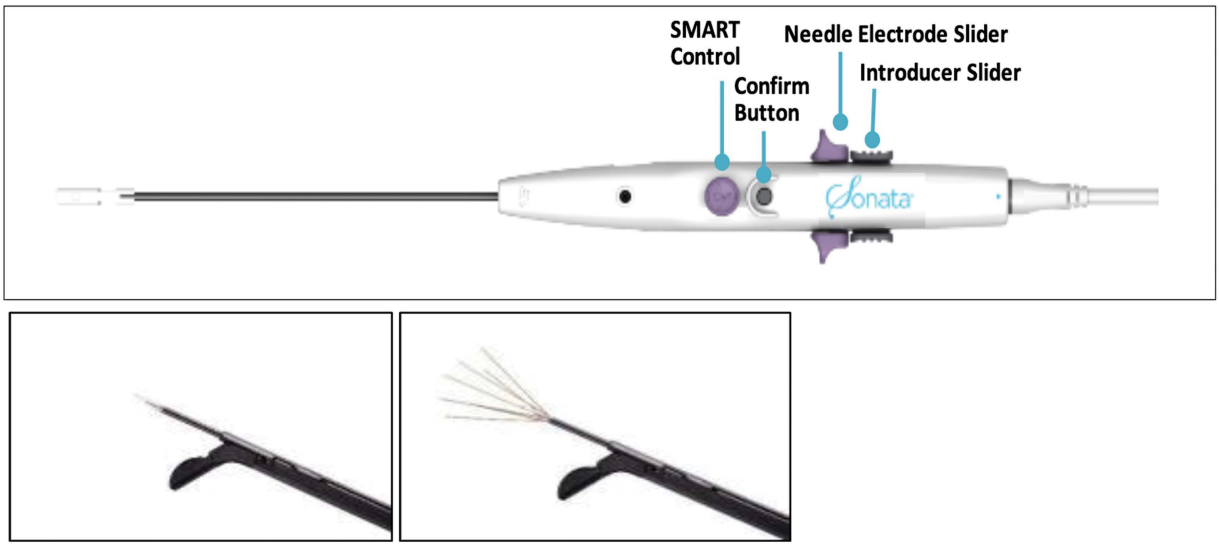


FIGURE 17.2 Components of the Sonata® system, including the combined intrauterine ultrasound probe and radiofrequency electrode handpiece (top). Detailed image of the handpiece tip including the articulating intrauterine ultrasound probe with introducer (bottom left) and with needle electrodes (bottom right). (Image of Sonata® system used with permission from Gynesonics, Redwood City, CA.)

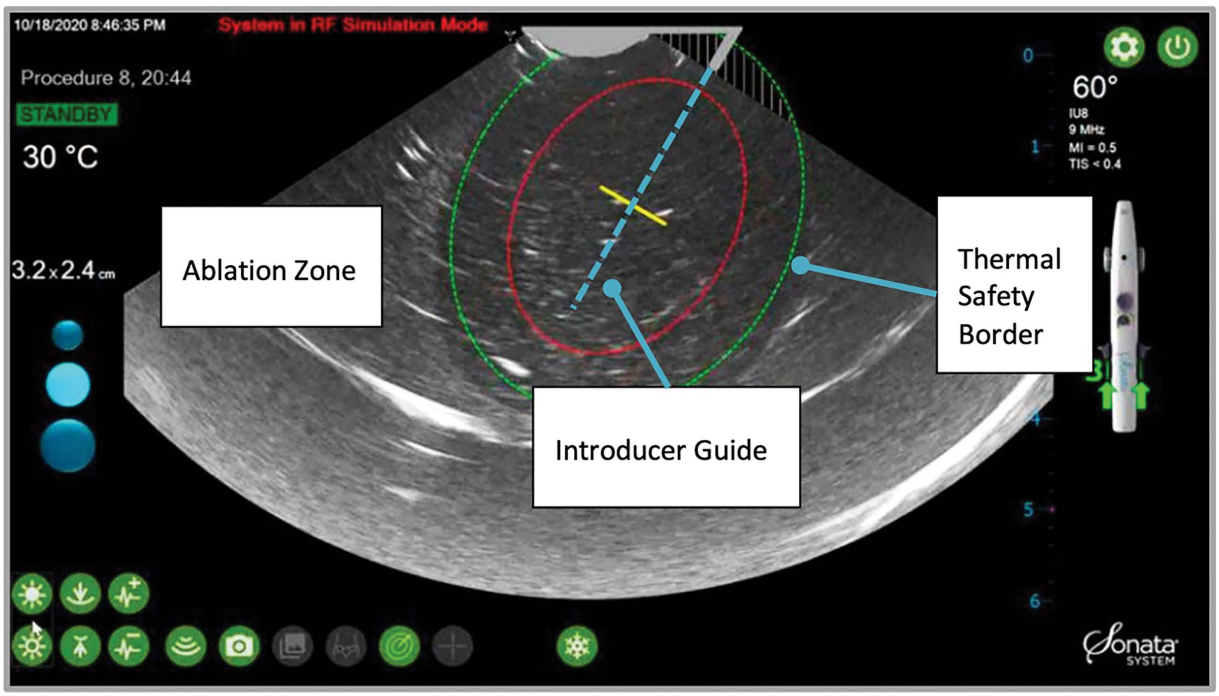


FIGURE 17.3 Illustration of the Sonata® system graphical overlay on the ultrasound image with ablation zone (red inner ellipse) and thermal safety border (green outer ellipse) and introducer guide (blue dashed line) displayed. (Image of Sonata® system used with permission from Gynesonics, Redwood City, CA.)

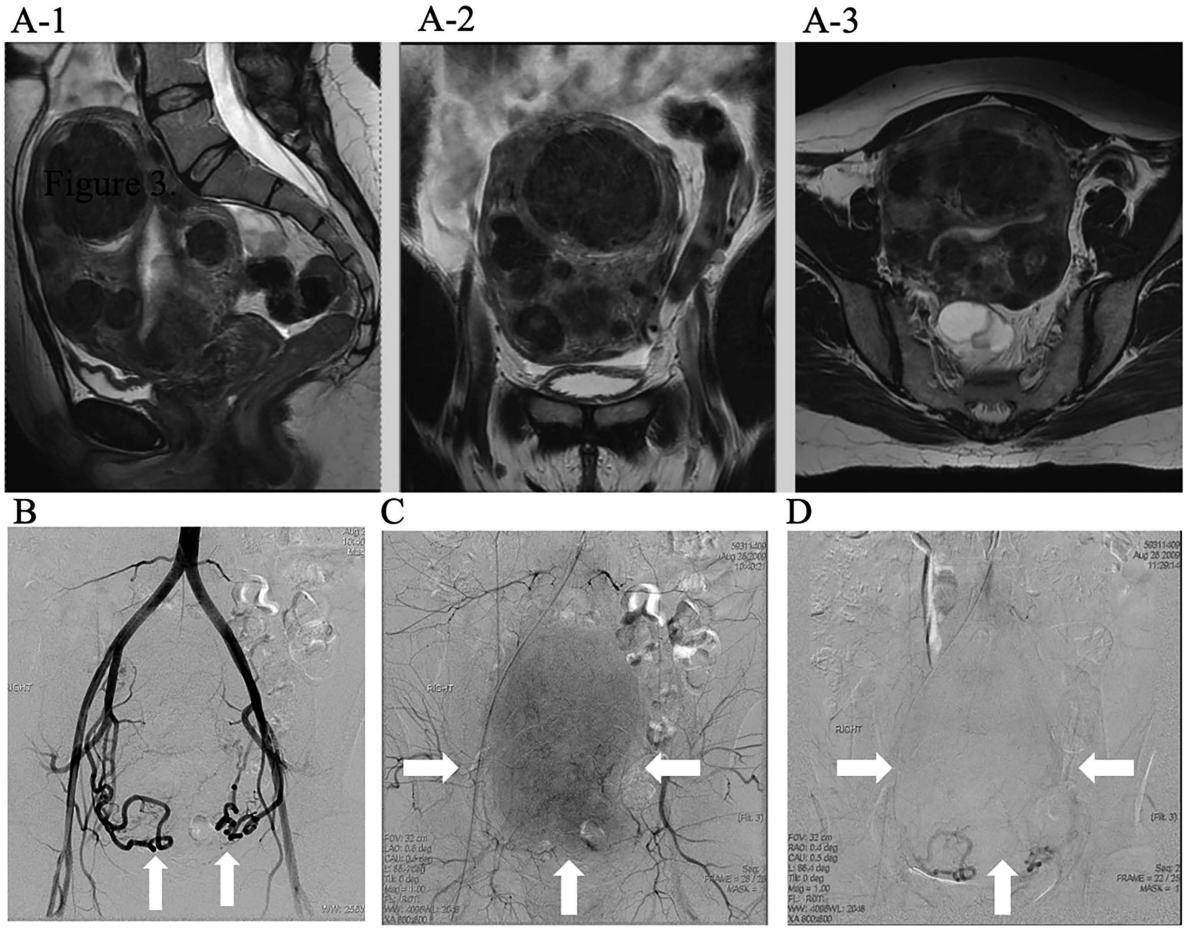


FIGURE 17.4 (A-1 through A-3) T2-weighted contrast-enhanced pelvic MRI of patient with symptomatic uterine myomas, in sagittal, coronal, and transverse views. (B) Digital subtraction angiography (DSA) demonstrating hypertrophic uterine arteries bilaterally (arrows). (C) Dense peri-fibroidal plexus before UAE (arrows) and (D) immediately following bilateral UAE (arrows). (Used with permission from Dr. Orons [10].

There is a direct relationship between the area of tissue requiring ablation and the time required to ablate the tissue, with larger ablation zones requiring longer time of ablation at target temperature. It is recommended to use multiple, overlapping eccentric ablations of approximately 2–3 cm for larger fibroids, to ensure effective treatment of the peripheral myoma tissue as well as maximize the efficiency of the procedure (1).

17.2.2 Uterine Fibroid Embolization

Uterine fibroid embolization, or uterine artery embolization (UAE), is a minimally invasive procedure during which the arteries supplying uterus are occluded with biocompatible particles, resulting in ischemic infarction and shrinkage of the leiomyomas. UAE has been used widely for treatment of symptomatic uterine fibroids since the early 2000s and is supported by ACOG as an accepted treatment option (2).

UAE is performed by an interventional radiologist under intravenous conscious sedation. A pelvic angiogram is obtained to demonstrate arterial anatomy and uterine artery origins. A microcatheter is placed through a transfemoral or transradial access point, threaded to the level of the uterine artery, and embolization particles are deployed to the target vasculature (9) (Figure 17.4).

UAE can be offered as an outpatient procedure, although median length of stay is 2 days. Inpatient admission is primarily indicated for pain control. While there is minimal pain during the procedure, over 90% of women experience pelvic pain following UAE. UAE is associated with a shorter procedural time, shorter length of hospital stay, less estimated blood loss, lower risk of blood transfusion, and faster return to daily activities compared to myomectomy and hysterectomy (11).

17.2.3 Magnetic Resonance-Guided Focused Ultrasound Surgery

Focused ultrasound treatment of fibroids is a noninvasive option for treatment of symptomatic uterine fibroids that uses a focused beam of ultrasonic energy to ablate fibroid tissue. The energy is delivered percutaneously to the targeted area without injuring tissue through which the beam travels or tissue surrounding the target area. This procedure is performed under image guidance, typically in the form of MRI, and is often referred to as magnetic resonance-guided focused ultrasound surgery (MRgFUS), or high-intensity focused ultrasound (HIFU) (12).

MRgFUS is an outpatient procedure performed under IV sedation. Treatment requires multiple small sonications per

fibroid, and can take upwards of 3 hours to treat a 7–8 cm sphere (12). Treatment of larger or multiple fibroids may require two 3-hour sessions, performed on two consecutive days (13). The majority of patients return to work within 1 day (14).

17.3 Patient Selection

Candidates for RFA, UAE, or MRgFUS have symptomatic uterine leiomyomas and desire uterine-sparing treatment. Patients must be appropriate candidates for the type of surgery, anesthesia, and imaging as required by type of procedure. These procedures should be avoided in patients with asymptomatic uterine leiomyomas, known or suspected pelvic malignancy, extrauterine masses, pelvic infection, or current pregnancy (3, 5, 12, 15).

17.3.1 Radiofrequency Ablation

For patients desiring RFA, the effectiveness and safety in patients with clinically significant adenomyosis, prior medical or surgical treatment of fibroids, or history of cervical dysplasia have not yet been established (3, 5). Neither the lap- nor T-RFA system is FDA approved for use in patients who desire future fertility. This warning is due to the limited data demonstrating evidence of safety in pregnancy. At the time of this publication, approximately 40 pregnancies have been reported following lap-RFA and 40 following T-RFA, with complication rates similar to the general population and no reported instances of uterine rupture (16, 17).

Lap-RFA can be used to treat FIGO types 2 through 6 and two to six myomas as well as type 7 with stalk width > 50% of fibroid diameter. Data is limited on the safety of treatment of cervical, round ligament, and broad ligament myomas, however safe and successful ablations of broad ligament myomas have been described in case reports using the lap-RFA system. T-RFA is intended for treatment for FIGO types 1 through 6 and two to five myomas. Neither system is intended for use in treatment of pedunculated FIGO type 0. Hysteroscopic and laparoscopic resection are recommended for FIGO type 0 or type 7 (stalk < 50%) myomas, respectively, and may be performed concomitantly with RFA (3, 5, 18).

Published outcomes are limited in the treatment of fibroids larger than 7 cm in diameter or uterine size greater than 14 weeks gestation or 300 cm^3. Case series have reported safe and successful treatment of uteri up to 22-week size and fibroids up to 15 cm for lap-RFA and fibroids > 10 cm for T-RFA (6, 18). Pretreatment of myomas with GnRH analogues prior to RFA is not recommended due to distortion of the myoma capsule resulting in difficulty visualizing the interface between the myoma and myometrium (3).

17.3.2 Uterine Artery Embolization

UAE is designed to treat FIGO type 1 through 6 or one to six myomas demonstrating adequate perfusion for occlusion by MRI. Special consideration must be taken into account with pedunculated subserosal/submucosal, cervical, or degenerated fibroids. For treatment of FIGO type 7 and 0 myomas, a stalk size of at least 25% and 50% are recommended (15,19). Myomas with extrauterine blood supply, such as cervical myomas, or those with evidence of degeneration are poor prognostic indicators for volumetric reduction (15,19). Case series have demonstrated successful treatment of fibroids > 10 cm and uteri with large fibroid burden (> 700 cm^3) as well as pretreatment with GnRH analogues (9, 20).

UAE is effective in the treatment of bulk symptoms in postmenopausal women and has been shown to improve symptoms by 88%–92% (18).

Recommendations for pregnancy following UAE have not been conclusively established, largely due to limited data (21, 22). The live birth rate following UAE has been reported as high as 70.8%. Delivery methods vary between studies with a vaginal birth rate from 53.3% to 87.5% and cesarean section rate from 61% to 78% (23).

The risk of diminished ovarian reserve and ovarian insufficiency following UAE is a concern, due to risk of incidental occlusion of collateral utero-ovarian vessels; however, multiple studies have demonstrated preservation of serum anti-Müllerian hormones and follicle-stimulating hormones following UAE (23, 24). The rate of ovarian insufficiency following UAE is approximately 7%, with almost all patients > 45 years of age (25).

17.3.3 Magnetic Resonance-Guided Focused Ultrasound Surgery

Ideal candidates for MRgFUS have a dominant fibroid that is amenable to MRgFUS based on size, location, and enhancement. Pedunculated fibroids and fibroids greater than 10–12 centimeters in diameter are typically not recommended for treatment; however, pretreatment with GnRH agonists has been used successfully for large fibroids (26, 27). MRgFUS is contraindicated if important structures are unable to be avoided in the path of the ultrasound beam, including cutaneous scars, bowel, pubic bone, intrauterine device, surgical clips, and hard implants (12).

In 2015, the FDA approved MRgFUS for treatment in women desiring future fertility; however, guidelines are controversial. At this time, a recommendation of MRgFUS prior to a planned pregnancy cannot be made. Current limited data demonstrates preserved AMH following MRgFUS (28).

17.4 Preprocedural Evaluation

MRI of the pelvis with contrast enhancement is the preferred imaging method prior to UAE and MRgFUS. Either pelvic ultrasound or pelvic MRI with contrast enhancement is recommended prior to radiofrequency ablation. Pelvic MRI with contrast enhancement has been shown to be more accurate than ultrasound for characterizing fibroid size, location, vascularity, and enhancement characteristics, in addition to determining other uterine pathologies that may mimic fibroid symptoms, such as adenomyosis (29).

17.5 Procedure Outcomes

17.5.1 Symptom and Quality of Life Improvement

Patients report a high level of satisfaction and significant improvements in health-related quality-of-life (HRQoL) scores and symptom severity scores (SSS) following all alternative treatment modalities. Lap-RFA and T-RFA have the greatest improvement in HRQoL scores and SSS from baseline to 3 months, which are maintained to 3-year follow-up (7, 30). At 36 months, 94% of patients who underwent lap-RFA or T-RFA are satisfied with their procedure (7, 30).

Following UAE, patients report significant improvement of HRQoL from baseline to 6 months, with scores remaining unchanged up to 10 years (31). Patient satisfaction is similar to myomectomy at 4 years and hysterectomy at 10 years (32, 33).

TABLE 17.1 Percentage of Mean Myoma Volume Reduction Following Treatment (4, 8, 30, 34–36)

Procedure	3 Months	12 Months	24 Months
Lap-RFA	39.8%	45%	
T-RFA	54.7%	67%	
UAE	44%	54%	60%
MRgFUS	21%	28%	49%

TABLE 17.2 Reintervention Rates Following Each Procedure (4, 39, 40)

Procedure	12 Months	24 Months	36 Months
Lap-RFA	3.8%	4.4%	11.0%
T-RFA	2.7%	5.2%	8.2%
UAE	7%	8%	14%
MRgFUS	12%	14%	22%

The largest improvement in SSS following MRgFUS is between 1 and 3 months. Symptoms continue to improve at 6 months and remain stable at 12 months. Compared to UAE, MRgFUS resulted significantly less improvement of fibroid symptoms and HRQoL at 6, 12, and 24 months (34).

17.5.2 Volume Reduction

RFA, UAE, and MRgFUS demonstrate statistically significant reductions in myoma volume as early as several weeks post-procedure and continue to decrease over time. Available percentage reductions in mean myoma volume from 3 to 24 months are summarized in Table 17.1.

It is difficult to draw a definitive conclusion as to the most effective means of volumetric reduction as there exists a large heterogeneity between studies when it comes to myoma size, number, and location treated. Additionally, it is important to note that initial studies using MRgFUS in the United States were limited by strict restrictions regarding ablation size by the Food and Drug Administration (FDA). These restrictions were changed in 2009 to include larger ablation zones, and subsequent studies may reflect further improvement in outcomes.

17.5.3 Improvement in Menstrual Bleeding

The majority of patients who have undergone lap-RFA, T-RFA, UAE, and MRgFUS have reported an improvement of heavy menstrual bleeding by 3 months post-procedure. By 12 months, 81.9% of lap-RFA, 95% of T-RFA, and 82%–90% of UAE patients reported a reduction in menstrual bleeding (7, 8, 21, 37). At 12 months following MRgFUS, patients reported, on average, a decrease in menstrual bleeding by 50% (38).

17.5.4 Reintervention Rate

The reintervention rates between RFA and UAE are comparable to traditional approaches, while MRgFUS appears to have the highest rate of the alternative procedures. The reintervention rates up to 36 months are summarized in Table 17.2.

The rate of major adverse events is low with reported rates of 1.78%–3.7% for lap-RFA, 1.4% for T-RFA, 4% for UAE, and 0.2% for MRgFUS, all of which are comparable to traditional fibroid treatment approaches (7, 8, 11, 39, 41).

17.6 Conclusion

RFA, UAE, and MRgFUS provide patients with minimally invasive, uterine-sparing alternative treatments for symptomatic uterine fibroids. These alternative treatments improve quality of life, with high levels of patient satisfaction and low rates of adverse events, comparable to traditional treatment methods. Due to their relative novelty, there is limited data to make concrete fertility recommendations following these procedures, although outcomes are promising. There are few studies that directly compare these treatment modalities, and additional prospective trials are needed to conclude which modality is the most effective.

References

* Denotes key reference

1. Lee BB et al. Radiofrequency ablation of uterine fibroids: a review. *Curr Obstet Gynecol Rep*. 2016;5(4):318–324.
2. American College of Obstetricians and Gynecologists (ACOG). Management of symptomatic uterine leiomyomas. ACOG practice bulletin 228. *Obstet Gynecol*. 2021;137(6):e100–e115.
3. Acessa System Clinical Compendium [Internet]. *Hologic*. Available at: https://hologiced.com/wp-content/uploads/2022/07/Clinical-Compendium.pdf (Accessed Apr 2023).
4. *Bradley LD et al. Clinical performance of radiofrequency ablation for treatment of uterine fibroids: systematic review and meta-analysis of prospective studies. *J Laparoendosc Adv Surg Tech A*. 2019;29(12):1507–1517.
5. Sonata system 2.2 instructions for use. Manual document number REF-009, LS 03818-009 [Internet]. *Gynesonics*. Available at: https://gynesonics.appdataroom.com/download/v/2016ae2466e85e9ff4a8b0e082cb19d9aa5ed091736758?source=media_manager&shared=20230614192909 (Accessed Apr 2023).
6. Christoffel L et al. Transcervical radiofrequency ablation of uterine fibroids global registry (SAGE): study protocol and preliminary results. *Med Devices*. 2021;15;14:85.
7. *Lukes A et al. Three-year results of the SONATA pivotal trial of transcervical fibroid ablation for symptomatic uterine myomata. *J Gynecol Surg*. 2020;36(5):228–233.
8. *Chudnoff SG et al. Outpatient procedure for the treatment and relief of symptomatic uterine myomas. *Obstet Gynecol*. 2013;121(5):1075–1082.
9. Kohi MP et al. Updates on uterine artery embolization. *Semin Intervent Radiol*. 2018;35(1):48–55.
10. Orons, P. MRI pelvis and digital subtraction angiography images during uterine artery embolization procedure. *UPMC Magee Womens-Hospital Imaging*, 2017.
11. *Gupta JK et al. Uterine artery embolization for symptomatic uterine fibroids. *Cochrane Database Syst Rev*. 2014;(12):CD005073.
12. *Summary of Safety and Effectiveness Data. Magnetic Resonance Guided Focused Ultrasound Surgery System: ExAblate 2000* [Internet]. Tirat-Carmel, Israel: InSightec, Ltd. Available at: www.accessdata.fda.gov/cdrh_docs/pdf4/P040003B.pdf.
13. Hesley GK et al. MR-guided focused ultrasound for the treatment of uterine fibroids. *Cardiovasc Intervent Radiol*. 2013;36(1):5–13.
14. Hesley GK et al. Noninvasive treatment of uterine fibroids: early mayo clinic experience with magnetic resonance imaging-guided focused ultrasound. *Mayo Clinic Proceedings*. 2006;81(7):396–942.
15. Smeets AJ et al. Safety and effectiveness of uterine artery embolization in patients with pedunculated fibroids. *J Vasc Interv Radiol*. 2009;20(9):1172–1175.
16. *Polin M et al. Radiofrequency ablation of uterine myomas and pregnancy outcomes: an updated review of the literature. *J Minim Invasive Gynecol*. 2022;29(6):709–715.

17. *Akhatova A et al. Reproductive and obstetric outcomes after UAE, HIFU, and TFA of uterine fibroids: systematic review and meta-analysis. *Int J Environ Res Public Health*. 2023;20(5):4480.
18. Lee SJ et al. Uterine artery embolization for symptomatic fibroids in postmenopausal women. *Clin Imaging*. 2016;40(01):106–109.
19. Kim YS et al. Uterine artery embolization for pedunculated subserosal leiomyomas: evidence of safety and efficacy. *J Vasc Interv Radiol*. 2018;29(4):497–501.
20. Smeets AJ et al. Uterine artery embolization in patients with a large fibroid burden: long-term clinical and MR follow-up. *Cardiovasc Intervent Radiol*. 2010;33(5):943–948.
21. Walker WJ et al. Pregnancy after uterine artery embolization for leiomyomata: a series of 56 completed pregnancies. *Am J Obstet Gynecol*. 2006;195:1266–1271.
22. Ludwig PE et al. Pregnancy success and outcomes after uterine fibroid embolization: updated review of published literature. *Br J Radiol*. 2020;93(1105):20190551.
23. Tropeano G et al. Long-term effects of uterine fibroid embolization on ovarian reserve: a prospective cohort study. *Fertil Steril*. 2010;94:2296–2300.
24. Shamy TE et al. The impact of uterine artery embilization on ovarian reserve: a systematic review and meta-analysis. *Acta Obstet Gynecol Scand*. 2019;99(1):16–23.
25. Spies J *et al*. The FIBROID Registry: symptom and quality-of-life status 1 year after therapy. *Obstet Gynaecol*. 2005; 106:1309–1318.
26. Napoli A et al. Uterine myomas: focused ultrasound surgery. *Semin Ultrasound CT MR*. 2021;42(1):25–36.
27. Smart OC et al. Gonadotrophin-releasing hormone and magnetic-resonance-guided ultrasound surgery for uterine leiomyomata. *Obstet Gynecol*. 2006;108:49–54.
28. Otonkoski S et al. Magnetic resonance guided high intensity focused ultrasound for uterine fibroids and adenomyosis has no effect on ovarian reserve. *Int J Hyperthermia*. 2023;40(1):2154575.
29. Rajan DK et al. Clinical utility of ultrasound versus magnetic resonance imaging for deciding to proceed with uterine artery embolization for presumed symptomatic fibroids. *Clin Radiol*. 2011;66(1):57–62.
30. *Berman J et al. Three years' outcome from the halt trial: a prospective analysis of radiofrequency volumetric thermal ablation of myomas. *J Minimal Invas Gynecol*. 2014;21(6).
31. Goodwin SC et al. Uterine artery embolization for treatment of leiomyomata: long-term outcomes from the FIBROID Registry. *Obstet Gynecol*. 2008;111(1):22–33.
32. *Manyonda I et al. FEMME Collaborative Group. Uterine-artery embolization or myomectomy for uterine fibroids. *N Engl J Med*. 2020;383(5):440–451.
33. Daniels J et al. On Behalf of the Femme Trial Collaborative Group. Uterine artery embolization or myomectomy for women with uterine fibroids: four-year follow-up of a randomised controlled trial. *Eur J Obstet Gynecol Reprod Biol X*. 2021;13:100139.
34. *Laughlin-Tommaso B et al. FIRSTT study: randomized controlled trial of uterine artery embolization vs focused ultrasound surgery. *Am J Obstet Gynecol*. 2019;220(2):174.e1–174.e13.
35. Taheri M et al. Nonresective treatments for uterine fibroids: a systematic review of uterine and fibroid volume reductions. *Int J Hyperthermia*. 2019;36(1):295–301.
36. Yerezhepbayeva M et al. Comparison of two invasive non-surgical treatment options for uterine myomas: uterine artery embolization and magnetic resonance guided high intensity focused ultrasound-systematic review. *BMC Womens Health*. 2022;22(1):55.
37. Spies JB et al. Uterine artery embolization for leiomyomata. *Obstet Gynecol*. 2001;98(1):29–34.
38. Huang Y et al. Efficacy and safety of magnetic resonance-guided focused ultrasound surgery ablation in the management of abnormal uterine bleeding due to uterine leiomyoma or adenomyosis. *Am J Transl Res*. 2022;14(1):656–663.
39. Sandberg EM et al. Reintervention risk and quality of life outcomes after uterine-sparing interventions for fibroids: a systematic review and meta-analysis. *Fertil Steril*. 2018;109(4).
40. Lin L et al. Quality of life, adverse events, and reintervention outcomes after laparoscopic radiofrequency ablation for symptomatic uterine fibroids: a meta-analysis. *J Minim Invasive Gynecol*. 2019;26(3):409–416.
41. Xu F et al. The comparison of myomectomy, UAE and MRgFUS in the treatment of uterine fibroids: a meta analysis. *Int J Hyperthermia*. 2021;38(2):24–29.

18 EVALUATION AND MANAGEMENT OF CHRONIC PELVIC PAIN

Erin T. Carey and Asha McClurg

18.1 Introduction

Chronic pelvic pain (CPP) is defined as intermittent or continuous pain from the pelvis or perceived to be from the pelvis, for at least 6 months not exclusively with menstruation or intercourse. CPP affects up to 26% of women worldwide, with the United States prevalence estimated at 15% of reproductive age women (1, 2). The annual costs for CPP evaluation and management, including office visits, emergency visits, medications, surgical interventions, and hospital admissions, was estimated at $2.8 billion in 1996, adjusted to approximately $5.8 billion annually in 2020 (1, 3).

Chronic pelvic pain can arise from various system-based etiologies involving the reproductive, gastrointestinal, genitourinary, and musculoskeletal systems. Conditions such as endometriosis, pelvic inflammatory disease, irritable bowel syndrome, interstitial cystitis/painful bladder syndrome, and musculoskeletal disorders can contribute to the development of chronic pelvic pain. Understanding the underlying system-based etiologies is essential for accurate diagnosis and tailored treatment approaches to address the specific contributing factors (Table 18.1).

18.2 Pathophysiology of CPP

The etiology of chronic pelvic pain is not fully understood. Current evidence suggests it is a complex and varied condition influenced by numerous factors with multiple potential etiologies and co-contributors. Patients experiencing CPP may also exhibit symptoms consistent with bladder pain syndrome or functional bowel pain absent of observable pathology, rather secondary to neural cross-signaling between neighboring pelvic structures. This cross-signaling, also known as cross-sensitization, refers to a phenomenon in which pain in one area of the body can sensitize or increase sensitivity to pain in another area (4). In the context of the pelvis, cross-sensitization occurs through various mechanisms involving the nervous system. The viscera has unique qualities, including its ability to radiate pain to remote regions. This occurs because the nerves responsible for transmitting visceral and somatic sensations converge within the spinal cord and higher centers of the central nervous system. The convergence of neural pathways in the pelvis is primed for abnormal, shared pathways between visceral structures (such as reproductive organs, bladder, and bowel) and somatic structures (like the skin, muscles, fascia, and bones) given the innervation structure (Figure 18.1).

The complex network that innervates the female pelvis provides both sensory and motor functions. The pelvic nerves are branches of the sacral plexus, formed by the spinal nerves originating from the sacral region of the spinal cord (S2–S4). These provide visceral innervation to the pelvic organs, including the uterus, vagina, bladder, and rectum, and also supply somatic innervation to the pelvic floor muscles (5). The pudendal nerve is a major nerve arising from the sacral plexus, traveling through the pelvis and innervating the external genitalia, including the clitoris, labia, perineum, and lower part of the vagina. The pudendal nerve also plays a role in controlling the muscles of the pelvic floor and contributes to sexual function. Sympathetic innervation of the pelvic organs, including the uterus, bladder, and rectum, are provided by the hypogastric nerves. They are involved in regulating functions such as blood flow, secretion, and smooth muscle contraction. Parasympathetic nerves from the sacral spinal cord (S2–S4) contribute to the autonomic innervation of the pelvic organs, controlling functions such as digestion, urination, and sexual arousal (5). Together this neural network works to provide sensory perception, motor control, and autonomic regulation of the pelvic organs and associated structures.

TABLE 18.1 System-Based Etiology of CPP

Psychological	Neurological	Musculoskeletal	Gastrointestinal	Genitourinary	Gynecologic	Integumentary
• Anxiety • Depression • Trauma • Somatization • Catastrophization	• Vuluodyrua • Pudendal • Neuralgia • Peripheral neuropathy • Small fiber neuropathy	• Myofascial pain • Tender points • Fibromyalgia • Chronic low back pain • Sacroiliac joint dysfunction • Face arthropathy • Tendonitis • Piriformis syndrome	• Irritable bowel syndrome • Inflammatory bowel disease • Chronic constipation/ outlet constipation • Diarrhea • Chronic anal fissures	• Bladder pain syndrome/ interstitial cystitis • Overactive bladder • Bladder spasms Recurrent urinary tract infections • Nephrolithiasis	• Primary dysmenorrhea • Endometriosis • Ovarian cysts • Adenomyosis • Fibroids • Genitourinary syndrome of menopause • Vaginismus • Vaginitis • Pelvic congestion syndrome • Pelvic inflammatory disease	• Lichen sclerosus • Lichen planus • Herpes simplex • Herpes zoster • Lichen simplex chronicus

* Disclosures: ETC provides expert witness testimony. She reports grant funding from the Eunice Kennedy Shriver National Institute of Child Health and Human Development and the North Carolina Collaboratory. ABM has no disclosures.

DOI: 10.1201/9781003312109-18

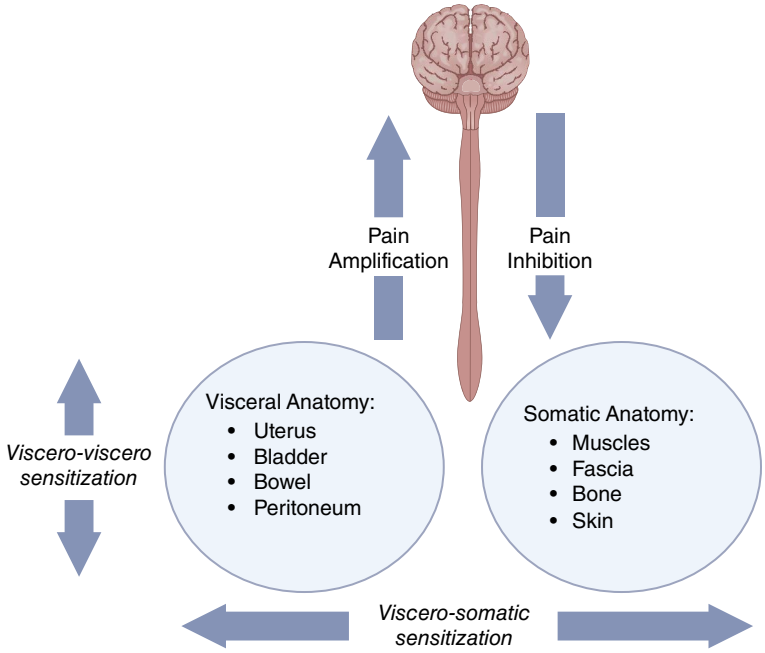


FIGURE 18.1 Viscero-viscero and viscero-somatic neural convergence pathways.

Apart from the innervation pathways, pain perception can be influenced by psychological and emotional factors, including stress, anxiety, and depression. These factors have the ability to interact with the nervous system and impact the way pain signals are processed, further confounding the clinical presentation.

18.3 Chronic Overlapping Pain Conditions

There is growing recognition that many common chronic pain conditions frequently coexist with other pain conditions, influenced by biological, psychological, and social factors that shape an individual's pain experience. The substantial overlap of these prevalent pain conditions is frequently overlooked in clinical care. Failing to recognize or screen for these cormorbid conditions may result in suboptimal treatment outcomes and persistent suffering for patients. When caring for patients with multiple chronic overlapping pain conditions (COPCs), one must consider all pain contributors in the clinical presentation to optimize pain management (Table 18.2) (6).

TABLE 18.2 Chronic Overlapping Pain Conditions

Chronic Low Back Pain
Chronic Migraine Headache
Chronic Tension-Type Headache
Endometriosis
Fibromyalgia
Interstitial Cystitis/Painful Bladder Syndrome
Irritable Bowel Syndrome
Myalgic Encephalomyelitis/Chronic Fatigue Syndrome
Temporomandibular Disorders
Vulvodynia

18.4 Trauma-Informed Care

Trauma-informed care is an approach to healthcare that recognizes and responds to the impact of trauma on an individual's physical, mental, and emotional well-being. It involves creating an environment that is sensitive, supportive, and empowering for individuals who have experienced trauma, aiming to promote their healing and resilience. Patients with chronic pelvic pain are significantly more likely to have experienced trauma and carry a diagnosis of posttraumatic stress disorder (7). Key components of providing trauma-informed care include informed consent, communication, patient choice, empowerment, privacy, comfort, and collaboration throughout the visit and exam to enhance their sense of safety.

Trauma survivors may have heightened sensitivity to touch, sounds, or sensations. The healthcare provider should aim to minimize potential triggers. Explaining each step before proceeding, using gentle touch, and allowing the patient to communicate any discomfort are fundamental components of the visit. Incorporating mind-body techniques, such as deep breathing exercises or guided imagery, can help patients manage any distress they may experience. After the visit, resources should be provided, such as information on counseling services or support groups, to address any ongoing emotional or psychological needs the patient may have. Ensuring the patient feels supported and cared for after the exam is an essential aspect of trauma-informed practice.

It is important to note that trauma-informed care is highly individualized, and specific approaches may vary depending on the patient's needs and preferences. By incorporating these trauma-informed practices, healthcare providers aim to create a safe and empowering environment for survivors of trauma during sensitive exams, including routine and focused pelvic exams.

18.5 Evaluation

A detailed patient history is essential in identifying a primary diagnosis in chronic pelvic pain along with overlapping chronic pain conditions. Obtaining a comprehensive chronic pain history under the time restraints of clinical care can be challenging, and allocating adequate time for complex pain patients is helpful. This may require scheduling a longer initial visit or utilizing multiple return visits at planned intervals. Extended clinical time is not only required for patient interview and details examination but is also essential for patient education and achieving collaboration on a patient-centered treatment plan.

Pain history should routinely include the onset, duration, chronicity, relationship to menses, variations in severity, aggravating and alleviating factors, quality, and location. A chronological timeline of these pain symptoms can elucidate the evolution of pain symptoms. Review of prior medications, procedures, and surgical interventions for pain and the relief or lack thereof with each will further narrow the primary diagnosis and overlapping contributors of pain and identify potential treatment gaps or unmet needs. A thorough social history including details on family dynamics, relationship, and employment status provides essential insight into the influence of psychosocial factors on a patient's pain experience and is key to developing a successful treatment plan. A sexual history should review components of dyspareunia including presence or absence of pain with external touch, insertion, deep penetration, arousal, orgasm, and the impact of positional changes on symptoms. Initial time of dyspareunia onset is also relevant, as well as pain with nonsexual touch including tampon placement, tight clothing, and particular activities. Use of a pain-focused intake form or validated pain questionnaires for the assessment of complex pain patients in advance of their scheduled appointment can be helpful in organizing and guiding a pain history. Such forms created by the International Pelvic Pain Society can be helpful (8).

Detailed physical examination is key to diagnosis in chronic pelvic pain and requires a transparent, gentle, and patient-centered approach utilizing trauma-informed care. Patients may have a history of trauma ranging from remote events to ongoing exposure, and gynecologic examination can be anxiety-provoking or triggering for or those with trauma histories. Patients with CPP have more than three times the odds of having a history of childhood abuse or witnessing domestic violence compared with patients without CPP (9). Given the high prevalence of trauma, examination of patients with chronic pelvic pain should be performed systematically, with a trauma-informed approach. The patient should be supported through the creation of a safe and calm environment. The patient should be encouraged to voice their needs during examination, and they must be informed that the exam can and should be paused or terminated for any reason at their request and that they should feel empowered to do so. Patients may choose the timing of exam and may prefer a future visit when greater patient-provider rapport has been developed. The provider should provide a detailed outline of what to expect throughout the examination including order of examination and use of digital touch or instruments such as a speculum or swab. A medical chaperone should be present during sensitive parts of an exam, and a patient may also prefer to have a support person present. Thoughtful language during the exam is critical, including gender-neutral language, with specific attention to historical, cultural, and gender issues, and triggering words and phrases such as "relax" or "take a deep breath" should be avoided. Creating and practicing a verbal script for this exam can help to avoid triggering language and create a safe environment.

The comprehensive physical is initiated with an inspection of the patient's gait and leg lengths for significant asymmetry. This is followed by the back and abdomen. These components of the exam can be performed with the patient fully dressed, with careful draping if clothing is manipulated for skin or scar evaluation and should be completed first as they are typically felt to be less invasive by the patient. When a pelvic exam is indicated, providers should leave the room to allow privacy while patients disrobe and dress. The patient's body should be covered throughout the pelvic exam, exposing only those areas as necessary and for the shortest time required. The patient is asked to move to the edge of the examination table and place their legs in the footrests or in a frog-leg position.

The evaluation of pelvic pain should begin with careful visual inspection of the external genitalia to evaluate for atrophy, lesions, fissures, or abnormal discharge. When patients describe vulvar complaints, a single lubricated cotton swab is serially applied to the labia majora, prepuce, clitoris, interlabial sulci, labia minora, and the vulvar vestibule in a semicircle from lateral to the urethra to the posterior fourchette. With each point of touch, the patient is asked to grade their pain response using the 0–10 visual assessment scale (VAS). A verbal pause to inquire about patient tolerability should be completed before proceeding with an internal exam.

The internal exam is initiated by inserting a single gloved and lubricated digit into the vagina. The urethra, bladder neck, and bladder are gently palpated, evaluating for pain or pressure and helping to identify overlapping urinary etiologies of pain. Examination of the pelvic floor follows by asking the patient to contract and release their pelvic floor muscles to assess for asymmetry, increased tension or limited mobility, or even paradoxical relaxation. The superficial transverse perineal muscle is palpable at the vaginal opening under the hymenal remnant, followed by evaluation of the levator ani muscles (puborectalis and pubococcygeus) at the 5 and 7 o'clock positions approximately 3–5 cm inside the vagina on the posterolateral vaginal walls. The obturator internus is also palpable, hooking the digit around the pubic rami and having the patient abduct their knee against the examiner's external hand, engaging the obturator internus. This is then repeated on the contralateral side. If patients describe pain predominantly on one side, initiate the exam on the contralateral side from their pain. When applying pressure to the pelvic floor muscles a gentle but firm pressure should be applied (approximately 2 kg of force); presence of tenderness to palpation of the pelvic floor is an abnormal finding.

A speculum exam may be performed when visualizing the vagina and cervix is indicated, and verbal pause should again be undertaken to assess patient tolerance. Following gentle placement and the opening of the speculum, a cotton swab is utilized to examine for pressure point tenderness along the vagina, cervix, or vaginal cuff in the setting of a prior hysterectomy. The bimanual exam is appropriate when deeper palpation of the pelvis is required. The uterine shape, mobility, and presence of tenderness can be assessed, and the parametria and adnexa can be palpated for tenderness or masses. A rectovaginal exam may be performed to assess for deep infiltrating endometriosis and rectovaginal nodules or uterosacral ligament disease.

18.6 Diagnostic Testing

Diagnostic testing for chronic pelvic pain includes both laboratory evaluation and diagnostic imaging. Laboratory workup may include a pregnancy test for patients of reproductive age, swab testing for vaginitis or sexually transmitted infection, and urinalysis and urine culture for urinary symptoms. Vulvar biopsy may be indicated if an abnormality is found on visual inspection of the vulva. Endometrial biopsy should be collected for chronic abnormal uterine bleeding, particularly for those with increased risk factors such as age > 45 years, obesity, and diabetes (10).

Imaging is helpful in both evaluating chronic pelvic pain and assessing pain exacerbation. Pelvic ultrasonography is the primary modality given its ability to evaluate multiple gynecologic causes of pelvic pain (including uterine pathology – adenomyosis, fibroids, polyps, ovarian pathology and cysts, endometriosis, and pelvic congestion syndrome). Transvaginal ultrasonography has improved detail and accuracy for evaluating the ovary for pathology. While a normal pelvic exam paired with normal pelvic ultrasound is reassuring, it does not eliminate the possibility of a primary pelvic pain etiology such as endometriosis. Magnetic resonance imaging can be helpful in evaluating some causes of chronic pelvic pain, including deep infiltrating endometriosis, adenomyosis, and uterine fibroids, but it may have a limited benefit when pelvic ultrasound is unremarkable.

18.7 Psychological Assessment

Patients with CPP have a higher risk of comorbid psychologic conditions with up to 50% reporting moderate to severe anxiety and 25% with moderate to severe depression (11). In addition to anxiety and depression, patients with chronic pelvic pain may also present with maladaptive coping mechanisms such as pain catastrophizing. Psychological assessment can be performed through patient interviews or via use of standardized psychological questionnaires. This is helpful to determine if additional psychological interventions including collaboration with a psychiatric provider, pharmacologic treatment of anxiety or depression, or cognitive behavioral therapy may be beneficial as a part of the comprehensive care plan.

Evaluation of the patient with chronic pelvic pain should conclude by eliciting the patient's treatment goals, expectations, and preferences. Creating a shared understanding of their goals is the foundation for a successful patient-centered treatment plan. Patients may have an already prolonged course with chronic pelvic pain that informs their expectations. The provider should explore the patient's experience with prior treatments and understand the patient's willingness to try new treatment modalities or retrial prior interventions. Discussion of time interval before expected change in symptoms and understanding of patient comfort with treatment risks and side effects should inform the recommended interventions.

18.8 Treatment

Building a multidisciplinary care team for patients with chronic pelvic pain involves assembling a group of healthcare professionals from different specialties to address the various aspects of the condition in a collaborative and complementary fashion. The core specialties that are typically involved in the management of chronic pelvic pain include gynecology, urology, gastrointestinal medicine, pain medicine, physical therapy, psychology/psychiatry, and possibly others depending on the specific needs of the patient.

In complex patients with multiple pain conditions, the designation of a team leader or care coordinator to oversee the patient's care and ensure all healthcare providers are working together towards a common treatment plan may increase satisfaction. Regardless of the exact approach, the development of personalized treatment plans based on the patient's specific needs, symptoms, and goals is necessary. Understandably, the composition and structure of a multidisciplinary care team will look different across teams and will vary based on local resources, healthcare system capabilities, and patient needs. Collaborating with experts in the field of chronic pelvic pain and considering existing guidelines or recommendations can help inform the development of an effective multidisciplinary care team.

18.9 Goal Setting

Goal setting can be an essential component of an effective pain management strategy, as it provides a clear direction for both the healthcare provider and the patient. While complete resolution of pain may not always be achievable, breaking the overall goal into smaller, attainable targets fosters a sense of progress and increases satisfaction for both parties involved. The primary focus shifts towards reducing the burden of symptoms and enhancing the overall quality of life.

Achievable goals may include increasing the duration of pain-free or reduced-pain intervals, incorporating behavioral response tools to enhance pain-coping mechanisms, and focusing on increasing functionality for a specific activity. Each patient's goals should be individualized to their unique circumstances and preferences, ensuring that their treatment plan aligns with their specific needs and aspirations. By setting clear objectives, collaborating with a diverse team of healthcare professionals, and tailoring interventions to the individual patient, the goals of pain management can enhance quality of life and greater satisfaction for both the provider and the patient.

Goal setting can conflict with the ability to achieve certain life goals set before chronic pain interference and therefore the concept of goal adjustment may be required for preexisting goals (i.e., college, career, family, etc.), depending on the individual patient. To adjust a goal, both effort towards the goal and commitment to the goal must be modified. These theoretical concepts relate specifically to adjusting life goals, factoring in the experiences of chronic pain in real time, and may be necessary depending on the patient and their personal pain experience (7).

Finally, the biopsychosocial model of pain should be introduced to the patient early in the treatment course. In addition to the biological factors, such as tissue damage or inflammation, pain management should consider the impact of sleep, mood, and environmental factors on pain experience.

18.10 Nonpharmacologic Treatments for CPP

18.10.1 Lifestyle Modifications

Lifestyle modifications play a crucial role in the management of chronic pelvic pain, offering patients the opportunity

to reduce symptom severity, improve overall well-being, and enhance their quality of life.

18.10.2 Diet

The importance of nutrition in preventing and treating various diseases is widely acknowledged. Although gastrointestinal symptoms and food intolerances are frequently associated with CPP, there is limited evidence to support the effectiveness of dietary changes in providing significant symptom relief. One dietary approach that has shown promise in patients with irritable bowel syndrome (IBS) is the restriction of low fermentable oligosaccharides, disaccharides, monosaccharides, and polyols (FODMAPs). These are carbohydrates present in a variety of foods, such as garlic, onions, legumes, wheat, and berries, which can be challenging to digest. Restricting FODMAP intake has been found to alleviate symptoms in patients with IBS (12, 13).

While endometriosis pain has the most extensive research data in the realm of nutrition and chronic pelvic pain in women, still only a limited body of data is available. Compared to women who follow lower inflammatory diets, those who consume diets with high inflammatory potential (red meat, ham, dairy, and trans-unsaturated fatty acids) have a significantly higher likelihood of developing endometriosis (14). Among various supplements, polyunsaturated fatty acids (PUFAs) have garnered extensive research attention, with numerous studies examining their role in endometriosis pathogenesis, symptom management, and treatment outcomes. A systematic review and meta-analysis showed a protective effect of omega-3 PUFAs supplementation in several chronic pain disorders and dysmenorrhea (15).

Chronic widespread musculoskeletal pain has been associated with changes in the gut microbiome, while low levels of vitamin D have been correlated with higher pain scores in different pain conditions. Vitamin D3 supplementation (cholecalciferol) has demonstrated potential in improving pain outcomes for fibromyalgia (16); however, its effectiveness in treating CPP secondary to endometriosis has not been replicated in research studies thus far.

18.11 Physical Activity and Exercise

Engaging in skeletal muscle movement to expend energy beyond resting levels has long been advocated for its potential benefits on pain management and overall health. In the context of patients with CPP, exercise has been linked to stress reduction and improvements in pain scores (13). In men, high levels of physical activity are associated with a lower risk of developing CPP compared to their sedentary counterparts (17). However, it is important to note that few studies in this area have directly explored the role of physical activity in women with CPP, which prevents drawing definitive conclusions from the available data.

18.11.1 Sleep

Sleep disturbances can exacerbate pain perception and impede the healing process, making it critical to address and improve sleep quality as part of the treatment plan. In fact, increasingly sleep disturbances have been recognized as a possible therapeutic target for a range of chronic conditions, including chronic pain (18). Among individuals with chronic pain, disrupted sleep reduces the body's natural pain inhibitory system, leading to alterations in the hypothalamic–pituitary–adrenal axis, and can trigger abnormal inflammatory responses (19). Women with CPP are more likely to experience poor sleep quality compared to controls without CPP (20). While there are limited data regarding sleep interventions in chronic pelvic pain, when left untreated, insomnia is considered a barrier for effective chronic pain management in other chronic pain disorders (21).

18.11.2 Pain Psychology

Mood and emotional well-being have a significant influence on pain perception and recovery. Managing mood disorders, such as anxiety and depression, can positively impact pain management outcomes (22). Additionally, promoting positive emotional states and providing appropriate psychological support can enhance pain coping mechanisms and overall well-being. Therapies including cognitive behavioral therapy (CBT) and self-modulation behavior therapy play fundamental roles in the management of chronic pain by addressing the interplay between thoughts, emotions, and behaviors. CBT is an evidence-based psychological intervention that identifies and modifies maladaptive thoughts and behaviors associated with pain, ultimately promoting improved coping strategies and overall well-being. Also known as "unguided CBT," self-modulation behavior therapy has similar goals to enhance self-efficacy and self-control over pain symptoms. Key components in both therapies involve self- monitoring (tracking symptoms, identifying triggers and factors that worsen or alleviate their pain), relaxation techniques to reduce muscle tension and anxiety (deep breathing, muscle relaxation, and guided imagery), activity pacing, cognitive restructuring (challenging negative or unhelpful thoughts regarding pain and replacing them with more realistic and positive thoughts), and goal setting. While limited data exists specific to chronic pelvic pain, pain psychology interventions are a key element in managing chronic pain disorders (23).

18.11.3 Physical Therapy

Pelvic floor physical therapy (PFPT) directed to reduce symptoms associated with CPP is well supported in patients with a myofascial component of their pelvic pain profile (13, 24). In addition to promoting physical activity and exercise, physical therapy incorporates relaxation, deep breathing, and meditation techniques, aiming to provide both physical and psychological benefits. Pelvic floor physical therapy programs usually involve weekly sessions over a duration of 8 to 12 weeks, followed by transitioning to a maintenance home exercise program.

18.11.4 Sexual Therapy

Sexual therapy plays a valuable role in patients with chronic pelvic pain by addressing the psychological and interpersonal aspects of their chronic condition. CPP can significantly impact a person's sexual well-being, leading to sexual dysfunction, decreased desire, and relationship strain (25). Sexual therapy aims to improve sexual functioning, reduce pain during intercourse, and enhance overall sexual satisfaction. Therapists may use various techniques such as CBT, education about pain and sexuality, communication exercises, and sensate focus exercises to help patients manage pain, alleviate anxiety, improve body image, and enhance intimacy. By addressing the sexual and emotional aspects of chronic pelvic pain, sexual therapy can contribute to the holistic management of the condition and improve the overall quality of life for patients.

18.11.5 Acupuncture

Acupuncture is an ancient therapeutic technique that involves the insertion of thin needles into specific points on the body to effect a systemic physiologic response. The mechanism of action is multifold, though its pain modulation effect is thought to be through the release of endogenous opioids that influence the transmission of pain signals in the central nervous system, helping to reduce pain perception. It has been used for centuries in traditional Chinese medicine and is gaining recognition as a complementary therapy for various health conditions, including CPP. While some studies suggest that acupuncture may be effective in reducing pain and improving quality of life in CPP, the evidence is still limited, and more research is needed to establish its efficacy and determine the optimal treatment protocols (26). In combination with conventional treatment, acupuncture improves pain outcomes in women with CPP (26).

18.11.6 Pharmacologic Treatments for CPP

Assessing patients for the appropriateness of medical management for CPP involves the previously described comprehensive evaluation to determine the underlying causes, contributing factors, and individual patient characteristics. Based on the assessment findings, the treatment plan can be built and may include pharmacological interventions (such as analgesics, hormonal therapies, and neuromodulators), targeted interventions (such as nerve blocks and tender point injections), and referral to specialized services (such as pelvic floor physical therapy and pain management clinics). Each pain program is individualized and based on best practices, incorporating shared decision making that is guided by the patient's preferences, coexisting conditions, and potential treatment interactions. Regular reassessment and close follow-up with the patient are essential to evaluate the effectiveness of medical management and make necessary adjustments to the treatment plan.

18.12 Analgesics

18.12.1 Acetaminophen

The mechanism of action of acetaminophen is not fully understood. It is believed to primarily inhibit the synthesis of prostaglandins in the central nervous system by blocking the enzyme cyclooxygenase (COX), but its exact mode of action is still under investigation. Unlike nonsteroidal anti-inflammatory drugs, acetaminophen has minimal anti-inflammatory effects and primarily functions as an analgesic and antipyretic.

Acetaminophen, known for its ability to enhance the effectiveness of other analgesic medications, achieves this by inhibiting the synthesis of central prostaglandins. While it is not typically a potent pain reliever on its own, combining it with other analgesics can lead to improved pain outcomes.

18.13 Nonsteroidal Anti-Inflammatory Drugs (NSAIDs)

NSAIDs, such as ibuprofen, naproxen, and diclofenac, are commonly used for their analgesic and anti-inflammatory properties. Their primary pharmacological effects are through the inhibition of COX, responsible to produce prostaglandins, inflammatory mediators involved in pain, inflammation, and fever. Traditional NSAIDs inhibit both COX-1 and COX-2 enzymes, while selective COX-2 inhibitors primarily target COX-2. By selectively inhibiting COX-2, these medications aim to minimize gastrointestinal risk associated with inhibiting COX-1, which is involved in maintaining the protective lining of the stomach (27). Long-term daily use of NSAID therapy is not recommended, but they can be included as an important component of pain flare plans or menstrual-related pain.

18.13.1 Opioids

The stigma surrounding opioid use for chronic pain often stems from concerns of addiction, misuse, and societal judgment. Individuals with chronic pain may face challenges in accessing adequate pain management due to the fear of being labeled as drug-seeking or the assumption that opioid use equates to addiction. The efficacy of opioids in chronic pain refractory to other treatments varies and should be carefully assessed on an individual basis, considering potential risks and benefits. The Centers for Disease Control and Prevention (CDC) guidelines for the use of opioids in the treatment of chronic pain recommend that other than malignancy or palliative care, opioids should not be considered first-line therapy (28). The CDC guidelines emphasize use of concurrent nonopioid medications for pain, regular assessment of pain and function, and strict guidance with avoiding the use of opioids and benzodiazepines concomitantly. Opioids carry the risk of tolerance, dependence, and potential side effects, therefore the current recommendations for its routine use in CPP is limited.

18.13.2 Hormonal Therapy

When gynecologic pain is considered a primary or contributing pain component, patients with CPP may benefit from menstrual suppression. Combined low-estrogenic, oral contraceptives are routinely used as first-line hormonal treatment for dysmenorrhea, adenomyosis, and endometriosis associated pain (29). Transitioning from cyclic to continuous monophasic active pills may be effective in dysmenorrhea management but is less effective in treating noncyclic pelvic pain and dyspareunia. Oral progestin-only treatment is recently considered first-line medical treatment for endometriosis-associated pain, and there is increasing data supporting oral gonadotropin-releasing hormone (GnRH) antagonists as reasonable second-line treatment for endometriosis-associated pain (30).

Similar to endometriosis, adenomyosis shares several clinical features and has a negative impact on women's quality of life secondary to abnormal uterine bleeding and pain. Medical management of adenomyosis is also progestin therapy, either local treatment with a levonorgestrel intrauterine system or systemic progestin therapy (31). Hormonal suppression with both progestins and GnRH agonists are also effective in decreasing pain symptoms in patients with suspicion for or diagnosis of pelvic congestion syndrome (32).

18.13.3 Antidepressants

Antidepressants modulate chronic pain through various physiological mechanisms, including their ability to alter neurotransmitter levels, particularly the inhibition of serotonin and norepinephrine reuptake in the central nervous system, which can influence pain perception and enhance inhibitory pain control. Additionally, antidepressants may also have anti-inflammatory effects and impact the functioning of descending pain pathways, leading to pain relief in some individuals with chronic pain. Limited evidence exists regarding the pain-relieving effects of these medications in individuals with visceral pain syndromes or CPP (33). While CPP is not exclusively

classified as a neuropathic pain disorder, the neuromodulatory effect of these medications, along with their impact on concurrent psychiatric conditions when present, may provide additional benefits.

Serotonin norepinephrine reuptake inhibitors (SNRI), such as duloxetine and venlafaxine, increase the available amount of norepinephrine and serotonin through the aforementioned mechanisms, which appears to decrease pain sensitivity in chronic pain conditions (34). SNRIs are generally well tolerated with few side effects as well as effective for the treatment of depression and anxiety, making it a good option for patients with comorbid psychiatric disorders. Duloxetine is FDA-approved for treatment of several chronic pain conditions, including fibromyalgia, chronic low back pain, and neuropathic pain. Similarly, milnacipram is approved for fibromyalgia and venlafaxine for neuropathic pain (35). Despite the evidence in other pain disorders, there is no available data for SNRIs in the treatment of CPP.

Tricyclic antidepressants (TCA), such as amitriptyline, nortriptyline, and desipramine, also increase the available amount of neurotransmitters norepinephrine and serotonin through similar mechanisms. While TCAs were primarily developed for the treatment of mood disorders, they have transitioned to off-label use for the pain management of chronic pain conditions (36). TCAs are frequently limited by significant anticholinergic side effects including sedation, drowsiness, dry mouth, and constipation. Data is limited in CPP, but one small study in 56 women with CPP noted that gabapentin alone or in combination with amitriptyline showed modest efficacy compared to amitriptyline alone (37).

18.13.4 Anticonvulsants

Anticonvulsant medications are commonly used in the management of neuropathic pain. They primarily target voltage-gated ion channels, particularly calcium and sodium channels, reducing neuronal excitability and dampening the transmission of pain signals. Additionally, anticonvulsants can modulate neurotransmitter release, augment inhibitory pathways, and exert anti-inflammatory effects, collectively contributing to their efficacy in pain management. The off-label use of gabapentin for the treatment of chronic pelvic pain is popular and may have some improvement in pain outcomes compared to baseline (38). Recently, however, a randomized double-blind placebo-controlled trial found no significant difference in pain reduction between gabapentin and placebo in patients with chronic pelvic pain, and women who took gabapentin experienced more serious adverse events compared to those on placebo (39). While gabapentin and pregabalin are often used interchangeably for chronic pelvic pain, there are no available data for pregabalin in the treatment of chronic pelvic pain.

18.13.5 Skeletal Muscle Relaxants

Skeletal muscle relaxants (SMRs) are widely prescribed in the United States. SMRs depress central nervous system activity, primarily targeting the spinal cord and brainstem. They exert their muscle-relaxing effects by enhancing the inhibitory neurotransmitter gamma-aminobutyric acid in the central nervous system, leading to decreased motor neuron activity and subsequently fewer muscle spasms. Additionally, some muscle relaxants have direct effects on skeletal muscle fibers, directly reducing muscle contractility and promoting relaxation.

While SMRs are not recommended as first-line treatment for myofascial pelvic pain, they can provide short-term pain relief for acute musculoskeletal pain (40). Despite high volume prescribing, there is limited data on long-term use. Prescribing patterns for SMRs among physicians in the United States from 2005 to 2016 showed that while new SMR prescriptions remained stable over time, the number of office visits where SMRs were refilled tripled from 2005 to 2016 (8.5–24.7 million visits), suggesting ongoing and long-term use (41). Two types of SMR exist – antispastic and antispasmodic relaxants. Antispastic agents target upper motor syndromes (e.g., multiple sclerosis, cerebral palsy, traumatic brain injury, spinal cord injury, and post-stroke syndrome) and have limited efficacy data in the treatment in musculoskeletal conditions, whereas antispasmodics are intended for peripheral muscle spasm. Among the various SMRs, cyclobenzaprine has been extensively studied and shown efficacy for musculoskeletal conditions, including pain relief in fibromyalgia (42). However, there are currently no specific data evaluating the use of SMRs in chronic pelvic pain, and the decision to use them should be based on individual factors, such as symptom severity, desired benefits, and potential side effects.

18.14 Cannabinoids

Medical cannabinoid therapy use for chronic pain is an ongoing area of study. Cannabis contains delta-9-tetrahydrocannabinol (THC) and cannabidiol (CBD), both which bind to endocannabinoid system receptors throughout the central and peripheral nervous system. The analgesic effect of cannabinoids is thought to be primarily neuropathic in nature resulting in the inhibition of neurotransmitter and neuropeptide release from presynaptic nerve endings, altering postsynaptic neuron excitability, activating the inhibitory pain pathways, and reducing neural inflammation. A systematic review of 11 randomized trials of various pain disorders (1219 patients) noted a statistically significant but small benefit of pain reduction by less than 1 point on a 0–10-point pain scale (43). Most studies exploring the pain outcomes of THC and CBD are neuropathic pain disorders and do not include CPP. A small cross-sectional survey of 119 women with pelvic and perineal pain, dyspareunia, or endometriosis identified almost 24% of patients with CPP regularly used cannabis as an adjunct to their pain therapy (44). Despite the widespread use of cannabinoids for pain management, there is a lack of high-quality evidence regarding their effectiveness in various pain conditions, including gynecologic disorders and chronic pelvic pain.

18.15 Bladder Symptom Management

Patients with CPP may also have overlapping bladder symptoms, even in the absence of comorbid pain disorders such as painful bladder syndrome (45). Symptoms are approached using a stepwise progression of treatments starting with conservative measures such as lifestyle modifications, dietary changes (e.g., bladder diet), and pelvic floor physical therapy. If these measures do not provide sufficient relief, oral medications such as bladder relaxants, antihistamines, and tricyclic antidepressants may be prescribed.

18.16 Gastrointestinal Symptom Management

Similar to bladder symptoms, many patients with CPP have functional bowel pain disorders or similar symptom

presentations. Most first-line therapies include a mirrored algorithm of lifestyle modifications, dietary changes (e.g., FODMAP diet), and pelvic floor physical therapy (46).

18.17 Interventions

18.17.1 Bladder Instillation

In patients with predominant bladder pain symptoms who have failed attempts at medical management, bladder instillations can be helpful. Therapeutic agents are instilled directly into the bladder and therefore have decreased systemic side effects compared to oral agents, which may be particularity helpful in patients for whom medical therapy was limited by side effects. Numerous agents have been studied including dimethyl sulfoxide, hyaluronic acid, chondroitin sulphate, heparin, and lidocaine, steroids, and antibiotics, as well as combinations of these medications (45). These medications have a variable success rate of 30%–90%, with lidocaine and heparin being more effective for short-term relief, while dimethyl sulfoxide and chondroitin sulfate may be more successful at long-term relief (45).

18.17.2 Neuromodulation

Neuromodulation has been studied for treatment of chronic pelvic pain, painful bladder, and functional bowel pain disorders. The main mechanism of action is the attenuation of pain signals to the central nervous system. This occurs via the gate-control theory of pain where large myelinated afferent nerves in the dorsal horn are activated and inhibit transmission in primary afferent nociceptive nerves (45).

Noninvasive techniques include transcutaneous electrical nerve stimulation (TENS) and percutaneous tibial nerve stimulation (PTNS). TENS been shown in small studies to be safe and effective at treating chronic pelvic pain (47, 48). PTNS is an office-based procedure to stimulate the posterior tibial nerve weekly for approximately 3 months followed by maintenance therapy. Limited studies on PTNS have found improved pelvic pain frequency, intensity, and decreased dyspareunia (47). Invasive techniques include sacral neuromodulation (SNM), pudendal nerve stimulation (PNS), and spinal cord stimulation (SCS) and are typically staged with a test phase initially followed by implantation of the stimulator if successful. SNM, which targets the S3 nerve root, is indicated for the management of refractory urinary urge incontinence and has been widely studied for treatment of CPP with conflicting results. Multiple studies with SNM have demonstrated that between 59% and 95% of patients have significant and durable pain relief (> 1 year) (47, 49). The pudendal nerve, originating from the S2, S3, S4 sacral nerve root, suggests that PNS may have broader sacral nerve root stimulation compared to SNM in patients with CPP. Some studies have shown that PNS may be superior to SNM or may be effective in patients who have failed SNM (47, 50). Patients with refractory pain despite trials of peripheral neuromodulation may be candidates for spinal cord stimulation; however, optimal lead position for CPP remains debated. Existing data indicates that 66%–86% of patients with refractory all-cause pain may respond to SCS (47).

18.18 Injections

Injections are a promising intervention for chronic pelvic pain, particularly those with evidence of myofascial pain on exam and history; however, future large, randomized trials are needed to understand the utility of this intervention further. Injection options include abdominal sites (abdominal trigger point injections, transabdominus plane blocks, ilioinguinal/iliohypogastric nerve blocks) as well as vaginal sites (levator ani trigger point injections, pudendal nerve blocks). Common injectates for trigger point injection include 1% lidocaine, 0.25% bupivacaine, and 0.5% ropivacaine with or without addition of a corticosteroid (triamcinolone acetonide), as well botulinum toxin A. The exact mechanism for trigger point injections remains unclear but may serve as mechanical disruption of skeletal muscle pain fibers, thereby interrupting the pain reflex arch. Injection may also lead to destruction of the trigger point or dilute nerve sensitized substances. One small study of 18 patients undergoing pelvic floor trigger point injection showed a 72% success rate with 50% or greater reduction in pelvic pain symptoms (51). Botulinum injections cause flaccid paralysis of the muscle at the injection site via permanent block of the presynaptic vesicle and prevention of acetylcholine release at the presynaptic plate of the neuromuscular junction. One study of 46 women with severe myofascial pelvic pain showed 74% of patients had improvement with pelvic floor botulinum injections (52), which may be particularly helpful when combined with pelvic floor physical therapy (53).

18.19 Surgery

18.19.1 Hysterectomy

Hysterectomy for treatment of chronic pelvic pain aims to remove the nociceptive source of chronic pelvic pain and may be highly effective in some patients. Initial studies of women who were thought to have uterine sources of pelvic pain showed 78% had significant improvement in pain, however 28% had persistent pain and 5% may develop new onset pain (54, 55). Recent studies have confirmed these results and indicate that the majority of women (74%–95%) experience significantly reduced pain and improved quality of life after hysterectomy; however, for patients whose primary indication for surgery is pelvic pain alone without clear pathology, 21%–40% have persistent postoperative pain. Among patients undergoing hysterectomy for any indication, those with preoperative pelvic pain have a significantly higher risk of persistent postoperative pain, and risk of postoperative pain is elevated in patients with comorbid depression and anxiety (54, 56, 57). Centralized pain is an important predictor of persistent pelvic pain after hysterectomy – one study showed that every 1 point increase in centralized pain before hysterectomy was associated with a 27% increase in odds of persistent pelvic pain (58).

Given the aforementioned findings, patients should be engaged in a discussion about the likelihood of pain relief with hysterectomy and the risk of persistent, worsening, or new pain, as well as possible prolonged recovery from surgery (54). Patients with or without discrete preoperative uterine pathology and increased risk factors for unresolved pain should still be considered candidates for hysterectomy, but they should be engaged in thoughtful shared decision making (58).

The role of oophorectomy at the time of hysterectomy for treatment of pelvic pain remains unclear, and oophorectomy should be considered with caution given evidence of increased risk of death during 20-year follow-up for women undergoing bilateral salpingo-oophorectomy at time of hysterectomy compared to age-matched controls who retained their ovaries (59). When clear pathology is present (such as endometrioma),

oophorectomy may be beneficial; however, oophorectomy for the potential of pain resolution in the setting of unexplained pain may not outweigh the known risks (54).

18.19.2 Adhesiolysis

In the absence of other identifiable sources for pelvic pain and in the setting of known prior surgical history, adhesion formation has been hypothesized as a source of pelvic pain symptoms. Small studies have shown conflicting results regarding efficacy of adhesiolysis for treatment of pelvic pain, but randomized trials have not shown a benefit (60). Adhesiolysis without targeted intervention, such as relief of obstruction, may expose patients to surgical risk without therapeutic benefit and may ultimately result in new adhesion formation.

18.20 Laparoscopic Uterosacral Nerve Ablation and Presacral Neurectomy

Surgical nerve ablation and presacral neurectomy aims to treat pelvic pain by interrupting afferent pain signals from the uterus and other pelvic structures to the central nervous system. A randomized controlled trial of laparoscopic uterosacral nerve ablation for chronic pelvic pain, dysmenorrhea, and dyspareunia showed no improvement in pain or quality of life compared to patients who did not undergo denervation (61). A similar randomized controlled trial confirmed these null findings (62). Retrospective studies have shown a benefit (success rate 65%–89%) for presacral neurectomy in the treatment of dysmenorrhea. In patients with endometriosis, randomized controlled trials have shown that presacral neurectomy has additional pain relief benefits compared to endometriosis excision alone (80% vs 50%) (29, 63). In patients with midline chronic pelvic pain and dysmenorrhea who are refractory to alternate interventions, presacral neurectomy may be of benefit.

18.21 Conclusion

Collaborative care involving a multidisciplinary team is often recommended to provide comprehensive and integrated support for individuals with CPP. Consider involving a multidisciplinary team, such as gynecologists, urologists, pain specialists, and psychologists, to provide a comprehensive assessment. By providing individuals with CPP the tools and skills to self-regulate their pain and improve their overall well-being, self-modulation behavior therapy empowers them to take an active role in their own pain management and enhances their sense of control and self-efficacy.

References

1. Mathias SD et al. Chronic pelvic pain: prevalence, health-related quality of life, and economic correlates. *Obstet. Gynecol*. 1996;87(3):321–327.
2. ACOG. Chronic pelvic pain. ACOG practice bulletin no. 128. *Obstet. Gynecol*. 2020;135(3):98–109.
3. Lamvu G et al. Chronic pelvic pain in women: a review. *JAMA*. 2021;325(23):2381–2391.
4. Majima T et al. Organ cross-sensitization mechanisms in chronic diseases related to the genitourinary tract. *J Smooth Muscle Res*. 2021;57:49–52.
5. Shoja MM et al. Neuroanatomy of the female abdominopelvic region: a review with application to pelvic pain syndromes. *Clin Anat*. 2013;26(1):66–76.
6. Chronic Pain Research Alliance. *About COPCs. Chronic pain research alliance* [Internet]. Available at: https://chronicpainresearch.org/about_copcs/ (Accessed Feb 2024).
7. Meltzer-Brody S et al. Trauma and posttraumatic stress disorder in women with chronic pelvic pain. *Obstet Gynecol*. 2007;109(4):902–908.
8. International Pelvic Pain Society. *Pelvic pain assessment form* [Internet]. Available at: www.pelvicpain.org/resources/documents-and-forms (Accessed Feb 2024).
9. Krantz TE et al. Adverse childhood experiences among gynecology patients with chronic pelvic pain. *Obstet Gynecol*. 2019;134(5):1087–1095.
10. Zhao J et al. Risk factors of endometrial cancer in patients with endometrial hyperplasia: implication for clinical treatments. *BMC Womens Health*. 2021;21(1):312.
11. Till SR et al. Psychology of chronic pelvic pain: prevalence, neurobiological vulnerabilities, and treatment. *Clin Obstet Gynecol*. 2019;62(1):22–36.
12. Black CJ et al. Efficacy of a low FODMAP diet in irritable bowel syndrome: systematic review and network meta-analysis. *Gut*. 2022;71(6):1117–1126.
13. Gutke A et al. Lifestyle and chronic pain in the pelvis: state of the art and future directions. *J Clin Med*. 2021;10(22):5397.
14. Liu P et al. Association between dietary inflammatory index and risk of endometriosis: a population-based analysis. *Front Nutr*. 2023;10:1077915.
15. Prego-Dominguez J et al. Polyunsaturated fatty acids and chronic pain: a systematic review and meta-analysis. *Pain Physician*. 2016;19(8):521–535.
16. Wepner F et al. Effects of vitamin D on patients with fibromyalgia syndrome: a randomized placebo-controlled trial. *Pain*. 2014;155(2):261–268.
17. Giubilei G et al. Physical activity of men with chronic prostatitis/chronic pelvic pain syndrome not satisfied with conventional treatments – could it represent a valid option? The physical activity and male pelvic pain trial: a double-blind, randomized study. *J Urol*. 2007;177(1):159–165.
18. Tang NK et al. Nonpharmacological treatments of insomnia for long-term painful conditions: a systematic review and meta-analysis of patient-reported outcomes in randomized controlled trials. *Sleep*. 2015;38(11):1751–1764.
19. Finan PH et al. The association of sleep and pain: an update and a path forward. *J Pain*. 2013;14(12):1539–1552.
20. Cosar E et al. Sleep disturbance among women with chronic pelvic pain. *Int J Gynaecol Obstet*. 2014;126(3):232–234.
21. McCracken LM et al. Disrupted sleep patterns and daily functioning in patients with chronic pain. *Pain Res Manag*. 2002;7(2):75–79.
22. Campbell LC et al. Persistent pain and depression: a biopsychosocial perspective. *Biol Psychiatry*. 2003;54(3):399–409.
23. Fordham B et al. Cognitive-behavioural therapy for a variety of conditions: an overview of systematic reviews and panoramic meta-analysis. *Health Technol Assess*. 2021;25(9):1–378.
24. Bittelbrunn CC et al. Pelvic floor physical therapy and mindfulness: approaches for chronic pelvic pain in women-a systematic review and meta-analysis. *Arch Gynecol Obstet*. 2023307(3):663–672.
25. Breton A et al. Enhancing the sexual function of women living with chronic pain: a cognitive-behavioural treatment group. *Pain Res Manag*. 2008 May;13(3):219–224.
26. Sung SH et al. Acupuncture treatment for chronic pelvic pain in women: a systematic review and meta-analysis of randomized controlled trials. *Evid Based Complement Alternat Med*. 2018;2018:9415897.
27. Rostom Aet al. Gastrointestinal safety of cyclooxygenase-2 inhibitors: a Cochrane Collaboration systematic review. *Clin Gastroenterol Hepatol*. 2007;5(7):818–828, 828.
28. Dowell Det al. CDC guideline for prescribing opioids for chronic pain – United States, 2016. *JAMA*. 2016;315(15):1624–1645.
29. Ramirez C et al. Pelvic denervation procedures for dysmenorrhea. *Curr Opin Obstet Gynecol*. 2017;29(4):225–230.

30. Falcone T et al. Clinical management of endometriosis. *Obstet Gynecol*. 2018;131(3):557–571.
31. Dueholm M. Minimally invasive treatment of adenomyosis. *Best Pract Res Clin Obstet Gynaecol*. 2018;51:119–137.
32. Tu FF et al. Pelvic congestion syndrome-associated pelvic pain: a systematic review of diagnosis and management. *Obstet Gynecol Surv*. 2010;65(5):332–340.
33. Andrade MA et al. The effect of neuromodulatory drugs on the intensity of chronic pelvic pain in women: a systematic review. *Rev Bras Ginecol Obstet*. 2022;44(9):891–898.
34. Schmidt-Wilcke T et al. Resting state connectivity correlates with drug and placebo response in fibromyalgia patients. *Neuroimage Clin*. 2014;6:252–261.
35. Gendreau RM et al. Efficacy of milnacipran in patients with fibromyalgia. *J Rheumatol*. 2005;32(10):1975–1985.
36. Moore RAet al. Amitriptyline for neuropathic pain and fibromyalgia in adults. *Cochrane Database Syst Rev*. 2012;12:CD008242.
37. Sator-Katzenschlager SM et al. Chronic pelvic pain treated with gabapentin and amitriptyline: a randomized controlled pilot study. *Wien Klin Wochenschr*. 2005;117(21–22):761–768.
38. He Y et al. Is gabapentin effective and safe in the treatment of chronic pelvic pain in women: a systematic review and meta-analysis. *Int Urogynecol J*. 2022:1071–1081.
39. Horne AW et al. GaPP2 collaborative. Gabapentin for chronic pelvic pain in women (GaPP2): a multicentre, randomised, double-blind, placebo-controlled trial. *Lancet*. 2020;396(10255):909–917.
40. Abdel Shaheed C et al. Efficacy and tolerability of muscle relaxants for low back pain: systematic review and meta-analysis. *Eur J Pain*. 2017;21(2):228–237.
41. Soprano SE et al. Assessment of physician prescribing of muscle relaxants in the United States, 2005–2016. *JAMA Netw Open*. 2023;3(6):1–9.
42. Kroenke K et al. Pharmacotherapy of chronic pain: a synthesis of recommendations from systematic reviews. *Gen Hosp Psychiatry*. 2009;31(3):206–219.
43. Meng H et al. Selective cannabinoids for chronic neuropathic pain: a systematic review and meta-analysis. *Anesth Analg*. 2017;125(5):1638–1652.
44. Carrubba AR et al. Use of cannabis for self-management of chronic pelvic pain. *J Women's Heal*. 2021;30(9):1344–1351.
45. Colemeadow J. Clinical management of bladder pain syndrome/interstitial cystitis: a review on current recommendations and emerging treatment options. *Res Rep Urol*. 2020:331–343.
46. Chey WD et al. Irritable bowel syndrome: a clinical review. *JAMA*. 2015;313(9):949–958.
47. Tam J et al. Neuromodulation for chronic pelvic pain. *Curr Urol Rep*. 2018;19(5):32.
48. Sharma N et al. Efficacy of transcutaneous electrical nerve stimulation in the treatment of chronic pelvic pain. *J Midlife Health*. 2017;8(1):36–39.
49. Martellucci J et al. Sacral nerve modulation in the treatment of chronic pelvic pain. *Colorectal Dis*. 2012;14(4):502–507.
50. Fan AKK et al. Neuromodulation for chronic urogenital pain: a comparison of pudendal and sacral nerve stimulation. *J Urol Suppl*. 2017;197:e1046–e1047.
51. Langford CF et al. Levator ani trigger point injections: an underutilized treatment for chronic pelvic pain. *Ref Neurourol Urodyn*. 2007;62:59–62.
52. Jha Set al. Botulinum injections for myofascial pelvic pain. *Int Urogynecol J*. 2021;32(5):1151–1156.
53. Halder GE et al. Botox combined with myofascial release physical therapy as a treatment for myofascial pelvic pain. *Investig Clin Urol*. 2017:134–139.
54. Lamvu G. Role of hysterectomy in the treatment of chronic pelvic pain. *Obstet Gynecol*. 2011;117(5):1175–1178.
55. Stovall TG et al. Hysterectomy for chronic pelvic pain of presumed uterine etiology. *Obstet Gynecol*. 1990;75(4):676–679.
56. Hartmann KE et al. Quality of life and sexual function after hysterectomy in women with preoperative pain and depression. *Obs Gynecol*. 2004;104:701–709.
57. Cockrum R et al. Hysterectomy for chronic pelvic pain. *Obstet Gynecol Clin North Am*. 2022;49(2):257–271.
58. As-Sanie S et al. Incidence and predictors of persistent pelvic pain following hysterectomy in women with chronic pelvic pain. *Am J Obs Gynecol*. 2021;255(5):568.
59. Rocca WA et al. Survival patterns after oophorectomy in premenopausal women: a population-based cohort study. *Lancet Oncol*. 2006;7(10):821–828.
60. Hammoud A et al. Adhesions in patients with chronic pelvic pain: a role for adhesiolysis? *Fertil Steril*. 2004;82(6):1483–1491.
61. Daniels J et al. Laparoscopic uterosacral nerve ablation for alleviating chronic pelvic pain: a randomized controlled trial. *JAMA*. 2009;302(9):955–961.
62. El-Din Shawki H. The efficacy of laparoscopic uterosacral nerve ablation (LUNA) in the treatment of unexplained chronic pelvic pain: a randomized controlled trial. *Gynecol Surg*. 2011;8(1):31–39.
63. Jedrzejczak P et al. Effects of presacral neurectomy on pelvic pain in women with and without endometriosis. *Ginekol Pol*. 2009;80(3):172–178.

19 PRINCIPLES OF NEUROPELVEOLOGY

Marc Possover, Varnita Vishwanath, and Ali Azadi

19.1 Introduction

Neuropelveology is an emerging discipline of medicine that was originally introduced over 20 years ago by Possover (1). It is now an established specialty reinforced by the International Society of Neuropelveology since 2014. The development of neuropelveology as a medical specialty has been driven by the combination of endoscopy and surgical procedures to improve and preserve pelvic nerve functions (2–5). This field consolidates knowledge from numerous medical specialties and focuses on diagnosing and treating pelvic nerve dysfunction and pathology. The range of conditions that are covered in neuropelveology includes neuropathic pain and malfunction caused by a variety of pathologies, pelvic organ dysfunction requiring nerve stimulation, and loss of function due to spinal cord injury (6). The state-of-the-art management of these conditions has therapeutic and preventative advantages.

The incidence of pelvic nerve pathology often goes underestimated. This is largely owed to the limited awareness of the disease processes, the complexity of the pelvic nerve system, and the restricted access to pelvic nerves for exploration and treatment. While neurosurgical procedures for upper limb lesions are well established, surgeries involving the pelvic nerves are still uncommon. A few open surgical approaches to the sacral plexus have been described for the treatment of traumatic pelvic plexopathies. These approaches, however, are laborious, are invasive, provide limited access to the entire scope of pelvic nerves, and pose a risk of severe vascular complications. For the same reasons, neuromodulation in the pelvis is restricted to certain nerves such as the spinal cord and sacral nerve roots, significantly compromising its effectiveness.

The practice of neuropelveology involves diagnosis, treatment, and post-therapeutic patient follow-up. There are four primary focuses within this field:

1. Diagnosis and treatment of pelvic neuropathic pain including the utilization of new techniques such as laparoscopic pelvic nerve decompression and neurolysis
2. Treatment of pelvic organ dysfunction through innovative methods such as genital nerve stimulation (GNS therapy)
3. Laparoscopic implantation of neuroprosthesis (LION procedure) to the pelvic nerves to restore lost function in patients with spinal cord injuries or pelvic nerve damage
4. Stimulation of the pelvic autonomic nervous system for prevention and/or treatment of general medical conditions such as osteoporosis, cardiovascular diseases, and the control of sarcopenia

The diagnostic stage in neuropelveology involves a comprehensive medical history that covers gynecology, urology, orthopedics, pelvic vessel pathology, and psychology of chronic pain and parapleology. The clinical examination involves the assessment of pelvic organs and their function, conducting a neurologic exam of the musculoskeletal system, and palpating the pelvic nerves by vaginal or rectal route (2). Upon establishing a diagnosis, neuropelveology employs a range of medical and surgical treatments tailored to the individual patient for addressing pelvic nerve pathologies. Neurosurgical techniques in neuropelveology include procedures such as decompression, neurolysis, reconstruction, and nerve resection (for conditions like sciatic nerve endometriosis).

19.2 Pelvic Neurofunctional Anatomy

Understanding the division of pelvic innervation is important as it is a fundamental aspect of managing pelvic pain conditions in neuropelveology. This field emphasizes the need to consider neuropathic pain and functional disorders of pelvic organs together. The more information obtained, the process of determining the affected nerves and pinpointing the anatomical location of the damage will be simpler. This reinforces the significance of a thorough patient history where every piece of information is valuable.

Pelvic innervation is a complex system including sensory and motor nerves. Sensory afferent nerves send information to the brain, while motor efferent nerves carry signals from the brain. The efferent nerves are further divided into somatic and autonomic nerves. Somatic pelvic nerves originate in the ventral roots of the spinal cord with the main ones involved in pelvic organ functions originating from the sacral plexus to innervate skeletal (voluntary) muscles. Autonomic pelvic nerves are responsible for innervating glands and smooth (involuntary) muscles. Autonomic nerves further divide into sympathetic nerves that originate from ventral roots of spinal nerves T1–L2 and parasympathetic nerves that originate from ventral roots of spinal nerves S2–S4/S5.

The sacral plexus (Figure 19.1) is made up of the lumbosacral trunk and the ventral rami of sacral nerve roots S1–S4/S5. The L5 nerve is primarily responsible for ankle dorsiflexion, with injury leading to drop foot. The S1 nerve controls ankle plantarflexion and the Achilles reflex, with injury leading to the inability to walk on heels.

Various nerve responses are observed during electrical stimulation of the sacral nerve roots using the laparoscopic neuro-navigation technique. Stimulation of the S4 nerve does not produce any motor actions in the lower extremities. Stimulation of the S3 nerve results in the bellows reflex (anal wink) and plantar dorsiflexion of the large toe and, to a lesser extent, of the smaller toes. Stimulation of the S2 nerve results in outward rotation of the leg, ankle plantar flexion, and contraction of the anal sphincter.

Branches of the sacral plexus include the superior gluteal nerve and the pudendal nerve, each with distinct functions:

1. The *superior gluteal nerve* originates from the lumbosacral trunk above the greater sciatic notch and exits through the greater sciatic foramen along with the superior gluteal artery and vein. It contributes to the stability of the pelvis by supplying the gluteus medius, gluteus minimus, and the tensor fascia lata muscles.
2. The *pudendal nerve* is a sensory and somatic nerve originating from the 2nd to 4th sacral nerve roots just proximal to the sacrospinous ligament. It exits the pelvis

DOI: 10.1201/9781003312109-19

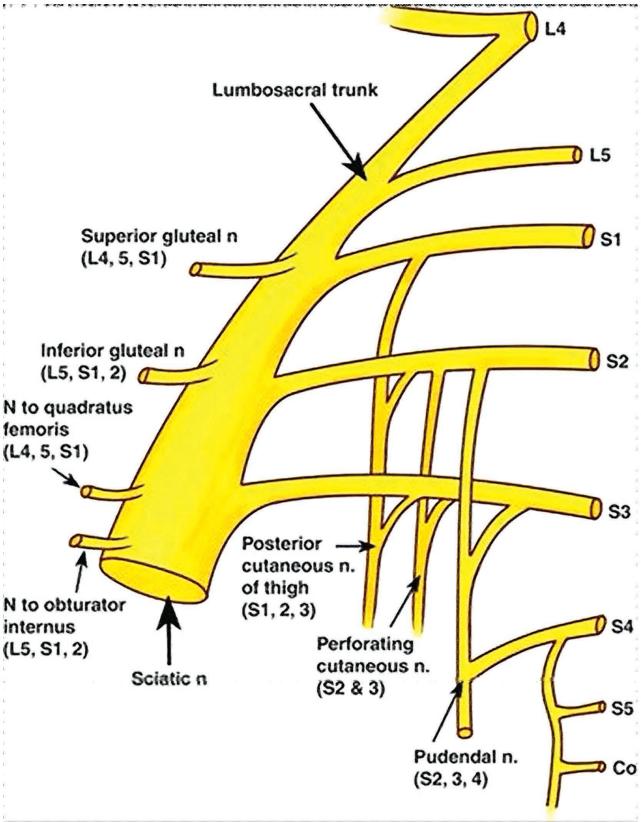


FIGURE 19.1 Sacral plexus. (From Walji AH et al. Clinical anatomy of the sacral plexus. In: Tsui B et al., eds. *Pediatric Atlas of Ultrasound- and Nerve Stimulation-Guided Regional Anesthesia.* Springer, New York, 2016: 165–175, with permission.)

through the greater sciatic notch, reenters the pelvis through the lesser sciatic notch, and then innervates three major regions: the gluteal region, the pudendal canal/Alcock canal, and the perineum. The three distal branches of the pudendal nerve include the inferior rectal nerve, the perineal nerve, and the dorsal nerve of the penis or the dorsal nerve of the clitoris. This nerve carries sensory information from the external genitalia, skin around the anus, and the perineum. It supplies motor innervation to the external urethral sphincter and the external anal sphincter.

- *Neurophysiology of micturition*: Micturition involves storage and emptying phases. Storage relies on sympathetic and somatic nerves to maintain internal and external urethral sphincter tone while the bladder wall relaxes. As the bladder fills, the pudendal nerve is activated to contract and maintain a higher pressure in the external urethral sphincter than in the bladder. Voiding is triggered by stretch receptors in the bladder activating the pontine micturition center. It is driven by parasympathetic stimulation for bladder contraction and relaxation of pelvic muscles and sphincters. In the voiding phase, the pudendal nerve causes the external urethral sphincter to relax and open. The pudendal nerve has somatic afferent fibers projecting on the sympathetic thoracolumbar neurons at the bladder neck. This neuromodulation works at the spinal level and appears to be at least partly responsible for urinary incontinence.

3. The parasympathetic innervation to the pelvis is supplied by the *pelvic splanchnic nerves* that originate from the sacral nerve roots S2 to S4/S5. These nerves transfix the sacral hypogastric fascia and form a mesh of smaller nerves. The meshwork of nerves connects to the pelvic plexus near the rectum as well as the bladder pillar and ureterovesical junction. The pelvic splanchnic nerves play a role in controlling the internal urethral sphincter to regulate bladder voiding, rectal motility, and sexual functions like erection. Surgical exposure of these nerves involves following the sacral nerves as through the S4 laterally to the sacral hypogastric fascia and then tracking them ventrally to their roots.

19.3 Sympathetic Pelvic Innervation of the Pelvis

The sympathetic innervation of the pelvis (Figure 19.2) originates from the following:

1. The *sympathetic trunk* stretches along both sides of the spine. The left sympathetic trunk lies beside the aorta while the right sympathetic trunk remains hidden behind the inferior vena cava, which can be damaged during a retrocaval lymphadenectomy. The lumbar sympathetic trunk runs along the medial insertion of the iliopsoas muscle and has four associated neural ganglia. Damage to the lumbar sympathetic trunk results in homolateral peripheral vasodilation resulting in calor of the homolateral foot. The sacral sympathetic trunk runs along the sacrum and consists of three sacral ganglia that anastomose to the inferior hypogastric plexus (IHP) ventral to the sacrum.
2. The *IHP* (also called plexus pelvicus) originates from the vegetative solar plexus and innervates the abdominal organs. It includes the intermesenteric plexus that forms the inferior mesenteric plexus running along the ventrolateral aspect of the aorta between the mesenteric arteries. The IHP is located deep in the pelvis lateral to the rectum and the craniodorsal part of the vagina. It appears as a net of fibers forming a sacrouterine ligament/rectovaginal pillar. The IHP plays a role in the autonomic nervous systems innervation of the pelvic organs and is involved in controlling the functions of the rectum and the reproductive organs.

19.4 Lumbar Plexus

Divisions of the L1–L4 and partly T12 nerves make up the lumbar plexus (Figure 19.3). Ventral rami of L4 pass communicating branches known as the lumbosacral trunk to the sacral plexus. This complex network of nerves plays a role in innervating the lower extremities and pelvis, providing motor and sensory functions to various muscles and organs in these regions.

There are several branches of the lumbar plexus that run into the pelvis:

1. The *iliohypogastric nerve* runs anterior to the psoas major and supplies motor branches to the quadratus lumborum and transversus abdominis. It supplies sensory branches to the lateral hip.

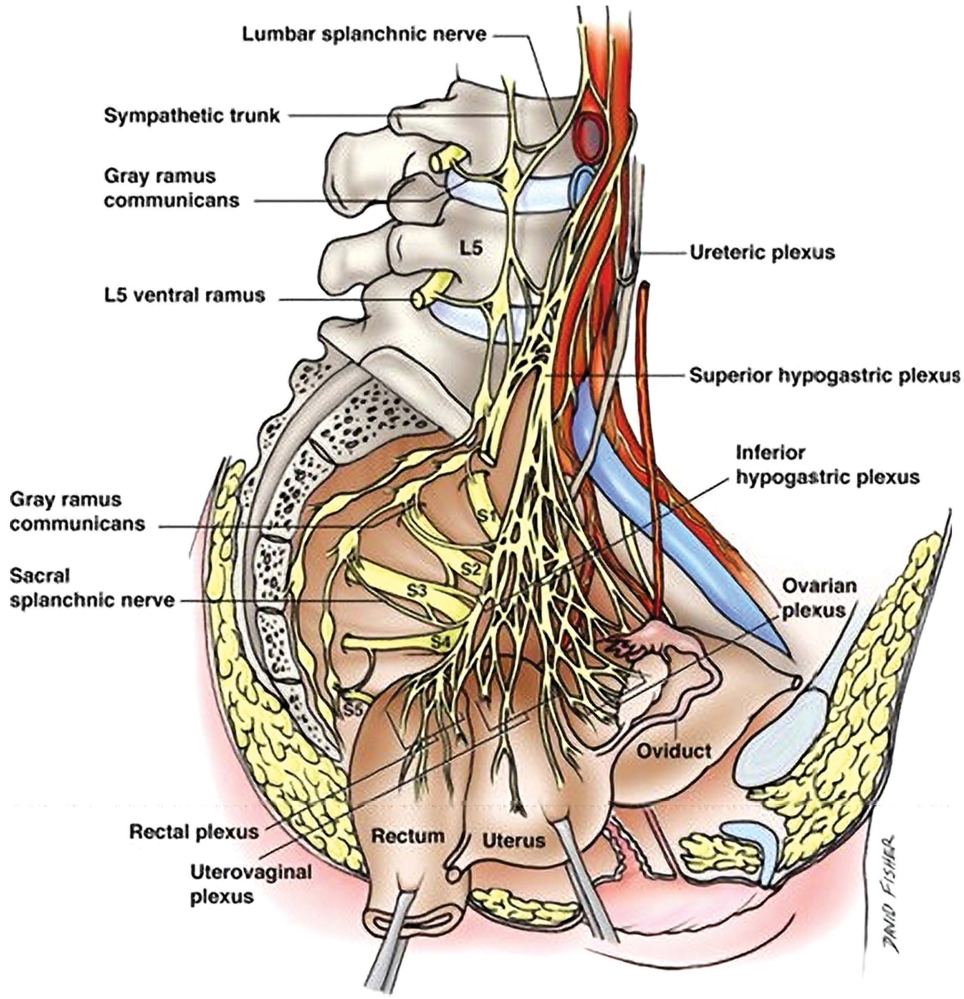


FIGURE 19.2 Pelvic side wall view of the sacral plexus. (From Shoja, M et al. Neuroanatomy of the female abdominopelvic region: A review with application to pelvic pain syndromes. *Clinical Anatomy*, 2013;26(1), 66–76, with permission.)

2. The *ilioinguinal nerve* runs caudally to the iliohypogastric nerve and supplies motor branches to the transverse abdominis. Its sensory branches are to the skin over the pubic symphysis and lateral aspect of the labia majora.
3. The *genitofemoral nerve* splits into two branches. The lateral femoral branch supplies sensory innervation below the inguinal ligament and the proximal lateral aspect of the femoral triangle. The genital branch sends sensory branches to the skin of the mons pubis and labia majora.
4. The *lateral cutaneous femoral nerve* pierces the psoas major and provides sensory innervation to the anterior and lateral aspects of the thigh.
5. The *obturator nerve* descends behind the psoas major and exits the pelvis through the obturator canal. It supplies motor branches to the adductor muscles and sensory branches to the upper medial thigh.
6. The *femoral nerve* is the largest branch of the lumbar plexus. It supplies sensory innervation to the anterior aspect of the thigh and knee and motor innervation to the quadriceps muscles. It runs between the psoas major and iliacus, giving off branches to these muscles, and exits the pelvis through the medial aspect of the muscular lacuna. Femoral neuropathy is the most common lumbosacral nerve injury during pelvic surgery and can occur via femoral nerve compression. The most common symptoms of femoral neuropathy include sensory loss over the anteromedial thigh and difficulty ambulating after surgery.

19.5 Nerve Injuries during Gynecologic Surgeries

All approaches of gynecologic surgery (vaginal/laparoscopic/laparotomy) can cause injury to the lumbosacral plexus. Nerve injury can occur in up to 2% of all gynecologic surgeries. Nerve injuries result from compression, stretching, or transection during surgery. While most nerve injuries resolve spontaneously, the more severe the injury the longer it will take to heal. Understanding basic neural anatomy is crucial in comprehending nerve injuries during surgery (Table 19.1).

Nerve fibers are divided into fascicles and are surrounded by loose connective tissue to protect it from injury.

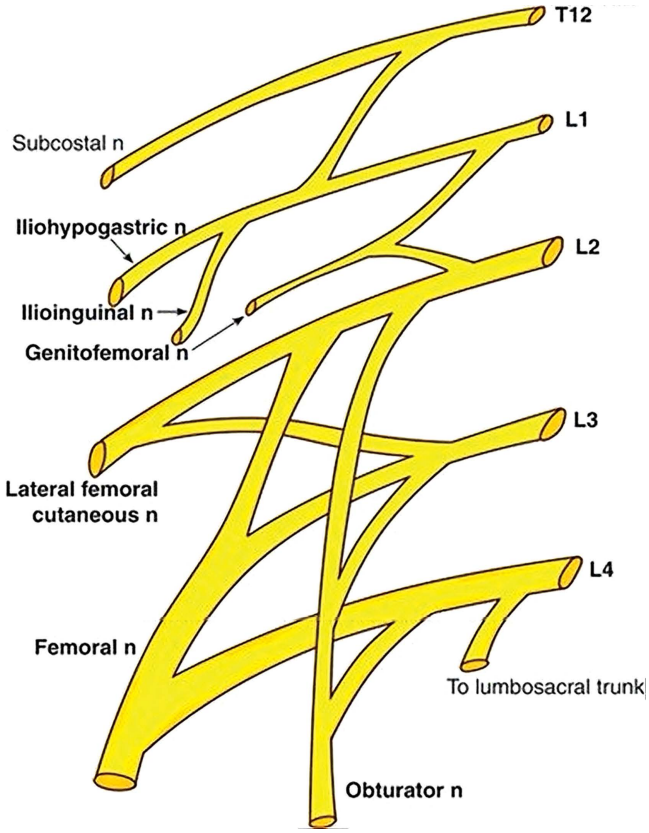


FIGURE 19.3 Lumbar plexus. (Reprinted from Walji AH, Tsui BCH, Clinical Anatomy of the Lumbar Plexus. In: Tsui B, Suresh S eds. *Pediatric Atlas of Ultrasound- and Nerve Stimulation-Guided Regional Anesthesia.* Springer, New York, 2016: 165–175, with permission.)

The Seddon classification helps surgeons anticipate prognosis and recovery. It categorizes nerve injuries into three types:

1. *Neuropraxia* (local conduction block) is caused by transient nerve ischemia. There is no damage to axons and Schwann cells. It often resolves within minutes unless prolonged, leading to demyelination.
2. *Axonotmesis* (axonal injury with preservation of Schwann cells) affects sensory, motor, and autonomic nerves. Wallerian degeneration begins within 1 to 2 days and recovery takes weeks to months.
3. *Neurotmesis* (complete disruption of the axon, Schwann cell, and connective tissue) is caused by a complete transaction of the nerve and requires surgical intervention.

19.6 Common Conditions

19.6.1 Bladder Hypersensitivity

Hypersensitive bladder symptoms refer to heightened bladder sensation. Symptoms include increased urinary frequency and nocturia, with or without bladder pain. Hypersensitivity results from the activation of sensory nerves in different regions including the inferior hypogastric nerves, sympathetic trunks, sacral nerve roots (S2–S4), pudendal nerve, and dorsal nerve of the clitoris (DNC). Bladder hypersensitivity associated with visceral pelvic pain is linked to the IHP, while hypersensitivity related to pelvic somatic pain is associated with the sacral nerve roots pudendal nerve and DNC.

19.6.2 Pathologies of the Inferior Hypogastric Plexus

Hypersensitivity of the bladder can be caused by endometriosis of the uterosacral ligaments. Symptoms include pelvic visceral pain, dysmenorrhea, rectal disorders, and dyspareunia as endometriosis infiltrates the cranial portion of the IHP (3). Pelvic sympathetic afferent fibers rising to the superior hypogastric plexus and crossing the promontory may cause ascending back pain and multiple vegetative symptoms (Table 19.2). Clinical examination focuses on vegetative disorders including pupil dilation, salivation inhibition, and tachycardia. Other causes of bladder hypersensitivity include surgical damage to the IHP during prolapse surgeries and radical pelvic surgery for malignancies (7–9).

19.6.3 Pathologies of the Pelvic Somatic Nerves

Neuropathy affecting the sacral nerves S2 to S4 and the pudendal nerve and its branches (particularly DNP) can lead to pelvic somatic pain and hypersensitivity of the bladder. Understanding the neuroanatomy is important in comprehending the combination of symptoms (10).

- *S1 and L5 radiculopathy* cause pain in the lower back, buttock, and dorsal/external leg. There is no genitoanal/pudendal pain. There may be issues with foot extension and leg movement, and gluteal muscle hypotrophy may also occur.
- *S2 radiculopathy* leads to pain in the buttock, dorsal/medial leg, perianal area, coccygodynia, and difficulties with toe motion.
- *S3 and S4 radiculopathy* specifically causes pudendal pain, mainly in the perineal and vulvar areas, resulting in vulvodynia without radiation to the buttocks or legs.
- *Pudendal neuralgia* causes pain in all three areas of the pudendal region without radiation to the buttocks or legs: ventral (vulvodynia), middle (perineal), and dorsal (perianal).

The neuropelveologic approach to the aforementioned pelvic neuropathies focuses on diagnostic methods, utilizing neurologic principles, and an in-depth knowledge of pelvic neurofunctional anatomy. Patient history plays a crucial role in understanding the pain history, irradiation, aggravating factors, and presence of vegetative and somatic symptoms.

For somatic pain, the location of pain and the underlying etiology are often different. Somatic pain is superficially located in the skin and can be described as allodynia, with specific locations and caudal irradiations to the genitoanal areas or lower extremity dermatomes (Figure 19.4). Somatic pain typically lacks vegetative symptoms.

The neuropelveologic workup scheme comprises six steps (7, 11):

1. Identifying the nerve pathways involved in transmitting pain signals to the brain
2. Identifying the location of neurologic irritation or injury (troncular, radicular, spinal, or cerebral)
3. Differentiating between nerve irritation and nerve injury (neurogenic neuropathy)
4. Confirming the diagnosis with neurologic examination and trigger point evaluation

TABLE 19.1 Mechanism of Nerve Injury during Gynecologic Procedures

Nerve	Origin	Type	Symptoms	Mechanism of Injury
Ilioinguinal and iliohypogastric	L1	Afferent	• Superficial pain and sensory deficit along the abdominal wall, suprapubic area, and inguinal ligament • Pain in medial groin labia majora or inner thigh	• Injury during trocar insertion • Injury during extended abdominal wall incision • Nerve entrapment during fascial closure
Obturator	L2–L4	Afferent Efferent	• Inability to adduct thigh • Sensory loss in medial thigh	• Prolonged hip flexion • Retropubic and deep pelvic sidewall dissection • Injury during transobturator tape placement • Injury during paravaginal repair
Femoral	L2–L4	Afferent Efferent	• Unable to flex hip, extend knee, adduct thigh • Sensory deficit in anterior thigh • Absent patellar reflex • Knee buckling	• Sidewall retractors during laparotomy • Hyperflexion of the hip (compression injury) or hyperextension of the hip (stretch injury) during positioning
Genitofemoral	L1–L2	Afferent Efferent	• Sensory deficit over the anterior thigh below the inguinal ligament and lateral labia • Paresthesia in groin area over the mons and labia majora	• Injury from retractors • Injury during retropubic sling placement
Lateral cutaneous femoral	L2–L3	Afferent	• Pain and sensory deficit in anterior lateral thigh to knee • Symptoms increase with standing, walking, or hip extension	• Hip hyperflexion • Abdominal retractors • Tight belt or clothing
Sciatic	L4–S3	Afferent Efferent	• Pain in posterior leg • Unable to extend thigh and flex leg • Sensory loss and posterior thigh, calf, and sole of the foot • Absent Achilles reflex	• Hyperflexion of the hip • Injury with sacrospinous ligament fixation • Sacroiliac fossa hemorrhage
Common peroneal	L4–S2	Afferent Efferent	• Foot drop/absent ankle dorsiflexion • Sensory deficit of lateral leg and foot	• Hip extension and rotation • Lateral pressure of the thigh in stirrups
Tibial	L4–S3	Afferent Efferent	• Loss of plantar flexion and foot inversion • Sensory loss over the sole and heel of the foot	• Compression during positioning
Pudendal	S2–S4	Afferent Efferent	• Pelvic pain • Urinary and fecal incontinence • Sensory loss in vulva, vagina, clitoris, perineum, and rectum	• Vaginal surgery/paravaginal repair • Vaginal birth
Sacral nerve roots	S1–S4	Afferent Efferent	• Sensation of perineum and vagina • Pelvic floor dysfunction, bladder and bowel dysfunction, arousal problems	• Injury during uterosacral ligament suspension

TABLE 19.2 Visceral versus Somatic Pain Symptoms

Visceral Pain	Somatic Pain
Pain quality • Vague, dull, poorly localized in the lower abdomen with radiation to the lower back **+ Vegetative symptoms** • Malaise/syncope • Fatigue • Irritability • Pupil dilation • Salivation inhibition • Tachycardia • Nausea/vomiting • Pallor • Diaphoresis • Anxiety	**Pain quality** • Allodynia, similar to electrical shock, precise location, clear pain description, lack of vegetative symptoms **+ Caudal radiation to the corresponding dermatome(s)** **+ Pelvic motor dysfunction** • Pelvic organ dysfunctions • Sexual dysfunction • Locomotion dysfunction

(From ref 1, with permission)

5. Identifying potential etiologies based on patient history and imaging, including sacral radiculopathy, compression of the sacral plexus, endometriosis, tumors, and postsurgical pelvic neuropathies
6. Providing individualized therapy, such as laparoscopic exploration/decompression for compression-related cases and neuromodulation for axonal nerve lesions with selectively placed electrodes for the management of neuropathic pain and pelvic organ dysfunction (12, 13)

19.7 General Treatment Principles

Treatment decisions should consider the patient's functional capacity, social support, and care goals. The ideal management strategy involves identifying the location and effects of the neurologic insults on storage, emptying, or both. Urodynamic testing is often used to help determine if there are issues with storage or emptying and whether they involve the detrusor

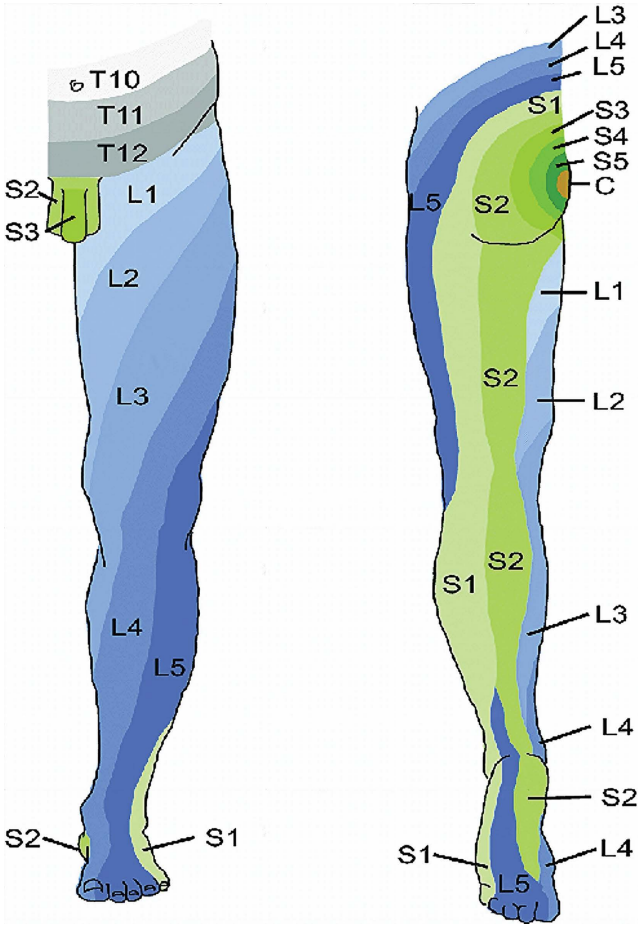


FIGURE 19.4 Genitoanal and lower extremity dermatome map. (From Ostelo RW, Physiotherapy management of sciatica, *J Physiother* 2020;66/2:83–88, with permission.)

muscle or outlet. Of note, if a patient exhibits abnormalities in both storage and emptying or both the detrusor and outlet, high-risk features that threaten upper tract deterioration should be addressed as a priority.

19.8 Novel Treatments

19.8.1 Laparoscopic Implantation of Neuroprosthesis (LION) Procedure

The LION procedure was introduced by Possover over 15 years ago for the primary treatment of bladder atony secondary to pelvic surgery. Since its development, it has increasingly been used for multiple applications including pelvic neuropathic pain, continence/voiding functions, and especially in paraplegia secondary to spinal cord injury to restore motor, sensory, and autonomic control (13).

The LION procedure involves neuromodulation, where electrical stimulation is used to help restore pelvic nerve function. The laparoscopic approach allows for the exploration of injured nerves. This potentiates the ability for etiologic treatment with nerve compression, reconstruction, or in the case of the LION procedure, the placement of a stimulation electrode directly on the nerve. The procedure consists of laparoscopic implantation by the transperitoneal approach of four stimulation lead electrodes to the bilateral sciatic, pudendal, and femoral nerves (Figure 19.5). All cables from the electrodes are connected to a multichannel generator implanted in a paraumbilical position, fixed to the abdominal fascia (13).

Early efficacy data from a case series of individuals undergoing the LION procedure for bladder dysfunction demonstrated promising results after its initial introduction. In this case series, 19 of 21 patients achieved success defined as the persistence of neuromodulation function up to 3 years postoperatively (14). Since then, the LION procedure has been especially evolving in the field of parapleology (13). A 2022 prospective randomized control trial evaluated the efficacy of the LION procedure in comparison to neuromuscular electrical stimulation (NMES) in spinal cord injury. The primary outcome measure was the Walking Index for Spinal Cord Injury (WISCI-II) that assesses the ability to ambulate. A statistically significant difference was observed in that the LION group participants gained 1 WISCI-II point in comparison to 0 points in the NMES group at 1-year follow-up (15).

19.8.2 Pudendal Nerve Stimulation

Sacral nerve stimulation (S3 root pelvic nerve stimulation) involves electrical stimulation of the nerve via implantation of

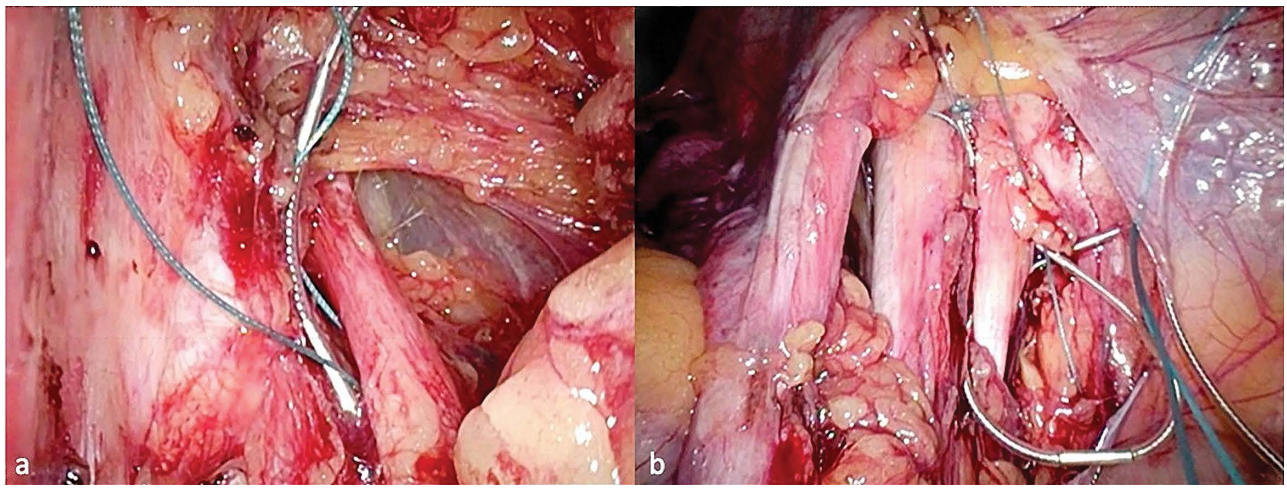


FIGURE 19.5 Sacral plexus LION procedure. Placement of the lead electrodes to (a) the left sciatic nerve and (b) the right femoral nerve (From ref 1, with permission).

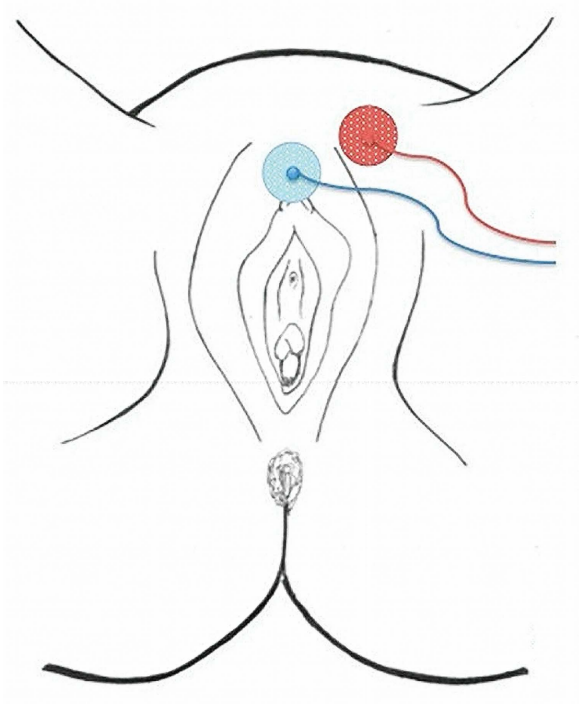


FIGURE 19.6 Position of the skin surface electrodes for the test phase (From ref 1 with permission).

a neuroprosthesis. Sacral nerve stimulation is primarily used to treat an overactive bladder, urinary incontinence, nonobstructive incomplete bladder emptying and fecal incontinence.

Pudendal nerve stimulation (PNS) can target a broader range of sphincter, vesical, and anal fibers compared to sacral nerve stimulation. PNS is a proposed solution for patients who do not respond to sacral nerve stimulation for bladder and fecal dysfunction.

Nerve stimulation involves two phases. The preoperative nonsurgical test phase can be performed using skin surface or needle electrodes near the genital nerves (Figure 19.6). This allows patients to trial and evaluate the effectiveness of the electrical stimulation in their daily environment or during urodynamic testing. If the preoperative test phase is successful, the patient may proceed to the permanent surgical implantation of the neuroprosthesis.

The surgical procedure involves the use of a hollow curved needle to transfix the urogenital diaphragm, enter the retropubic space, and exit through the skin in the suprapubic area. A quadripolar lead electrode is retrogradely introduced into the shaft of the curved needle driver, and the electrode lead remains in place with the stimulator's pole emerging through the vulvar incision. Through a second supravulvar incision, an applicator is introduced to ensure a deep location of the cable electrode near the pubic bone. The final step involves connecting the lead electrode to the generator which is fixed behind the pubic bone through a suprapubic minilaparotomy. This approach reduces the risk of bleeding and nerve injury as it avoids the need for dissection. In a recent case series of 24 individuals with neurogenic detrusor overactivity, genital nerve stimulation showed promising results. Nerve stimulation at tolerable amplitudes individualized to the patient inhibited reflexive bladder contractions and increased bladder capacities by 135 ± 109 mL (16). In a similar study with 15 neurogenic patients, average daily incontinence episodes decreased from 7 ± 3.3 to 2.6 ± 3.3 ($p < 0.02$). In the same study participants on 6 months follow-up, urodynamics revealed an increase in bladder capacity from 153.3 ± 49.9 to 331.4 ± 110.7 mL ($p < 0.01$) (17).

19.8.3 Nerve-Preserving Surgeries

Pelvic autonomic nerves (PANs) are challenging to visualize without magnification. They can be found on the lateral side of the uterosacral and vesicouterine ligaments, as well as on the medial side of the parametria. PANs may be affected by endometriosis lesions or malignancies. To prevent damage to PANs, they must be carefully identified during surgical excisions of these conditions. Three important areas to intentionally identify include the superior hypogastric plexus (SHP), inferior hypogastric plexus (IHP), and pelvic splanchnic nerves (PSN) (Figure 19.7). The SHP can be visualized at the sacral promontory where it divides into the right and left pelvic branches that run dorsomedially to the ureters. The IHP is immediately lateral to the uterosacral ligaments. The parasympathetic nerves originate from S2 to S4 and can be located below the deep uterine vein (18).

- *Nerve-sparing endometriosis surgery*
  Surgical treatment of deep infiltrating endometriosis has the potential to damage the autonomic nervous system of the pelvis during excisional techniques. The autonomic nervous system, including the bilateral hypogastric nerves and inferior hypogastric system, controls urinary, anorectal, and sexual functions, which is important to preserve when exercising endometriosis lesions. The surgical approach involves identifying the right or left hypogastric nerve in relation to the other pelvic landmarks and using it as a reference point to preserve other autonomic bundles in the pelvis. The hypogastric nerve is the most superficial and readily identifiable component of the inferior hypogastric plexus. It can be identified as coursing along the inferior margin of the pelvic side wall bilaterally, roughly 14.5 mm medial to the ureter. For confirmation of the hypogastric nerve, the pulling maneuver can be performed with gentle traction on the nerve that causes a caudal movement of the superior hypogastric plexus (over the sacral promontory). Next, the retroperitoneum is dissected at the pelvic brim inferomedially to the external iliac vessels. The underlying tissue must be gently dissected until the ureter is identified and lateralized. Ongoing dissection along the peritoneum is then carried deeper into the pelvis until the hypogastric nerve can be identified and lateralized. The peritoneum containing endometriosis can now be freely resected (19).
- *Nerve-sparing radical hysterectomy*
  Bladder dysfunction is one of the most unavoidable complications after a radical hysterectomy secondary to resection of the neural portion of the cardinal ligament. It can be significantly prevented with careful attention to nerve preservation.

  The first step of nerve-preserving radical hysterectomy involves isolating and transecting the vesical veins in the vesicovaginal ligament. This ligament contains the vesical veins that drain into the dorsal uterosacral ligament, fatty connective tissue, and a vesical nerve bundle. In this procedure, the paravaginal space is not created. The vesical veins are transected which effectively disconnects the bladder from the cervix and

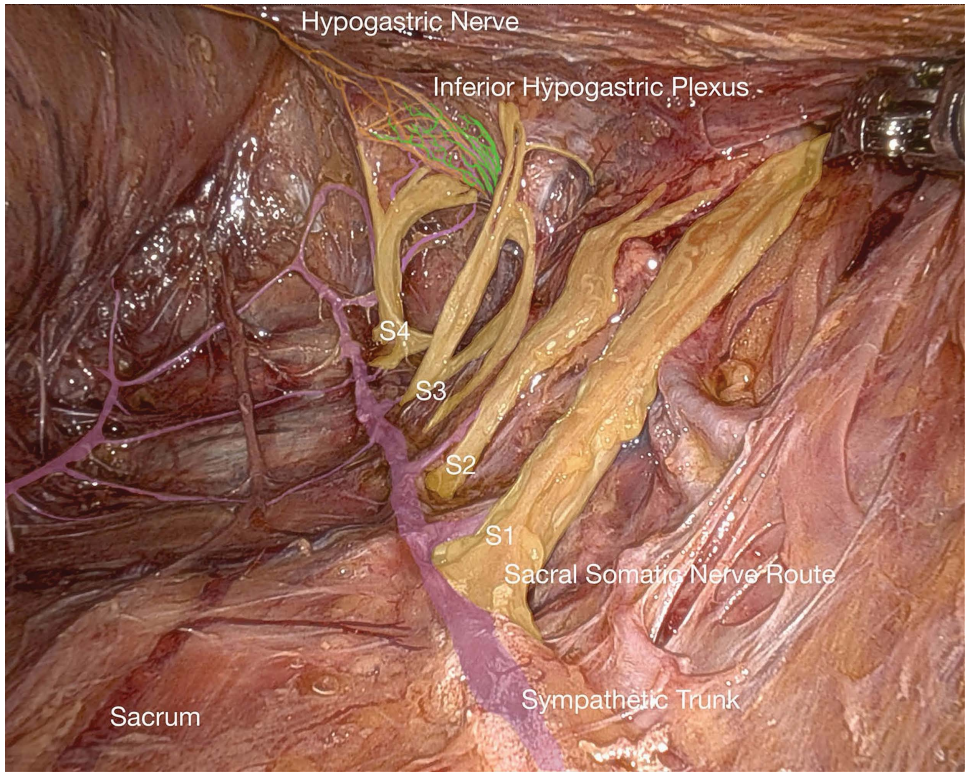


FIGURE 19.7 Robotic surgical view of the sacral nerve roots (yellow) S1–S4, the sacral sympathetic trunk (purple), the hypogastric nerve (orange), and PSN (green) (Reprinted from Alkatout I, Wedel T, Pape J, et al. Review: Pelvic nerves – from anatomy and physiology to clinical applications. *Translational Neuroscience*, 2021;*12*(1), 362–378, with permission).

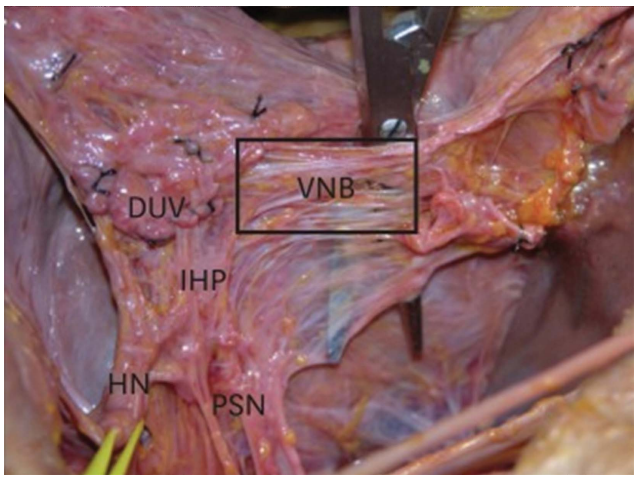


FIGURE 19.8 Identification of the IHP and the UNB. *Abbreviations*: *DUV*: deep uterine vein; *HN*: hypogastric nerve; *IHP*: inferior hypogastric plexus; *PSN*: pelvic splanchnic nerve; *UNB*: uterine nerve branches. *VNB*: vesical nerve branches (From Sakuragi N et al. Nerve-sparing radical hysterectomy in the precision surgery for cervical cancer. *J Gynecol Oncol*. 2020;31(3):e49, with permission.)

vagina. The second step is to identify the hypogastric nerve and uterine nerve bundle to separate the vesicle nerve bundle from the paracervix and paracolpium (Figure 19.8). The cut end of the dorsal uterosacral ligament is separated from the pelvic splanchnic nerves and the IHP. This allows for the recognition of vesical nerve fibers on the upper lateral surface of the peracolpium. The hypogastric nerve is detached from the rectal vaginal ligament which extends just below the dorsal uterosacral ligament. The uterine and vesical nerve branches are then identified posteriorly and anteriorly. The uterine nerve fibers are then selectively transected. This will cause the IHP and VNB to retract dorsolaterally. The third step involves the excision of the rectal vaginal ligament and paracolpium (20).

References

1. Possover M. Neuropelveology: an emerging discipline for the management of pelvic neuropathies and bladder dysfunctions through to spinal cord injury, anti-ageing and the mars mission. *J Clin Med*. 2020;9(10).
2. Possover M et al. Neuropelveological assessment of neuropathic pelvic pain. *Gynecol Surg*. 2014;11:139–144. https://doi.org/10.1007/s10397-014-0838-4.
3. Possover M et al. The "laparoscopic neuro-navigation" – LANN: from a functional cartography of the pelvic autonomous neurosystem to a new field of laparoscopic surgery. *Minim Invasive Ther Allied Technol*. 2004;13(5):362–367.
4. Possover M et al. The LANN technique to reduce postoperative functional morbidity in laparoscopic radical pelvic surgery. *J Am Coll Surg*. 2005;201(6):913–917.
5. Possover M et al. Anatomy of the sacral roots and the pelvic splanchnic nerves in women using the LANN technique. *Surg Laparosc Endosc Percutan Tech*. 2007;17(6):508–510.

6. Possover M et al. Neuropelveology: new groundbreaking discipline in medicine. *J Minim Invasive Gynecol*. 2015;22(7):1140–1141.
7. Possover M. Laparoscopic management of neural pelvic pain in women secondary to pelvic surgery. *Fertil Steril*. 2009;91(6): 2720–2725.
8. Possover M et al. Risks, symptoms, and management of pelvic nerve damage secondary to surgery for pelvic organ prolapse: a report of 95 cases. *Int Urogynecol J*. 2011;22(12):1485–1490.
9. Possover M. Pathophysiologic explanation for bladder retention in patients after laparoscopic surgery for deeply infiltrating rectovaginal and/or parametric endometriosis. *Fertil Steril*. 2014;101(3):754–758.
10. Possover M et al. Voiding dysfunction associated with pudendal nerve entrapment. *Curr Bladder Dysfunct Rep*. 2012;7(4):281–285.
11. Possover M et al. Laparoscopic therapy for endometriosis and vascular entrapment of sacral plexus. *Fertil Steril*. 2011;95(2): 756–758.
12. Possover M et al. The laparoscopic approach to control intractable pelvic neuralgia: from laparoscopic pelvic neurosurgery to the LION procedure. *Clin J Pain*. 2007;23(9):821–825.
13. Possover M. The "possover-LION procedure" to the pelvic somatic nerves in people with a spinal cord injury. *J Minim Invasive Gynecol*. 2022;29(3):340.
14. Possover M. The laparoscopic implantation of neuroprothesis to the sacral plexus for therapy of neurogenic bladder dysfunctions after failure of percutaneous sacral nerve stimulation. *Neuromodulation*. 2010;13(2):141–144.
15. Kasch H et al. Effect of pelvic laparoscopic implantation of neuroprosthesis in spinal cord injured subjects: a 1-year prospective randomized controlled study. *Spinal Cord*. 2022;60(3): 251–255.
16. Brose SW et al. Genital nerve stimulation is tolerable and effective for bladder inhibition in sensate individuals with incomplete SCI. *J Spinal Cord Med*. 2018;41(2):174–181.
17. Spinelli M et al. A new minimally invasive procedure for pudendal nerve stimulation to treat neurogenic bladder: description of the method and preliminary data. *Neurourol Urodyn*. 2005;24(4):305–309.
18. Magrina J et al. Nerve-sparing in gynecologic surgery: a perspective. *J Minim Invasive Gynecol*. 2021;28(3):475–480.
19. Zakhari A et al. Keep your landmarks close and the hypogastric nerve closer: an approach to nerve-sparing endometriosis surgery. *J Minim Invasive Gynecol*. 2020;27(4):813–814.
20. Sakuragi N et al. Nerve-sparing radical hysterectomy in the precision surgery for cervical cancer. *J Gynecol Oncol*. 2020; 31(3):e49.

20 ENDOMETRIOSIS: DIAGNOSIS AND PATHOPHYSIOLOGY

Guilherme Henrique Zanluchi, Marina Paula Andres, and Mauricio S. Abrão

20.1 Introduction

The term endometriosis was first introduced by Sampson in 1927 in a classical study that attributed this pathology to retrograde menstruation (1). The etiology of this disease is not completely understood but has been widely studied in recent years.

Endometriosis is a chronic hormone-dependent inflammatory condition characterized by the presence of functional endometrial glands and stroma outside the uterine cavity (2). According to Nisolle and Donnez (1997), endometriosis is classically subdivided into the following three distinct forms: peritoneal, ovarian, and rectovaginal endometriosis (presently referred to as deep infiltrating endometriosis). In addition to these frequent sites, they can also affect the colon, bladder, ureter, diaphragm, and other organs (3–5).

Endometriosis affects 6%–10% of women of reproductive age and is one of the most prevalent benign gynecological illnesses (6). It is also associated with infertility and pelvic pain. When considering only patients with these symptoms, the estimated prevalence increases to 35%–50% (6). Endometriosis also has detrimental effects on social, occupational, and psychological performance (7).

20.2 Pathophysiology

Many theories are known about the onset of endometriosis, but none explain all cases. It is considered a multifactorial disease involving impaired immunity, imbalanced cell proliferation, apoptosis, and genetic factors (2, 4, 5).

20.2.1 Sampson's Theory (Retrograde Menstruation)

This is currently one of the primary theories of endometriosis. This theory states that during the menstrual cycle, retrograde menstruation occurs through fallopian tube fragments of the viable endometrium, which are implanted in the pelvis. This blood accumulates in the lowest portions of the pelvic cavity, such as the ovarian fossa, the cul-de-sac of Douglas, the uterosacral ligaments, and the posterior part of the broad ligaments, which are the places in the pelvis where the peritoneal endometriosis is most commonly found (8).

Patients with a bicornuate uterus, vaginal atresia, hymenal imperforation or microperforation, transverse vaginal septum, and other obstructive genital malformations have an increased risk of experiencing menstrual reflux and may therefore develop endometriosis as well (9).

However, while up to 90% of women have retrograde menstruation, only 10%–15% develop endometriosis, indicating that additional elements, including immunological factors and microbiome, are involved (10–12).

20.2.2 Metaplasia Theory

The peritoneum, ovarian germinal epithelium, and Müllerian ducts (where the endometrium originates) share a common embryological origin. Therefore, all of its cells can undergo metaplasia and become endometrial cells, leading to peritoneal endometriosis, a phenomenon related to irritating factors that may be present in the menstrual blood itself (9). This theory also explains why endometrial lesions in teenagers disappear after the repair of obstructive deformities by transforming endometrial lesions into normal peritoneum (9).

This theory would explain endometriosis in amenorrheic women and extrapelvic endometriosis (13).

20.2.3 Immune Factors

Recent research has largely focused on the immune system as a complex and multifaceted component in the etiology of endometriosis. An increase in the concentrations of activated macrophages, cytokines, and T and B cells has been observed in the peritoneal fluid of women with endometriosis (14). Poor macrophage activation and signaling may promote the survival of ectopic endometrial cells (15).

20.2.4 Precursor Cell Theory

Endogenous ovarian hormones can induce remnants of Müllerian embryonic tissues of genital origin that persist in the peritoneum and can grow and transform into endometrial tissue. This theory explains infiltrative lesions in young individuals without accompanying peritoneal lesions, peritoneal lesions (9), and endometriosis in premenstrual patients (16, 17).

20.2.5 Genetic Factors

When investigating the genetic predisposition for endometriosis, a study showed that 6.9% of females with first-degree relatives with endometriosis also had the disease and 1% of those did not have a familiar history, indicating a significant genetic propensity in the development of the disease (18). In 2015, a retrospective analysis revealed that 34.5% of cases had a positive family history of endometriosis, and in 25.5% of those cases, a first-degree relative had the condition (19). These findings suggest that genetic heritage may also be involved.

20.2.6 Environmental Factors

Recent research on dietary and lifestyle variables has revealed an association between these variables and susceptibility to endometriosis. According to their findings, endometriosis can be prevented by consuming a diet rich in fruits and vegetables but low in meat. In addition, endometriosis is more likely to occur in women with low body mass indices (20, 21).

20.3 Lesion Phenotypes and Histology

Endometrial glands and stroma are frequently observed in endometriotic lesions. These lesions may contain cysts and blood and are frequently surrounded by fibrous tissue (4).

20.3.1 Lesion Phenotypes

Endometriotic lesions can be categorized as superficial, ovarian, and infiltrating endometriosis (3–5):

1. *Superficial*: Lesions are < 5 mm deep (4) categorized as red, black, or white lesions (Figure 20.1). Microscopically, these lesions appear as small glands with a large

* The authors report no financial conflicts of interest.

DOI: 10.1201/9781003312109-20

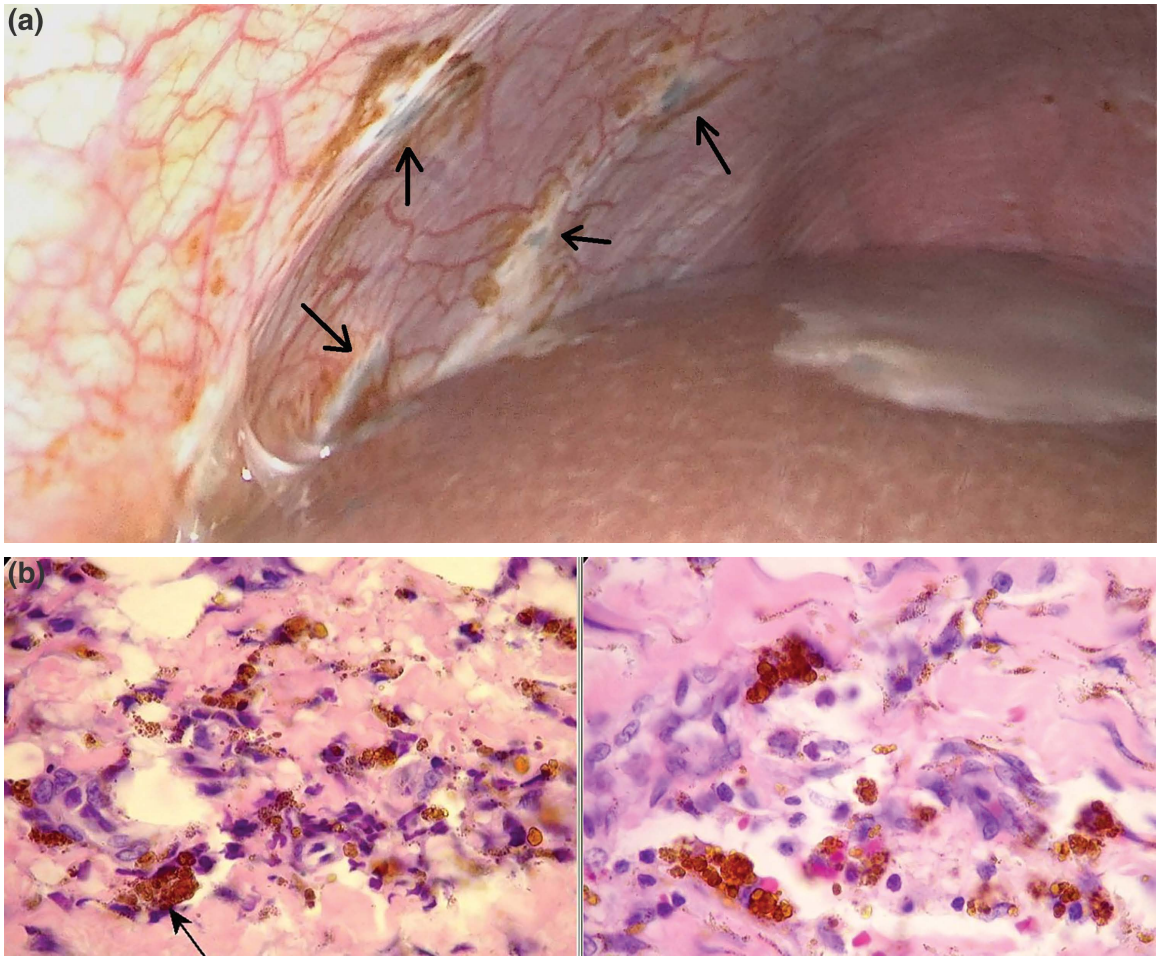


FIGURE 20.1 (a) Laparoscopic image of the black lesion in the diaphragm. Black arrows indicate the endometriotic tissue surrounded by fibrotic tissue and active glands. (b) Microscopic imaging of a black superficial endometriotic lesion showing active glands and hemosiderin deposition (From anatpat.unicamp.br, with permission).

number of infiltrating inflammatory cells and hemosiderin deposits.

2. *Ovarian endometrioma*: Ovarian endometriotic cysts are frequently filled with chocolate-like fluid (4, 5) (Figure 20.2).
3. *Deep endometriosis*: These are lesions that extend > 5 mm deep into the peritoneum (4, 5). It commonly affects the retrocervical region, rectosigmoid colon, bladder, ureter, and vagina (4) (Figure 20.3).

20.4 Diagnosis

20.4.1 Clinical Symptoms

While a considerable proportion of women with endometriosis are asymptomatic, others may experience severe and progressive pain symptoms such as dysmenorrhea, noncyclical chronic pelvic pain, deep dyspareunia, dyschezia, and painful cyclic urinary incontinence (22). However, the disease severity and its symptoms may not necessarily correlate.

In some cases, there may be a correlation between the type of symptoms and lesion location. Vaginal and retrocervical lesions often cause deep dyspareunia, bladder endometriosis may be associated with dysuria and urinary urgency, and rectosigmoid lesions may result in cyclic intestinal symptoms such as pain during defecation and diarrhea during menstruation (23).

Physical examinations are usually advisable and helpful for evaluation, particularly in cases of severe endometriosis. Common findings include the presence of nodules or uncomfortable thickening in the retrocervical region, an increase in the adnexal region (suggestive of ovarian endometriomas), a retroverted uterus with reduced mobility, and posterior cul-de-sac nodules (associated with uterosacral and intestinal diseases). Physical gynecological examinations can detect up to 80% of endometriotic lesions in the rectosigmoid (6, 22, 24). It is crucial to assess and diagnose additional causes of dyspareunia and pelvic pain, such as vaginismus and myofascial pain (24).

20.4.2 Imaging

Imaging tests should be used for further diagnostic investigation if the disease is suspected. Transvaginal ultrasonography with bowel preparation is a sensitive (49%–100%) and specific (93%–100%) examination that is inexpensive and accessible, and it should be used as the initial step in the diagnosis and choice of treatment. However, the outcomes may

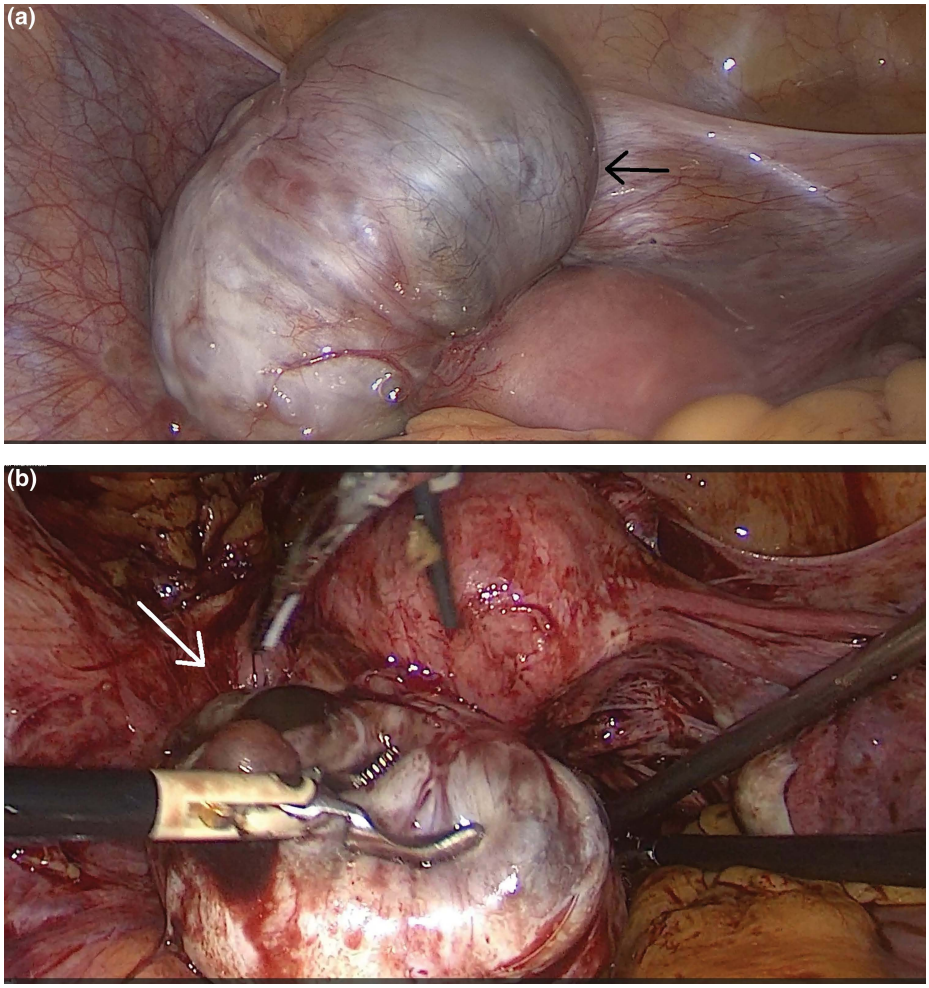


FIGURE 20.2 Laparoscopic image of a left ovarian endometrioma (arrow) before (a) and after (b) drainage. A chocolate-like fluid is observed after drainage.

vary depending on the technique used, the quality of the equipment utilized, and the experience of the professional executing it; therefore, it should be performed by a trained team (23). Bowel preparation before examination lowers the likelihood of image artifacts caused by the presence of air and feces in the rectal cavity.

To diagnose deep endometriosis, pelvic magnetic resonance imaging (MRI) should be performed with the gel in the vaginal cavity. This examination has high sensitivity and specificity (83% and 90%, respectively). Compared to transvaginal ultrasonography, MRI has a higher sensitivity for lesions in the uterosacral ligaments, rectovaginal septum, and vagina (85%, 77%, and 82%, respectively), but lower specificity (80%, 95%, and 90%, respectively). MRI and transvaginal ultrasonography show 73% sensitivity and 90% and 86% specificity for evaluating rectosigmoid lesions, respectively (23).

20.4.3 Laboratory Diagnosis

For the noninvasive diagnosis of endometriosis, several biochemical markers have been investigated, including CA 19–9, CEA, CA-125, α-fetoprotein, beta-2 microglobulin, anticardiolipin antibodies, and cytokines, including interleukin (IL)-2, 4, 6, 10, 12, 18, tumor necrosis factor-α, and interferon-Ɣ. One of the most studied biomarkers so far, CA-125, is an epithelial antigen and is expressed in tissues originating from the coelomic epithelium, including the endometrium, endocervix, fallopian tubes, peritoneum, pleura, and pericardium. However, despite being related to the disease, several studies have shown that it has low sensitivity and negative predictive value for the diagnosis of endometriosis; therefore, it is not recommended (12, 14, 15, 22, 25).

Despite improvements in noninvasive imaging techniques, laparoscopy with direct visualization of diseased implants and histological confirmation remains the gold standard for confirming a conclusive diagnosis of endometriosis. These procedures are no longer necessary for disease diagnosis. The disease should not only be diagnosed but also completely treated at the same time that the patient is developing pneumoperitoneum with all the associated surgical risks (24, 26).

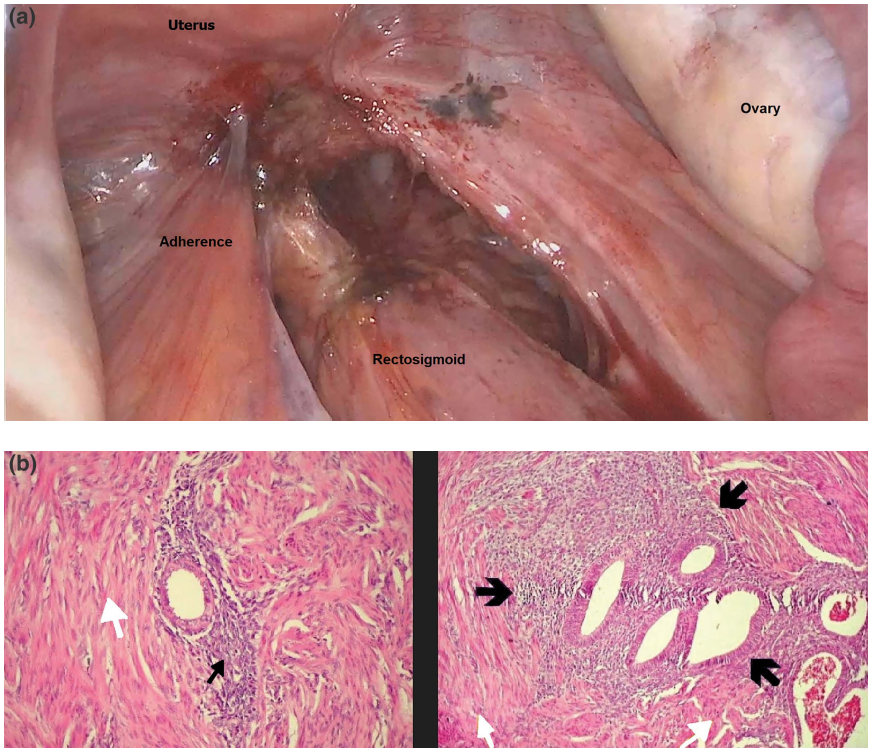


FIGURE 20.3 (a) Laparoscopic image of deep rectosigmoid endometriosis with partial cul-de-sac blockage. (b) Microscopic view of endometrial glands surrounded by inflammatory infiltrates (black arrows) in the intestinal muscle (white arrows) (From anatpat.unicamp.br, with permission).

References

1. Dastur AE et al. John A Sampson and the origins of endometriosis. *J Obstet Gynaecol India*. 2010;60(4):299–300.
2. Olive DL. *Endometriosis in Clinical Practice*. London: Taylor and Francis; 2005.
3. Nisolle M et al. Peritoneal endometriosis, ovarian endometriosis, and adenomyotic nodules of the rectovaginal septum are three different entities. *Fertil Steril*. 1997;68:585.
4. International Working Group of AAGL, ESGE, ESHRE, and WES et al. An international terminology for endometriosis. *J Minim Invasive Gynecol*. 2021;28:1849.
5. Royal College of Obstetricians and Gynaecologists. *The Investigation and Management of Endometriosis. Green-top Guideline No. 24*. London: Royal College of Obstetricians and Gynaecologists; 2002.
6. Mattos LA et al. Structured ultrasound and magnetic resonance imaging reports for patients with suspected endometriosis: guide for imagers and clinicians. *J Minim Invasive Gynecol*. 2019;26(6):1016–1025.
7. Mounsey A et al. Diagnosis and management of endometriosis. *Am Fam Phys*. 2006;74:594–600.
8. Sampson JA. Peritoneal endometriosis due to menstrual dissemination of endometrial tissue into the peritoneal cavity. *Am J Obstet Gynecol*. 1927;14:422–469.
9. Bourdel N et al. Endométriose et adolescente [Endometriosis in teenagers]. *Gynecol Obstet Fertil*. 2006 Sep;34(9):727–734.
10. Vercellini P et al. Endometriosis: pathogenesis and treatment. *Nat Rev Endocrinol*. 2014;10:261.
11. Halme J et al. Retrograde menstruation in healthy women and in patients with endometriosis. *Obstet Gynecol*. 1984;64:151.
12. Barcena de Arellano ML et al. Immunohistochemical characterization of endometriosis-associated smooth muscle cells in human peritoneal endometriotic lesions. *Hum Reprod*. 2011;26:2721–2730.
13. Jubanyik KJ et al. Extrapelvic endometriosis. *Obstet Gynecol Clin North Am*. 1997;24:411–440.
14. Podgaec S et al. Th1 and Th2 immune responses related to pelvic endometriosis. *Rev Assoc Med Bras*. 2010;56(1):92–98.
15. Szyllo K. The involvement of T lymphocytes in the pathogenesis of endometriotic tissues overgrowth in women with endometriosis. *Mediators Inflamm*. 2003;12:131–138.
16. Marsh EE et al. Endometriosis in premenarcheal girls who do not have an associated obstructive anomaly. *Fertil Steril*. 2005;83:758.
17. Figueira PG et al. Stem cells in endometrium and their role in the pathogenesis of endometriosis. *Ann NY Acad Sci*. 2011;1221:10.
18. Laufer MR et al. Adolescent endometriosis: diagnosis and treatment approaches. 2003 Jun;16(3):s3–s11. Review.
19. Audebert A et al. Adolecent endometriosis: report of a series of 55 cases with a focus on clinical presentation and long-term issues. *J Minim Invasive Gynecol*. 2015;22(5):834–840.
20. Fjerbaek A et al. Endometriosis, dysmenorrhea and diet – what is the evidence? *Eur J Obstet Gynecol Reprod Biol*. 2007;132:140–147.
21. Parazzini F. Selected food intake and risk of endometriosis. *Hum Reprod*. 2004;19:1755–1759.
22. ESHRE Special Interest Group for Endometriosis and Endometrium Guideline Development Group. ESHRE guideline for the diagnosis and treatment of endometriosis. *Hum Reprod*. 2005;120:2698–2704.
23. Abrao MS et al. Comparison between clinical examination, transvaginal sonography and magnetic resonance imaging for the diagnosis of deep endometriosis. *Hum Reprod*. 2007;22(12):3092–3097.
24. Kho RM et al. Surgical treatment of different types of endometriosis: comparison of major society guidelines and preferred clinical algorithms. *Best Pract Res Clin Obstet Gynaecol*. 2018;51:102–110.
25. Abrao MS et al. Histological classification of endometriosis as a predictor of response to treatment. *Int J Gynaecol Obstet*. 2003;82(1):31–40.
26. Abrão MS et al. Deep endometriosis infiltrating therectosigmoid: critical factors to consider before management. *Hum Reprod Update*. 2015;21(3):329–339.

21 MEDICAL MANAGEMENT OF ENDOMETRIOSIS

Papri Sarkar, Devon Marks, Maha Al Jumaily, and Emad Mikhail

21.1 Introduction

Endometriosis is a benign complex, estrogen-dependent, chronic inflammatory disease that affects 5%–10% of women of reproductive age (1–4). Endometriosis is characterized by the existence of ectopic endometrial-like tissue (stroma and glands) outside the uterus primarily in the pelvic area which is observed as ovarian cysts (endometrioma) and peritoneal and deep lesions (5, 6).

Symptoms of endometriosis can range widely from being asymptomatic to causing infertility problems and endometriosis-associated pain including chronic pelvic pain, pain with menstruation (dysmenorrhea), intercourse (dyspareunia), urination (dysuria), and defecation (dyschezia) (5). Endometriosis-associated pain might occur due to nerve infiltration and irritation by the endometriosis lesions and a high level of inflammatory mediators (7, 8).

Medical treatment for endometriosis includes hormonal and nonhormonal options. The main goal of medical treatment in endometriosis is to manage the endometriosis-associated pain and possibly impede the growth of the ectopic endometriosis foci, but these might reoccur again after stopping the therapy (8, 9). Medical therapy is usually indicated for short-term periods, as long-term medical management is limited due to the side effects and cost. Medical treatment lessens the endometriosis-associated pain level by reducing the production of estrogen and decreasing the level of inflammatory mediators (9). Empiric hormonal therapy can be used for 3 months in women with no history of histopathological confirmed endometriosis (4). Medication for endometriosis should be changed if there are no satisfactory results achieved after a few months of treatment (10).

Hormonal therapy can be used for long-term maintenance, especially for women who underwent surgical resection.

21.2 The First and Second Lines of Medical Management

The first line of medical treatment for endometriosis would include nonsteroidal anti-inflammatory drugs (NSAIDs), combined hormonal contraceptive pills, and progestins (11) (Table 21.1). Second-line treatment is recommended for women with persistent endometriosis-associated pain despite first-line medications and would include gonadotropin-releasing hormone (GnRH) agonists, GnRH antagonists, aromatase inhibitors, danazol, gestrinone, and selective estrogen receptor modulators (SERM) (11) (Table 21.2).

21.3 Role of Medical Therapy in Different Types of Endometriosis

Medical management of endometriosis is considered the first line of treatment with the overall goal to improve the endometriosis-associated symptoms by reducing the need for surgical intervention, preventing recurrence after surgical resection, improving quality of life, and preserving fertility (12–14). It is the first line of management for women who have no plans for immediate pregnancy to inhibit ovulation (15, 16). Hormonal therapy reduces the size of endometriotic lesions through inducing atrophy within the estrogen-dependent ectopic endometrium, which helps with reducing the endometriosis-associated pelvic pain through blockage of estrogen receptors and activation of progesterone receptors (15, 17).

The role of medical management in endometriosis depends on the phenotype. There are three different phenotypes of endometriosis: superficial peritoneal endometriosis (SUP), deep endometriosis (DE), and ovarian endometrioma (OMA) (18).

Ovarian endometrioma is common and present in 17% to 44% of women with endometriosis (19). It can cause mechanical damage to the ovaries, interrupt the blood supply to ovarian tissue, and lower the ovarian reserve (20, 21). The goal and approach of OMA management depends on the associated symptoms, the size of the endometrioma, and patients' preferences. The role of medical treatment includes pausing menstruation, inhibiting ovulation, achieving a hypohormonal state, and controlling pain (22). If chronic pelvic pain is the main symptom, then medical management will be the first line of treatment, but if infertility is the presenting symptom, then surgical resection of endometrioma and/or in vitro fertilization (IVF) would be the first line of treatment (20, 23). Medical management of endometriomas is associated with a higher ovarian reserve and is preferred over the surgical approach for a cyst that is 3 cm or smaller (20). Hormonal therapy should not be used to manage ovarian endometrioma in women with infertility as this will inhibit ovarian function (20).

There are a few advantages and disadvantages of using medical therapy in the management of endometriomas. The advantages include avoiding postoperative complications of surgery like lower ovarian reserve and avoiding the delay in starting in vitro fertilization, whereas the disadvantages include recurrence of pelvic pain, increasing the size of the cyst and associated damage to the ovarian tissue, and difficulty of accessing ovarian tissue during IVF (21).

Superficial peritoneal endometriosis is the most common phenotype of endometriosis where endometriosis spots are located on the surface of the peritoneum (24). The first line of peritoneal endometriosis management is hormonal therapy especially when there is no sonographic evidence of endometriosis and there is no immediate desire for pregnancy (25).

Hormonal therapy is recommended postoperatively for peritoneal endometriosis to improve and control chronic pelvic pain. Results of a retrospective cohort study of 94 women who underwent laparoscopic surgery for peritoneal endometriosis from January 2014 to June 2019 show a significant decrease in endometriosis-associated pain for the group who used hormonal therapy postoperatively (29.87%) compared to the group who did not use hormonal therapy (25).

Deep endometriosis presents in 20% of women with endometriosis and the management approach depends on the woman's preference, the severity of the symptoms, and the stage of endometriosis (26). The role of medical therapy in DE would include controlling the endometriosis-associated pain and other symptoms, preventing the development of new endometriotic lesions, and lowering the risk of recurrence after the surgery (26).

DOI: 10.1201/9781003312109-21

TABLE 21.1 First-Line Medical Treatment

Nonsteroidal anti-inflammatory drugs (NSAIDs)
Combined oral contraceptive pills
Progestines
Dienogest
Medroxyprogesterone acetate
Levonorgestrel intrauterine system (LNG-IUS)

TABLE 21.2 Second-Line Medical Treatment

Gonadotropin-releasing hormone (GnRH) agonists
Gonadotropin-releasing hormone (GnRH) antagonists
Aromatase inhibitors
Danazol
Gestrinone
Selective estrogen receptor modulators (SERMs)
Selective progesterone receptor modulators (SPRMs)

A retrospective cohort study of 122 women subjects with DE of the bowel shows that both medical and surgical approaches improve DE-associated pain when 61 women underwent surgery while 61 women received medical therapy (hormonal). However, the improvement in pain symptoms was higher and lasted for a longer period with the surgical approach compared to the medical therapy (27).

Medical treatment of deep endometriosis helps to decrease the pain level and is a treatment until surgery (28). Endometrial thickness is one of the tools used to monitor the response to hormonal therapy in controlling the symptoms in women with DE as higher responses have been noticed in women with thin endometrial thickness (< 3.3 mm) (29). Management with 6 months of gonadotropin-releasing hormone agonist (GnRH-a) postoperatively in women with superficial peritoneal endometriosis and deep infiltrative endometriosis is cost-effective in preventing the recurrence (30).

It is first important to note that all available medical treatments for endometriosis aim to improve symptoms and prevent progression. There is no available medical treatment that can provide a cure for endometriosis. Symptoms often recur after discontinuation of therapy. The focus of treatment is to address endometriosis-associated pain and infertility in women.

21.4 Nonhormonal Therapies

21.4.1 NSAIDs

Nonsteroidal anti-inflammatory drugs work to decrease inflammation by inhibiting prostaglandin production through inhibition of the cyclo-oxygenase enzymes. One proposed mechanism of endometriosis-related pain is inflammation caused by ectopic endometrial tissue; this provides the biological plausibility on how the use of NSAIDs may be effective. One placebo-controlled double-blind study of 18 women examined the effect of prostaglandin biosynthesis inhibitors acetylsalicylic acid, indomethacin, and tolfenamic acid on endometriosis-related dysmenorrhea. Results showed decreased reported symptoms in those treated with tolfenamic acid, a drug that inhibits both synthesis and action of prostaglandins (31, 32). Gastrointestinal side effects were higher in those treated with indomethacin and acetylsalicylic acid (31). Another study examined the effect of naproxen sodium on 24 women with dysmenorrhea secondary to endometriosis and showed significant reduction in pain and decreased need for supplemental analgesics with treatment compared to placebo (33). Cochrane library review deemed this evidence of naproxen efficacy to be very low quality, and no other trials were identified for Cochrane review 2016 update (34). While these studies demonstrate potential relief of symptoms by prostaglandin inhibition and anti-inflammatory effects, there are limited data showing significant relief of pain with NSAIDs alone. Due to low-quality evidence and side effects from long-term use, NSAIDs are often used in conjunction with other treatments (35). As NSAIDs are widely available with low risk overall, the European Society of Human Reproduction and Embryology (ESHRE) gives weak recommendation that NSAIDs be offered alone or in combination with other treatments (35). It is important to be aware that NSAIDs taken in high doses for long periods can have significant adverse gastrointestinal side effects, and patients should be counseled appropriately (36).

21.4.2 Neuromodulators

Neuromodulators act by affecting the central nervous system's modulation of pain rather than peripheral mediators. They are used mainly by pain medicine specialists. Some examples of this class of medications are anti-depressants, selective serotonin uptake inhibitors, and anticonvulsants. These medications have proven effective in treating other chronic pain conditions and propose a different mechanism of action than other available options. One randomized control study compared gabapentin vs placebo in treatment of chronic pelvic pain and found no significant difference in pain scores. Additionally, increased reports of side effects were associated with gabapentin, such as dizziness, drowsiness, and visual disturbances (37). Another study using a rat model showed significantly reduced endometriosis lesion size in rats treated with valproic acid compared to untreated rats. Moreover, rats treated with valproic acid had significantly increased weight gain (38). Unfortunately, the generalizability of these studies is limited. High-quality studies examining efficacy of neuromodulators on endometriosis-related symptoms are scarce. Neuromodulators are a promising alternative option, however in randomized clinical trials for the management of chronic pelvic pain, they have not been proven to be clearly superior to placebo and are sometimes associated with severe, dose-limiting side effects (35). Of note, women with endometriosis have high incidence of psychiatric disturbances (this is generally believed to be related to depression that results from chronic pain) and myofascial pain syndrome which may be treated with neuromodulators (39, 40). The use of neuromodulators may be particularly beneficial in patients with such comorbid conditions. More research is needed to better understand their utility in endometriosis.

21.5 Hormonal Therapies

Normal endometrium within the uterus expresses receptors that bind estrogens, androgens, progestins, and glucocorticoids (2). Hormonal therapy for endometriosis is based on the theory that endometrial-like tissue outside of the uterus remains hormonally responsive and is steroid dependent. Hormonal therapies aim to induce atrophy and decrease activity in ectopic endometrium that is presumed to be causative of symptoms. They modify the hormonal environment either by suppressing ovarian activity or acting directly on steroid

receptors and enzymes found in the lesions. These include progestogens, anti-progestogens, combined oral contraceptives, GnRH agonists, GnRH antagonists, the levonorgestrel intrauterine system (LNG-IUS), danazol, and aromatase inhibitors (e.g., letrozole). Per ESHRE guidelines it is recommended to offer women hormone treatment as one of the options to reduce endometriosis-associated pain (35).

21.5.1 Combined Hormonal Contraceptives

Combined hormonal contraceptives contain the two most important hormones in the female reproductive system, estrogen and progesterone. Synthetic formulations of these hormones act on endogenous hormone pathways to alter the menstrual cycle. Together they prevent follicular development and ovulation. Progestin, synthetic progesterone, also acts to induce endometrial atrophy, leading to a thinning of the endometrium. These mechanisms are mediated via negative feedback to the hypothalamus and anterior pituitary affecting GnRH, FSH, and LH secretion (41). Combined hormonal contraceptives include oral contraceptive pills (OCPs), vaginal ring, and transdermal patch. As most data have been collected on oral formulations, our discussion will focus on OCPs. OCPs reduce menstrual flow, thereby decreasing prostaglandin synthesis via arachidonic acid breakdown, and cause decidualization of endometriotic implants via decreased cell proliferation and increased apoptosis (42). They can be taken in cyclic, extended cycle, or continuous use formulations based on patient needs and preference. OCPs are a good option for those not currently desiring fertility and without cardiovascular disease, clotting disorders, or migraine with aura. OCPs should also be avoided in women with a personal history of breast or endometrial cancer, in the immediate postpartum period and in those who smoke, particularly over the age of 35 (41). OCPs have proven efficacious in both randomized control trials and observational studies with clinically and statistically significant results for endometriosis-related pain. This is demonstrated in the Cochrane review reporting OCP to be more effective than placebo (43). The ESHRE gives strong recommendation that OCPs can be prescribed to treat endometriosis-associated dyspareunia, dysmenorrhea, and non-menstrual pain (35). Based on smaller studies, ESHRE gives a weak recommendation that continuous use of OCPs can also be offered in patients desiring amenorrhea (35). One benefit of treatment with OCPs is that they are generally cost-effective and well tolerated by patients without significant side effects. Their action is also quickly reversible for women who may desire fertility in the future. Additionally, they can be taken consecutively for long periods of time safely (43). The largest side effect of OCPs is prevention of pregnancy, which may be desired by many women of reproductive age affected by endometriosis. Most other side effects are mild and resolve with time or switching formulations. Some potential side effects include breakthrough bleeding, nausea, headache, breast tenderness, and decreased libido (41). A randomized clinical trial of 47 women with endometriosis shows that both leuprolide and continuous oral contraceptives are equally effective in controlling endometriosis-associated pelvic pain (44).

21.5.2 Progesterone-Only Contraceptives

Progesterone-only medications are available as oral formulations, injections, implants, and intrauterine devices (IUDs). These medications use various formulations of progestins, synthetic compounds that mimic the effects of the natural hormone progesterone. Progestins inhibit cell proliferation, inflammation, neovascularization, and neurogenesis in endometriosis. Their suppressive action on the endometrium appears to be most important in reducing endometriosis-related pain. However, endometriotic lesions can demonstrate progesterone resistance through decreased receptor expression, expression of less active isoforms, and oxidative stress (45). Many formulations of progestin pills are available, although there is no evidence to suggest one is superior to another in the treatment of endometriosis (35). Some commonly used oral progestins are norethindrone acetate and desogestrel. Depot medroxyprogesterone is available as a subcutaneous or intramuscular injection. Levonorgestrel-releasing IUD can be placed in the office and is generally well tolerated by patients without need for anesthesia or analgesics. There are multiple levonorgestrel-releasing IUDs on the market, with approval for use between 3 and 8 years depending on the specific type. These are a good option for women looking for a lower maintenance treatment option and not desiring fertility in the near future. Similarly, etonogestrel-releasing subdermal implants can be safely placed in office with local anesthetic and are approved for 3 years. A 2012 Cochrane review comparing oral progestins and injectable medroxyprogesterone acetate with placebo and other drugs found medroxyprogesterone acetate to significantly reduce endometriosis-related symptoms compared with placebo. Studies comparing oral progestins with combined oral contraceptive pills have shown reduction in symptoms in both groups without significant difference between treatments (46). A review of five RCTs showed levonorgestrel-releasing IUDs to reduce pain scores and improve health-related quality of life (HRQoL) (35). There is less available data on subdermal implants; however, a 2020 RCT of 103 women showed significantly reduced endometriosis-related pain, dysmenorrhea, and chronic pelvic pain with both levonorgestrel-releasing IUDs and etonogestrel-releasing subdermal implants (47). Based on this data, ESHRE gives a strong recommendation to prescribe women progestins to reduce endometriosis-related pain. All progesterone-only medications provide the benefit of being reversible and safe for long-term use. Progesterone-only contraception is safe in the immediate postpartum period, and other contraindications are the same as noted earlier for OCPs. IUDs should not be placed with cervical cancer or suspected uterine infection. Side effect profiles vary by mode of administration and formulation. Providers should work with patients to understand which side effect profile may be best tolerated. Oral progestins may be associated with increased reports of headache, bleeding, and amenorrhea. Reported adverse effects of medroxyprogesterone include injection site reaction, bloating, weight gain, intermenstrual bleeding, and nausea (35).

21.5.3 Selective Progesterone Receptor Modulators (SPRMs)

Selective progesterone receptor modulators are a class of synthetic molecules that can interact with the progesterone receptor (PR) as an agonist, antagonist, or with mixed agonist/antagonist function. These molecules have recently become of interest as they have a wide spectrum of action and potential uses. Due to the ability of mixed action, SPRMs can have selective inhibition of endometrial proliferation to reduce disease burden without estrogen deprivation and undesired side effects (45). Unique, benign histological changes have been observed in endometrium of women treated with SPRMs, termed progesterone-associated endometrial changes (PAECs). These changes are described as cystic glandular dilation, inactive glands and epithelia lining, low mitotic activity, and increased apoptosis. Various studies have examined gene expression in these

changes, but none have shown expression of genes involved in endometrial cancer pathways (48). Mifepristone was the first SPRM discovered in 1980 for anti-glucocorticoid properties, and it wasn't until 1988 that its antiprogesterone role was observed. Mifepristone's antiproliferative effect is mediated via inhibition of PR. Some studies have also shown inhibition of estrogen receptor (ER) and increased expression of androgen receptor (AR). As androgens can act as antagonists of E2 action, mifepristone's increased AR expression could play a role in its antiproliferative effect. In clinical trial, regression of endometriosis lesions seems to be dependent on dose and duration of treatment. A 2017 Cochrane review reports moderate evidence that mifepristone reduces dysmenorrhea and low-quality evidence in reduction of dyspareunia. While more data is needed, it appears that higher doses are more effective than the 2.5 mg dose (49). Multiple RCTs comparing mifepristone and placebo show the prevalence of dysmenorrhea and pelvic pain were significantly reduced in treatment group at 3 and 6 months. There is some limited data to suggest that 6 months of treatment with mifepristone may lead to reduction in visible endometriosis, although this was based on a small sample size. Hot flashes, nausea and vomiting, and fatigue were reported significantly more in treatment groups. Additionally, an increased number of women developed transaminitis and PAECs (48). Another SPRM, ulipristal acetate, showed regression of endometriosis lesions studied in rats was mediated by apoptosis induction, reduction of cell proliferation, and increased expression adhesion molecules and anti-inflammatory effect. In current studies, ulipristal decreased PR expression and did not affect ER expression. In vivo studies have shown decreased endometrial proliferation, and regrowth after treatment interruption was slower than with progestins (50). There is insufficient data to make a recommendation on ulipristal efficacy on improving endometriosis-related symptoms. The 2017 Cochrane review found available data on ulipristal not suitable for analysis (49). Similar to mifepristone, PAEC has been observed after treatment for 6 months but was reversible. There is also concern for hepatotoxicity, and SPRMs should be avoided in those with liver disease (45). It is important to note that neither ESHRE nor ACOG mention SPRMs in their current recommendations (35).

21.5.4 GnRH Agonists

Another class of drugs used to treat endometriosis is gonadotropin-releasing hormone agonists. GnRH agonists differ from natural GnRH at amino acid sequence positions 6 and 10. Endogenous GnRH is released from the hypothalamus in a pulsatile manner that acts to stimulate the anterior pituitary to secrete FSH and LH, which regulate sex hormones. Upon initial administration of GnRH agonists, symptoms may flare as they act to increase estrogen production for approximately 10 days. However, when GnRH agonists are administered in a continuous, non-pulsatile manner, they downregulate the anterior pituitary resulting in a hypogonadotropic hypogonadal state. This ultimately means that ovarian estrogen production is suppressed. As discussed previously, hormonal treatment is based on the principle that ectopic endometrial deposits are hormone responsive. The downregulation of reproductive hormones caused by GnRH agonists aims to decrease activity in these deposits. One commonly available GnRH agonist is leuprolide, which is given as an intramuscular (IM) injection in 1- or 3-month intervals depending on dosage. Treatment duration is usually 6 months. Leuprolide IM injections may be given with or without add-back hormonal therapy of norethindrone acetate. Both regimens are FDA approved for treatment of endometriosis. The purpose of norethindrone acetate is to dimmish negative side effects of the hypoestrogenic state like vasomotor symptoms and loss of bone mineral density. Leuprolide is not suitable for women who are breastfeeding, are pregnant, or may become pregnant. Add-back therapy with norethindrone acetate is contraindicated in women with cardiovascular disease, impaired liver function, hypercoagulable state, and breast cancer. A 2010 Cochrane review examined efficacy of GnRH agonists compared with no treatment, placebo, danazol, and progestin IUDs. GnRH agonists were superior to no treatment/placebo and no significant difference in pain relief was identified between GnRH agonists and danazol or LNG-IUD (51). ESHRE guidelines give strong recommendation to GnRH agonists to reduce endometriosis-related pain, although dosage and duration need to be further studied. There is moderate-quality evidence to suggest that add-back therapy resulted in reduced bone mineral density loss without affecting efficacy of GnRH agonist on reducing symptoms. For this reason, the guidelines strongly recommend that clinicians consider prescribing hormonal add-back therapy to prevent hypoestrogenic side effects. Due to these potentially serious side effects like bone loss, they consider GnRH agonist second line after a safer alternative such as OCP or progestin has been ineffective. Special consideration on long-term bone health should be taken in adolescents who may not have achieved maximum bone density and all young women (35).

21.5.5 GnRH Antagonists

GnRH antagonists suppress GnRH hormone production by competing with endogenous hormone for pituitary receptors. Like GnRH agonists, these medications act to suppress anterior pituitary release of FSH and LH leading to a hypogonadotropic hypogonadal state. Unlike GnRH agonists, there is no flare phase and therapeutic effect can be quickly achieved. In addition, GnRH antagonists are shorter acting, which may be beneficial as rapid reversal of hypoestrogenic adverse effects is possible (52). Common GnRH antagonists include elagolix and relugolix, which are available as oral formulations of varying doses. Both elagolix and relugolix are FDA approved for treatment of endometriosis. Multiple RCTs have shown elagolix and relugolix to be effective in relieving endometriosis-associated pain compared with placebo in a dose-dependent manner. Data show significant reduction in dysmenorrhea and nonmenstrual pelvic pain. In available studies, elagolix improved dyspareunia compared with placebo, while relugolix showed no significant difference (53). Reported side effects also appear to be dose dependent and include hot flushes, headache, and nausea. Significant decrease in spinal bone mineral density in patients treated with elagolix has been noted in a dose-dependent manner (53). There is insufficient data on dosage and duration of treatment, need for add-back therapy and effects on bone health. In August 2022 the FDA approved a combination therapy of relugolix, estradiol, and norethindrone as a once daily pill in premenopausal women for treatment of endometriosis. Preliminary studies claim decreased amounts of bone mineral density (BMD) loss with this new formulation. ESHRE guidelines give weak recommendation to consideration of GnRH antagonists to reduce endometriosis-related pain, stating more evidence is needed. Similar to GnRH agonists, these drugs should be considered second line due to side effect profile, and special consideration should be taken for adolescents and young women on the long-term effects on bone health (35).

21.5.6 Aromatase Inhibitors

Aromatase is an enzyme involved in conversion of androgens to estrogen. Aromatase is expressed in eutropic endometrium as well as ectopic endometrial lesions. Molecular studies have

identified aromatase P540 inside of endometriotic tissue, suggesting local synthesis of estradiol contributing to disease process. Based upon this, aromatase inhibitors present a unique and specific option to manage endometriosis-related pain and infertility (54). Aromatase inhibitors (AI) block estrogen synthesis in the periphery and in the ovaries. They have traditionally been used and are FDA approved for medical treatment of hormone receptor positive breast cancer. They are not yet approved by the FDA for treatment of endometriosis. Studies have shown third-generation aromatase inhibitors letrozole and anastrozole to reduce endometriosis-related pain symptoms. Studies have examined the use of AI in oral formulations and vaginal suppositories, in combination with progestins and OCP. There is insufficient data to state one superior to another, although it appears letrozole has been studied more. One study showed a 50% decrease in the size of endometrioma after 3 months of treatment with letrozole and add-back progestin (55). ESHRE guidelines give strong recommendation to use of AI for endometriosis-related pain that is refractory to other medical or surgical therapy, as they reduce associated pain. One benefit of AI is that they can be prescribed in adjunct to OCP, progestins, GnRH agonists, and GnRH antagonists (35). However, AI use is limited by adverse effects that are difficult to tolerate for patients. These include bone, joint, and muscle pain, as well as fatigue (52). Further studies are needed to assess long-term safety and generalizability of results. It is unclear if there is any role of letrozole's ovulation-inducing effect in treatment of endometriosis-associated infertility and assistive reproductive technologies.

21.5.7 Danazol

Danazol is a synthetic steroid derived from ethinyl testosterone with a high affinity to androgen receptors and moderate affinity to progesterone preceptors and gonadotropin receptors. Oral danazol was approved by the FDA to treat endometriosis in 1971 and used for many years in treatment of endometriosis-related symptoms. However, there are other medical therapies available with more favorable side effect profiles. Significant side effects related to danazol's androgenic properties have limited its use. These include LDL increase, HDL decrease, acne, edema, weight gain, muscle cramps, and hirsutism (35, 52). More recently, vaginal danazol has been studied particularly in deep endometriosis and rectovaginal endometriosis and shown improvement in endometriosis-related symptoms, reduction in heavy menstrual bleeding, and reduction in volume of the lesion. The results were achieved without significant androgenic adverse effects as seen with oral danazol. More robust RCTs with larger sample size is needed to make recommendation on vaginal danazol use and further assess its safety profile (56).

21.6 Medical Treatment of Endometriosis in Adolescent Populations

Adolescents are defined as females under the age of 20 years, a group which experience high rates of dysmenorrhea. Endometriosis and associated pain in this age group can be detrimental during a pivotal time of self-growth and affect school performance. In cases of suspected endometriosis first-line therapy remains NSAIDs, OCPS, and progestins. These medications are effective, safe, well studied, and reasonably priced. It is important to note that some progestins may decrease BMD in a reversible manner. Studies of GnRH agonist use in adolescents suggest they are best used with combined add-back therapy to increase quality of life and mitigate BMD side effects. Still, careful consideration must be taken regarding potential long-term side effects (35). Surveillance should be performed with DEXA scan and therapy discontinued if bone mineral density loss occurs despite add-back therapy. There is no evidence to support that medical treatment is helpful in stopping or slowing the progression of endometriosis in the adolescent population.

21.7 Endometriosis and Infertility

Approximately 30%–50% of women with endometriosis experience infertility. The relationship between endometriosis and infertility is complex. In treatment of infertility, a Cochrane review of 12 studies showed ovulation suppression by hormonal therapy appears to have no benefit on pregnancy rate when compared with no treatment (57). Based upon this data, ovulation suppression should not be used to treat infertility (35). Also, ovulation suppression used in adjunct to surgery in perioperative period has an unclear role. The 2020 Cochrane review of 25 RCTs concludes that postsurgical hormonal suppression therapy may improve pregnancy rate when compared with no medical therapy (32). However, the quality of this evidence is low due to the indirectness of outcomes measured and inconsistency across studies. It may be better interpreted that postsurgical hormonal suppression does not appear to negatively affect fertility and may be prescribed for pain management. For these reasons, ESHRE guidelines recommend postsurgical hormone suppression should not be used solely to enhance pregnancy rates but may be used to treat pain. Another RCT compared treatment with letrozole, an aromatase inhibitor, with triptorelin, a GnRH agonist and no medication after surgical intervention. Pregnancy rates at 1 year after restoration of normal cycle were similar in all groups. Therefore, when used for its antiestrogen properties, letrozole is not recommended to improve natural pregnancy rates (35). Anti-inflammatories have also been studied as a treatment for endometriosis-associated infertility. Pentoxifylline, a xanthine derivative often used to treat lower extremity claudication, has anti-inflammatory properties that have been studied for their use in endometriosis. A Cochrane review of three RCTs showed uncertain results if pentoxifylline improved pregnancy rate, and no trial reported live birth rate (58). It is unclear if targeting the chronic inflammation of endometriosis may improve fertility but based upon current studies there is insufficient evidence to prescribe anti-inflammatory drugs such as pentoxifylline to do so and it is not recommended (35).

The mainstay of treatment for endometriosis-associated infertility remains surgery. A prospective RCT comparing postsurgical treatment with clomiphene citrate and letrozole significantly increased ovulation compared with control, without change in pregnancy rate or live birth rate (59). While these findings may suggest that paired with intrauterine insemination (IUI) clomiphene and letrozole may increase pregnancy rate, there are no studies examining these outcomes in women with endometriosis.

21.8 Endometriosis and Pregnancy

Endometriosis-associated pain improves in many women during pregnancy, which is not surprising as the hormonal changes in the body reflect similar mechanisms to hormonal treatments. The most important hormonal changes are thought to be cessation of ovulation and increased levels of progesterone during pregnancy. As ovulation suppression and progestins

are two first-line methods in which we treat endometriosis, this improvement makes sense. However, the behavior of lesions seems to vary, with some lesions increasing in size and some decidualizing. Decidualization of endometrioma may resemble a malignant ovarian tumor and present a difficult diagnostic challenge (35). In these cases first-line treatment is with expectant management via serial monitoring by US or MRI. If malignancy is suspected and surgery needed, the best option is minimally invasive laparoscopic approach no later than 23 weeks at a tertiary care center (60). For some women, it may be difficult to decipher if their endometriosis-related pain has improved as pregnancy itself is frequently associated with pelvic pain. Some common causes of pelvic pain in pregnancy are round ligament pain, muscle spasms, pelvic girdle pain, and pressure on local structures from the growing fetus. For these reasons there is limited high-quality data examining change in endometriosis-related pain in pregnancy. Symptoms frequently recur after pregnancy, although breastfeeding may delay the return. The ovulatory changes may last several months with variation by breast feeding frequency. Once normal ovulatory cyclicity has returned, similar to women who did not breastfeed, symptoms often recur. Overall, women should not be advised to become pregnant for the sole purpose of treating endometriosis, as symptoms do not always improve and often recur (35). Recent studies have focused on the effect of endometriosis on the pregnancy, as opposed to the other direction. There appears to be an increased risk of spontaneous hemoperitoneum, bowel and ovarian complications, and placenta previa. Some data also suggest an increased risk of first trimester miscarriage, ectopic pregnancy, and several other risk factors based on low-quality evidence. More studies are needed before conclusions cannot be drawn on such risks. As there are no data to suggest that treatment prior to pregnancy minimizes these risks, women with endometriosis should receive routine prenatal care. However, clinicians should be aware of these risks and take a careful, detailed history at each appointment, as they are uncommon but serious (35, 60).

21.9 Endometriosis in Peri- and Post-Menopause

Endometriosis is a steroid-dependent disease state. With cessation of ovarian function creating a hypoestrogenic state in natural or surgically induced menopause, with bilateral oophorectomy, most women experience improvement of symptoms and regression of disease. Some women, however, report continued symptoms, likely due to the complex pathogenesis of endometriosis-related hormonal pathways. It is speculated this may be due to extraovarian estrogen production or local overproduction within lesions via aromatase overexpression and other androgenic genes. Alternatively, the hypoestrogenic state of menopause causes significant symptoms that impair their quality of life. Commonly these symptoms are treated with hormone replacement therapy, which is the most effective therapy to treat vasomotor symptoms and urogenital atrophy. A systematic review along with a 2009 Cochrane review report a small association between menopausal hormone replacement and endometriosis recurrence, although this wasn't significant in any of the included studies (61). More data are needed to clarify risk of recurrence and ideal regimen. In summary, combined menopausal hormone replacement therapy can be prescribed in women with a history of endometriosis, although patients should be counseled appropriately on the possibility of symptom recurrence. Women with surgically induced menopause should be treated with hormone replacement until age of menopause (35). Any postmenopausal woman on hormone therapy with recurrence of symptoms should stop hormone therapy before exploring other treatment, understanding vasomotor symptoms may recur. Despite operative risks, surgical excision of lesions may be considered first line in some patients as medical therapy is limited. Aromatase inhibitors present one option for medical management as they block extraovarian estrogen production. This presents a theoretically appealing option as this is the predominant source of estrogen in postmenopausal women. As discussed previously, aromatase inhibitors have shown to be effective in reducing endometriosis-associated pain in premenopausal women, although side effects of hot flushes and BMD must be considered. Data specific to AI use in postmenopausal women are limited to case reports, which suggest similar improvement in symptoms as those in premenopausal women. AI can be considered as a treatment option in postmenopausal women, particularly when surgery is not feasible (35).

21.10 Role of Medical Therapy in Perioperative Period

Treatment approach for endometriosis involves employing both surgical and medical therapies to minimize the recurrence of the condition, which includes control of pain, dysmenorrhea, dyspareunia, and disease burden. However, the optimal timing for administering medical therapy in relation to surgery – that is, before, after, or both before and after surgery – is to optimize treatment response remains unclear, despite the apparent benefits of the combined approach.

21.10.1 Preoperative Medical Management Options

Current literature does not support the use of preoperative hormone treatment to improve immediate outcome of surgery for pain in women with endometriosis. It shows no benefit of preoperative use of medical therapies with respect to pain, dysmenorrhea, or dyspareunia recurrence post-surgery (35, 62). Chen et al. performed a metanalysis to determine the effectiveness of medical therapies for hormonal suppression before, after, or both before and after surgery for endometriosis for improving painful symptoms, reducing disease recurrence, and increasing pregnancy rates. For this, they included 25 RCTs with 3378 women with endometriosis. When comparing "surgery-alone" with presurgical hormonal suppression, the results were inconclusive if presurgical hormonal suppression reduced pain recurrence at 12-month (RR 1.10, 95% CI: 0.72 to 1.66; 1 RCT, $n = 262$; very low-quality evidence), or if it reduced disease recurrence at 12 months or less as compared to surgery alone (RR 0.88, 95% CI: 0.78 to 1.00; 1 RCT, $n = 262$; very low-quality evidence). They were uncertain if presurgical medical hormonal suppression improved pregnancy rates compared to surgery alone (RR 1.18, 95% CI: 0.97 to 1.45; 1 RCT, $n = 262$; very low-quality evidence) (32). From the patient's viewpoint, medical treatment should be administered before surgery to women experiencing painful symptoms during the waiting period before surgery, with the aim of alleviating pain before, rather than after, the procedure.

21.10.2 Postoperative Medical Management Options

If a woman with endometriosis does not wish to become pregnant immediately after surgery, she may be recommended postoperative hormone therapy to enhance the surgical outcomes for pain relief. Postoperative medical management can be considered for short-term goals and long-term goals.

Chen et al. presented the best available data on short-term (≤ 12 months) pain and disease recurrence post-surgery. The interventions included were GnRH agonists, danazol, letrozole, OCP, and progestogens. Compared to surgery alone, postsurgical medical therapy may decrease pain recurrence at 12 months or less (RR 0.70; 95% CI: 0.52 to 0.94; 5 RCTs; 657 patients) and disease recurrence (RR 0.30; 95% CI: 0.17 to 0.54; 4 RCTs; 433 patients) (62). In a randomized control trial of 55 patients with endometriosis and moderate to severe dysmenorrhea, significantly lower median values were obtained if dysmenorrhea and noncyclical pelvic pain score was reported in patients at 12-month follow-up who received LNG-IUS as compared to expectant management. However, this is not an option for patients who want to get pregnant immediately. According to the ESHRE guidelines, postoperative hormone therapy within 6 months of surgery has only a slight advantage in enhancing surgical outcomes. Nonetheless, hormone therapy may be given for other reasons, such as contraception or secondary prevention, without any demonstrated harm. In a recent study that included 1092 patients for a long-term follow-up period up to 10 years found that the recurrence rate can be as low as 28%. It is noteworthy that the majority of patients in that study used postoperative hormonal suppression. Based on that study population, it is justified to consider postoperative hormonal suppression in patients who do not have an immediate desire to get pregnant and do not report tolerance issues (63).

Almost all currently available treatments of endometriosis are suppressive, not curative. On treatment discontinuation, recurrence of the symptoms is the rule. For instance, endometriosis-associated pain can continue after medical treatment or conservative surgery. After medical treatment or surgical treatment, the recurrence of endometriosis was estimated to be 21.5% at 2 years and 40% to 50% at 5 years (64). For short-term medical therapy (< 6 months), no benefit of oral contraceptive (either cyclic or continuous) was seen in reducing pain recurrence. However, some studies have shown that long-term (> 6month) administration of postoperative medications (Table 21.1) can prevent recurrence of symptoms (65).

For prevention of ovarian endometriosis (endometrioma) recurrence, several studies have reported use of different medications, which are listed in Table 21.2. Many studies have evaluated the use of oral contraceptive (OC) from 6-month to 36-month follow-up and collectively demonstrate that postoperative OC conveys a protective effect against recurrence of ovarian endometrioma, but the effect seems to vanish rapidly after discontinuation (66–69). In an RCT by Cucinella, different regimens of OCs with different progestins (i.e., desogestrel, gestodene, and dienogest) were compared and no significant difference was seen in the recurrence rate between these agents (26.5%, 31.8%, and 20.5%), although the recurrence rate in nonusers (74.7%) was significantly higher than that in all OC groups (P <.005). Other options to consider are progestins which includes dienogest, LNG-IUS, and depo MPA. Wong et al. demonstrated that both LNG-IUS and depot MPA administered for 3 years after laparoscopy can inhibit lesion recurrence (recurrence was not detected in any patient in either group). In this study, the authors also found that LNG-IUS was associated with better compliance (reduced vaginal bleeding) and greater safety (reduced bone mineral density loss) than MPA (70). Other studies have reported that LNG-IUS is as effective as OC; however, the patient satisfaction is higher with LNG-IUS (71).

For prevention of deep lesion recurrence, the data are sparse. When followed up for > 2 years, the rate of deep lesion recurrence was reported to be 10%. A prospective study involving 500 women treated with shave excision of rectovaginal endometriosis showed that women who received continuous postoperative progestin had a very low recurrence rate (1%), as did women who had interrupted medical treatment and quickly conceived (2%), compared to women who discontinued treatment but did not become pregnant (20%). This indicates that postoperative medical treatment is important for women who do not want to conceive. According to a review article by Roman et al., continuous medical treatment can prevent recurrence of deep endometriosis after surgical management. The article suggests that instead of choosing either medical or surgical management, both therapies should be combined for optimal effectiveness (72).

References

1. Bulun SE et al. Endometriosis. *Endocr Rev*. 2019;40:1048–1079.
2. Saunders PTK et al. Endometriosis: etiology, pathobiology, and therapeutic prospects. *Cell*. 2021;184:2807–2824.
3. Zondervan KT et al. Endometriosis. *Nat Rev Dis Primers*. 2018;4:9.
4. Smolarz B et al. Endometriosis: epidemiology, classification, pathogenesis, treatment and genetics (review of literature). *Int J Mol Sci*. 2021;22.
5. Parasar P et al. Endometriosis: epidemiology, diagnosis and clinical management. *Curr Obstet Gynecol Rep*. 2017;6:34–41.
6. Foti PV et al. Endometriosis: clinical features, MR imaging findings and pathologic correlation. *Insights Imaging*. 2018;9:149–172.
7. Filip Lv et al. Endometriosis associated infertility: a critical review and analysis on etiopathogenesis and therapeutic approaches. *Medicina* (Kaunas). 2020;56.
8. Rafique S et al. Medical management of endometriosis. *Clin Obstet Gynecol*. 2017;60:485–496.
9. Nezhat C et al. Optimal management of endometriosis and pain. *Obstet Gynecol*. 2019;134:834–839.
10. Amro B et al. New understanding of diagnosis, treatment and prevention of endometriosis. *Int J Environ Res Public Health*. 2022;19.
11. Kalaitzopoulos DR et al. Treatment of endometriosis: a review with comparison of 8 guidelines. *BMC Womens Health*. 2021;21:397.
12. Martone S et al. Role of medical treatment of endometriosis. *Minerva Obstet Gynecol*. 2021;73:304–316.
13. Muzii L et al. Management of endometriomas. *Semin Reprod Med*. 2017;35:25–30.
14. Chantalat E et al. Estrogen receptors and endometriosis. *Int J Mol Sci*. 2020;21.
15. Kim MR et al. Clinical diagnosis and early medical management for endometriosis: consensus from Asian Expert Group. *Healthcare* (Basel). 2022;10.
16. Chauhan S et al. Endometriosis: a review of clinical diagnosis, treatment, and pathogenesis. *Cureus*. 2022;14:e28864.
17. Gheorghisan-Galateanu AA et al. Hormonal therapy in women of reproductive age with endometriosis: an update. *Acta Endocrinol* (Buchar). 2019;15:276–281.
18. Reis FM et al. Superficial peritoneal endometriosis: clinical characteristics of 203 confirmed cases and 1292 endometriosis - free controls. *Reprod Sci*. 2020;27:309–315.
19. Jee BC. Efficacy of ablation and sclerotherapy for the management of ovarian endometrioma: a narrative review. *Clin Exp Reprod Med*. 2022;49:76–86.
20. Muzii L et al. Expectant, medical, and surgical management of ovarian endometriomas. *J Clin Med*. 2023;12.
21. Lee D et al. Management of endometriosis-related infertility: considerations and treatment options. *Clin Exp Reprod Med*. 2020;47:1–11.
22. Vignali M et al. Approaching ovarian endometrioma with medical therapy. *Minerva Obstet Gynecol*. 2021;73:215–225.
23. Muzii L et al. Current management of ovarian endometriomas. *Minerva Ginecol*. 2018;70:286–294.
24. Allaire C et al. Diagnosis and management of endometriosis. *CMAJ*. 2023;195:E363–E371.

25. Duckelmann AM et al. When and how should peritoneal endometriosis be operated on in order to improve fertility rates and symptoms? The experience and outcomes of nearly 100 cases. *Arch Gynecol Obstet*. 2021;304:143–155.
26. D'Alterio MN et al. Management challenges of deep infiltrating endometriosis. *Int J Fertil Steril*. 2021;15:88–94.
27. Rezende GP et al. Surgery vs. hormone-based treatment for pain control in deep infiltrating endometriosis: a retrospective cohort study. *Curr Med Res Opin*. 2022;38:641–647.
28. Koninckx PR et al. Treatment of deeply infiltrating endometriosis. *Curr Opin Obstet Gynecol*. 1994;6:231–241.
29. Mariani LL et al. Endometrial thickness in the evaluation of clinical response to medical treatment for deep infiltrating endometriosis: a retrospective study. *Arch Gynecol Obstet*. 2021;303:161–168.
30. Wu B et al. Medical therapy for preventing recurrent endometriosis after conservative surgery: a cost-effectiveness analysis. *BJOG*. 2018;125:469–477.
31. Kauppila A et al. Prostaglandin biosynthesis inhibitors and endometriosis. *Prostaglandins*. 1979;18:655–661.
32. Chen I et al. Pre- and postsurgical medical therapy for endometriosis surgery. *Cochrane Database Syst Rev*. 2020;11: Cd003678.
33. Kauppila A et al. Naproxen sodium in dysmenorrhea secondary to endometriosis. *Obstet Gynecol*. 1985;65:379–383.
34. Brown J et al. Nonsteroidal anti-inflammatory drugs for pain in women with endometriosis. *Cochrane Database Syst Rev*. 2017;1:Cd004753.
35. Becker CM et al. ESHRE guideline: endometriosis. *Hum Reprod Open*. 2022;2022:hoac009.
36. Allen C et al. Nonsteroidal anti-inflammatory drugs for pain in women with endometriosis. *Cochrane Database Syst Rev*. 2009:CD004753.
37. Horne AW et al. Gabapentin for chronic pelvic pain in women (GaPP2): a multicentre, randomised, double-blind, placebo-controlled trial. *Lancet*. 2020;396:909–917.
38. Liu M et al. Valproic acid and progestin inhibit lesion growth and reduce hyperalgesia in experimentally induced endometriosis in rats. *Reprod Sci*. 2012;19:360–373.
39. Pope CJ et al. A systematic review of the association between psychiatric disturbances and endometriosis. *J Obstet Gynaecol Can*. 2015;37:1006–1015.
40. Galasso A et al. A comprehensive review of the treatment and management of myofascial pain syndrome. *Curr Pain Headache Rep*. 2020;24:43.
41. Cooper DB et al. Oral contraceptive pills [Internet]. In: *StatPearls*. Treasure Island: StatPearls Publishing; 2022.
42. Meresman GF et al. Oral contraceptives suppress cell proliferation and enhance apoptosis of eutopic endometrial tissue from patients with endometriosis. *Fertil Steril*. 2002;77: 1141–1147.
43. Brown J et al. Oral contraceptives for pain associated with endometriosis. *Cochrane Database Syst Rev*. 2018;5:Cd001019.
44. Guzick DS et al. Randomized trial of leuprolide versus continuous oral contraceptives in the treatment of endometriosis-associated pelvic pain. *Fertil Steril*. 2011;95:1568–1573.
45. Reis FM et al. Progesterone receptor ligands for the treatment of endometriosis: the mechanisms behind therapeutic success and failure. *Hum Reprod Update*. 2020;26:565–585.
46. Brown J et al. Progestagens and anti-progestagens for pain associated with endometriosis. *Cochrane Database Syst Rev*. 2012;2012:Cd002122.
47. Margatho D et al. Endometriosis-associated pain scores and biomarkers in users of the etonogestrel-releasing subdermal implant or the 52-mg levonorgestrel-releasing intrauterine system for up to 24 months. *Eur J Contracept Reprod Health Care*. 2020;25:133–140.
48. Islam MS et al. Selective progesterone receptor modulators-mechanisms and therapeutic utility. *Endocr Rev*. 2020;41.
49. Fu J et al. Progesterone receptor modulators for endometriosis. *Cochrane Database Syst Rev*. 2017;7:Cd009881.
50. Liang B et al. Efficacy, safety and recurrence of new progestins and selective progesterone receptor modulator for the treatment of endometriosis: a comparison study in mice. *Reprod Biol Endocrinol*. 2018;16:32.
51. Brown J et al. Gonadotrophin-releasing hormone analogues for pain associated with endometriosis. *Cochrane Database Syst Rev*. 2010;2010:Cd008475.
52. Vannuccini S et al. Hormonal treatments for endometriosis: the endocrine background. *Rev Endocr Metab Disord*. 2022;23:333–355.
53. Xin L et al. Efficacy and safety of oral gonadotropin-releasing hormone antagonists in moderate-to-severe endometriosis-associated pain: a systematic review and network meta-analysis. *Arch Gynecol Obstet*. 2023;308(4):1047–1056.
54. Abu Hashim H. Potential role of aromatase inhibitors in the treatment of endometriosis. *Int J Womens Health*. 2014;6:671–680.
55. Agarwal SK et al. Reduction in endometrioma size with three months of aromatase inhibition and progestin add-back. *Biomed Res Int*. 2015;2015:878517.
56. Godin R et al. Vaginally administered danazol: an overlooked option in the treatment of rectovaginal endometriosis? *J Obstet Gynaecol Can*. 2015;37:1098–1103.
57. Hughes E et al. Ovulation suppression for endometriosis. *Cochrane Database Syst Rev*. 2007;2007:Cd000155.
58. Grammatis AL et al. Pentoxifylline for the treatment of endometriosis-associated pain and infertility. *Cochrane Database Syst Rev*. 2021;8:Cd007677.
59. Zhou L et al. Ovulation induction with clomiphene citrate or letrozole following laparoscopy in infertile women with minimal to mild endometriosis: a prospective randomised controlled trial. *J Obstet Gynaecol*. 2022;42:316–321.
60. Maggiore LRU et al. A systematic review on endometriosis during pregnancy: diagnosis, misdiagnosis, complications and outcomes. *Hum Reprod Update*. 2016;22:70–103.
61. Gemmell LC et al. The management of menopause in women with a history of endometriosis: a systematic review. *Hum Reprod Update*. 2017;23:481–500.
62. Yang L et al. The role of oxidative stress and natural antioxidants in ovarian aging. *Front Pharmacol*. 2020;11:617843.
63. Roman H et al. Long-term risk of repeated surgeries in women managed for endometriosis: a 1,092 patient-series. *Fertil Steril*. 2023;120(4):870–879.
64. Guo SW. Recurrence of endometriosis and its control. *Hum Reprod Update*. 2009;15:441–461.
65. Koga K et al. Prevention of the recurrence of symptom and lesions after conservative surgery for endometriosis. *Fertil Steril*. 2015;104:793–801.
66. Vercellini P et al. Postoperative oral contraceptive exposure and risk of endometrioma recurrence. *Am J Obstet Gynecol*. 2008;198:504 e1–504 e5.
67. Ouchi N et al. Recurrence of ovarian endometrioma after laparoscopic excision: risk factors and prevention. *J Obstet Gynaecol Res*. 2014;40:230–236.
68. Takamura M et al. Post-operative oral contraceptive use reduces the risk of ovarian endometrioma recurrence after laparoscopic excision. *Hum Reprod*. 2009;24:3042–3048.
69. Muzii L et al. Postoperative administration of monophasic combined oral contraceptives after laparoscopic treatment of ovarian endometriomas: a prospective, randomized trial. *Am J Obstet Gynecol*. 2000;183:588–592.
70. Wong AY et al. Levonorgestrel-releasing intrauterine system (Mirena) and depot medroxyprogesterone acetate (Depoprovera) as long-term maintenance therapy for patients with moderate and severe endometriosis: a randomised controlled trial. *Aust NZ J Obstet Gynaecol*. 2010;50:273–279.
71. Cho S et al. Postoperative levonorgestrel-releasing intrauterine system versus oral contraceptives after gonadotropin-releasing hormone agonist treatment for preventing endometrioma recurrence. *Acta Obstet Gynecol Scand*. 2014;93:38–44.
72. Roman H et al. Surgical management of deep infiltrating endometriosis of the rectum: pleading for a symptom-guided approach. *Hum Reprod*. 2011;26:274–281.

22 SURGICAL MANAGEMENT OF PELVIC ENDOMETRIOSIS AND ENDOMETRIOMA

Mario Malzoni, Megan Wasson, Luca Nardone, Giorgia Poppi, Maria Cristina Solazzo, Alessia Oliviero, and Francesca Falcone

The vast majority of endometriosis is located in the pelvis and is reported to represent 96.4% of all lesion locations. This can include the ovary with or without posterior cul-de-sac obliteration (1). Surgical management of pelvic endometriosis requires a high index of suspicion, thorough evaluation of the entire pelvis, and a sound understanding of intraperitoneal and retroperitoneal anatomy. Superficial endometriosis, which involves less than 5 mm of invasion, is more prevalent than deep infiltrating endometriosis and is not consistently visible on diagnostic imaging studies. As a result, multiple national obstetrics and gynecology organizations from around the world recommend surgery to be considered in patients with suspected superficial endometriosis (2).

22.1 Indications for Surgery in Women with Confirmed or Suspected Endometriosis

The decision to proceed with surgery for treatment of suspected or confirmed endometriosis is multifactorial. Definitive diagnosis of endometriosis continues to require histopathologic confirmation of the presence of endometrial glands and stroma. Given the lack of reliable noninvasive tests for endometriosis, such as blood biomarkers, surgery remains the gold standard for diagnosis.

In women with signs or symptoms of endometriosis, the main indications for surgery are represented by one or more of the following situations:

1. Endometriosis-associated pain refractory to medical therapies
2. Endometriosis-associated pain in cases where medical therapies are not well tolerated or contraindicated
3. Organ (bladder, bowel, ureteral, etc.) dysfunction in cases where medical therapies are not effective, not well tolerated, or contraindicated
4. Endometriosis/endometrioma-associated infertility

Therefore, the decision to perform surgery should be mainly guided by the presence or absence of pain symptoms, response or contraindication to medical therapy, patient age and preferences, history of previous surgery, presence or absence of infertility factors, and ovarian reserve. Minimally invasive (laparoscopic or robotic) surgery is the preferred approach for endometriotic patients suitable for surgery, due to the less postoperative pain, shorter hospital stay, quicker recovery, and better cosmesis compared to open surgery. Additionally, a minimally invasive approach affords the surgeon enhanced visualization, increased precision, and improved access to deeper areas in the pelvis.

The two mainstays of surgical treatment for endometriosis include ablation or fulguration of all visible endometriosis lesions versus excision. Excision of endometriosis is the preferred approach as it allows for histopathologic evaluation and definitive diagnosis and reduction in disease burden. In contrast, ablation or fulguration of endometriosis relies on visual inspection of lesions and limits destruction of the lesions to the superficial areas that are clearly visible. With fulguration, there is risk of thermal injury to surrounding structures. Studies have shown that excision also results in a greater reduction in endometriosis-related symptoms, long-term improvement in symptoms, and decreased risk of symptom recurrence (3–4). Furthermore, there are data to support posterior compartment peritonectomy when treating endometriosis, with reduced recurrence rates and overall symptom improvement (5).

When surgically treating endometriosis, a sound understanding of anatomy, proximity and relationships of intraperitoneal and retroperitoneal structures, and the avascular spaces of the pelvis is essential. Excision of superficial endometriosis will frequently require dissection of the space of Okabayashia (medial pararectal space) with development of the ureteric tunnel as well as development of the rectovaginal septum and paravesical spaces.

22.2 Visual Detection of Superficial Endometriosis

Excision of lesions suspected to be endometriosis relies on accurate visual detection of the disease. Lesions can appear to be clear, white, red, or powder burn or as a peritoneal pocket (Figures 22.1–22.5). The multitude of presentations can pose a significant challenge in accurate detection, especially to the untrained eye. Furthermore, 11.3% of normal appearing peritoneum without macroscopic disease has been shown to have microscopic evidence of endometriosis on histopathology. Additionally, the typical powder burn appearance of endometriosis is only present in 27.4% of lesions confirmed to have endometriosis, and an atypical appearance represents the majority of endometriotic lesions (6).

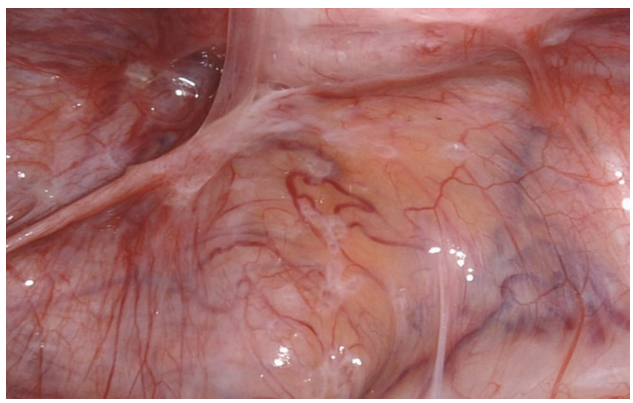


FIGURE 22.1 Superficial endometriosis lesion with clear vesicular appearance involving the posterior cul-de-sac.

DOI: 10.1201/9781003312109-22

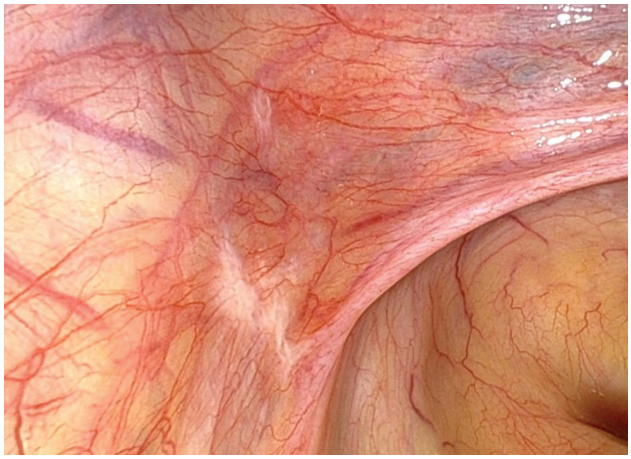


FIGURE 22.2 Superficial endometriosis lesion with white scarred appearance involving the left pelvic sidewall.

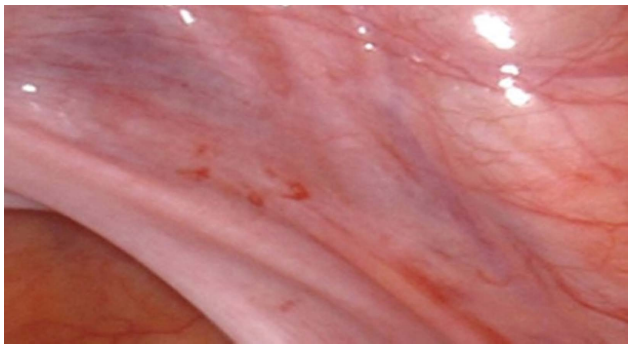


FIGURE 22.3 Superficial endometriosis lesion with red flame appearance involving the right pelvic sidewall.

FIGURE 22.4 Superficial endometriosis lesion with powder burn appearance involving the posterior cul-de-sac.

During the initial survey of the pelvis for endometriosis, thorough inspection of all pelvic structures should be completed. This includes evaluation of the fallopian tubes and adnexa, pelvic sidewalls, and posterior and anterior cul-de-sacs. It is essential to closely inspect these areas to ensure no subtle lesions are present. Structures should also be moved to allow for complete visualization under and around pelvic structures, assessing for any restrictions in mobility, scarring, or lesions not readily visible. Utilization of an accessory port or angled laparoscope can help assist in a thorough pelvic survey.

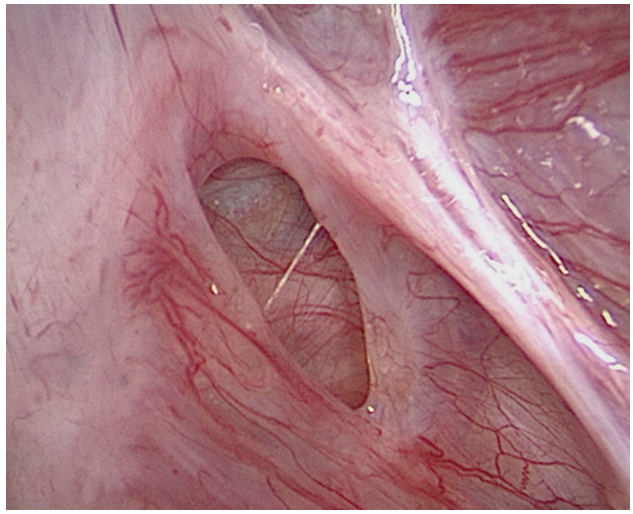


FIGURE 22.5 Superficial endometriosis lesion with peritoneal pocket involving the posterior cul-de-sac.

22.3 Surgical Treatment of Ovarian Endometriomas

Endometriomas, also known as "chocolate cysts" or "endometriotic cysts," are localized forms of ovarian endometriosis (Figure 22.6) and represent the most frequent form of endometriotic disease, likely related to their typical ultrasound features allowing easy and accurate diagnosis. It has been reported that endometriomas occur in 17%–44% of endometriotic women (7), and their detection is often associated with other disease locations. To date, treatment options for all types of endometriosis are mainly represented by hormone therapies, surgery, or a combination of both. Endometriomas, however, frequently present a clinical dilemma as to whether and how to treat when found during imaging. Endometriotic cysts lead per se to a decrease in ovarian reserve and often form adhesions with the pelvic peritonipsilateral fallopian tube and uterus, which also impair fertility (8). Surgical treatment of endometrioma could be considered in infertile women, as it may increase the chance of natural pregnancy. In individuals with endometrioma, decreased ovulation, decreased response to ovarian stimulation, and decreased number of follicles and oocytes retrieved during ovarian stimulation and oocyte retrieval have been noted. Surgical treatment of endometriomas has been shown to increase spontaneous pregnancy rates, improve response to ovarian stimulation, and reduce cyst and associated pelvic pain recurrence.

In infertile women with endometrioma, surgery is particularly indicated in case of intact ovarian reserve, no previous ovarian surgery, rapid growth of the ovarian lesion(s), unilateral disease, or abnormal ultrasound appearance. In contrast, poor ovarian reserve, previous ovarian surgery, bilateral endometriomas, and young age represent relative contraindications to surgical treatment in this setting of patients.

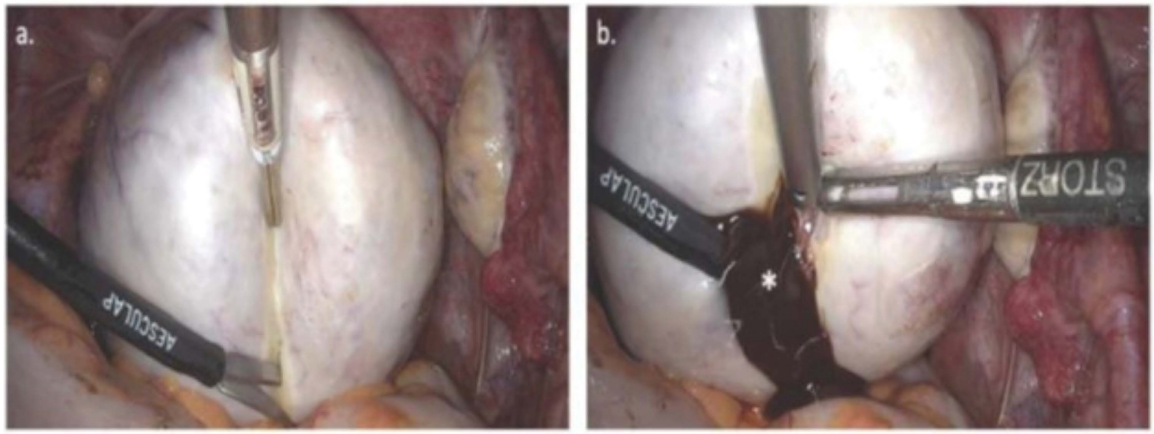


FIGURE 22.6 Left ovarian endometrioma before (a) and after (b) capsule incision. * Chocolate cyst fluid.

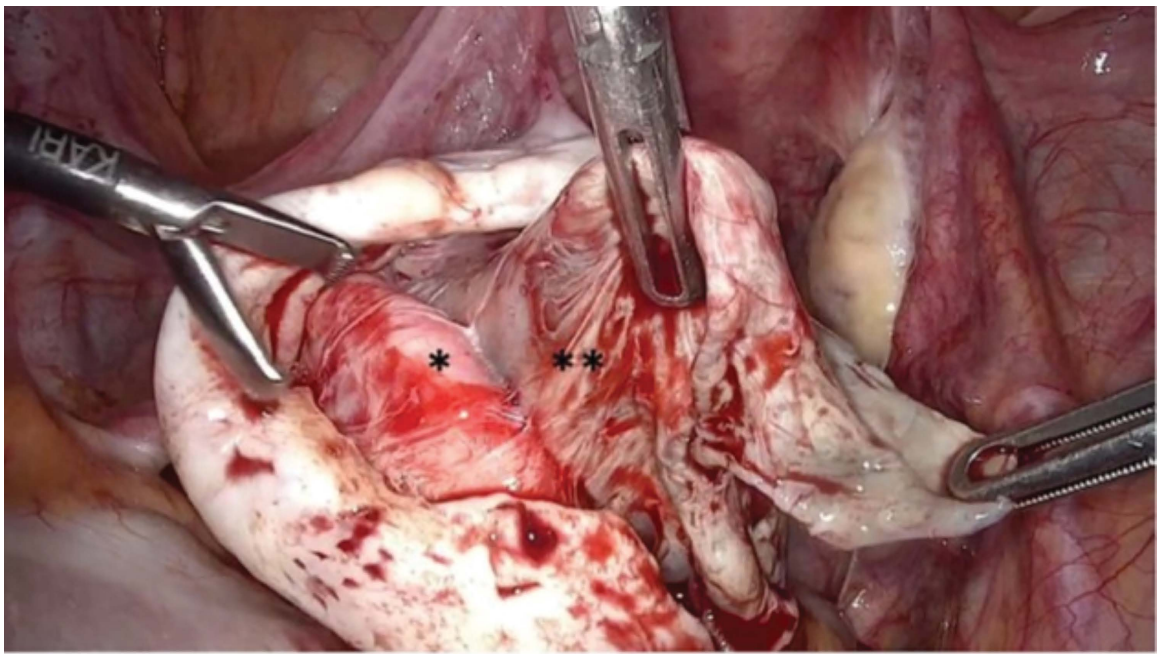


FIGURE 22.7 Surgical excision of left ovarian endometrioma with stripping technique. * Ovarian parenchyma. ** Cyst capsule.

Minimally invasive (laparoscopic or robotic) surgery is the preferred and recommended approach for the management of patients with endometriomas eligible for surgical treatment. In women desiring to preserve their reproductive potential, surgical treatment of endometrioma(s) (if needed) should be aimed to remove the endometriotic tissue preserving the maximum possible amount of normal ovarian tissue. It has been shown, however, that surgical treatment of endometriotic cysts is associated with the unavoidable and unintentional removal or destruction of ovarian follicles, which can be objectified by a measurable postoperative reduction in serum anti-Müllerian hormone levels or antral follicle count on ultrasound. Patients undergoing ovarian cystectomy for ovarian endometriomas have higher rates of perioperative adverse events than patients undergoing ovarian cystectomy for other benign neoplasms (9).

Conservative surgical techniques for the treatment of endometriomas are mainly represented by cystectomy, electrocoagulation, laser or plasma energy ablation, or methods combining excision and ablation (10). Cyst drainage is not recommended as there is a high likelihood of rapid cyst recurrence. Laparoscopic cystectomy (Figure 22.7) has been traditionally considered the method of choice for surgical management of endometrioma. Such technique consists of bluntly removing the cyst capsule from the ovarian parenchyma using gentle traction and countertraction with appropriate instruments (stripping technique); careful identification of cleavage plane and precise spot application of monopolar or bipolar electrosurgery is the key to achieve hemostasis, prevent unnecessary damage to healthy tissue, and avoid blind or excessive diathermy. If necessary, suture can be employed to achieve hemostasis.

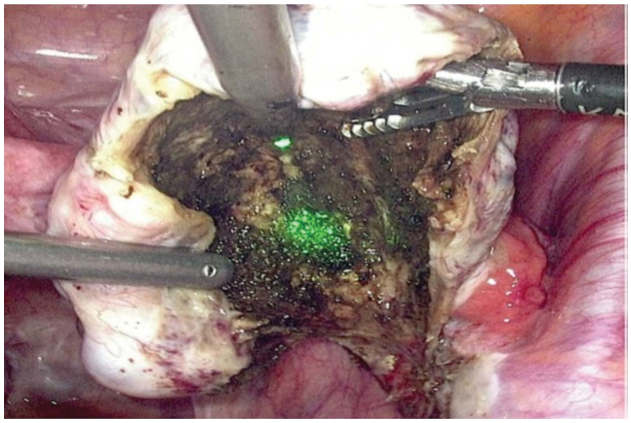


FIGURE 22.8 Diode laser treatment of right ovarian endometrioma.

Drainage and coagulation has been proposed as an alternative method to stripping technique, with the aim to minimize the risk of damage to ovarian reserve following cystectomy due to the inadvertent removal of healthy ovarian cortex together with the endometrioma wall. In fact, randomized trials and a Cochrane database systematic review support that cystectomy is to be preferred in appropriate candidates, showing lower recurrence rates of endometrioma and endometriosis-associated pain compared with drainage and coagulation (11–13).

In the last decade, laser and plasma energy ablations have been increasingly investigated (14). CO_2 laser and plasma energy have a low thermal spread (1–1.5 mm). These techniques appear to destroy the filmy superficial internal lining of the cyst selectively without reaching the fibrotic capsule surrounding the endometrioma or the adjacent healthy ovarian cortex (Figure 22.8). Randomized trials and retrospective studies show that the long-term recurrence rate is similar after CO_2laser vaporization and cystectomy for endometriomas, with the former having less harmful effects on ovarian reserve (14–16). Therefore, current guidelines indicate that clinicians can consider both cystectomy and CO_2 laser vaporization for performing surgery in women with ovarian endometrioma(s) (17).

A combined technique, using both excision and ablation, can be used to prevent excessive bleeding and ovarian tissue removal/damage, particularly in case of large endometriomas. However, a small multicenter randomized trial, comparing stripping and combined excision/ablation techniques for the treatment of bilateral ovarian endometriomas larger than 3 cm, reports similar recurrence rates and postoperative antral follicle count for the two techniques (18).

Finally, oophorectomy may be considered after careful discussion with the woman, particularly in the presence of recurrent or large unilateral endometriomas or suspicion of potential malignancy.

22.4 Hysterectomy for Abnormal Menstrual Bleeding in Setting of Endometriosis-Associated Pain

Hysterectomy, with or without oophorectomy, is considered as an option for managing abnormal menstrual bleeding and chronic pelvic pain that is the result of uterine pathology, such as adenomyosis. Hysterectomy is not considered a primary treatment of endometriosis but can be considered in patients who have fulfilled their reproductive desire and pelvic pain symptoms do not respond to conservative treatments (i.e., medical therapy, laparoscopic excision of endometriotic lesions). It is important to note that evidence supporting this approach is primarily based on retrospective case series and limited prospective studies. The decision to perform hysterectomy in the setting of endometriosis is complex, with several factors to weigh and potential consequences to consider (19). The absence of randomized controlled trials has made it challenging to draw definitive conclusions regarding the effectiveness of hysterectomy in alleviating chronic pelvic pain. A nonsystematic literature review shows the mixed outcomes of this surgical approach, indicating that not all women experience pain relief (20). The difficulties in evaluating the role of hysterectomy for treating chronic pelvic pain are numerous, also due to the challenge of distinguishing cyclical from noncyclical pain, establishing causality between endometriosis and chronic pelvic pain, and the variability in the success rates among studies.

Several studies support including hysterectomy for treatment of chronic pelvic pain. Shakiba et al. demonstrated that women undergoing hysterectomy, with or without oophorectomy, were less likely to require further surgery compared to those undergoing conservative surgery (21). Similarly, a Swedish population-based study (22) supported the effectiveness of hysterectomy in significantly reducing painful symptoms over the long term.

To minimize the risk of persistent/recurrent pain and reoperation, current guidelines recommend to perform hysterectomy together with the complete removal of all visible endometriotic lesions (19). This is of paramount importance, especially if bilateral salpingo-oophorectomy (BSO) is not performed, since ovarian preservation increases sixfold the risk of recurrent pain and eightfold the risk of reoperation (20). Decision regarding bilateral oophorectomy should take into account the (i) long-term harmful effects of premature/early menopause (including adverse effects on cognition, mood, cardiovascular, bone, and sexual health, and an increased risk of early mortality) (23–24); (ii) genetic/familial risk for ovarian cancer. Of course, the risk of ovarian cancer is reduced in patients with endometriosis undergoing BSO compared to those keeping their ovaries. It should be noted, however, that BSO becomes a cost-effective intervention when the lifetime ovarian cancer risk exceeds 4% (25). Given that the overall lifetime risk of ovarian cancer in endometriotic patients is 2.5%, decision regarding BSO should be tailored depending on each patient's personal/familial history of ovarian cancer (26).

Minimally invasive (laparoscopic or robotic) surgery is the preferred approach for performing hysterectomy in women with endometriosis. As far as the type of hysterectomy to be performed, a total hysterectomy is strongly recommended. This preference stems from concerns about the possible persistence of adenomyosis and endometriosis within the retained cervix or adjacent areas in case of subtotal hysterectomy (27).

It has to be emphasized that some women may continue to experience pain after hysterectomy, potentially due to residual endometriosis or centralization of pain (28). This underlines the need for adequate preoperative counseling and comprehensive perioperative assistance including long-term symptoms management (if any).

References

1. Lee HJ et al. Various anatomic locations of surgically proved endometriosis: a single-center experience. *Obstet Gynecol Sci*. 2015;58(1):53–58.
2. Goncalves MO et al. Systematic evaluation of endometriosis by transvaginal ultrasound can accurately replace diagnostic laparoscopy, mainly for deep and ovarian endometriosis. *Human Reproduction*. 2021;36(6):1492–1500.
3. Pundir JY et al. Laparoscopic excision versus ablation for endometriosis-associated pain: an updated systematic review and meta-analysis. *J Mnim Invas Gynecoly*. 2017;24(5):747–756.
4. Misal M et al. Histologic-proven recurrence of endometriosis after previous ablation vs. excision surgery. *J Minim Invas Gynecol*. 2021;28(11):S108–S109.
5. Abesadze E et al. Possible role of the posterior compartment peritonectomy, as a part of the complex surgery, regarding recurrence rate, improvement of symptoms and fertility rate in patients with endometriosis, long-term follow-up. *J Minim Invas Gynecol*. 2020;27(5):1103–1111.
6. McKee DC et al. Diagnosis of endometriosis: the surgeon's eye compared to histopathology. *J Gynecol Surg*. 2023;39(5): 235–239.
7. Ajossa S et al. The prevalence of endometriosis in premenopausal women undergoing gynecological surgery. *Clin Exp Obstet Gynecol*. 1994;21:195–197.
8. Ofer A et al. Improving the treatment and management of endometriosis: an overview of current and novel approaches. *Am J Obstet Gynecol*. 2016;214:672.
9. Orlando MS et al. Perioperative outcomes in a nationwide sample of patients undergoing surgical treatment of ovarian endometriomas. *Fertil Steril*. 2022;117(2):444–453.
10. Saridogan E et al. Recommendations for the surgical treatment of endometriosis. Part 1: ovarian endometrioma. *Hum Reprod Open*. 2017;14(1):27.
11. Brown J et al. Endometriosis: an overview of Cochrane Reviews. *Cochrane Database Syst Rev*. 2014;(3):CD009590.
12. Alborzi S et al. A prospective, randomized study comparing laparoscopic ovarian cystectomy versus fenestration and coagulation in patients with endometriomas. *Fert Steril*. 2004;82(6):1633–1637.
13. Beretta P et al. Randomized clinical trial of two laparoscopic treatments of endometriomas: Cystectomy versus drainage and coagulation. *Fertil Steril*. 1998;70:1176–1180.
14. Candiani M et al. Recurrence rate after "one-step" CO2 fiber laser vaporization versus cystectomy for ovarian endometrioma: a 3-year follow-up study. *J Minim Invasive Gynecol*. 2020;27:901–908.
15. Tsolakidis D et al. The impact on ovarian reserve after laparoscopic ovarian cystectomy versus three-stage management in patients with endometriomas: a prospective randomized study. *Fertil Steril*. 2010;94:71–77.
16. Carmona F et al. Ovarian cystectomy versus laser vaporization in the treatment of ovarian endometriomas: a randomized clinical trial with a five-year follow-up. *Fertil Steril*. 2011;96:251–254.
17. Dunselman GAJ et al. ESHRE guideline: management of women with endometriosis. *Human Reproduction*. 2014;29:400–412.
18. Muzii L et al. Comparison between the stripping technique and the combined excisional/ablative technique for the treatment of bilateral ovarian endometriomas: a multicentre RCT. *Human Reprod*. 2016;31:339–344.
19. Becker CM et al. ESHRE guideline: endometriosis. *Hum Reprod Open*. 2022;2022:1–26.
20. Martin DC. Hysterectomy for treatment of pain associated with endometriosis. *J Minim Invasive Gynecol*. 2006;13:566–572.
21. Shakiba K et al. Surgical treatment of endometriosis: a 7-year follow-up on the requirement for further surgery. *Obstet Gynecoly*. 2008;111.
22. Sandström A et al. Effect of hysterectomy on pain in women with endometriosis: a population-based registry study. *BJOG*. 2020;127:1628–1635.
23. Laughlin-Tommaso SK et al. Cardiovascular and metabolic morbidity after hysterectomy with ovarian conservation: a cohort study. *Menopause*. 2018;25.
24. Rocca WA et al. Hysterectomy, oophorectomy, estrogen, and the risk of dementia. *Neurodegener Dis*. 2012;10:175–178.
25. Manchanda R et al. Specifying the ovarian cancer risk threshold of "premenopausal risk-reducing salpingooophorectomy" for ovarian cancer prevention: a cost-effectiveness analysis. *J Med Genet*. 2016;53:591–599.
26. Hermens M et al. Incidence of ovarian cancer after bilateral salpingo-oophorectomy in women with histologically proven endometriosis. *Fertil Steril*. 2022;117:938–945.
27. Keckstein J et al. Recommendations for the surgical treatment of endometriosis. Part 2: deep endometriosis. *Hum Reprod Open*. 2020;(1):hoaa002.
28. Long AJ et al. Reoperation and pain-related outcomes after hysterectomy for endometriosis by oophorectomy status. *Am J Obstet Gynecol*. 2023;228:57.e1–57.e18.

23 EXTRAPELVIC ENDOMETRIOSIS

Ricardo M.A. Pereira

23.1 Introduction

"Extrapelvic endometriosis" is a misleading term used in medical literature in several specialties, making it difficult and challenging to analyze comparative data and contributing to a confused understanding of the multiple forms of endometriosis. This inaccuracy has led to guidelines describing different management based on scarce evidence for recommendations (1). The occurrence of lesions in extrapelvic locations in patients diagnosed with pelvic endometriosis is estimated at 5%–10% (2) and they may be underdiagnosed (3), making a correct understanding even more difficult. Lesions can occur in various anatomical regions, and sometimes mimic several other conditions such as appendicitis (4), gastrointestinal disorders (5), orthopedic problems (6), and thoracic (7, 8), dermatologic (9), neurological, and psychiatric diseases (10). Surgical management of extrapelvic endometriosis requires a site-specific approach for each anatomical region affected, with each of their particularities and associated physiopathological knowledge and characteristics of each patient considered. They are often evaluated by different medical specialties, resulting in differing points of view and approaches and, therefore, contributing to scarce evidence-based recommendations.

Mesothelial cells form a monolayer (mesothelium) lining of the serosal cavities (pleural, pericardial, and peritoneal) and the organs within (11). Superficial lesions may be restricted to the mesothelial coverage of the serous cavities, mainly the pelvic and abdominal peritoneal recesses, while deep lesions progress beyond the mesothelium and may infiltrate the subperitoneal connective tissues (ligaments, fascia, areolar connective tissue), avascular anatomical spaces, muscles, nerves, and vessels to varying degrees. Infiltrative lesions often affect organs located in the pelvic cavities but are less common in the organs of the abdominal and thoracic cavities (visceral endometriosis).

The various theories proposed to explain the onset of endometriosis have not been able to clearly answer the origin of the ectopic endometrium; however, clockwise flow of intraperitoneal fluid may exert an important influence on the distribution of lesions in abdominal extrapelvic endometriosis, while clinical forms of thoracic endometriosis syndrome may be related to the one-way transdiaphragmatic flow of fluid from the peritoneal to the pleural cavity (12, 13). Unlike pelvic endometriosis, in abdominal and thoracic extrapelvic endometriosis, there is a marked predominance of lesions located in the right hemiabdomen (appendix, cecum, ileum, psoas muscle, Morison's pouch, and diaphragm) and pleural cavity (pleura and lung). Extrapelvic endometriosis located in the inguinal region also has an interesting predominance towards the right side (14).

The three mesothelium-lined serous cavities – peritoneal, pleural, and mediastinal – are separate and independent. The diaphragm is a muscular–tendinous structure that separates the thorax from the abdomen and contains three major openings: the aortic hiatus, the esophageal hiatus, and the inferior vena cava foramen. Smaller openings allow for the passage of nerves and veins. The inferior vena cava foramen is located in the midportion of the central tendon in the posteromedial part of the right diaphragm. This opening enlarges with inspiration and with blood flow inside the heart. Radioisotope 99rnTc-sulfur colloid demonstrates the one-way transdiaphragmatic flow of fluid from the peritoneal to the pleural cavity. In contrast, radioisotope injected into the pleural cavity fails to traverse the diaphragm and sits in the pleural space (12). Dr. Paul Kirschner eloquently described the anatomical defects that allow for passage of fluids, cells, tissue, and gases through holes in the diaphragm (15). These smaller defects called fenestrations have been identified occurring within the tendinous portion of the central diaphragm and are more common in the right hemidiaphragm (16). In 1958, Maurer (13) was the first to describe the association among openings in the diaphragm (fenestrations) and catamenial pneumothorax with endometriosis. And again, over 90% of lesions occur on the right side, but they may also be left-sided or bilateral (17).

Extrapelvic endometriosis originating from scars located outside the mesothelial cavities may occur due to accidental transplantation of viable endometrial cells during procedures such as episiotomy, C-section, or trocar insertion. Extrapelvic endometriosis located in the abdominal or thoracic cavity is invariably in contact with the mesothelial tissue that lines these two cavities, for example the appendix, small intestine, colon, stomach (18, 19, 56), liver, kidney, adrenal glands, and pancreas. The surgical techniques related to these organs will not be considered in this chapter.

Extrapelvic endometriosis identified in distant sites from the mesothelial tissue (nonabdominal, nonthoracic) such as the central nervous system, skin, nasolacrimal, and in isolated muscles in the limbs and unrelated to this scarring is extremely rare (20) and will also not be considered in this chapter.

23.2 Endometriosis in the Thoracic Cavity

Thoracic endometriosis syndrome (TES) refers to the presence of endometriotic lesions in the lungs or visceral pleura and comprises four clinical entities: the catamenial pneumothorax, the catamenial hemothorax, the catamenial hemoptysis, and the lung nodules (18).

23.3 Endometriosis in the Abdominal Cavity

The abdominal peritoneal cavity is anatomically divided by the transverse mesocolon into the supramesocolic and inframesocolic compartments. These two compartments are then divided into right and left by the falciform ligament and small bowel mesenterium, respectively. The right and left parietocolic gutters are located laterally in the inframesocolic compartment.

23.3.1 Endometriosis in the Supramesocolic Compartment

23.3.1.1 Diaphragmatic and Pericardial Endometriosis

In diaphragmatic endometriosis, the lesion begins on the abdominal surface of the diaphragm (peritoneum) and may extend to the thoracic surface of the diaphragm (parietal pleura), the so-called full-thickness lesion.

DOI: 10.1201/9781003312109-23

Since diaphragmatic endometriosis is associated with severe pelvic disease (18), it can be considered a possible extension of pelvic disease and is considered extrapelvic endometriosis for being located in the upper abdomen (supramesocolic compartment). The right diaphragm is by far the most frequently affected by endometriosis when compared to the left; 90% and 10%, respectively (18).

There are two types of lesions: infiltrative lesions and fenestrations. Infiltrative lesions are characterized by a thickening, can be of different sizes from tiny lesions to larger lesions measuring several centimeters, can be isolated or confluent, and often form cystic areas with blood and compromising the entire thickness of the diaphragm from the peritoneum muscle layer to the parietal pleura (full-thickness lesion). Diaphragmatic defects or fenestrations are small, multiple openings (holes) measuring from 1 to 3 millimeters and rarely measuring more than 10 mm (21, 22) (Figure 23.1). Through laparoscopic visualization it is sometimes possible to see the sliding movement of the parietal pleura, while through thoracoscopy visualization, it is possible to observe the sliding movement of the hepatic capsule. Cyclical shoulder pain during the menstrual period and sometimes in the ovulatory period is the predominant symptom of infiltrative lesions, while catamenial pneumothorax is the usual clinical form in diaphragmatic defects (13).

Types of diaphragmatic lesions:

- Diaphragmatic implant (thickening)
- Diaphragmatic defect (fenestration, holes, pores)

Types of Diaphragmatic Endometriotic Implants

- *Peritoneal (superficial implant)* – Involves only the diaphragmatic peritoneum.
- *Muscular (partial-thickness infiltration, nodule)* – extends into, but not through, the diaphragmatic muscle fibers.
- *Full-thickness (transdiaphragmatic infiltration, nodule)* – infiltrates the entire thickness of the diaphragm, reaching or penetrating the parietal pleura.

Due to the close anatomical relationship between the diaphragm and the liver, we can didactically use the same classic segmentation system used in liver surgery described by Couinaud (23) to topographically classify the diaphragmatic endometriosis lesions of the diaphragm (Figure 23.2).

Location of diaphragmatic lesions corresponding to liver segmentation:

1. Segment V lesions (hepatorenal recess)
2. Segment VI lesions
3. Segment VII lesions
4. Segment VIII lesions
5. Segment IVa lesions
6. Segment II lesions

The right subphrenic recess is the most frequent site of diaphragmatic lesions. The visualization of the right subphrenic recess (hepatic segments VII, VIII, IVa) requires a 30° 10 mm laparoscope placement, usually in the right midclavicular line at the inferior edge of the tenth costal cartilage margin. This approach allows optimal exposure of the superior surface of the right hemidiaphragm and the adjacent hepatic dome.

The left subphrenic recess (segment II) is easily visualized during an inspection with the laparoscope inserted through the umbilical port.

Lesions located on the lateral part of the right diaphragm (segment VI) are usually present when we identify lesions in the right subphrenic recess (segments VII, VIII, IVa). Lesions located in the most anterior part of both sides of the diaphragm

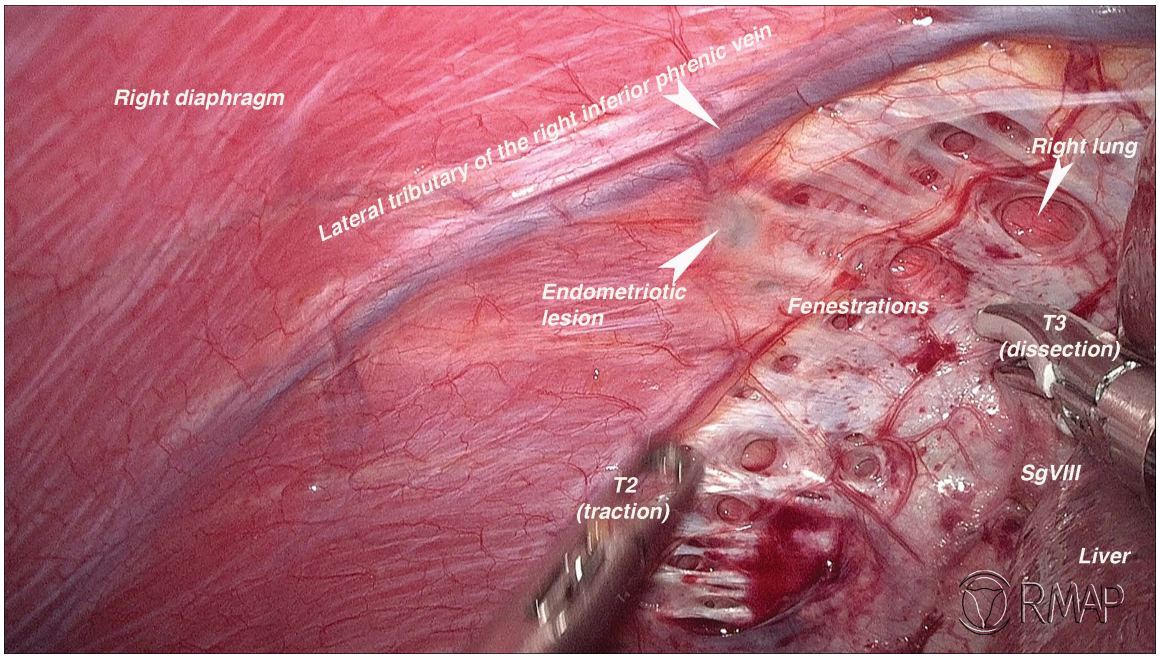


FIGURE 23.1 Diaphragmatic defects or fenestrations.

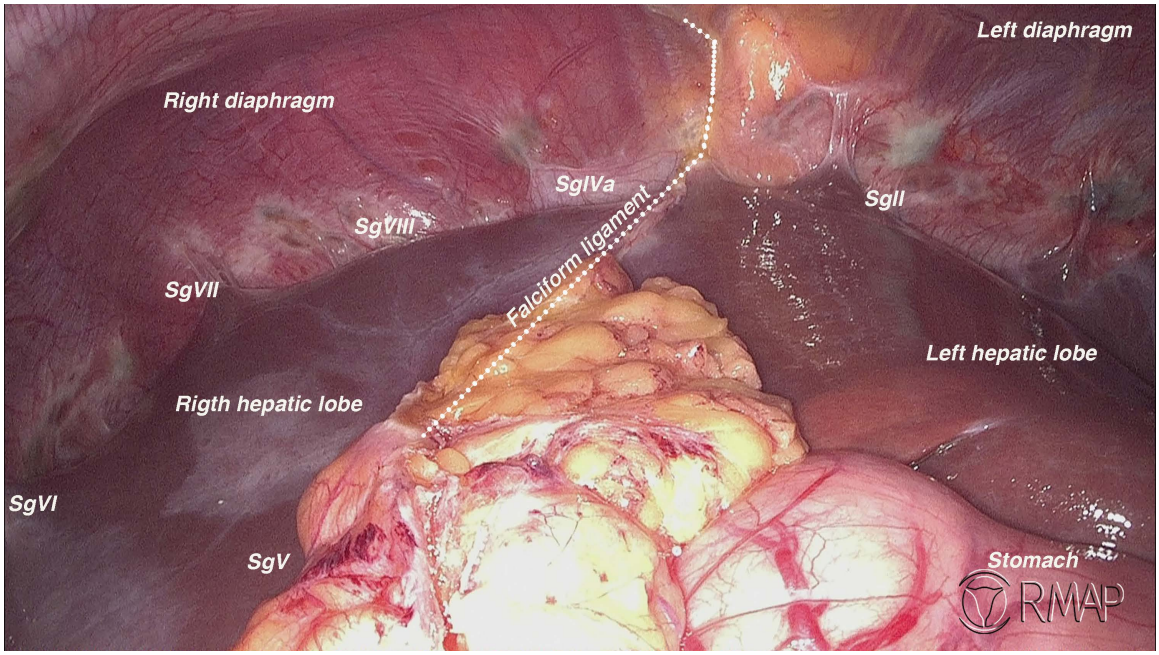


FIGURE 23.2 Endometriotic lesions in the diaphragm correlated with classic hepatic segmentation.

(ventral) are smaller, less infiltrative, and less frequent but easier to visualize laparoscopically when compared to those located in the subphrenic recesses. Lesions are rarely found infiltrating the posterior part of the right diaphragm close to its insertion at the level of L1–L2. When this occurs, they are usually extensions of large lesions affecting the hepatorenal recess (Morison's pouch).

More extensive and infiltrative lesions (full-thickness) are more frequent in the right diaphragm, as well as with TES, in all of its four clinical entities: the catamenial pneumothorax, the catamenial hemothorax, the hemoptysis, and the pulmonary nodules.

Left diaphragmatic endometriosis generally affects the mediastinal portion of the diaphragm adjacent to the fibrous pericardium and may infiltrate the parietal layer of the serous pericardium (full-thickness). The lateral portion of the left diaphragm is less frequently affected.

Fenestrations are frequently located in the right diaphragm in the nonmuscular portion (central tendon) at the level of hepatic segments VII and VIII, which makes them difficult to identify during visualization with the laparoscope positioned on the umbilical trocar. Maurer et al. (13), in 1958, were the first to correlate catamenial pneumothorax with fenestrations of the right diaphragm and also the first to record the instance of a successful surgical treatment of chronic recurring pneumothorax through the excision of a defect. Since then, several case reports and systematic reviews have confirmed this correlation (24, 25).

It is possible to draw an anatomical and pathological analogy between the hepatorenal recess (Morison's pouch), located in the supramesocolic compartment, and the recto-uterine pouch (pouch of Douglas) located in the pelvic cavity, both in the dynamics and in the accumulation of physiological peritoneal fluid, as well as in pathological situations such as hemoperitoneum, purulent peritonitis, and the spread of peritoneal metastasis. Meyers et al. (26) demonstrated the direct flow of fluids coming from the recto-uterine pouch (pouch of Douglas) through the right parietocolic gutter to the hepatorenal recess (Morison's pouch). A better understanding of supramesocolic compartment endometriosis may shed light on the process of the distribution of endometriotic lesions within the peritoneal cavity. Extrapelvic endometriosis located in the supramesocolic compartment, especially in the hepatorenal recess, is probably being underdiagnosed as this space is rarely inspected during the surgical treatment of pelvic endometriosis or even during the resection of lesions on the right diaphragm.

Laparoscopic Technique for the Inspection of the Supramesocolic Compartment during Endometriosis Pelvic Surgery

Upper abdomen endometriosis is probably underdiagnosed since gynecologists are focused primarily on the pelvis, and all aspects of the supramesocolic compartment are not systematically checked during gynecological laparoscopy.

While performing a laparoscopic surgical procedure in the pelvis, the surgeon can investigate the presence of extrapelvic endometriosis affecting the supramesocolic and the inframesocolic compartments.

- *Patient Positioning*: A broader view of the supramesocolic compartment is better achieved with the reverse Trendelenburg position. This together with partial left lateral decubitus provides a slight displacement of the right lobe of the liver caudally and medially, making it easier to inspect the right subphrenic recess. Morison's pouch inspection is facilitated by placing the patient in a slight Trendelenburg position (10°) and moving the right lobe of the liver cranially with a long snake laparoscopic liver retractor.
- *Trocar Placement*: Inspection of the supramesocolic compartment must be performed after the inspection of the pelvis using the same positioning of the pelvic surgery auxiliary trocars (6 mm): (1) Central: positioned over the midline, 10–12 cm below the umbilicus.

(2) Lateral: bilaterally positioned on the line between the anterior superior iliac spine and the umbilicus at the junction of the lower and middle thirds. The laparoscope is inserted into the trocar positioned in the umbilicus. Long snake laparoscopic liver retractors aided by atraumatic grasping forceps and using slow and smooth movements are used to move the liver and organs in the supramesocolic compartment in order to inspect and provide visual access to the peritoneal recesses. A 30° 10 mm laparoscope positioned on the umbilical trocar provides a better inspection of the peritoneal recesses, especially the subphrenic and subhepatic (Morison's pouch).

Laparoscopic Technique for Resection of Endometriosis on the Right Side of the Diaphragm

- *Patient Positioning*: The patient is placed in the modified lithotomy position and Allen stirrups are used to position the patient's legs.

The patient is positioned in a reverse Trendelenburg together with a partial left lateral decubitus with a trunk angulation of approximately 20°. The patient's arms are covered with foam egg crate; the hands are kept in a loose position and protected by putting a small piece of padding into the palms. An atraumatic restraint system is used to prevent the patient from sliding during position changes, especially when steep Trendelenburg, reverse Trendelenburg, or lateral decubitus is used.

- *Trocar Placement* (Figure 23.3).
  - *T1*: 11 mm trocar positioned at the umbilicus
  - *T2*: 6 mm trocar positioned inferiorly and close to the costal margin, on the right midaxillary line
  - *T3*: 11 mm trocar positioned inferiorly to the edge of the tenth costal cartilage, 2 cm medial to the right midclavicular line
  - *T4*: 6 mm trocar positioned in the anterior median line, 2 cm inferiorly to the xiphoid process
  - *T5*: 6 mm trocar positioned on the left midclavicular line, 5 cm inferior to the costal margin edge of the tenth costal cartilage

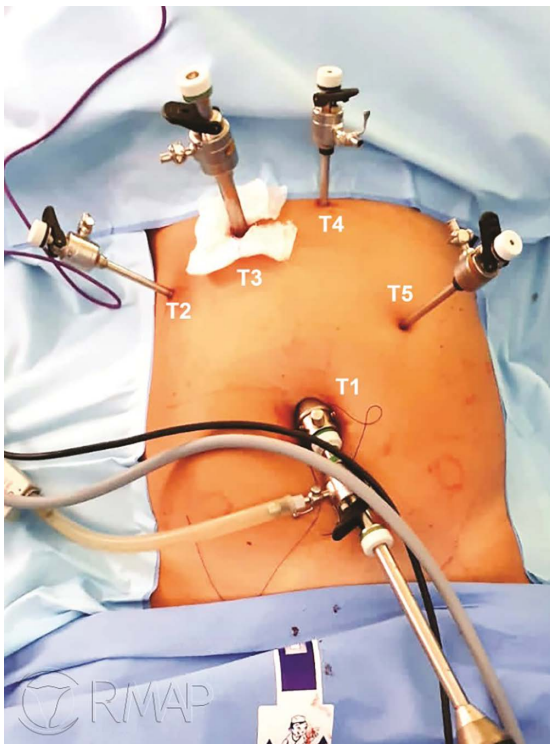


FIGURE 23.3 Trocar placement in supramesocolic compartment surgery.

23.3.2 Visualization and Surgical Access to Right Diaphragm Lesions

The lesions located in the ventral part of the diaphragm are less infiltrative, smaller, and less symptomatic, and they are also easily identified during visualization of the upper part of the abdomen and thus do not require displacement of the liver. The opposite occurs with those located in the subphrenic recess, which are more frequent, more infiltrative (full-thickness) (Figure 23.4), more symptomatic, and require the medial and caudal displacement of the hepatic parenchyma to visualize and access the right subphrenic recess. Hepatorenal recess (Morison's pouch) lesions are frequently associated with small lesions of the right subphrenic recess and usually infiltrate the peritoneum (Figure 23.5). When large nodules are present (infrequent), they may infiltrate the subperitoneal tissue or one or more of the following structures: the adjacent posterior diaphragm, the renal fascia (Gerota's), and/or the adrenal glands.

The use of a 30° 10 mm laparoscope, alternating between T1 and T3, is extremely helpful as it provides a wider and more adequate visual field of the recesses. The use of one or two snake laparoscopic liver retractors (5 mm), 36 mm in length, assisting in the displacement of the hepatic parenchyma, are essential for exposing the subhepatic and subphrenic recesses. The identification, dissection, and resection of the diaphragmatic lesions are possible through medial and caudal displacement of the hepatic parenchyma utilizing two important surgical maneuvers.

23.3.2.1 Medial Displacement of the Right Hepatic Lobe

This maneuver is used to visualize as well as to excise the right diaphragmatic lesions corresponding to hepatic segments VI, VII, and VIII. Displacement is achieved by sectioning the right coronary ligament (inferior leaflet and superior leaflet) and the right triangular ligament. The patient is positioned in the reverse Trendelenburg position together with partial left lateral decubitus, with a trunk angulation of approximately 20°. The hepatorenal recess is accessed by introducing a 5 mm laparoscopic liver retractor at T5, causing the right hepatic lobe to be displaced cranially, and exposing the inferior leaflet of the right coronary ligament which is sectioned using grasping forceps at T2 (traction) and a long vessel sealer, 44 cm in T3 (dissection, coagulation, cut).

This dissection begins approximately 1 cm laterally to the inferior vena cava where an avascular space is constructed through a craniolateral dissection until the part of the posterior diaphragm open toward the bare area of the liver is exposed. Another similar retractor can be introduced at T4 to aid in medial displacement as the dissection progresses. Next, the section of the inferior leaflet of the right coronary ligament is completed to its junction with that of the superior leaflet of the right coronary ligament at the level of the right triangular ligament (Figure 23.6). Thus, the medial displacement of the right hepatic lobe gradually occurs and the visualization of the diaphragmatic area corresponding

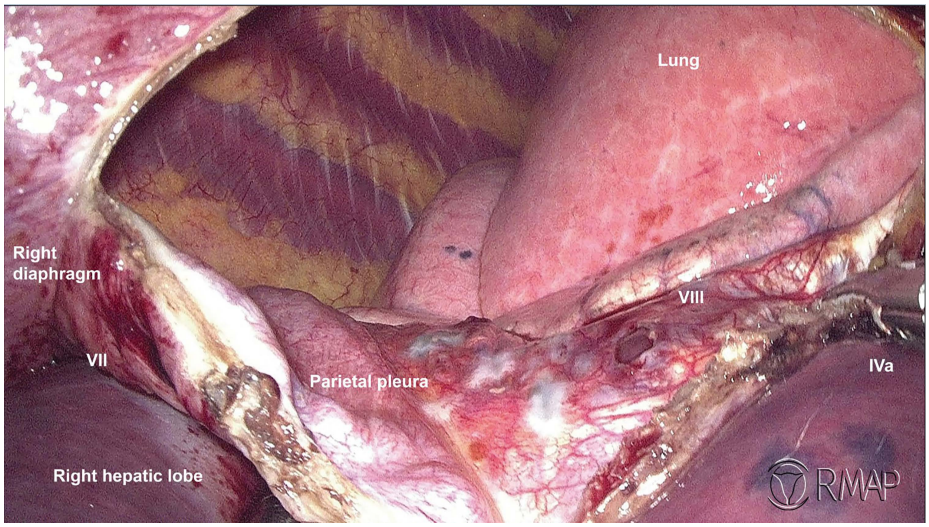


FIGURE 23.4 Endometriotic lesion on the right diaphragm (full-thickness).

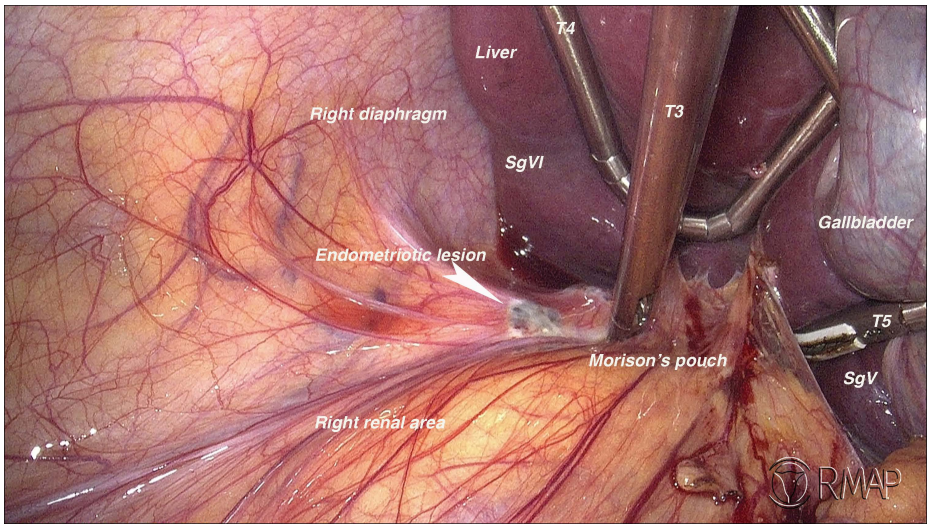


FIGURE 23.5 Endometriosis in the hepatorenal recess (Morison's pouch).

to hepatic segment VI and the entire hepatorenal recess is achieved. Next, the section of the superior leaflet of the right coronary ligament begins, from lateral to medial, until the diaphragm corresponding to segments VII and VIII is exposed.

Diaphragmatic endometriosis located in areas corresponding to liver segments VI, VII, and part of VIII, as well as those located in the Morison's pouch, can be fully visualized and excised through adequate exposure with two retractors at T4 and T5, grasping forceps for traction (T2), and a long vessel sealer, 44 cm (T3), for dissection, excision, and hemostasis. The resection of lesions in the hepatorenal recess, dissection and section of the inferior leaflet of the right coronary ligament, triangular ligament, of the superior leaflet of the most lateral part of the right coronary ligament, corresponding to the hepatic segments V, VI, VII, and part of VIII, was named by us as the "safe zone," because it does not involve the dissection of large vessels or the nerve trunk in this area.

23.3.2.2 Caudal Hepatic Displacement

The caudal displacement of the liver is used to visualize and excise right diaphragmatic lesions corresponding to hepatic segments VII, VIII, and IVa. By sectioning the round ligament (ligamentum teres) and falciform ligament, the liver may be displaced caudally (Figure 23.7). Here the patient is also positioned in the reverse Trendelenburg position together with a right lateral decubitus with a trunk angle of approximately 20°. The 30° 10 mm laparoscope is positioned at T1, facilitating the visualization of the falciform ligament and the round ligament. The vessel sealer and grasping forceps can alternately be positioned at T5 or T2.

The most cranial portion of the falciform ligament joins the hepatic peritoneum to become the superior leaflet of the left and right coronary ligaments.

The 30° 10 mm laparoscope is repositioned at T3 for better visual control of the subphrenic recess. The grasping forceps are positioned at T2 and the vessel sealer at T1. The retractor positioned at T5 draws caudally and gently compresses the liver

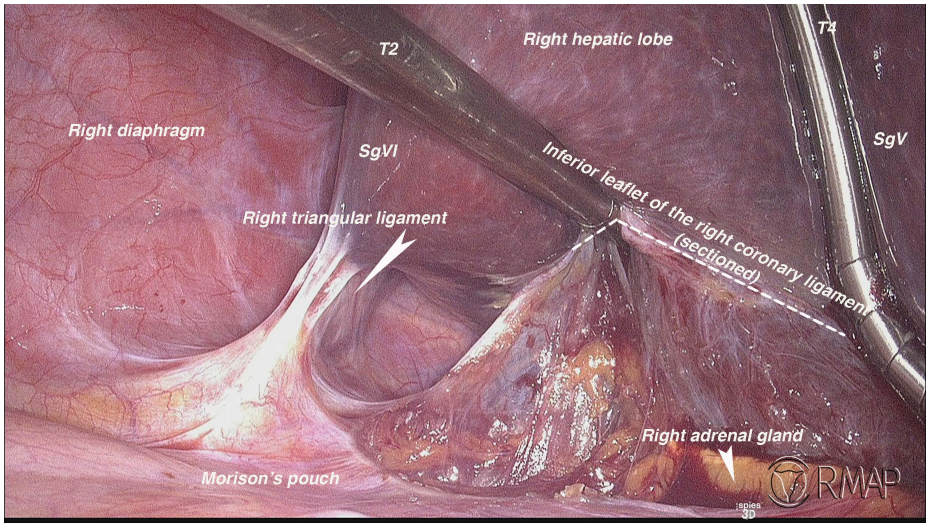


FIGURE 23.6 Medial displacement of the right hepatic lobe.

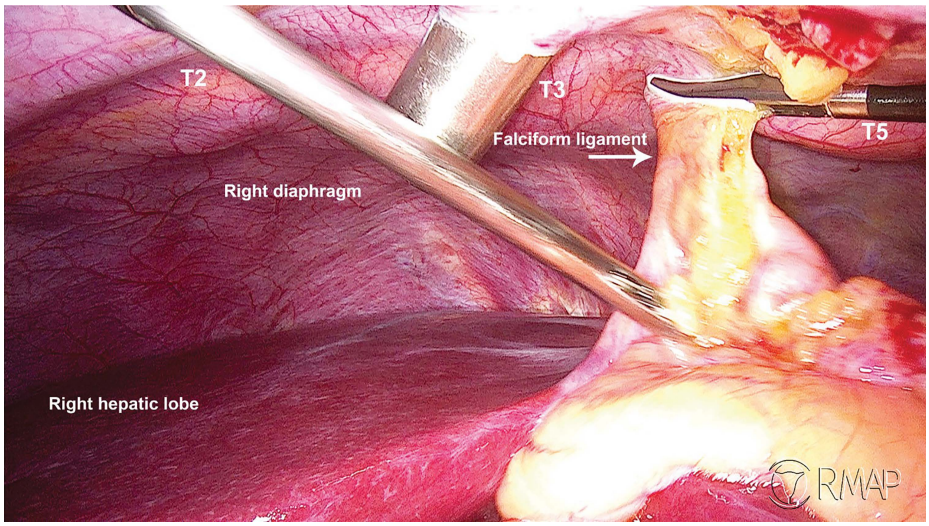


FIGURE 23.7 Caudal hepatic displacement.

posteriorly, further facilitating visual control of the subphrenic recess. Thus, the superior leaflet of the right coronary ligament is completely dissected and sectioned safely with the previously sectioned junction with the inferior leaflet

Endometriotic lesions corresponding to segments IVa, VIII, and VII are visualized and can be excised. This caudal displacement and section of the superior leaflet of the right coronary ligament allows better control of the vena cava foramen and also prevents lesions to the vena cava, which can be fatal. An important landmark is to follow the course of the anterior and lateral tributaries of the right inferior phrenic vein in the right diaphragm which drain into the inferior vena cava close to the area corresponding to hepatic segment IVa and along the medial part of the superior portion of the right coronary ligament. Another important aspect is the visualization of the area of the diaphragm that corresponds to segment VIII where the right phrenic nerve penetrates the diaphragm, in order to avoid damaging the nerve and the resulting paralysis of the right diaphragm. The dissection and sectioning in the most cranial part of the falciform ligament and the initial part of the superior leaflet of the right coronary ligament corresponding to hepatic segments IVa and VIII was named by us as the "danger zone."

23.3.2.3 Suturing of the Right Diaphragm

One or two laparoscopic liver retractors can help by accentuating caudal or medial displacement, depending on the need. The 30° 10 mm laparoscope can be positioned in T1 as the caudal and medial displacement of the liver provides an adequate view of the right diaphragmatic opening. Using an assistant needle holder in T2 and a needle holder in T3, careful, continuous laparoscopic intracorporeal techniques are performed using barbed sutures with PDS Plus-00. Immediately before completing the suture, pneumothorax and fluids are aspirated simultaneously with pulmonary hyperventilation (Valsalva maneuver). The thoracic cavity is fully closed, and a thoracic drain is not necessary. In cases of extensive resection of the diaphragm, closing may require the use of a double-faced polypropylene mesh with a hydrogel safety coating on the surface that is sutured to the pleural cavity (Figure 23.8).

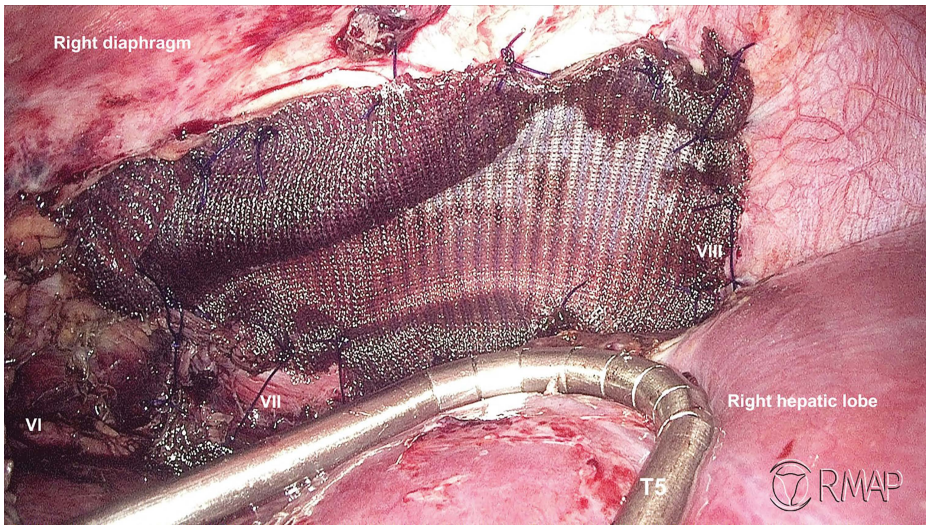


FIGURE 23.8 Placement of mesh in the closure of the right diaphragm.

Laparoscopic Technique for Resection of Endometriosis on the Left Diaphragm and Pericardium

- *Patient Positioning*: Positioning is similar to that used for the right diaphragm except for the partial lateral decubitus, which is on the right.
- *Trocar Placement*:
  - T1: 0° or 30° 10 mm laparoscope
  - T2: 5 mm laparoscopic liver retractor can help with the caudal displacement of the liver by enlarging the view of the left diaphragm and enlarging the field of action.
  - T3: A grasper can be positioned for traction, or an assistant needle holder can be used for suturing.
  - T4: Expendable
  - T5: Vessel sealer is positioned for resection or a needle holder for suturing

There are similarities with the technique described earlier for the right diaphragm, however the 0° or 30° laparoscope is positioned on T1. In T3, a grasper for traction or an assistant needle holder for suturing can be introduced during lesion resection. In T5, a vessel sealer for dissection, coagulation, and section, or the needle holder to suture the diaphragm and pericardium, is positioned. Monopolar current is contraindicated due to propagation and transmission to the cardiac conduction system.

23.3.3 Visualization and Surgical Access to Left Diaphragm Lesions and Pericardium

Endometriotic lesions on the left diaphragm are less frequent and less symptomatic compared to those on the right diaphragm. They are usually located in the mediastinal area where the diaphragm is lined internally by part of the fibrous pericardium.

The round and falciform ligaments are sectioned using the same technique described for the right diaphragm. Caudal displacement of the liver is used to visualize and excise the left diaphragmatic lesions corresponding to hepatic segment II.

23.3.4 Pericardial Endometriosis Resection: Surgical Technique

The technique used consists of adequate visualization of the mediastinal area of the left diaphragm, using grasping forceps to pull the lesion at T3 and a vessel sealer to cut, coagulate, and resect the lesion area at T5 (27). Upon entering the mediastinal cavity, a stream of pericardial serous fluid normally flows through the opening towards the laparoscope. As the opening increases, the movements of the heart within the pericardial sac and the lesion affecting the fibrous pericardium are clearly visualized. Caudal traction of the lesion easily moves it away from the cardiac area due to the mobility of the diaphragmatic muscle, allowing the safe release of the entire pericardial lesion through the coagulation and sectioning of the free edges of the diaphragmatic muscle and fibrous pericardium (Figure 23.9). Endometriotic lesions infiltrating the left hemidiaphragm and located in the area corresponding to the fibrous pericardium do not always invade it. The lesion may be merely juxtaposed to its surface, and during dissection it can often be removed without the need for fibrous pericardium resection. The necessity for pericardial resection and consequent entry into the mediastinum can only be determined intraoperatively during the dissection.

23.4 Suturing the Left Diaphragm (Mediastinal Portion) and the Fibrous Pericardium

The needle holder positioned in T5, the assistant needle holder in T3, and a laparoscopic liver retractor in T2 are usually sufficient to close the diaphragmatic defect including the fibrous pericardium. Careful interrupted or continuous laparoscopic intracorporeal suturing techniques are made using barbed sutures with PDS Plus-00. Laparoscopic intracorporeal suturing with needle movements from the inside to the outside of the mediastinum cavity, accompanying the systolic movements, allows for the safe closure of the pericardium. Minor pericardial resections may not require closure.

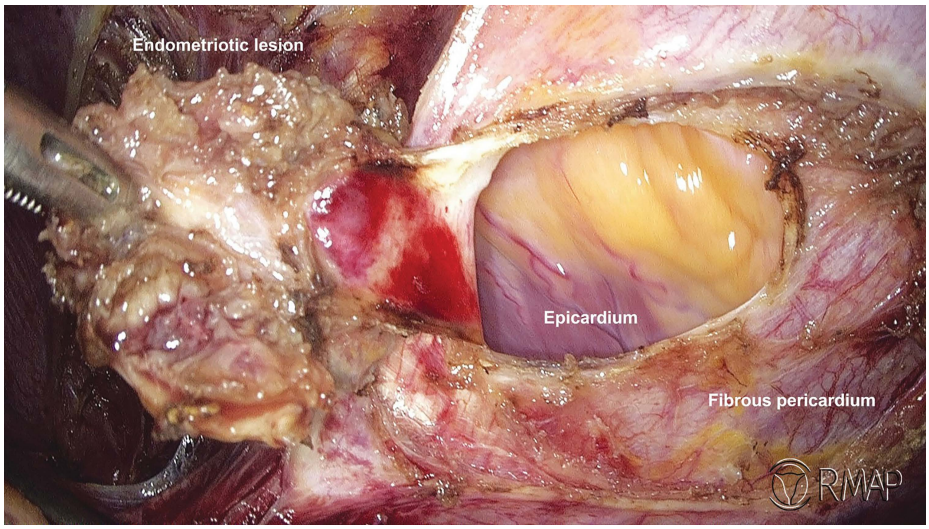


FIGURE 23.9 Pericardial endometriosis.

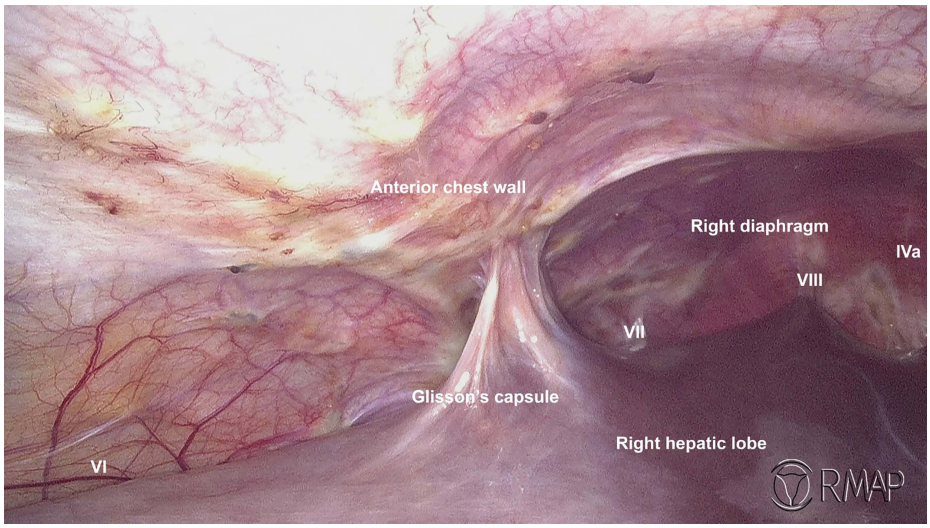


FIGURE 23.10 Endometriosis infiltrating Glisson's capsule and anterior thoracic wall.

23.5 Endometriosis Infiltrating the Left Diaphragm, Excluding the Mediastinal Area

The diaphragmatic area corresponding to the left parietal pleura and the left thoracic cavity are the least frequent sites affected by diaphragmatic endometriosis, but it is an area of easy visualization, resection, and suturing due to the anatomy of the left subphrenic recess being more easily exposed. The technique for positioning the patient and trocar placement is similar to that described for the pericardium. Careful, continuous laparoscopic intracorporeal techniques using barbed sutures with PDS Plus-00 are used for the closure of the left thoracic cavity. Immediately before completing the suture, similar to the technique of suturing the right diaphragm, the pneumothorax and fluids retained in the thoracic cavity are aspirated simultaneously with pulmonary hyperventilation (Valsalva maneuver). The thoracic cavity is hermetically closed and a thoracic drain is not necessary.

23.5.1 Endometriosis Infiltrating the Liver (Glisson's Capsule and Parenchyma)

Hepatic endometriosis is associated with endometriosis of the diaphragm and may be part of the same pathology (19, 28). Glisson's capsule infiltration (Figure 23.10) is often present in diaphragmatic endometriosis, unlike parenchymal involvement (cystic mass), which is extremely rare. Resection of lesions infiltrating Glisson's capsule can be performed using cutting together with bipolar coagulation. Large cystic lesions may require partial hepatectomy for complete excision (28).

23.5.2 Endometriosis Infiltrating Anterior Thoracic Wall

Endometriotic lesions may be present laterally and ventrally on the right thoracic wall at the level of diaphragmatic attachments in the costal cartilage of ribs 7 to 10 and direct attachment to ribs 11 to 12. In this topography, lesions are commonly restricted to the peritoneum but in rare cases can infiltrate the

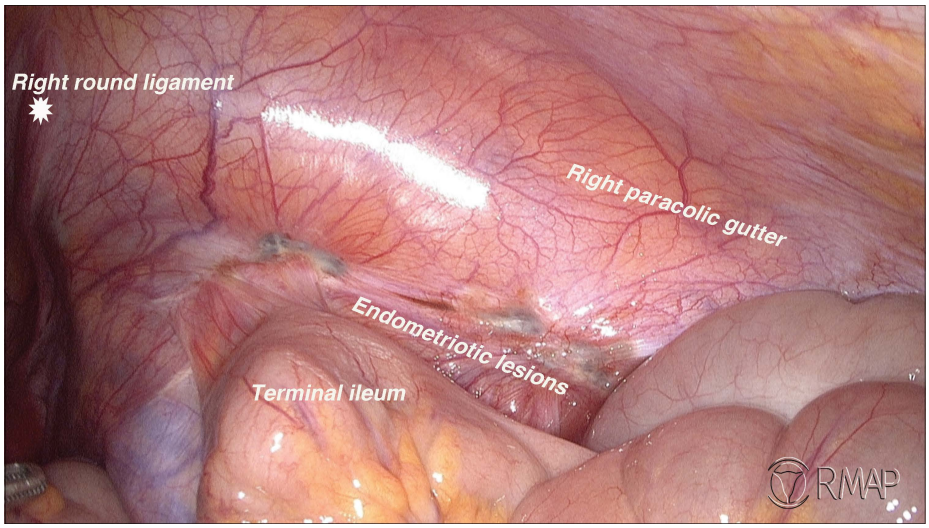


FIGURE 23.11 Endometriosis infiltrating right paracolic gutter.

thoracic wall muscles (internal and innermost intercostal muscles) and even the costal periosteum. Visualization of the area using a 30° 10 mm laparoscope provides a substantial improvement in the visual field, facilitating resection in symptomatic patients through the traction of the lesion with a grasping tool and hemostatic section with vessel sealer.

23.5.3 Endometriosis in the Inframesocolic Compartment

Endometriosis located in the inframesocolic compartment may involve the small bowel (terminal ileum), ileocecal junction, appendix, cecum, ascending, transverse, and descending colons as well as their respective mesenteriums. The greater omentum may also have endometriotic implants. These will not be considered in this chapter.

23.5.4 Endometriosis in the Paracolic Gutters

Paracolic gutters are spaces lateral to the ascending and descending colon. The right paracolic gutter is larger and deeper than the left and communicates freely with the right subhepatic and subphrenic spaces. Fluid ascends the right external paracolic gutter from the pelvic cavity to enter Morison's pouch before progressing to the right subphrenic space. The left paracolic gutter has restricted pelvic fluid circulation to the left parietocolic groove due to the sigmoid curvature which forms the intersigmoid recess. The phrenicocolic ligament at the level of the splenic flexure restricts flow in either direction between the left paracolic gutter and perisplenic space and left diaphragm. These anatomical characteristics associated with the physical barrier represented by the falciform ligament may explain the predominance of endometriotic lesions in the right upper abdomen. In addition to paracolic gutters playing an important role in the distribution of extrapelvic endometriosis, we can identify endometriotic lesions throughout the extension of the paracolic gutters. There is a predominance of superficial lesions mainly at the level of the intersigmoid and retrocecal recesses and in the upper parts at the level of the flexures. Deep lesions are more common in the right paracolic gutter (Figure 23.11) and can affect the muscles and even the nerves of the posterior (psoas muscle, femoral nerve) or the anterior (transversus abdominis, internal oblique) abdominal walls.

23.6 Abdominal Wall Endometriosis (AWE)

Abdominal wall endometriosis is characterized by the involvement of endometriotic tissue in the anterior or posterior abdominal walls or inguinal canal. The abdominal wall includes primary lesions, considered spontaneous and secondary due to a surgical incision (scar endometriosis), and represents 20% and 80%, respectively (29). The most common form of endometriosis in the anterior abdominal wall occurs in the surgical scar after cesarean (secondary) (30). Endometriosis has also been documented in the scar tissue of abdominal incisions including laparoscopic port sites, hernia repairs, and laparotomy for hysterectomy and myomectomy and is collectively referred to as abdominal wall endometriosis (AWE) (29–31). Endometriotic lesions have been reported to involve the adipose layer (91.4%–96.9%), fascia (65.7%–67.2%), and muscular layer (17.2%–20.7%) (30). Medical therapy has not been found to be effective for treatment of AWE. Surgical excision is considered the criterion standard for treatment of AWE (32).

The spontaneous form is more commonly located in the inguinal canal and umbilicus (29, 30). Lesions in the posterior abdominal wall are very rare, spontaneous, and located in the parietocolic gutters and can infiltrate muscles such as the psoas, iliacus, and quadratus lumborum after penetrating the fascial covering called the transversalis fascia (33). Abdominal mass (96%) and cyclical pain (87%) are the most common presenting symptoms in AWE (29). Extensive resection is recommended to avoid postoperative recurrence. MRI and USG are useful in determining the extent of the lesion before surgery (29).

23.6.1 Endometriosis in Abdominal Scars

Cesarean scars on the abdominal wall are the main risk factor for scar endometriosis (29–31). The rate of formation after cesarean delivery has been reported to be between 0.03% and 1.08% (32). A long clinical history of cyclical pain in the lower abdomen, often incapacitating, may be present. Malignant transformation of scar endometriosis has been reported to have a very poor prognosis (29, 34). Extensive incisional resection is

recommended to avoid postoperative recurrence (29, 30). The use of mesh may be necessary in the case of larger nodules infiltrating the muscular layers and extensive fascial areas.

23.6.2 Umbilical Endometriosis (UE)

Umbilical endometriosis or Villar's nodule is a rare form of endometriosis with a frequency of around 0.4%–4% of extragenital lesions and around 0.5%–1% of all cases of endometriosis and has been reported to represent 30%–40% of cases of AWE (35). Patients present symptoms in 97% of cases: edema in 86% and cyclical pain in the umbilical region in 81%, and in cases that infiltrate the dermis (full-thickness) it presents with umbilical bleeding during the menstrual period in 45% of cases (36). Umbilical hernias in women may be associated with umbilical endometriosis (37). Two types of UE have been described. Primary UE occurs in the absence of a surgical history, whereas secondary UE arises with scar tissue following procedures such as laparoscopy. Extensive resection followed by reconstruction of the area represents the primary treatment (36). Resection of large nodules may require the placement of mesh, and umbilical reconstruction should be considered to create a new navel (plastic surgery).

23.6.3 Inguinal Endometriosis

- Internal inguinal ring (deep)
- Inguinal canal
- External inguinal ring (superficial)
- Canal of Nuck
- Hernia sac
- Vulvar (labia majora)

The inguinal canal is a short, narrow, diagonal passage in the lower anterior abdominal wall measuring approximately 4 cm in length and lined by the aponeuroses of three muscles: the external oblique, the internal oblique, and the transversus abdominis (38). In women, the development of the inguinal canal is determined by the invagination of the parietal peritoneum forming the processus vaginalis (PV) and by the gubernaculum which forms the round ligament and passes through the canal and terminates in the labia majora. Normally, the superior portion of the PV closes in the last weeks of pregnancy and the obliteration proceeds gradually and inferiorly to the labia majora. A persistently patent PV is called the canal of Nuck. The inguinal canal contains blood and lymphatic vessels, the genital branch of the genitofemoral nerve, the ilioinguinal nerve, and the round ligament. Endometriosis in the inguinal canal can be located in three anatomical areas: the inguinal canal itself, the internal inguinal ring (deep), and the external inguinal ring (superficial). Endometriotic lesions seem to start in the internal inguinal ring and may progressively infiltrate towards the inguinal canal and less frequently reach the external inguinal ring. Endometriosis of the internal inguinal ring is underdiagnosed before surgery (14). The lesions are smaller, less infiltrative, and less symptomatic (39). In contrast, lesions infiltrating the external inguinal ring are less frequent, larger, and more symptomatic. Laparoscopic resection is possible in most internal lesions, whereas those located in the external inguinal ring are excised through a skin incision. The great surgical challenge is laparoscopic dissection at the level of the inguinal canal (Figure 23.12). Knowledge of the anatomy of the external iliac and inferior epigastric vessels next to the inguinal ligament, important anatomical landmarks, are vital for the surgical technique. Right-side dominance of inguinal endometriosis has been suggested by several authors reporting that 86%–90% occurred on the right side (14).

Laparoscopic Technique for Resection of Inguinal Endometriosis

- *Patient Positioning and Trocar Placement*: The same technique for laparoscopic pelvic surgery can be used as described earlier. The 30° 10 mm laparoscope is extremely valuable for adequate visualization of the ceiling and floor of the inguinal canal.

23.6.3.1 Lesions Involving the Internal Inguinal Ring (Deep)

The lesion does not reach the interior of the canal and the external inguinal ring. There is a strong association between the presence of a patent canal of Nuck and endometriosis in the canal of Nuck (14, 44). It is possible to identify the

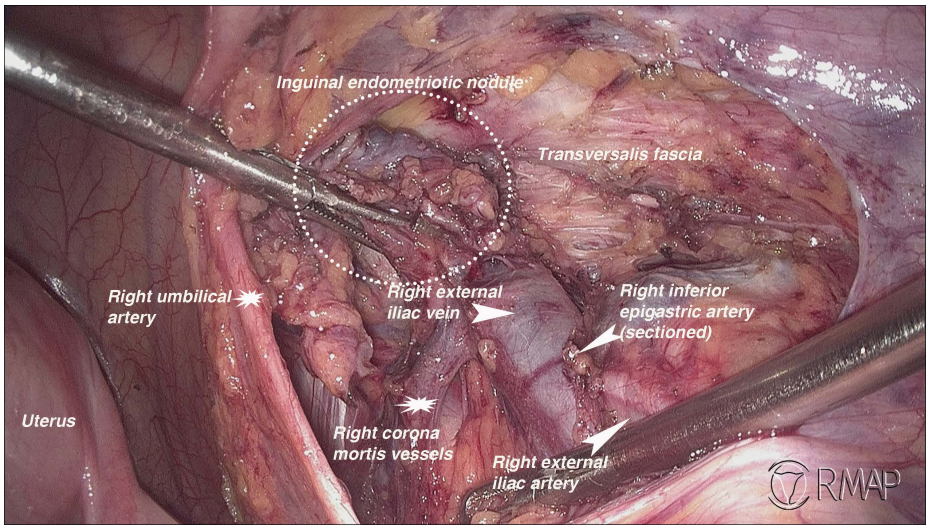


FIGURE 23.12 Endometriosis involving inguinal canal.

lesion while inspecting the region, but when the round ligament is pulled towards the peritoneal cavity, an inversion of the ring occurs and there will be visual access to the often-hidden lesions. A dissection of the peritoneum involving the ring makes it possible to excise the lesion which is normally peritoneal and has an atypical or typical appearance. The peritoneum can be easily closed with a purse-string suture. Nodular lesions usually extend into the canal and/or to the external inguinal ring.

23.6.3.2 Lesions Involving the Inguinal Canal

The lesion is normally of typical appearance: nodular shaped, variable sized, and affecting the round ligament, muscle layers, and nerves. The genital branch of the genitofemoral nerve enters the canal together with the round ligament while the ilioinguinal nerve penetrates approximately 1–2 cm beyond the internal inguinal ring. The inferior epigastric vessels, external iliac vessels, and their arterial and venous connections with the obturator vessels (corona mortis) constitute an important anatomic landmark for dissecting and excising the lesion. As described by Rogers Jr. and Taylor: "The purpose of surgical dissection is to expose anatomic structures while safeguarding their structural and physiological integrity. Progression of dissection is a purposeful millimeter by millimeter" (40).

Meticulous hemostasis using bipolar energy and placement of metal clips facilitates the separation of the lesion from the external iliac vessels and inferior epigastric vessels. Identification of the genital branch of genitofemoral nerve and ilioinguinal nerve is important for nerve sparing, neurolysis, or neurectomy if the nerve is infiltrated.

23.6.3.3 Lesions Involving the External Inguinal Ring (Superficial)

This is normally an extension of the lesion beginning in the internal inguinal ring, continuing to the inguinal canal, and possibly extending to the subcutaneous tissue. They are larger in size, more symptomatic, and their palpation during the menstrual period is highly painful. A skin incision is necessary to completely remove the lesion.

23.7 Perineal Scar Endometriosis

Perineal scar endometriosis at the episiotomy scar site is very rare, occurring in only about 0.03%–0.37% of cases (41–43). The classical clinical complaint includes a history of episiotomy, a tender nodule at the scar site, and cyclical pain. In a series of 130 cases of perineal endometriosis, Zhu et al. (43) describe perineal scar endometriosis as predominantly associated with injuries caused by episiotomies or obstetrical tears.

Diagnostic imaging through MRI is the preferred imaging method. All endometriotic masses in the perineum must be completely excised to avoid recurrences. Early diagnosis is vital as delayed diagnosis can lead to increased morbidity resulting from anal sphincter, vaginal, or rectal involvement (41, 43).

References

1. Members of the Endometriosis Guideline Core Group. ESHRE guideline: endometriosis. *Hum Reprod Open*. 2022;2022: hoac009.
2. Lukac S et al. Extragenital endometriosis in the differential diagnosis of non-gynecological diseases. *Dtsch Arztebl Int*. 2022;119:361–367.
3. Machairiotis N et al. Extrapelvic endometriosis: a rare entity or anunder diagnosed condition? *Diagn Pathol*. 2013;8:194.
4. Huang YM et al. Chronic appendicitis secondary to endometriosis: a case report. *Int J Color Dis*. 2015;30:289–290.
5. Podgaec S et al. Epigastric pain relating to menses can be a symptom of bowel endometriosis. *São Paulo Med J*. 2008;126:242–244.
6. Nair A et al. Endometriosis of the sciatic nerve masquerading as lumbar spondylosis in a 40-year-old Chinese woman. *BMJ Case Rep*. 2021;14:e244584.
7. Hwang et al. Clinical features of thoracic endometriosis: a single center analysis. *Obstet Gynecol Sci*. 2015;58(3):223–231.
8. Nair SS et al. Thoracic endometriosis syndrome: a veritable Pandora's box. *J Clin Diagn Res*. 2016;10:QR04–QR08.
9. Kyamidis K et al. Spontaneous cutaneous umbilical endometriosis: report of a new case with immunohistochemical study and literature review. *Dermatol Online J*. 2011;17:5.
10. Gao M et al. Psychiatric comorbidity among women with endometriosis: nationwide cohort study in Sweden. *Am J Obstet Gynecol*. 2020;223(3):415.e1–415.e16.
11. Mutsaers SM. The mesothelial cell. *Int J Biochem Cell Biology*. 2004;36:9–16.
12. Rubinstein D et al. Hepatic hydrothorax in the absence of clinical ascites (diagnosis and management). *Gastroenterol*. 1985;88:188–191.
13. Maurer ER et al. Chronic recurring spontaneous pneumothorax due to endometriosis of the diaphragm. *J Am Med Assoc*. 1958;168(15):2013–2014.
14. Nagase S et al. Hydrocele of the canal of nuck with endometriosis: right-side dominance confirmed by literature review and statistical analysis. *Case Rep Pathol*. 2020:2567267.
15. Kirschner PA. Porous diaphragm syndromes. *Chest Surg Clin N Am*. 1998;8:449–472.
16. Guest S. The curious right-sided predominance of peritoneal dialysis-related hydrothorax. *Clin Kidney J*. 2015;8:212–214.
17. Korom S et al. Catamenial pneumothorax revisited: clinical approach and systematic review of the literature. *J Thorac Cardiovasc Surg*. 2004;128:502e8.
18. Soriano D et al. Thoracic endometriosis syndrome is strongly associated with severe pelvic endometriosis and infertility. *J Minim Invasive Gynecol*. 2012;19:742–748.
19. Nezhat C et al. Laparoscopic management of hepatic endometriosis: report of two cases and review of the literature. *J Minim Invasive Gynecol*. 2005;12:196–200.
20. Andres MP et al. Extrapelvic endometriosis: a systematic review. *J Minim Invasive Gynecol*. 2020;27:373–389.
21. Cowl CT et al. Visualization of diaphragmatic fenestration associated with catamenial pneumothorax. *Ann Thorac Surg*. 1999;68:1413–1414.
22. Leong AC et al. Catamenial pneumothorax: surgical repair of the diaphragm and hormone treatment. *Ann R Coll Surg Engl*. 2006;88:547–549.
23. Couinaud C. *Le foie: études anatomiques et chirurgicales*. Paris: Masson; 1957.
24. Gil Y et al. Diagnosis and treatment of catamenial pneumothorax: a systematic review. *J Minim Invasive Gynecol*. 2020;27:48–53.
25. Lillington GA et al. Catamenial pneumothorax. *JAMA*. 1972;219:1328–1332.
26. Meyers MA et al. The peritoneal ligaments and mesenteries: pathways of intraabdominal spread of disease. *Radiol*. 1987;163:593–604.
27. Pereira RM et al. Pericardial endometriosis: laparoscopic resection approach. *J Minimal Invas Gynecol*. 2018;25/7(Suppl S15).
28. Rivkine E et al. Hepatic endometrioma: a case report and review of the literature: report of a case. *Surg Today*. 2013;43:1188–1193.
29. Hirata T et al. Extra-pelvic endometriosis: a review. *Reprod Med Biol*. 2020;19:323–333.
30. Ecker AM et al. Abdominal wall endometriosis: 12 years of experience at a large academic institution. *Am J Obstet Gynecol*. 2014;211(4):363.e1–363.e5.

31. Khan Z et al. Risk factors, clinical presentation, and outcomes for abdominal wall endometriosis. *J Minim Invasive Gynecol*. 2017;24(3):478–484.
32. Rindos NB et al. Diagnosis and management of abdominal wall endometriosis: a systematic review and clinical recommendations. *Obstet Gynecol Surv*. 2017;72(2):116–122.
33. Bailey AP et al. Florid endometriosis in a post- menopausal woman. *Fertil Steril*. 2010;94(7):2769.e1–2769.e4.
34. Taburiaux L et al. Endometriosis associated abdominal wall cancer: a poor prognosis? *Int J Gynecol Cancer*. 2015;25(9):1633–1638.
35. Brambilla M et al. Umbilical endometriosis: a systematic literature review and pathogenic theory proposal. *J Clin Med*. 2022;11(4):995. PMID: 35207266.
36. Hirata T et al. A national survey of umbilical endometriosis in Japan. *J Minim Invasive Gynecol*. 2020;27:80–87.
37. Brătilă E et al. Umbilical hernia masking primary umbilical endometriosis – a case report. *Rom J Morphol Embryol*. 2016;57:825–829.
38. Bhosale PR et al. The inguinal canal: anatomy and imaging features of common and uncommon masses. *RadioGraphics*. 2008;28(3):819–835; quiz 913.
39. Niitsu H et al. Clinical characteristics and surgical treatment for inguinal endometriosis in young women of reproductive age. *Dig Surg*. 2019;36(2):166–172.
40. Rogers RM Jr. et al. The core of a competent surgeon: a working knowledge of surgical anatomy and safe dissection techniques. *Obstet Gynecol Clin North Am*. 2011;38:777–788.
41. Li J et al. Diagnosis and treatment of perineal endometriosis: review of 17 cases. *Arch Gynecol Obstet*. 2015;292:1295–1299.
42. Saloum NM et al. A rare case report of endometriosis in an episiotomy scar without anal sphincter involvement. *EC Gynaecol*. 2018;7:466–470.
43. Zhu S et al. Clinical presentation of perineal endometriosis and prognostic nomogram after surgical resection. *BMC Womens Health*. 2022;22(1):476.
44. Prodromidou A et al. Endometriosis of the canal of nuck: a systematic review of the literature. *Diagnostics*. 2020 Dec 22;11(1):3.
45. Albutt K et al. Endometriosis within a left-sided inguinal hernia sac. *J Surg Case Rep*. 2014;2014(5):rju046.
46. Sampson JA. Inguinal endometriosis. Often reported as endometrial tissue in the groin, adenomyoma in the groin, and adenomyoma of the round ligament. *Am J Obstet Gynecol* 195;10:462–503.
47. Brainwood M et al. Persistence of the processus vaginalis and its related disorders. *Australas J Ultrasound Med*. 2020;23:22–29.
48. May J et al. Porous diaphragm syndrome: haemothorax secondary to haemoperitoneum following laparoscopic hysterectomy. *BMJ Case Rep*. 2013:bcr2013201088.
49. Arakawa T et al. Clinical aspects and management of inguinal endometriosis: a case series of 20 patients. *J Obstet Gynaecol Res*. 2019;45(10):2029–2036.
50. Niitsu H et al. Clinical characteristics and surgical treatment for inguinal endometriosis in young women of reproductive age. *Dig Surg*. 2019;36:166–172.
51. Kim DH et al. Inguinal endometriosis in a patient without a previous history of gynecologic surgery. *Obstet Gynecol Sci*. 2014;57(2):172.
52. Solass W et al. Morphology of the peritoneal cavity and pathophysiological consequences. *Pleura and Peritoneum*. 2016 Dec 1;1(4):193–201.
53. Meyers M. The spread and localization of acute intraperitoneal effusions. *Radiology*. 1970 Jun;95:547–554.
54. Zhang P et al. Cesarean scar endometriosis: presentation of 198 cases and literature review. *BMC Womens Health*. 2019;19(1):14.
55. Moulder JK et al. Risk of appendiceal endometriosis among women with deep-infiltrating endometriosis. *Int J Gynecol Obstet*. 2017;139:149–154.
56. Allahqoli L et al. Appendiceal endometriosis: a comprehensive review of the literature. *Diagnostics*. 2023;13:1827.

24 SURGICAL MANAGEMENT OF GASTROINTESTINAL AND GENITOURINARY ENDOMETRIOSIS

Eung-Mi Lee and Ted Lee

24.1 Background

Endometriosis is the presence of endometrium-like tissue outside the uterus and can take many forms that include superficial peritoneal lesions, cysts in the ovaries known as endometriomas, and deep endometriosis penetrating at least 5 mm into surrounding tissue (1). This last type of endometriosis is accompanied by fibrosis and adhesions leading to distorted anatomical planes that commonly manifest as an obliterated posterior cul-de-sac. Deep endometriosis is overall rare, and its prevalence is estimated to be 1%–2% of the population (2). However, deep endometriosis presents a surgical challenge, given extensive scarring as well as the involvement of other organ systems. These systems include the gastrointestinal tract – most commonly, the rectum, rectosigmoid, or sigmoid colon – as well as the genitourinary tract – most commonly, the bladder (80% of cases) or the ureters (14% of cases) (3). Given the involvement of other organ systems in addition to distorted surgical planes and fibrotic tissue, surgery for deep endometriosis can be associated with a high complication rate. One retrospective cohort study including 165 patients at a tertiary referral center for patients with deep endometriosis found that the overall rate of postoperative complications was 16.2%, with severe postoperative complications of 2.42% (4). As such, it is imperative for all gynecologic surgeons to be aware of the surgical principles to follow when encountering advanced deep endometriosis. This chapter will focus on deep endometriosis affecting the gastrointestinal and genitourinary systems (Figure 24.1).

24.2 General Principles

For any patient who is going to the operating room for pelvic pain, it is essential to consider endometriosis on the differential. Encountering a frozen pelvis during surgery can either be planned or unexpected. Even for surgeons who have the skill to operate on advanced endometriosis, finding unexpected, advanced disease can pose several issues. The first is that there is a lack of informed consent – excising all disease may require surgery on nearby visceral organs including the bladder, ureters, and bowel. In addition, it is important to understand the patient's fertility desires and to obtain consent from patients any time a surgery may impact future fertility. The second is that there may be insufficient time scheduled for the surgery. Surgery for advanced endometriosis is very time and resource intensive, and the consequences of extending operating time for the unexpected frozen pelvis affect not only the surgeon and the patient, but also the operating room team and other patients scheduled that day. Performing surgery on advanced endometriosis also increases the risk of visceral injury and may require involvement of other surgical specialists such as general or colorectal surgeons and urologists, and planning a multidisciplinary approach preoperatively is preferable to an intraoperative consult. The alternative to extending surgical time on an unexpected encounter would be to end the surgery or provide incomplete surgical treatment. This can be devastating to patients who have arranged for and been waiting for surgical treatment.

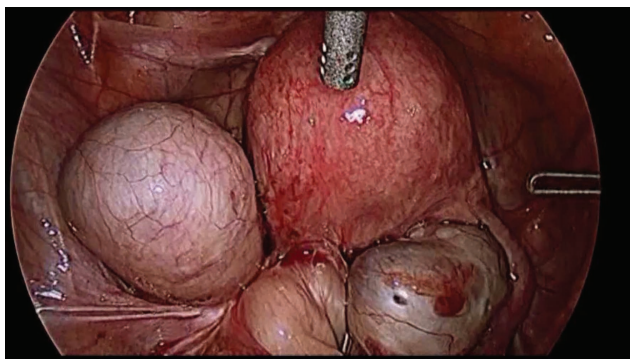


FIGURE 24.1 Advanced endometriosis with obliteration of the posterior cul-de-sac.

24.2.1 Consent Process

There are three key principles to follow during the surgical consent process that will optimize treatment success for the patient with endometriosis. The first is to set realistic expectations of the surgery. For patients desiring surgery for pelvic pain who have undergone past surgeries or do not have focalizing symptoms on exam, it is important to be clear that surgery may or may not help with pain. For patients with extensive disease desiring fertility-sparing surgery, it is important to clarify that reproductive organs left behind such as the uterus may be generators of pain. In addition, it is important to be clear with patients that endometriosis is a chronic condition and that there is the risk for reoperation in the future.

The second is to explore the goals of the patient and their main objectives in undergoing surgery. These objectives may include pain relief or optimizing fertility, and these goals will guide what will be done during surgery. As such, clarifying goals should prompt a discussion on what things the patient would like done based on what is encountered – including incidental findings for which the patient may not have symptoms. For example, in the case of a rectal nodule, discerning whether the patient would want this removed, even if it commits them to a resection and reanastomosis or possibly an ostomy, or whether, given the absence of symptoms, it would be better to avoid the risks of bowel surgery. Each patient will be motivated by different values and so it is paramount to understand these goals in order to provide the best care that is aligned with the patient's interests.

The third principle is to be transparent about the risks. There is an increased risk of visceral injury during surgery for advanced endometriosis, even in the most skilled of hands. It is important that patients understand this risk and the measures that may be taken in the event of a complication.

DOI: 10.1201/9781003312109-24

24.2.2 Multidisciplinary Involvement

Advanced endometriosis may require multidisciplinary involvement, as endometriosis may be found invading the bowel or genitourinary system, which may be outside of the scope of the gynecologic surgeon. As such, it is important to establish a connection between departments to provide the best care for patients with advanced endometriosis. A thorough evaluation will allow for the early identification of genitourinary and bowel involvement, which should prompt a preoperative consultation with urology, colorectal, or general surgery. Whenever possible, a preoperative consultation is always preferred to an intraoperative consultation and engenders trust and confidence among colleagues.

When involving other specialists, it is important to clarify what portions each surgeon will be responsible for. There may be scenarios where the gynecologic surgeon can complete portions of a particular procedure with the assistance and guidance of a specialist, and there are other times when the specialist will complete procedures that are outside of the scope of the gynecologic surgeon's practice. It is important to discuss beforehand the extent of involvement that will be required of each specialist.

24.3 Gastrointestinal Endometriosis

The gastrointestinal tract is the most common site of extragenital endometriosis, and the prevalence of bowel endometriosis is estimated to be 3.8%–37% in patients with endometriosis (5). Although there are case reports of endometriosis affecting the upper portion of the gastrointestinal tract, it is far more likely to be found on the rectosigmoid colon, followed by the rectum, the ileum, the appendix, and the cecum (6). Bowel endometriosis can be superficial and affect the serosa or deeply infiltrative and extend into the muscularis or all the way through to the mucosa, which has implications on surgical management. This section will review the presentation, diagnosis, and treatment of patients with gastrointestinal endometriosis.

24.3.1 History

Taking a thorough patient history is important in the clinical diagnosis of endometriosis. All patients should be assessed for dysmenorrhea, dyschezia, and dyspareunia (also known as the "3Ds of endometriosis"). It is our recommendation that gynecologic surgeons bringing patients to the operating room for any type of intrabdominal surgery should routinely incorporate these questions into their preoperative consult review of systems as it may signal the presence of endometriosis. Although patients may not have all three of these symptoms, presence of these symptoms should prompt a high index of suspicion for endometriosis. Dysmenorrhea is the most common symptom of endometriosis, and pelvic pain without dysmenorrhea makes endometriosis less likely. In assessing the dysmenorrhea, it is important to ask when the dysmenorrhea started and about the nature and location of the pelvic pain. For dyspareunia, it is helpful to understand whether there are certain locations that trigger the pain, as this may help with lateralizing any lesions of endometriosis.

For patients with gastrointestinal involvement, many will have the typical symptoms of endometriosis including pelvic pain, dysmenorrhea, dyspareunia, and/or dyschezia. Patients with advanced involvement of the bowel may report cyclic constipation around menses which can be suggestive of bowel narrowing, or cyclic hematochezia, which occurs when endometriosis infiltrates the mucosa of the bowel. However, it is important to note that generalized bowel symptoms are common among many patients with peritoneal endometriosis, and so symptoms similar to irritable bowel syndrome such as bloating, intermittent constipation, and diarrhea do not necessarily signal the presence of deep endometriosis within the gastrointestinal tract.

24.3.2 Physical Exam

The physical exam is an important diagnostic tool that can help guide surgical planning. In addition to a general physical assessment, all patients should have an abdominal and pelvic exam. A trauma-informed approach should be taken in every single encounter. This includes counseling the patient on what to expect during the exam, the rationale behind each step of the exam, and that the exam can be stopped at any point.

During the abdominal exam, surgical scars should be noted. For patients with a prior cesarean section, the scar should be palpated for any nodularity or tenderness in case there is the presence of abdominal wall endometriosis.

On pelvic exam, a speculum exam is helpful to note whether the cervix is midline or deviated, as deviation may indicate tethering or nodularity from endometriosis that distorts the anatomy. On speculum exam, findings that are highly suggestive of bowel involvement are deviation of the cervix with visible endometriosis in the posterior fornix (Figure 24.2).

A monomanual and bimanual exam are also informative, and a systematic approach should be adopted in completing these assessments. The purpose of the monomanual exam is to localize and reproduce focal tenderness. During the monomanual exam, one or two fingers are used to palpate the anterior vaginal wall, the levator and obturator muscles bilaterally, and the posterior fornix. Muscle spasm or tenderness on the levator and obturator muscles signal myofascial pain, whereas localized tenderness in the posterior fornix may indicate endometriosis. Patients may exhibit a classic visceral reaction upon palpating endometriosis with a marked, involuntary response to exquisite tenderness. A bimanual exam is done to palpate the size, shape, version, and tenderness of the uterus, evaluate the size and tenderness of the adnexa, and assess for the mobility of pelvic organs.

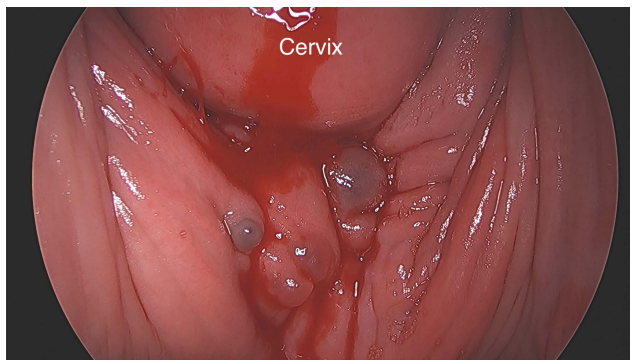


FIGURE 24.2 A speculum exam with endometriosis in the posterior fornix is highly suggestive of deep endometriosis involving the bowel.

A rectovaginal exam is also informative, but many providers may not routinely perform this exam. This could be for many reasons including that the findings have not yielded any additional information. However, when done with a specific purpose, this exam can yield important information, particularly for patients with suspected advanced involvement of the bowel. In order to perform the rectovaginal exam, one finger is placed in the vagina and the other in the rectum. The finger in the rectum is directed anteriorly to palpate the cervix through the rectum, as this is a consistent anatomical landmark. Once the cervix has been found, the finger is swept laterally on either side to feel the uterosacral ligament. By doing this, the examiner can feel any nodularity or focal tenderness that may be present on the uterosacral ligaments, cul-de-sac, and rectovaginal septum, or assess for any tethering which may be indicative of deeply infiltrating endometriosis. The physical exam may also reveal bowel nodules in the most distal 5 cm of the rectum but will not detect nodules that are more proximal.

24.3.3 Imaging

For patients with suspicion of advanced endometriosis, the MRI is very helpful in preoperative planning. However, MRI is not ordered routinely for every patient with pelvic pain and suspected endometriosis. The findings that may prompt MRI imaging include decreased mobility or nodularity on pelvic exam as well as findings of an endometrioma on ultrasound. In general, the presence of an endometrioma, or a persistent debris-filled cyst, may indicate deep infiltrating disease (7), with some studies citing at least a fivefold increased risk of deep infiltrating disease as well as obliteration of the cul-de-sac, or bowel involvement (8). In circumstances where the suspicion for bowel endometriosis is high but is above the level of the cervix in the sigmoid colon, obtaining an endorectal ultrasound may be a useful tool given the limitations of MRI (see later). When deep infiltrating endometriosis of the bowel is identified, it is important to note the size and depth of the lesion and whether it invades all the way through the mucosa of the bowel. One sign of endometriosis involving the rectal wall is the "mushroom cap sign" (Figure 24.3). This occurs when endometriotic implants invade the muscular layer of rectosigmoid colon, which causes smooth muscle proliferation, nodular thickening, and fibrosis whereas the overlying mucosa overlying mucosa is intact. As such, the fibrotic endometriosis will appear hypointense on T2-weighted imaging, but then also have an overlying higher signal intensity representing the mucosal layer (9).

Other than MRI, an endoanal ultrasound can also be considered and used to detect lesions within the bowel. This will also help to show the size and depth of the lesion and whether the

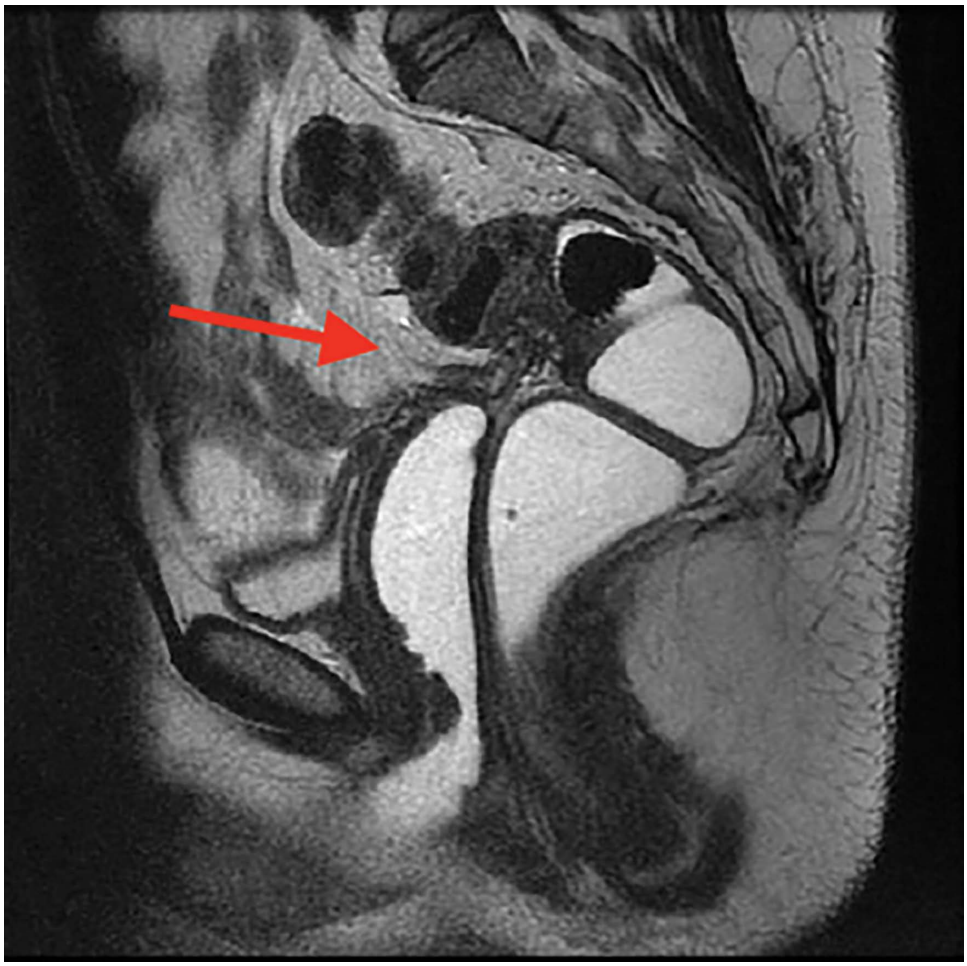


FIGURE 24.3 Note the "mushroom cap sign" on the sagittal view of MRI.

FIGURE 24.4 Endorectal ultrasound showing a bowel nodule of endometriosis.

lesion invades all the way through the bowel. Endorectal ultrasound is especially helpful for invasive endometriotic nodule on the upper rectum or sigmoid colon, as MRI is less sensitive because rectal contrast does not reach the upper rectum. Patients with cyclic hematochezia without palpable nodularity on rectovaginal exam will benefit from endorectal ultrasound (Figure 24.4).

In addition, some endometriosis centers are able to use ultrasonography for surgical planning. However, this typically requires ultrasonographers specially trained in endometriosis who are able to detect other signs of advanced disease. In these cases, a systematic scan of the anterior, middle, and posterior compartments are essential and should include visualization of the ureters, the vaginal wall and fornices, the rectovaginal septum, the uterosacral ligaments, and the anterior rectal wall to assess for the sliding sign of the uterus against the rectum for identification of tethered organs or an obliterated posterior cul-de-sac (10).

Having a radiologist familiar with endometriosis can help pick up nuances on imaging exams regardless of modality, and in practices and settings where advanced endometriosis is frequently encountered, it is recommended to hold interdisciplinary conferences to review MRI images and correlate them with findings and the pictures and/or videos from surgery.

24.4 Surgical Technique

In planning for surgical treatment of bowel endometriosis, it is especially important to have a sense of the size, location, and depth of the endometriosis impacting the bowel. This will help to determine the type of strategy to use to excise the endometriosis.

In general, for patients undergoing surgery for bowel endometriosis, it is important to address all other lesions of endometriosis first and normalize anatomy (Figure 24.5). For patients undergoing a hysterectomy, this should also be completed prior to addressing the bowel endometriosis. This allows for optimal visualization. We recommend performing a ureterolysis to

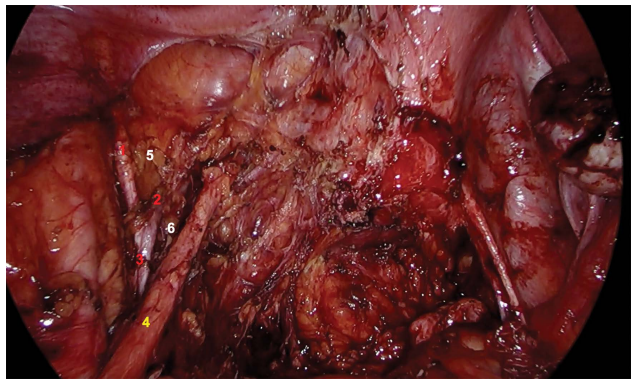


FIGURE 24.5 We recommend addressing other lesions of endometriosis which will often include ureterolysis and dissection of the avascular spaces. Legend: (1) medial umbilical ligament; (2) uterine artery; (3) anterior division of the internal iliac artery; (4) ureter; (5) paravesical space; (6) pararectal space.

mobilize the ureters as well as a bilateral oophoropexy to keep the adnexa out of the surgical field and to maximize the use of the first-assist, as they will no longer need to hold up the ovaries while the surgeon is working near the pelvic side wall. An oophoropexy can be completed as an external or internal pexy.

There are several ways to accomplish an external oophoropexy. The first is to use a Keith straight needle on a monofilament suture and place it through the abdominal wall (inferior and lateral to the lateral trocar sites), pierce the ovary through the distal third (close to the utero-ovarian ligament) and then back out through the distal third of the ovary, and finally back out from the site where it was placed in the abdomen. A hemostat can be placed on the sutures right as they exit the skin to hold the pexy in place during surgery. Placing the stitch on the distal one-third of the ovary provides maximum exposure in holding back the ovaries. Another way to achieve this would be to use a monofilament suture on a regular curved

needle. A stitch is placed through the distal one-third of the ovary, the needle is cut and removed from the body, and then a 2 mm incision inferior and lateral to the trocar site is made. A Carter–Thomason suture passer is then placed through this incision so that the ends of the monofilament suture is handed to the Carter–Thomason. The suture ends can then be pulled out of the abdomen and tagged with a hemostat at the exit site from the skin to hold the ovaries in place. Once the surgery is complete, the external oophoropexy stitch can be removed. An internal oophoropexy stitch can also be done by placing a stitch on the distal third of the ovary and affixing this to the round ligament and tying this down with an intracorporeal knot.

Most rectosigmoid endometriosis is associated with obliteration of the cul-de-sac, and it is rare to find a solitary nodule on the rectosigmoid without obliteration of the cul-de-sac. In general, bowel endometriosis is found on the medial portion of the rectosigmoid colon, but the pararectal spaces laterally are typically unaffected. Dissecting the medial pararectal spaces (space of Okabayashi) can be used to isolate the bowel and its attachment to the uterus and posterior aspect of the vagina. The space of Okabayashi can be opened by entering the peritoneum just medial to the uterosacral ligament. By doing this, the uterus and vagina can be separated from the bowel, thereby opening up the rectovaginal space. During this process, electrosurgery should be used sparingly to prevent thermal injury.

Once the rectosigmoid colon is isolated, the bowel should be palpated using an atraumatic grasper. This can help identify the location and size of the nodule (Figure 24.6). The surgeon should have a general sense of the size and location of these nodules based on the preoperative imaging.

There are three general approaches to removal of bowel lesions which are (1) bowel shaving, (2) discoid resection, and (3) segmental resection. The approach will depend on the depth, size, and location of the lesions. In general, bowel shaving is used for lesions that are superficial in nature, extending no deeper than the seromuscular layer. Discoid resection is the removal of an endometriotic nodule in the bowel. General guidelines suggest that this technique is best utilized for nodules that invade all or almost all the way into the mucosa but are less than 3 cm in size, or take up less than 1/3 of the bowel lumen. Segmental resection with reanastomosis is used for lesions that are larger than 3 cm in size, take up more than 1/3 of the bowel lumen, or are multifocal in nature (6). In addition, when a segmental resection is performed close to the anal verge (typically < 5 cm from the anal verge), a temporary diverting ileostomy may be performed at the same time to ensure full healing of the anastomosis without breakdown.

One important caveat is that since the caliber of the rectum and the rectosigmoid colon varies depending on the level of disease, the size differentiation (nodule less than 3 cm or less than 1/3 of the bowel lumen) is not absolute when it comes to the decision between anterior discoid vs segmental resection. For example, if the nodule is greater than 3 cm but a rectal probe can easily pass around the nodule, anterior discoid resection may still be feasible. If the caliber of the rectosigmoid is narrower, a segmental resection may be preferred even if the nodule is smaller than 3 cm, as discoid resection and the associated repair may result in significant stricture.

24.4.1 Bowel Shaving Technique

Bowel shaving is typically reserved for lesions that are superficial and impact the serosal layer of the bowel. Superficial lesions of the serosal layer of the bowel can often be removed without disrupting the deeper muscular or mucosal layers. There have been multiple studies published on bowel shaving, and in these studies, various techniques to bowel shaving have been described (11). Although different techniques may be used, the general principle is to excise any endometriotic or fibrotic lesion on the bowel without disrupting the lumen. We favor using scissors if bowel shaving is performed. The superficial lesion is grasped and the scissors are used to begin cutting into the serosal layer on the anterior surface of the bowel until the lesion is completely undermined and circumscribed. If the serosal layer is removed with minimal disruption of the underlying muscularis layer, sutures may not need to be utilized. However, if there is disruption to the muscularis layer, sutures

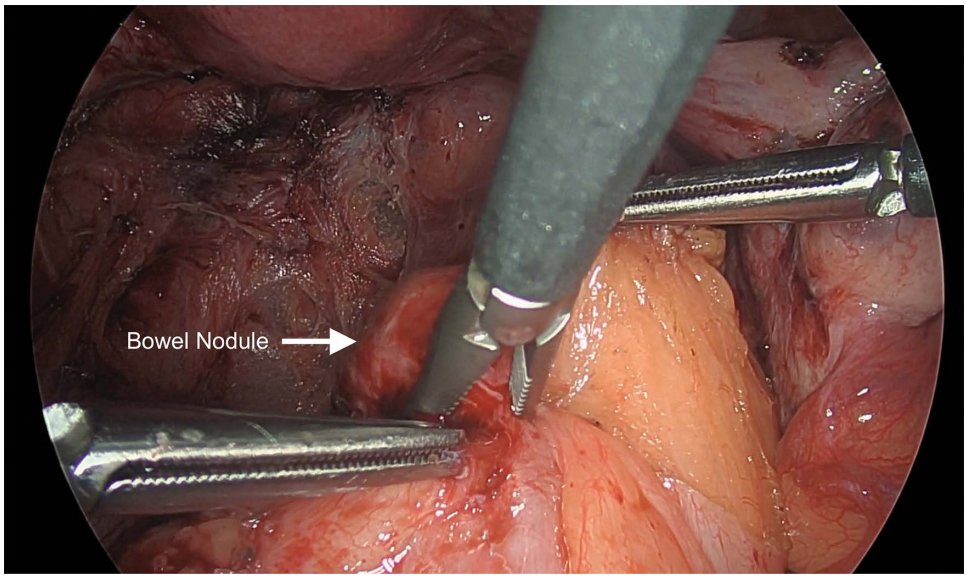


FIGURE 24.6 The bowel should be palpated with an atraumatic grasper to get a sense of the size of the endometriotic nodule.

may be used to reinforce or oversew the seromuscular layer. We typically use interrupted sutures or a horizontal mattress suture using a 2–0 or 3–0 delayed absorbable suture such as polyglactin. Typically, for superficial layers on the rectosigmoid colon, reapproximating the seromuscular layer will not cause stricture. After bowel shaving, the patient does not need to be placed on a modified diet.

24.4.2 Discoid Resection Technique

Discoid resection is used for endometriotic nodules that extend deeply into the muscularis of the bowel or all the way into the mucosa, but are less than 3 cm in size, or take up less than 1/3 of the entire bowel lumen (6). However, as discussed previously, this is a general guideline and exceptions can be made depending on the size of the nodule relative to the caliber of the affected bowel. For lesions that are very low and close to the anal verge, we recommend consideration of a segmental resection with possible temporary ileostomy in order to allow for adequate healing and prevent breakdown of the repair.

There are multiple techniques that have been described to perform a discoid resection. One method is to use a circular stapler to resect the portion of diseased bowel while also reapproximating the anterior wall of the bowel with the stapler at the same time. We typically use an advanced bipolar device with a cutting blade (ENSEAL bipolar; Ethicon – Somerville, NJ) to resect the nodule and then do a primary closure of the bowel, which we will describe in this chapter.

In our approach, the bowel is isolated and the advanced bipolar is then used to squeeze the nodule and bounce off the nodule in order to get a sense of the boundaries and size of the nodule. The serosa is then opened with the advanced bipolar device. Once the serosa is entered, the nodule is again evaluated in order to begin circumscribing the entire nodule. A suture can be placed through the bowel nodule to help with retraction and manipulation of the nodule. The nodule is manipulated frequently to get a sense of the boundaries and to preserve as much of the surrounding normal rectum as possible. We use this particular advanced bipolar device as it will not cut through the endometriosis nodule but will bounce off of it, leaving the entire lesion intact. During the removal of the nodule, sharp dissection along with electrosurgery can be used, but we recommend minimizing the use of electrosurgery to prevent thermal injury and to ensure that the tissue will heal well once repaired.

Once the lesion is removed in its entirety, the defect in the colon can be repaired. A rectal probe can be placed to guide the repair and prevent narrowing of the lumen (Figure 24.7). If the defect ends up spanning larger than 1/3 of the lumen, a reanastomosis should be considered in order to achieve the best result and prevent breakdown or leakage. Although defects in the small bowel necessitate closure perpendicular to the axis of the small bowel to prevent stricture, defects in the colon can sometimes be closed parallel to the axis of the colon given the larger caliber of the lumen. In either case, we recommend using the rectal probe to ensure patency of the lumen. When the defect is closed perpendicular to the lumen, the lateral apices of the defect can be anchored with a delayed absorbable suture to provide better exposure of the entire defect and ensure a symmetric closure of both edges of the bowel. The bowel is then closed in two layers. We use a 2–0, delayed absorbable unidirectional barbed suture. The first layer will reapproximate the mucosa, whereas the second layer will bring together the muscularis. The closure should ensure a tight seal, but cinching the tissue too tightly with the suture may cause ischemic necrosis and breakdown of the wound. As such, we have found that the barbed suture provides a secure but tension-free closure.

After closure of the defect, the rectal probe is removed and an air-leak test is completed to ensure a secure closure. This can be done by placing a rigid proctoscope in the rectum, filling the pelvis with saline, and ensuring the defect is submerged in the saline. A laparoscopic bowel clamp should then be placed above the level of the repair. Air is introduced into the rectum using the proctoscope, and the saline should be carefully assessed for bubbles. If there are any bubbles, this indicates that there is a leak in the repair, and this defect needs to be addressed.

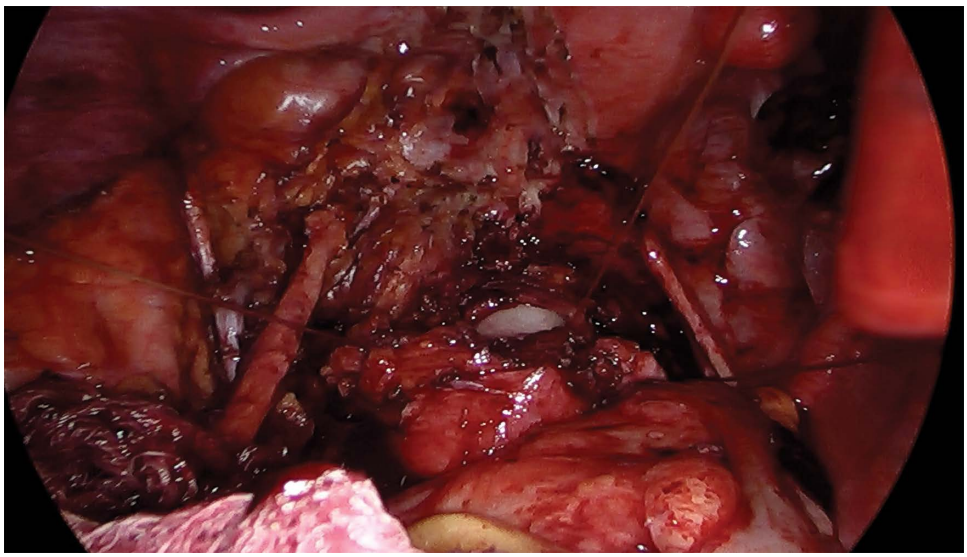


FIGURE 24.7 A rectal or bowel probe should be used to ensure patency of the lumen. The lateral apices of the defect can also be anchored to provide better exposure of the entire defect and ensure symmetric closure.

24.4.3 Segmental Resection Technique

Segmental resection involves complete resection of an affected portion of bowel followed by reanastomosis. This is typically reserved for large lesions greater than 3 cm, lesions that take up more than 1/3 of the bowel lumen, or multifocal lesions (6). Segmental resection should be performed by a colorectal surgeon, gynecologic oncologist, or other specialist with training in bowel resections. Segmental resections can be performed end to end or side by side. Based on the level of the segmental resection, there is a possibility that the patient may need a temporary diverting ileostomy to allow for full healing of the reanastomosis. This is often the case for resections that occur close to the anal verge. Another important consideration is that segmental resection may require aggressive dissection, including retrorectal dissection, which involves important neurovascular structures that may be disrupted, leading to undesired sequelae such as severe constipation and urinary retention (6).

There have been many studies published on the outcomes of bowel shaving, discoid resection, and segmental resection for endometriosis. In a meta-analysis published in 2020 that included 60 studies with a total of 17,495 total patients, the mean postoperative complication rate was 5.7%, with 2.2% after shaving, 9.7% after disc excision, and 9.9% after segmental resection (11). This study examined rates of bowel perforation requiring colostomy, rectovaginal fistula, leakage, intraoperative hemorrhage requiring blood transfusion, voiding dysfunction < 30 days, voiding dysfunction > 30 days, ureteral injury, and anastomotic stenosis. In this meta-analysis, the authors reasoned that if the studies involving rectal shaving only referred to removal of the rectal serosa, this would reduce the postoperative risk of complications compared to discoid excision and segmental resection – however, the studies all described different techniques with some disrupting the muscularis layer and so it is hard to draw a true comparison using shaving techniques. In addition, shaving may not always be suitable given the depth of the lesion. However, the authors were able to conclude from the analysis that discoid excision appears to be associated with fewer postoperative complications than segmental resection does.

In our experience, we determine surgical approach on a case-by-case basis with a plan to remove all diseased tissue while leaving as much normal tissue behind as possible. This may include bowel shaving, but our goal is not necessarily to avoid entering the muscularis layer or even the lumen, as our objective is to remove all of the endometriosis. However, we recognize that there are logistical challenges to this approach as any type of repair of the bowel, even reapproximation of the seromuscular layer, may necessitate assistance by colorectal surgery or general surgery. In addition, we described the squeeze technique to complete a discoid resection, but we acknowledge that the use of a circular stapler has been well described in the literature and is also another feasible option to complete this approach. The advantage of using the circular stapler is that it is very time efficient and will allow reapproximation of the anterior wall of the affected bowel at the same time that the lesion is resected. The disadvantage is that there are preset sizes to the circular stapler, so this may involve removing some amount of healthy tissue or, for endometriosis that is too large to fit into the stapler, may require additional bowel shaving to debulk the size of the nodule before using the stapler. In addition, the reapproximation of the bowel wall will always be the same with the circular stapler, whereas the squeeze technique allows for closure in a horizontal, oblique, or vertical fashion as long as the rectal probe is used as a template to preserve the patency of the bowel lumen.

Deep infiltrating endometriosis of the gastrointestinal tract requires careful preoperative workup with involvement of multidisciplinary teams. The surgical technique should be chosen based on the size, location, depth, and number of lesions.

24.5 Endometriosis of the Genitourinary Tract

Endometriosis of the genitourinary tract is estimated to affect 0.3%–12% of patients with endometriosis (12). In a systematic review, bladder endometriosis accounted for 80% of genitourinary tract involvement, whereas ureteral endometriosis occurred 14% of the time and was frequently associated with rectovaginal and/or uterosacral endometriosis (13). Bladder endometriosis can also be iatrogenic from a prior cesarean section.

Endometriosis of the ureter is seen more frequently on the left side and in a distal rather than proximal segment. The location of ureteral endometriosis has been thought to align with the theory of retrograde menstruation, as menstrual fluid carries endometriotic cells to the most dependent portion of the pelvis, which would impact the distal ureter, and because the presence of the sigmoid colon on the left side of the pelvis allows for collection of menstrual fluid in the left pelvis, leading to more cases of left ureteral endometriosis over right ureteral endometriosis (13).

Although superficial lesions of endometriosis may impact the peritoneum overlying the ureters or the bladder, for the purposes of our review, we will discuss the management of lesions that deeply infiltrate the genitourinary system or cause significant fibrosis to require more than excision of peritoneal lesions.

24.6 Preoperative Workup

24.6.1 History

As outlined earlier in the chapter, the office workup of the patient is a key component in detecting genitourinary endometriosis and appropriately planning for surgical treatment. The clinical presentation of bladder and ureteral endometriosis can be varied. Patients with bladder endometriosis may complain of dysuria, suprapubic pain, urinary frequency, or hematuria and have symptoms similar to cystitis. However, it is possible for patients without genitourinary endometriosis to have similar urinary symptoms as well. Many patients with genitourinary endometriosis may present with other symptoms of endometriosis such as dysmenorrhea, dyspareunia, and dyschezia. In a systematic review of 18 studies with 700 patients with ureteral endometriosis, the most reported symptoms were dysmenorrhea (81.4%), pelvic pain (70.2%), and dyspareunia (66.4%), whereas dysuria and other urinary symptoms were only reported in approximately 34.7% of patients (12). Some patients may also experience pelvic, flank, or back pain. However, given the nonspecific nature of symptoms, ureteral endometriosis may be found entirely incidentally on imaging by detecting a hydroureter.

24.6.2 Physical Exam

All patients with endometriosis should be examined using a systematic approach. Although genitourinary endometriosis itself cannot be detected with a physical exam, the physical

exam provides important information that can inform the type of imaging modality to use in surgical planning. Any patients with suspected deep infiltrating endometriosis on physical exam should have an MRI for surgical planning. The steps of the systematic physical exam have been reviewed earlier in this chapter.

24.6.3 Imaging

As with the workup for endometriosis of the bowel, if there are signs of deep endometriosis on ultrasound such as bilateral endometriomas or lack of a "sliding sign" indicating tethering of pelvic organs, further workup should be pursued with MRI.

On MRI, it is important to assess the anterior compartment and look for any nodules in the bladder. On T2 imaging, this will appear as a hypointense mass contrasted against the bright signal seen in the bladder. On T1 imaging, this will typically have an intermediate signal with possible hyperintense foci representing glandular endometriosis. It is important to take note of the size, the location, and the proximity to the ureters and trigone, as these will all inform surgical planning. If MRI suggests the endometriotic nodule is on the trigone or near the trigone (Figure 24.8), a diagnostic cystoscopy is helpful for surgical planning. For ureteral endometriosis, it is important to look for any signs of hydroureter and to identify where the blockage is occurring. Ureteral endometriosis may appear to be fibrotic, which on T2 imaging appears hypointense with irregular or stellate margins. It can be very hard to differentiate whether ureteral endometriosis is extrinsic or intrinsic, but it is important to note the location of the endometriosis, so that it can be focused on in surgery, and to assist in surgical planning in case resection of that portion of the ureter is needed.

24.6.4 Surgical Treatment of Bladder Endometriosis

Bladder endometriosis is defined as endometriosis that infiltrates into the detrusor muscle of the bladder. When planning for surgical treatment of endometriosis nodules within the bladder, careful surgical planning is paramount. For these types of lesions, involvement of a urologist is important for success, particularly for nodules that may be sizeable or located in an area other than the dome of the bladder. Factors to consider in surgical planning include the size and the location of the nodule. For nodules located in the bladder dome, the surgical treatment is excision of the nodule with simple partial cystectomy with a two-layer closure. For nodules located near the trigone or the vesicoureteral junction, ureteral stents are recommended. For nodules that are very close to or involving the ureteral orifice, a ureteroneocystostomy may be necessary.

Since bladder endometriosis nodules invade the detrusor muscle, there may not be any evidence of the lesion on the actual peritoneum overlying the bladder. However, most nodules on the dome are easily located and palpated by gently squeezing along the bladder, being careful not to mistake the Foley bulb for the nodule. However, nodules on the trigone or near the trigone may pose a challenge because they are not easily palpated and are seen after creation of cystotomy. In order to get direct access to bladder nodules, it may be helpful to approach the bladder laterally. This can be done by entering the retroperitoneum and developing the avascular paravesical space, which is bordered by the medial umbilical ligament, the uterine artery, and the bladder. Once the nodule is palpated by gently squeezing the nodule, an incision can be made along the border of the

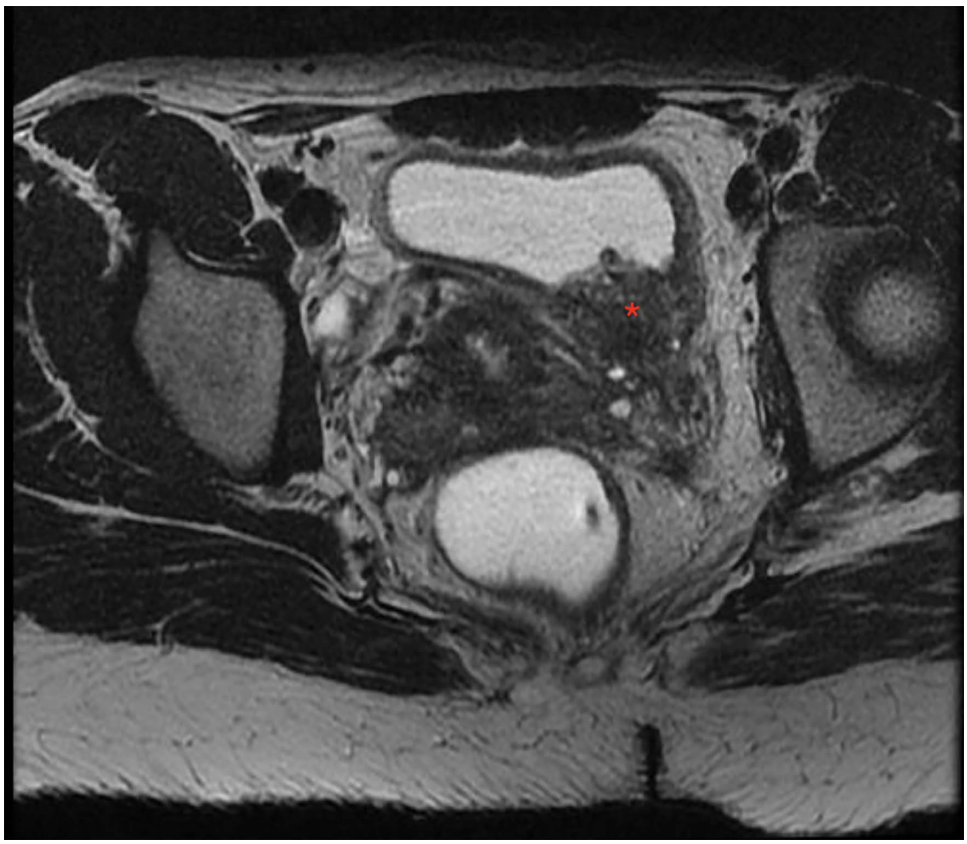


FIGURE 24.8 MRI T2-weighted axial image of the pelvis showing a nodule of bladder endometriosis (*) near the trigone.

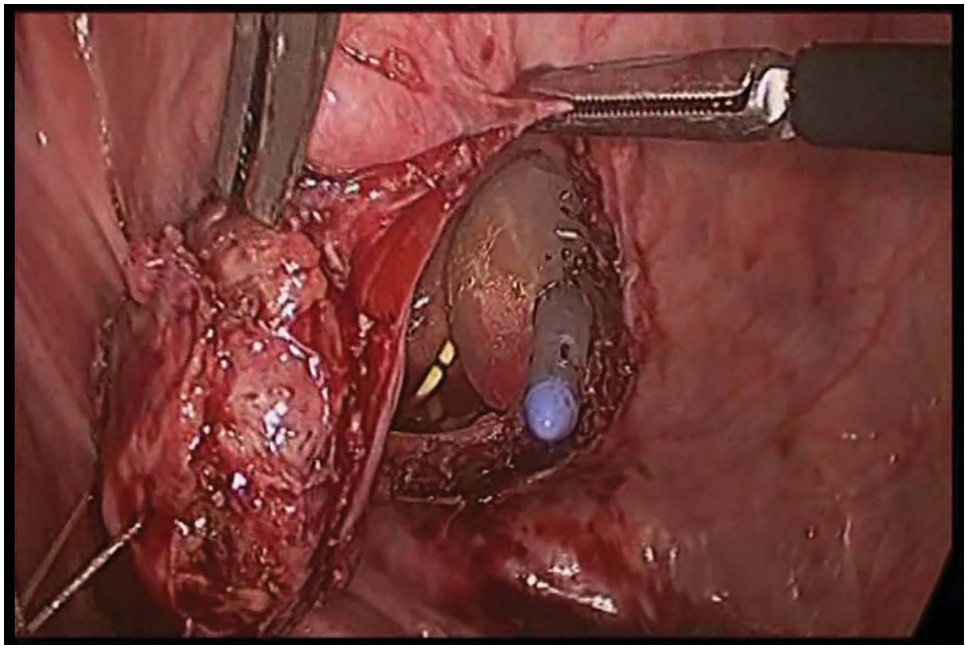


FIGURE 24.9 Endometriosis nodule of the bladder with urinary Foley and left ureteral stent visible.

nodule. Once the cystotomy is made, the lesion can be directly visualized, and the entire nodule can be circumscribed and removed. Note that for nodules within the vesicouterine junction, partial resection of the myometrium may be necessary, as these nodules may also invade into the neighboring uterus. In addition, when nodules are within 2 cm of the vesicouterine junction, double J stents should be kept in place for 2 weeks as postoperative inflammation may cause temporary obstruction of the proximal ureter (13). See Figure 24.9.

After the lesion is removed, the bladder needs to be reapproximated. The bladder should be closed in two layers with the first layer reapproximating the mucosa and part of the muscularis. The second layer is an imbricating layer incorporating the muscularis and serosa and provides additional reinforcement. In these repairs, an absorbable synthetic suture can be used, whereas permanent suture such as silk should be avoided as they can be a nidus for stone formation (14). For these cystotomy closures, we make use of a 2–0 barbed suture. The barbs in the suture keep the incision closed, with less reliance on an assistant to hold the incision closed while avoiding strangulation of the tissue, and allow for an equal distribution of tension along the closure. For these reasons, the barbed suture can also facilitate more efficient repair of the bladder. The use of barbed suture has been studied in a retrospective review and showed no major complications and appears to be an acceptable alternative to non-barbed absorbable suture (15).

For a large defect, it may be necessary to release the bladder in order to achieve a tension-free closure. The retropubic space, or the space of Retzius, should be developed to allow greater mobility (Figure 24.10). This can be done by opening the peritoneal layer by using the median umbilical ligament at the midline of the pelvis as a landmark. Once the peritoneal layer is opened, pneumodissection will reveal thin, alveolar tissue that can be bluntly dissected. If additional mobility is required, the bladder can also be mobilized by developing the vesicovaginal space and bringing the bladder base off the vagina. An instrument such as a Breisky–Navratil retractor can be placed into the anterior vaginal fornix to help delineate this space and provide a surface against which traction can be applied to develop this space.

Once the bladder has been repaired in two layers, the bladder should be backfilled with at least 300 cc to ensure a watertight seal. An indwelling Foley catheter should be left in place for 7–10 days, and we recommend obtaining a voiding cystourethrogram at removal.

24.6.5 Surgical Treatment of Ureteral Endometriosis

Ureteral endometriosis can be intrinsic or extrinsic. Approximately 80% of all cases of ureteral endometriosis are extrinsic, meaning that the endometrial glandular and stromal tissue is found within the submucosal and adventitial layers of the ureter (16). In these cases, the distortion of the ureter is primarily caused by fibrosis. Intrinsic endometriosis represents 20% of cases and occurs when endometriosis invades into the uroepithelial and submucosal layers (16). In situations of ureteral endometriosis, medical treatment is largely ineffective, as the main cause of distortion is fibrosis, which does not typically respond to hormonal suppression. In addition, there may be progression of disease which can lead to worsening hydroureter and loss of kidney function.

The surgical treatment of ureteral endometriosis will largely depend on the location and whether the lesion is extrinsic or intrinsic. For all patients with suspected ureteral endometriosis, it is important to obtain imaging, if it has not already been done. For many patients, the suspicion of ureteral endometriosis will come from findings on MRI or a CT scan which shows hydronephrosis. In addition to this, a screening renal ultrasound can help determine the extent of renal damage. Other imaging modalities that have been used include intravenous pyelogram, ureteroscopy, and endoluminal ultrasound. Since these imaging modalities are not commonly used by most gynecologic surgeons, consulting a urologist is important.

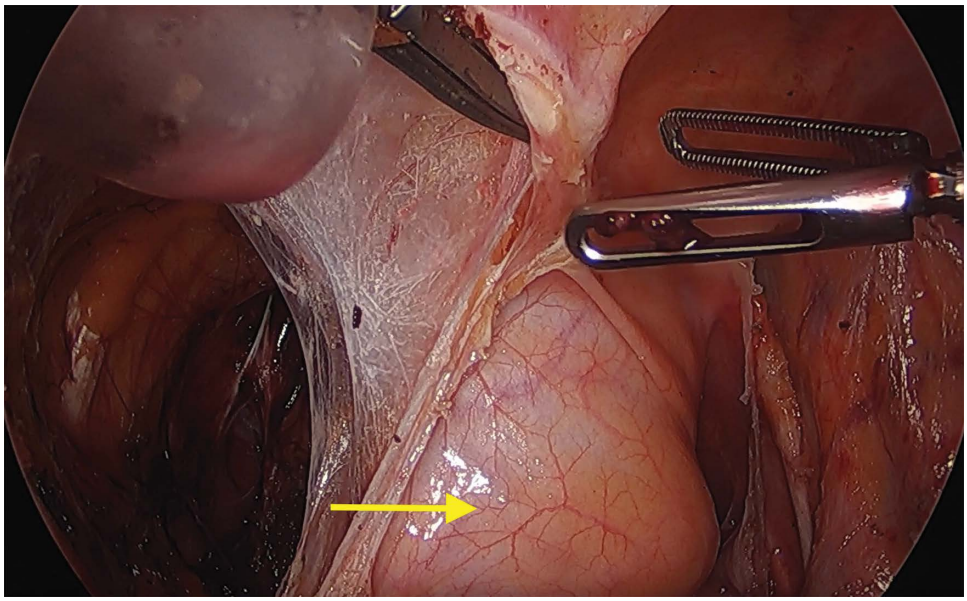


FIGURE 24.10 Dissecting the space of Retzius can provide additional bladder mobility to facilitate tension-free closure (arrow, bladder).

Unfortunately, it is very difficult to distinguish between extrinsic and intrinsic ureteral endometriosis on imaging including MRI, and so it is crucial to thoroughly counsel the patient on the potential surgical strategies that may be undertaken to treat the ureteral endometriosis, as well as the surgical outcomes. The different types of surgical treatment can include extensive ureterolysis, ureteroureterostomy, and ureteroneocystostomy, and so the surgeon should plan for ample operating room time, ensure that the proper surgical team is assembled, including involvement of a urologist, and plan for all necessary equipment to complete any of these procedures.

Extrinsic ureteral endometriosis typically requires complete ureterolysis to free the ureter from the surrounding endometriotic fibrosis. Performing this type of ureterolysis can be technically challenging given the fibrotic tissue surrounding the ureter which may distort normal tissue planes. In order to complete the ureterolysis, it is advisable to open the paravesical and pararectal spaces and identify the uterine artery. Depending on the location of the nodule, it may be advisable to temporarily clamp the uterine artery proximally to prevent bleeding in case the uterine artery is injured in a distal location while dissecting through the fibrotic tissue. To begin the ureterolysis, the peritoneum should be opened in an area more proximal to the fibrosis, if possible. This will allow the dissection to begin in an area of normal tissue planes. There is typically an avascular plane close to the ureter but outside of the adventitia, or the vascular sheath of the ureter. At times, there may be fibrotic tissue overlying the ureter that cannot be dissected bluntly, and so this layer must be entered by sharp dissection. When in close proximity to the ureter, cold scissors should be used to avoid the risk of thermal injury. As the dissection progresses closer to the area of constriction, there is often a very fibrotic nodule encasing the ureter. This can be difficult to dissect, but a plane can generally be found at 12 o'clock. When this plane is found, the nodule constricting the ureter can be bivalved and dissected completely off the ureter. There are several other tools that can help with retracting the ureter atraumatically, which can include a laparoscopic Babcock as well as a vessel loop. Once ureterolysis is complete, it is recommended to leave a double J stent for 2–4 weeks to protect the ureter and prevent delayed injury, as the vascular sheath may have been compromised during the process of ureterolysis, and to help with any constriction due to postoperative inflammation of the ureter.

Intrinsic ureteral endometriosis typically requires resection followed by a ureteroureterostomy or a ureteroneocystostomy. The decision to perform a ureteroureterostomy or a ureteroneocystostomy will depend on the location of the endometriosis to be excised, as the main goal is to achieve a tension-free repair. In most cases, ureteral endometriosis is found distally in the pelvis. However, when it is found more proximally, a ureteroureterostomy can be performed. In general, when the lesion is in the proximal two-thirds of the ureter, a ureteroureterostomy can be performed, whereas lesions found in the distal 1/3 of the ureter will likely require a ureteroneocystostomy. In addition, a ureteroureterostomy is typically only suitable for shorter defects that can be brought back together in an anastomosis without excessive tension. In our experience collaborating with the urology team, a ureteroneocystostomy is typically preferred as the risk of stricture is higher with ureteroureterostomy.

In a ureteroureterostomy, ureterolysis is performed to allow for the greatest mobility of the ureter. The lesion of endometriosis infiltrating the ureter is excised using cold scissors to avoid electrosurgery, which may impair healing. The lesion is removed in its entirety, and then both ends of the ureter are spatulated. A double J stent can be placed at this time to facilitate bringing the ends together. A delayed absorbable 3–0 or 4–0 suture is then used to place interrupted sutures to bring the apex of the proximal spatulated end of the ureter to its matching distal component. The suture is then tied down, bringing the two ends of the ureter together. Another interrupted stitch is placed on the opposite apex. After this, several other interrupted sutures can be placed all the way around the reanastomosis. Once this is complete, the double J stent should stay in place for 6 weeks. In addition, a closed-suction drain

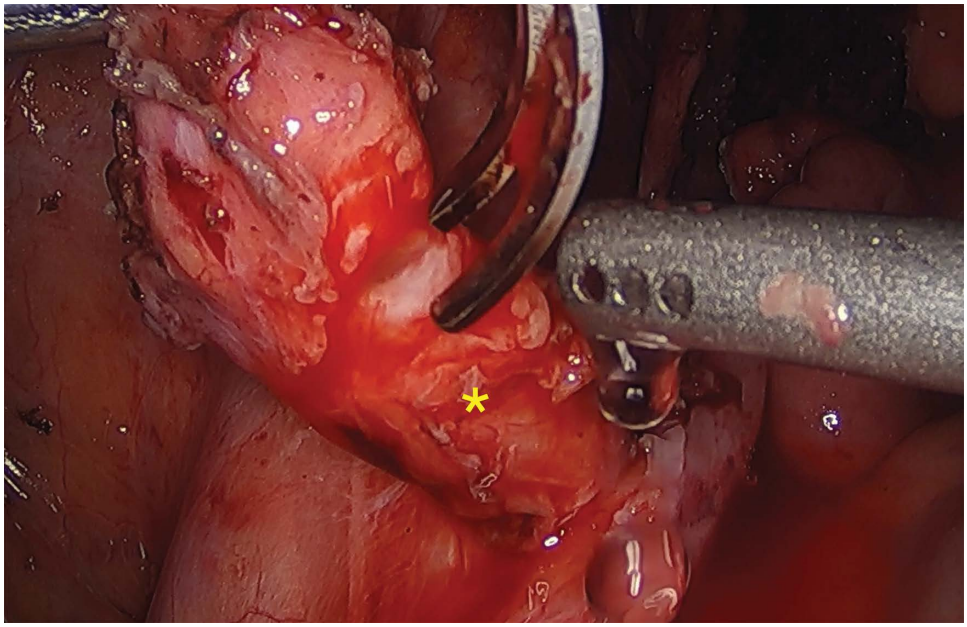


FIGURE 24.11 The ureter (*) is trimmed to remove any excess tissue that may be ischemic. The ureter is then spatulated.

can be left near the site of the reanastomosis to detect leakage from the site. Fluid collected in the drain-bulb can be sent for a creatinine to detect leakage.

Ureteroneocystostomy can be done when endometriotic lesions infiltrate the distal 1/3 of the ureter. The lesion of endometriosis is completely removed using cold scissors to preserve as much of the ureter as possible and avoid thermal injury which may compromise healing. Next, the ureter will be implanted back into the bladder. In doing this, the main goal is to achieve a tension-free repair. There are several strategies to help achieve this – the first is to ensure that adequate ureterolysis has been completed to mobilize the ureter. The second is to mobilize the bladder by dissecting the space of Retzius. The vesicovaginal space can also be dissected. The tension between the ureter and the bladder can be checked several times during this process to guide how much dissection needs to be done in order to achieve a tension-free repair. If there is still not adequate mobility of the ureter, a psoas hitch can be performed to help bring the bladder closer to the ureter. A psoas hitch is performed by placing several interrupted stitches of delayed 2–0 absorbable suture between the bladder and the psoas tendon. It is important to avoid incorporating the genitofemoral nerve, which runs along the psoas tendon.

Once the bladder and ureter have been sufficiently mobilized, the ureter is spatulated with cold scissors, and a cystotomy is created at the dome of the bladder where the ureter will be reimplanted. See Figure 24.11.

A double J stent is then placed to help guide the repair. A delayed 3–0 or 4–0 absorbable suture is then used to place sutures between the apex of the spatulated end of the ureter to the bladder. Sutures are placed circumferentially either in a running or interrupted fashion until the reimplantation is complete. In our experience, we use two 4–0 monofilament sutures. The first is used to anchor the ureter to the bladder and then secure the medial aspect of the ureter to the bladder in a running fashion, ensuring that the ureter is on the inside of the bladder. The second is then used to reapproximate the lateral aspect of the ureter and bladder. In addition, to protect the reimplantation, an imbricating stitch over the ureter can be completed using a 3–0 barbed suture. This can be done by taking small bites of the bladder on either side of the ureter and cinching the tissue together. As with a ureteroureterostomy, we recommend leaving the stent in place for 6 weeks and leaving a closed-suction drain by the site of reimplantation to detect spillage. See Figure 24.12.

Key Points

- Advanced endometriosis presents a surgical challenge due to extensive scarring, obliteration of normal surgical planes, and distorted anatomy.
- Encounters with advanced endometriosis can be planned or unexpected. It is imperative to collect a thorough history and perform a physical exam in order to anticipate when the presence of advanced endometriosis, allowing for appropriate surgical planning and proper informed consent from the patient.
- MRI is a helpful preoperative tool for surgical planning and should be obtained when deep endometriosis is suspected.
- Endometriosis invading the gastrointestinal tract or the genitourinary tract requires careful preoperative planning with other specialties such as colorectal surgery and urology.
- Endometriosis invading the bowel can be removed using bowel shaving, discoid excision, or segmental resection.

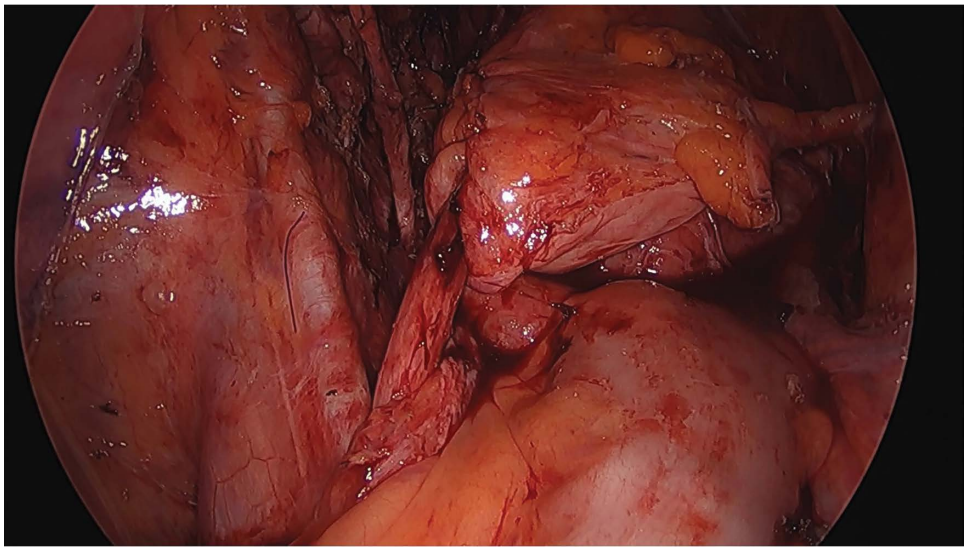


FIGURE 24.12 Resection of bladder endometriosis with primary repair and reimplantation of the ureter.

- Bowel shaving should be used primarily for superficial lesions involving the bowel, whereas discoid excision can be used for endometriotic nodules < 3 cm or taking up less than one-third of the lumen. Segmental resection is best for endometriotic nodules in bowel that are larger than 3 cm, greater than one-third of the lumen, or multifocal.
- Endometriosis more commonly affects the bladder over the ureters. When there is an endometriotic nodule invading the bowel, the nodule may need to be excised with repair of cystotomy.
- Ureteral endometriosis may be extrinsic or intrinsic. Extrinsic endometriosis requires ureterolysis to remove fibrotic tissue. Intrinsic endometriosis requires excision of the lesion from the ureter with subsequent repair of the ureter. Depending on the location of the nodule, this may require a ureteroureterostomy or a ureteroneocystostomy.

References

1. Zondervan KT et al. Endometriosis. *N Engl J Med*. 2020;382(13):1244–1256.
2. Koninckx PR et al. Deep endometriosis: definition, diagnosis, and treatment. *Fertil Steril*. 2012;98(3):564–571.
3. Cavaco-Gomes J et al. Laparoscopic management of ureteral endometriosis: a systematic review. *Eur J Obstet Gynecol Reprod Biol*. 2017;210:94–101.
4. Leborne P et al. Clinical outcomes following surgical management of deep infiltrating endometriosis. *Sci Rep*. 2022;12(1): 21800.
5. Remorgida V et al. Bowel endometriosis: presentation, diagnosis, and treatment. *Obstet Gynecol Surv*. 2007;62(7):461–470.
6. Nezhat C et al. Bowel endometriosis: diagnosis and management. *Am J Obstet Gynecol*. 2018;218(6):549–562.
7. Chapron C et al. Associated ovarian endometrioma is a marker for greater severity of deeply infiltrating endometriosis. *Fertil Steril*. 2009;92(2):453–457.
8. Banerjee SK et al. Endometriomas as a marker of disease severity. *J Minim Invasive Gynecol*. 2008;15(5):538–540.
9. Arévalo N et al. "Mushroom cap" sign in deep rectosigmoid endometriosis. *Abdom Radiol* (NY). 2018;43(11):3201–3203.
10. Van den Bosch T et al. Ultrasound diagnosis of endometriosis and adenomyosis: state of the art. *Best Pract Res Clin Obstet Gynaecol*. 2018;51:16–24.
11. Bendifallah S et al. Surgical outcomes after colorectal surgery for endometriosis: a systematic review and meta-analysis. *J Minim Invasive Gynecol*. 2021;28(3):453–466.
12. Cavaco-Gomes J et al. Laparoscopic management of ureteral endometriosis: a systematic review. *Eur J Obstet Gynecol Reprod Biol*. 2017;210:94–101.
13. Nezhat C et al. Pathophysiology and management of urinary tract endometriosis. *Nat Rev Urol*. 2017;14(6):359–372.
14. Glaser LM et al. Bowel and bladder injury repair and follow-up after gynecologic surgery. *Obstet Gynecol*. 2019 Feb;133(2):313–322.
15. Chamsy D et al. The use of barbed suture for bladder and bowel repair. *J Minim Invasive Gynecol*. 2015;22(4):648–652.
16. Yohannes P. Ureteral endometriosis. *J Urol*. 2003;170(1): 20–25.

25 FERTILITY CONSIDERATIONS IN MANAGEMENT OF ENDOMETRIOSIS

Jack Przebienda, Elliott G. Richards, and Tommaso Falcone

25.1 Introduction

Endometriosis in infertile patients has an unknown prevalence and a variable presentation, in large part because an invasive procedure is required to confirm the diagnosis. The prevalence in infertility patients is unclear because laparoscopy is no longer considered an integral part of the investigation of an infertile couple.

While diagnosis of endometriosis is arguably straightforward in the histologic confirmation of ectopic endometrial glands and stroma, the pathogenesis, clinical investigation, classification, and management of endometriosis is complex, particularly in the setting of infertility. The prevailing wisdom is that endometriosis is present in 5%–15% of reproductive aged women and up to 50% of women with unexplained infertility, yet many of these patients with infertility will not experience hallmark symptoms such as pelvic pain, nor will they have characteristic signs on noninvasive imaging, leading to difficulty in knowing when and how to pursue diagnosis and treatment. Furthermore, conventional suppressive medical therapies for endometriosis are not compatible with conception, and even excisional surgical therapies can harm future fertility.

Despite considerable advances in the last decade, the relationship between endometriosis and infertility is not fully understood and the subject of considerable controversy. For the patient diagnosed with endometriosis and their clinician caring for them, management of endometriosis in the context of fertility can be a daunting task.

25.1.1 Endometriosis and Infertility: A Brief History

First discussions of a link between endometriosis and infertility occurred as early as the 1940s (1). However, it was not until the 1950s that Dr. Robert Kistner's work truly brought the issue into the spotlight (2). Through his extensive writings on the topic, he outlined potential therapeutic measures for addressing infertility issues linked to endometriosis, which significantly helped shape the early understanding of the relationship between these two conditions.

During the period of the 1960s and 1970s, the connection between endometriosis and infertility was explored in greater depth (3–6). Scientific investigations found that endometriotic lesions and associated adhesions could disrupt the pelvic anatomical structure, impairing normal function of the ovaries and fallopian tubes, ultimately giving rise to fertility issues.

During the 1980s and 1990s, technological advancements in medical imaging, like ultrasound and laparoscopy, allowed for better visualization and diagnosis of endometriosis (7, 8). With this enhanced capability, more studies found a higher prevalence of endometriosis in women who were struggling with infertility. Many researchers during this time proposed that endometriosis could potentially cause infertility through other mechanisms beyond just mechanical disruption, such as molecular and cellular changes, inflammatory responses, and compromised egg quality.

By the 21st century, the association between endometriosis and infertility was well established. A growing body of research suggested that endometriosis could cause infertility not only through anatomical disruption but also by inducing changes at the molecular and cellular level and impairing the immunological environment within the reproductive tract. The proinflammatory microenvironment has been shown to be present in peritoneal, follicular, and endometrial fluids (9–11).

25.1.2 Endometriosis Classification Systems

In 1996, the American Society for Reproductive Medicine (ASRM) revised their classification system for endometriosis, providing a framework for physicians to describe and communicate features of the condition with greater precision (12). The ASRM classification system uses a point total based on the location, extent, and depth of endometrial tissue growth, as well as the presence and severity of adhesions and other associated factors. This point total is then used to classify endometriosis into four stages: stage I (minimal), stage II (mild), stage III (moderate), and stage IV (severe). This system has been widely adopted and has helped standardize the diagnosis and management of endometriosis, yet it has not been without drawbacks and alone it has limited utility in predicting the fertility potential of a patient.

Introduced in 2008, the Endometriosis Fertility Index (EFI) is a tool to predict the chance of pregnancy for patients with surgically documented endometriosis (Figure 25.1) (13). The EFI takes into account both historical factors and surgical factors (the "least function score," or LFS) to provide a more comprehensive assessment of fertility potential. Historical factors, such as age, years of infertility, and prior pregnancy, account for half of the points in the EFI scoring system. The other half comes from the LFS, which is determined at the conclusion of endometriosis surgery. The LFS measures the extent of damage to the reproductive organs caused by endometriosis and assigns a score based on the severity of damage. The EFI scoring system ranges from 0 to 10, with a score of 0 indicating the poorest prognosis; a score of 0 to 3 is associated with a very low probability of achieving a successful pregnancy; scores between 4 and 7 are associated with intermediate probability of success; a score of 8 to 10 is associated with a high probability of pregnancy success; and a score of 10 indicates the best prognosis. The EFI has been shown to be a reliable predictor of pregnancy outcomes in women with endometriosis who have not undergone IVF. The EFI can help guide treatment decisions, as patients with a low EFI score may benefit from more aggressive treatment options such as IVF, while those with higher scores may be good candidates for less invasive treatments such as intrauterine insemination (IUI) or attempt at spontaneous pregnancy. The EFI is a valuable tool for clinicians in assessing and counseling patients with endometriosis regarding their fertility potential.

The Enzian classification was developed in 2016 by a group of international experts (14). The system is named after the Enzian flower, which grows in the Alps and has petals arranged in a spiral pattern, reflecting the spiral nature of endometriosis lesions. The Enzian system includes both imaging and surgical

DOI: 10.1201/9781003312109-25

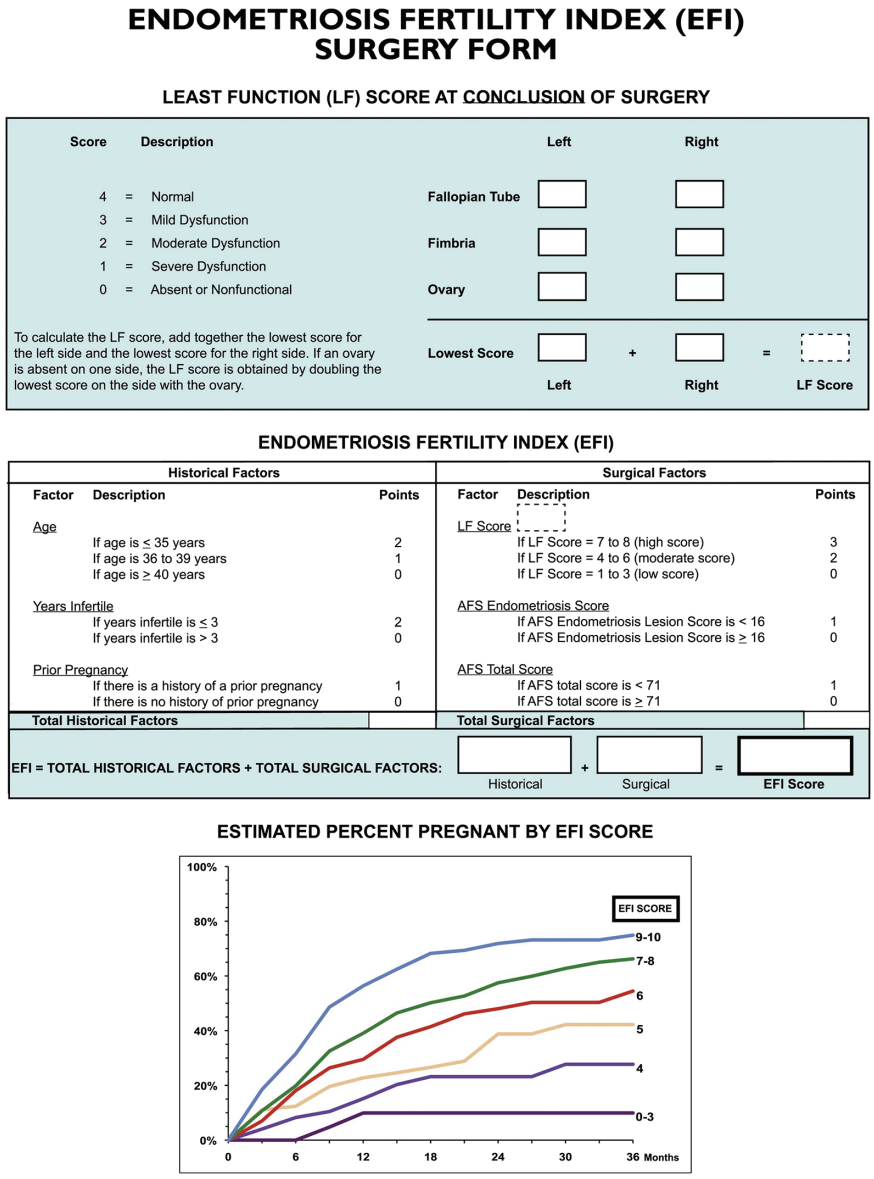


FIGURE 25.1 Endometriosis Fertility Index. (From Ref. 13 with permission.)

features of endometriosis, providing a more complete picture of the disease. The imaging component of the system includes transvaginal ultrasound (TVUS) and magnetic resonance imaging (MRI) findings, while the surgical component includes the extent and depth of endometriosis lesions, as well as their location and characteristics. One of the main strengths of the Enzian system is that it allows for a more precise and detailed classification of endometriosis, which can help guide treatment decisions and improve patient outcomes. For example, the system provides specific criteria for diagnosing deep endometriosis (DE), which is a particularly severe form of the disease that can cause significant pain and infertility. The Enzian system includes six main categories of endometriosis, which are further divided into subcategories based on the extent and severity of the disease. The categories include peritoneal endometriosis, ovarian endometriosis, deep endometriosis, adenomyosis, endometriotic scars, and extragenital endometriosis. Compared to the ASRM and EFI classification systems, the Enzian system offers several advantages. For one, it allows for a more accurate diagnosis of endometriosis by incorporating both imaging and surgical features of the disease. Additionally, it offers a more detailed description of endometriosis lesions and their characteristics, which can aid in surgical planning and improve outcomes. The Enzian system also includes a scoring system that takes into account the extent and severity of endometriosis, allowing for a more nuanced and individualized approach to treatment. However, the Enzian system is still relatively new and has not yet been widely adopted in clinical practice. Additionally, its use may require specialized training and expertise in both imaging and surgery. The ASRM and EFI classification systems, on the other hand, are more established and widely recognized, making them more accessible and easier to use for clinicians.

The AAGL introduced a new classification system to consider the complexity of phenotype (15). However, the AAGL severity stage correlates comparably with pain and infertility symptoms with the ASRM staging system. Furthermore, the classification was not validated for fertility outcomes. For this

reason, the EFI score is currently the system with the most robust predication of fertility surgical outcome.

25.2 Mechanisms of Infertility in Endometriosis Patients

Endometriosis has been implicated in infertility through a variety of interconnected mechanisms. These multifaceted pathways are not fully elucidated, each involving anatomical, biochemical, immunological, and endocrine aspects.

Several proposed mechanisms have been put forward as mechanisms behind endometriosis-associated infertility (16):

- *Adhesions*: Endometriosis can lead to the formation of pelvic adhesions which can distort the anatomical orientation of the female reproductive organs. This can hinder the normal function of the ovaries and fallopian tubes, affecting processes such as ovulation, fertilization, and implantation.
- *Chronic Intraperitoneal Inflammation*: The presence of endometriotic lesions is associated with an elevated inflammatory response within the peritoneal cavity and the endometrial cavity. This chronic inflammation can produce a hostile environment for gametes and embryos, reducing fertility.
- *Disturbed Folliculogenesis*: The formation of endometriotic cysts, or endometriomas, can cause local inflammation and oxidative stress, which may disturb normal folliculogenesis. This can negatively affect oocyte quality and quantity, impairing fertility.
- *Progesterone Resistance*: Endometriosis is associated with a reduced responsiveness of the endometrium to progesterone. This progesterone resistance could lead to impaired endometrial preparation for embryo implantation, contributing to infertility.
- *Effects on Spermatozoa*: The inflammatory environment in the peritoneal cavity in endometriosis can negatively affect sperm function and survival, further decreasing the chances of successful fertilization.
- *Anti-Endometrial Antibodies*: The presence of anti-endometrial antibodies has been observed in some women with endometriosis. These antibodies might potentially interfere with implantation, though the exact mechanisms are not clear.
- *Dysfunctional Uterotubal Motility*: Endometriosis can lead to impaired uterotubal transport mechanisms, potentially preventing the successful transport of the oocyte to the site of fertilization or of the embryo to the site of implantation.
- *Luteal Phase Defects*: Endometriosis may interfere with normal luteal phase function, reducing the length of the luteal phase and the level of progesterone, which could impair endometrial receptivity and embryo implantation.
- *Luteinized Unruptured Follicle (LUF) Syndrome*: Some studies suggest that women with endometriosis are more likely to have LUF syndrome, where the dominant follicle luteinizes but does not rupture. This would prevent the release of an oocyte, preventing fertilization.

These proposed mechanisms are not all proven, nor are they mutually exclusive. It is likely that endometriosis impacts fertility in a complex and multifactorial manner in a given individual patient. More basic and translational research is required to better understand underlying cellular mechanisms and genetic predispositions. A more complete understanding of these mechanisms is vital for developing effective therapeutic strategies for managing infertility in patients with endometriosis.

25.3 Treatments for Infertility in Endometriosis Patients

25.3.1 Conventional Medical Therapies for Endometriosis and Timed Intercourse

Conventional medical therapies for endometriosis include NSAIDs, combined oral contraceptives, progestin only therapies, GnRH agonists/antagonists with or without add-back therapy, aromatase inhibitors, and danazol; nearly all of these involve hormonal and ovarian suppression and none are compatible with immediate conception. Suppression with one or more of these agents prior to attempting to conceive has long been proposed as a strategy to theoretically improve odds of successful pregnancy.

However, multiple studies demonstrate no benefit to pretreatment with suppression therapy prior to trying to conceive spontaneously. A Cochrane review of 23 trials involving a total of more than 3000 women found no differences in pregnancy rates among subfertile women with endometriosis who undergo prior ovulation suppression using oral contraceptives, progestins, or danazol (odds ratio [OR]: 1.02, confidence interval [CI]: 0.70 to 1.52, $p = 0.82$) (17). Loverro et al. (2008) further considered ovarian suppression in the setting of advanced endometriosis (stage III/IV disease) and found that pretreatment does not improve natural conception compared to expectant management (18).

Therefore, the initiation of medical management in such cases only serves to postpone attempts at conception and does not improve pregnancy rates outside of IVF. While treatment of pelvic pain with medical therapies in a patient desiring future childbearing is reasonable, use of these therapies for the sole purpose of improving fertility outcomes is largely counterproductive, as it delays care.

25.3.2 In Vitro Fertilization in the Context of Endometriosis

Endometriosis has been consistently shown to adversely affect IVF parameters but not overall IVF pregnancy rates following transfer of a high-quality embryo. A systematic review and meta-analysis conducted by Huiling Qu et al. (2022) found a decreased number of oocytes retrieved ($p < 0.00001$) in patients with endometriosis versus those without (19). This is consistent with Li et al. (2020), who found that patients with surgically treated endometriosis had significantly fewer mature oocytes retrieved and viable embryos compared with controls, leading to a lower pregnancy rate per cycle (20).

Study of morphokinetics of embryos generated from endometriosis patients reveal impairments in early and late development including progress to morula, blastocyst, and expanded blastocyst stage (21). However, patients with endometriosis have similar rates of fertilization, pregnancy, and live birth as their age-matched controls. Similarly, Vigano et al. (2023) found no difference in fertilization rates when comparing intracytoplasmic sperm injection (ICSI) versus conventional in vitro fertilization in patients with endometriosis, as well as similar cumulative clinical pregnancy and live birth rates between endometriosis cases and controls (22).

The observation that embryo transfer success between endometriosis cases and controls is equivalent suggests the primary mechanisms by which endometriosis leads to diminished pregnancy rates in spontaneous conceptions involve the ovary, fallopian tube, and peritoneal cavity, and less so the uterine environment. However, some investigators have reported aberrant BCL6 *and/or beta-3 integrin* expression in the endometrium of patients with unexplained infertility to be associated with poor reproductive outcomes in IVF cycles (23). For these patients, it is argued, excisional surgery or suppressive therapy enhances subsequent embryo transfer outcomes. It is important to note that BCL6 *and/or beta-3 integrin* testing is not considered standard of care, and future work is needed to validate these findings.

It is not clear whether ovarian suppression is beneficial prior to IVF for patients with endometriosis. A Cochrane review in 2006 concluded that ovarian suppression for stage II/III/IV disease prior to IVF increases pregnancy rates fourfold (24). However, a subsequent review in 2019 concluded that all of the studies to date had high risk of bias and low-quality data and that no definitive conclusions can be made at this time (25).

Adenomyosis often occurs in women with endometriosis. There is some evidence that long-term suppression before IVF may improve fertility outcome (26, 27).

Finally, for patients concerned that IVF might exacerbate endometriosis, a 2018 systematic review found that IVF does not increase endometriosis-related pain symptoms or the risk of disease recurrence (28).

25.3.3 Surgical Excision of Endometriosis in the Context of Desired Fertility

Surgery is often warranted for diagnosis and treatment of endometriosis-related symptoms, and it may have a fertility benefit. A Cochrane review reported moderate-quality evidence from three RCTs (528 women) that laparoscopic excision improves ongoing pregnancy rate compared to diagnostic laparoscopy (OR: 1.89, 95% CI: 1.25 to 2.86; I2 = 0%) (29). However, it is important to note that although pregnancy rates are improved after surgical treatment, the number needed to treat is 12 patients. If assuming the prevalence of disease at diagnostic laparoscopy to be 20%, then it would take 60 laparoscopies to achieve one extra pregnancy.

For patients with advanced stage disease, surgical resection may be warranted for endometriomas greater than 4–5 cm in size if associated with pain, difficult oocyte retrieval, recurrent IVF failures, or concern for malignancy (30, 31). However, it is important to note that excision of an endometrioma improves spontaneous pregnancies but not IVF pregnancies (32, 33). Therefore, excision should be attempted for the aforementioned reasons as well as when spontaneous pregnancy is desired or recommended, such as when the EFI score is high. Surgery is most appropriate when patients desire both optimization of fertility and alleviation of pain symptoms (34).

In patients contemplating surgical intervention, the risk of iatrogenic injury during surgery is a pivotal consideration when it comes to preserving fertility potential. Specifically, when dealing with endometrioma removal, there is abundant evidence of the adverse impact of surgery on ovarian reserve, manifesting in substantial declines in anti-Müllerian hormone levels (as much as 30% in unilateral and up to 44% in bilateral endometriomas).

While each case should be individualized, fertility preservation should be at least considered before undertaking any surgical intervention (30, 35). The pursuit of such a strategy necessitates comprehensive and thoughtful discussion with the patient. This dialogue should focus on their reproductive aspirations, while also providing a clear understanding of the potential risks and benefits associated with the various fertility preservation options available.

The counseling can include exploration of the available fertility preservation options, which include tissue, embryo, and oocyte cryopreservation, as described next. Such discussion is crucial to ensuring patients are thoroughly informed and empowered to make decisions that align with their personal circumstances and reproductive goals.

25.4 Fertility Preservation in the Context of Endometriosis

Fertility preservation in the context of endometriosis can present unique challenges. One major challenge stems from the inherently diminished ovarian reserve and compromised oocyte/embryo quality present in patients suffering from endometriomas. Endometriomas of the ovary are known to negatively impact the ovarian reserve due to mechanical stress on the ovarian cortex and inflammation-induced damage. This is evident in histological evaluations of affected ovaries, showcasing diminished follicular density, increased follicular atresia, and heightened activation of primordial follicles relative to an unaffected ovary. Consequently, women with endometriomas have reduced ovarian reserve compared to healthy controls, with more pronounced declines in those with bilateral endometriomas. However, the clinical implications of these observations remain unclear, as markers of ovarian reserve poorly predict spontaneous conception, and women with endometriomas undergoing in vitro fertilization maintain similar pregnancy and live birth rates as those without endometriomas, notwithstanding a diminished response to gonadotropins and lower oocyte yields.

As discussed, a challenge faced with endometriosis is the potential decrease in oocyte and embryo quality. Systematic reviews suggest that endometriosis correlates with fewer mature oocytes retrieved relative to other infertility causes, reduced fertilization rates especially in minimal/mild disease, and abnormal embryo development patterns including mitochondrial dysfunction, diminished mitochondrial mass, slower growth rates, and heightened chances of developmental arrest (21, 36). Despite these distinct hurdles, as discussed earlier, the majority of studies suggest minimal impact of endometriosis on IVF outcomes when compared to women with other infertility causes. This underscores the value of IVF and other fertility preservation methods in optimizing fertility prospects for patients with endometriosis.

25.4.1 Oocyte/Embryo Cryopreservation

Oocyte retrieval and cryopreservation have increasingly become a cornerstone in fertility preservation for patients with endometriosis who are preparing for surgical interventions (37). These procedures offer a way to secure viable oocytes prior to surgery, mitigating the risk of ovarian reserve depletion as a result of surgical treatment. Indeed, such preemptive steps provide a pool of viable oocytes that can later be used in assisted reproductive technologies (ART), offering a valuable assurance for those whose ovarian reserve may be further compromised post-surgery.

The procedure for oocyte retrieval, usually performed as part of an IVF cycle, involves ovarian stimulation with exogenous

gonadotropins to promote the development of multiple follicles. Once the follicles have reached an appropriate size, final oocyte maturation is triggered, and the oocytes are retrieved transvaginally under ultrasound guidance. Following retrieval, the oocytes are cryopreserved using vitrification, a rapid-freezing method that prevents the formation of ice crystals and enhances the survival rate of thawed oocytes (38).

However, it is important to note that patients with endometriosis often exhibit a lower response to controlled ovarian stimulation, leading to a fewer number of retrieved oocytes when compared to patients without the condition. This observation is linked to the inherent diminished ovarian reserve and compromised oocyte quality associated with endometriosis.

Moreover, the decision to pursue oocyte cryopreservation should be personalized, taking into account the patient's age, severity of endometriosis, and baseline ovarian reserve. Evidence suggests that to have a realistic prospect of achieving one or more live births, a minimum of 10–15 oocytes should be cryopreserved in women aged 35 years or younger, and over 20 in those above 35 years. This recommendation underscores the importance of a careful, individualized approach to oocyte retrieval and preservation as part of a comprehensive fertility preservation strategy in endometriosis management (37).

25.4.2 Ovarian Tissue Cryopreservation

An emerging alternative approach for fertility preservation in endometriosis patients is ovarian tissue cryopreservation (OTC). This technique provides a feasible solution for young patients who need to undergo immediate surgery or those who cannot undergo hormonal stimulation for oocyte or embryo cryopreservation due to various reasons. This approach has particular relevance for patients with severe endometriosis, where the risk of significant damage to ovarian reserve from surgery is high.

OTC involves the surgical removal of an ovary or ovarian tissue, which is then subjected to cryopreservation. This technique allows the preservation of thousands of immature follicles in cortical tissue, which could potentially be used for future fertility treatments. The ovarian tissue can be transplanted back into the patient when she is ready for pregnancy, and natural conception may occur if the graft restores normal ovarian function. If not, IVF can be pursued using the oocytes matured from the transplanted tissue.

However, ovarian tissue cryopreservation and transplantation are not without challenges. The invasive nature of the procedure, technical demands, and the potential risk of reintroducing endometriotic tissue at the time of transplantation are factors that need consideration. Additionally, while successful live births have been reported following OTC, and the procedure is no longer considered experimental, data are still limited (39). This underscores the importance of comprehensive counseling to discuss the potential risks and benefits with patients considering OTC (37).

25.5 Future Directions

Ongoing research efforts, bolstered by recent increases in federal funding and attention, aim to improve diagnosis, treatment, and fertility outcomes for endometriosis patients. Understanding the mechanisms of infertility in endometriosis is crucial for the development of targeted therapies and interventions. Further research into the role of inflammation, altered immune function, and hormonal imbalances in the disease process will help elucidate the complex interplay between endometriosis and fertility.

To develop novel pharmaceutical agents that reduce off-target effects and enhance fertility will require a greater understanding of underlying molecular pathways and variability of these pathways between patients. The identification of additional gene markers associated with endometriosis will enable earlier and more accurate diagnosis of the disease, facilitating earlier intervention and improving fertility outcomes. Noninvasive biomarkers in blood or urine is a significant focus of ongoing research which could offer a less invasive means of diagnosing endometriosis, monitoring disease progression, and evaluating treatment response.

Technological advancements, such as the use of in vitro maturation (IVM) of oocytes, single cell RNA sequencing of endometriosis lesions, and the application of artificial intelligence in embryo selection, represent promising future directions in the realm of fertility management in endometriosis patients. All these efforts in combination hold the promise of significantly transforming the way endometriosis and associated infertility are managed in the future.

25.6 Conclusion

In conclusion, the management of endometriosis and its impact on fertility is a complex and multifaceted challenge that requires a comprehensive understanding of the disease process, its relationship with fertility, and the available treatment options. Although oral contraceptive pills, progestins, and GnRH agonists and antagonists can exhibit considerable efficacy in alleviating endometriosis symptoms both before and after pregnancy, pretreatment with these agents does not appear to enhance fertility. Conservative surgery can have fertility benefits, but fertility preservation prior to surgery should always be considered given risk of iatrogenic harm to ovarian reserve. IVF is the mainstay of fertility treatment in the setting of endometriosis. Ongoing research, fortified by recent increases in federal funding and attention, aims to enhance our understanding of endometriosis, with a specific focus on improving diagnostic methods, treatment modalities, and fertility outcomes. The mechanisms underpinning infertility associated with endometriosis remain a crucial area for exploration, informing the development of targeted therapies and interventions.

References

1. Randall CL. Management of complications of endometriosis. *JAMA*. 1949;139(15):972.
2. Kistner RW. Endometriosis and infertility. *Clin Obstet Gynecol*. 1959;2:877–889.
3. Petersohn L. Fertility in patients with ovarian endometriosis before and after treatment. *Acta Obstet Gynecol Scand*. 1970;49(4):331–333.
4. Hanton EM et al. Endometriosis in young women. *Am J Obstet Gynecol*. 1967;98(1):116–120.
5. Peterson EP et al. Laparoscopy of the infertile patient. *Obstet Gynecol*. 1970;36(3):363–367.
6. García CR et al. Pelvic endometriosis: infertility and pelvic pain. *Am J Obstet Gynecol*. 1977;129(7):740–744.
7. Weed JC et al. Endometriosis: can it produce an autoimmune response resulting in infertility? *Clin Obstet Gynecol*. 1980;23(3):885–893.
8. Ascher SM et al. Endometriosis: appearance and detection with conventional and contrast-enhanced fat-suppressed spin-echo techniques. *J Magn Reson Imaging*. 1995;5(3):251–257.
9. Bedaiwy M et al. Differential expression of follicular fluid cytokines: relationship to subsequent pregnancy in IVF cycles. *Reproductive BioMedicine Online*. 2007;15(3):321–325.

10. Bedaiwy MA et al. Effect of ovarian involvement on peritoneal fluid cytokine concentrations in endometriosis patients. *Reprod Biomed Online*. 2007;14(5):620–625.
11. Llarena NC et al. Characterizing the endometrial fluid cytokine profile in women with endometriosis. *J Assist Reprod Genet*. 2020;37(12):2999–3006.
12. Revised American Society for Reproductive Medicine classification of endometriosis: 1996. *Fertil Steril*. 1997;67(5):817–821.
13. Adamson GD et al. Endometriosis fertility index: the new, validated endometriosis staging system. *Fertil Steril*. 2010;94(5):1609–1615.
14. Tuttlies F et al. [ENZIAN-score, a classification of deep infiltrating endometriosis]. *Zentralbl Gynakol*. 2005;127(5):275–281.
15. Abrao MS et al. AAGL 2021 endometriosis classification: an anatomy-based surgical complexity score. *J Minim Invasive Gynecol*. 2021;28(11):1941–1950.e1.
16. Tanbo T et al. Endometriosis-associated infertility: aspects of pathophysiological mechanisms and treatment options. *Acta Obstet Gynecol Scand*. 2017;96(6):659–667.
17. Hughes E et al. Ovulation suppression for endometriosis. *Cochrane Database Syst Rev*. 2007;2007(3):CD000155.
18. Loverro G et al. A randomized study comparing triptorelin or expectant management following conservative laparoscopic surgery for symptomatic stage III–IV endometriosis. *Eur J Obstet Gynecol Reprod Biol*. 2008;136(2):194–198.
19. Qu H et al. The effect of endometriosis on IVF/ICSI and perinatal outcome: a systematic review and meta-analysis. *J Gynecol Obstet Human Reprod*. 2022;51(9):102446.
20. Li A et al. Analysis of IVF/ICSI-FET outcomes in women with advanced endometriosis: influence on ovarian response and oocyte competence. *Front Endocrinol*. 2020;11:427.
21. Llarena NC et al. The impact of endometriosis on embryo morphokinetics: embryos from endometriosis patients exhibit delayed cell cycle milestones and decreased blastulation rates. *J Assist Reprod Genet*. 2022;39(3):619–628.
22. Viganò P et al. Conventional IVF performs similarly in women with and without endometriosis. *J Assist Reprod Genet*. 2023;40(3):599–607.
23. Almquist LD et al. Endometrial BCL6 testing for the prediction of IVF outcomes: a cohort study. *Fertil Steril*. 2017;108(6):1063–1069.
24. Sallam HN et al. Long-term pituitary down-regulation before in vitro fertilization (IVF) for women with endometriosis. *Cochrane Database Syst Rev*. 2006;2006(1):CD004635.
25. Georgiou EX et al. Long-term GnRH agonist therapy before in vitro fertilisation (IVF) for improving fertility outcomes in women with endometriosis. *Cochrane Database Syst Rev*. 2019;2019(11):CD013240.
26. Donnez J et al. Evolution of uterine adenomyosis volume during and after GnRH antagonist (linzagolix) treatment: lessons for further clinical trials. *Fertil Steril*. 2023 Nov;120(5):1071–1073.
27. Rocha TP et al. Fertility-sparing treatment of adenomyosis in patients with infertility: a systematic review of current options. *Reprod Sci*. 2018;25(4):480–486.
28. Somigliana E et al. Ovarian stimulation and endometriosis progression or recurrence: a systematic review. *Reprod Biomed Online*. 2019;38(2):185–194.
29. Bafort C et al. Laparoscopic surgery for endometriosis. *Cochrane Database Syst Rev*. 2020;10(10):CD011031.
30. Llarena NC et al. Fertility preservation in women with endometriosis. *Clin Med Insights Reprod Health*. 2019;13:1179558119873386.
31. Rehmer JM et al. Management of endometriomas. *Obstet Gynecol Surv*. 2019;74(4):232–240.
32. Tsoumpou I et al. The effect of surgical treatment for endometrioma on in vitro fertilization outcomes: a systematic review and meta-analysis. *Fertil Steril*. 2009;92(1):75–87.
33. Benschop L et al. Interventions for women with endometrioma prior to assisted reproductive technology. *Cochrane Database Syst Rev*. 2010;(11):CD008571.
34. Berlanda N et al. Role of surgery in endometriosis-associated subfertility. *Semin Reprod Med*. 2013;31(2):133–143.
35. Santulli P et al. Fertility preservation for patients affected by endometriosis should ideally be carried out before surgery. *Reprod BioMedicine Online*. 2021;43(5):853–863.
36. Sanchez AM et al. Is the oocyte quality affected by endometriosis? A review of the literature. *J Ovarian Res*. 2017;10:43.
37. Rangi S et al. Fertility preservation in women with endometriosis. *J Clin Med*. 2023;12(13):4331.
38. Cobo A et al. Oocyte vitrification for fertility preservation in women with endometriosis: an observational study. *Fertil Steril*. 2020;113(4):836–844.
39. Practice Committee of the American Society for Reproductive Medicine. Fertility preservation in patients undergoing gonadotoxic therapy or gonadectomy: a committee opinion. *Fertil Steril*. 2019;112(6):1022–1033.

26 OFFICE HYSTEROSCOPY

Aparna Ramanathan, Mariam Barseghyan, and James K. Robinson

26.1 Background

In office hysteroscopy, miniaturized endoscopic equipment is used to visualize and examine the endometrial cavity without need for an operating room or general or regional anesthesia (1). The first hysteroscopy was performed in 1869 using a cystoscope to diagnose and treat an endometrial polyp in a 60-year-old patient with postmenopausal bleeding (2). Office hysteroscopy began in the 1980s (3). The basic instrument used in office hysteroscopy is a hysteroscope, which is a long, narrow telescope attached to a light source which acts to illuminate the area being viewed (4). Office hysteroscopy is the gold standard for diagnosis of abnormal uterine bleeding, as it provides direct visualization of the endometrial cavity. It is fast, precise, and effective in detecting intrauterine abnormalities (5).

26.2 Gynecologic Aspects

26.2.1 Indications

The indications for performance of office hysteroscopy are illustrated in Figure 1 and described later. There is significant overlap in the indications for office and operating room–based hysteroscopy. This list is not exhaustive, and other scenarios where office hysteroscopy is useful can emerge based on individual patient pathologies and scenarios (3).

Abnormal uterine bleeding. Hysteroscopy is the gold standard for diagnosis of abnormal uterine bleeding. Office hysteroscopy is becoming progressively more accessible for the diagnosis and treatment of pathologies known to cause abnormal uterine bleeding, including polyps, leiomyomas, retained products of conception, and malignancy (6, 7). Blind endometrial biopsy, which is currently widely used in the diagnosis of abnormal uterine bleeding, may fail to be completed in the office up to 11% of the time due to factors such as cervical stenosis and patient discomfort. In postmenopausal women, it fails up to 21% of the time. In a retrospective study of 68 women who underwent office hysteroscopy after failed endometrial biopsy, hysteroscopies were successfully completed in 96% of cases. Overall, 10% of patients subsequently required operating room–based hysteroscopy to address fibroids or polyps or to allow for general anesthesia (8). A randomized controlled trial demonstrated that treatment of endometrial polyps with office hysteroscopy resulted in minimal discomfort, shorter time away from home, and faster recovery when compared with hysteroscopy completed in the operating room (5).

The incidence of retained products of conception is estimated to range between 2% and 6% of all pregnancies and is associated with complications including bleeding, infections, intrauterine adhesions, and decreased fertility. Studies have shown the superiority in targeted hysteroscopic resection of retained products of conception over ultrasound-guided curettage in reducing complications and increasing the probability of a subsequent successful pregnancy. Women treated for retained products of conception with suction curettage have an increased risk of recurrence and of placenta accreta in subsequent pregnancies compared with women treated with office hysteroscopy (9).

Infertility and congenital anomalies. Patients with infertility who are experiencing recurrent pregnancy loss or recurrent implantation failure or who have a previous uterine scar can benefit from office hysteroscopy for evaluation of the uterine cavity. Suspicion for congenital anomalies are another indication for office hysteroscopy (6, 7). A randomized controlled trial showed that hysteroscopic polypectomy improved fertility in women who were undergoing intrauterine insemination (4).

Intrauterine adhesions. Intrauterine adhesions can form as a result of intrauterine instrumentation (myomectomy, dilation and curettage, etc.). Office hysteroscopy used for evaluation of the endometrial cavity after these procedures allows for both reassurance of complete removal of the uterine pathology and maintenance of cavity patency, as intrauterine instrumentation is a known risk factor for the development of intrauterine adhesions (10). Indications for evaluation for intrauterine adhesions include secondary amenorrhea, irregular menstruation, and imaging evidence of adhesions in women pursuing fertility (3).

Posttreatment. Posttreatment follow-up is a broad indication that can apply to follow-up for various medical or surgical treatments. Surgical treatments include following myomectomy or septoplasty for evaluation and treatment of any postsurgical treatment. Office hysteroscopy can also be performed after tamoxifen use to evaluate for malignancy (3). Vaginoscopy allows for direct visualization of the cervical canal and the capability to perform blunt and sharp dissection of intracervical adhesions (8).

Foreign body. Foreign bodies, such as retained intrauterine devices, can be diagnosed and removed via office hysteroscopy. Vaginoscopy offers a less traumatic approach to evaluation and treatment of retained foreign bodies in pediatric and adolescent populations (8).

26.2.2 Efficacy

Hysteroscopic evaluation offers better accuracy in diagnosis of endometrial lesions, missing less than 0.5% of serious disease. Compared with transvaginal ultrasound, hysteroscopy has fewer false positive and false negative results in the detection of polyps, submucosal leiomyomas, and endometrial hyperplasia (11). The sensitivity and specificity of transvaginal ultrasound in detecting intracavitary abnormalities were 56.3% and 72%, respectively, compared with 87.5% and 100% for office hysteroscopy. Ultrasound is limited in delineating endometrial thickening from other intrauterine lesions (3). For saline-infused sonohysterography, the sensitivity and specificity were 81.3% and 100%, which was roughly equivalent to office hysteroscopy without, however, the ability to treat pathology in the same visit (12). In addition, saline-infused sonohysterography has limitations in identifying pathology specifics. It cannot, for example, distinguish a cluster of polyps from a submucous leiomyoma (3).

A systematic review and meta-analysis were performed to evaluate the effectiveness of office hysteroscopy compared with hysteroscopy in the operating room to diagnose and/or treat intrauterine pathology. The primary outcome was diagnostic accuracy; secondary outcomes included treatment success, fewer adverse events, patient satisfaction, and lower cost.

DOI: 10.1201/9781003312109-26

Twenty studies were included for analysis; however, no study compared the primary outcome. There were no significant differences between office hysteroscopy and hysteroscopy in the operating room with regard to treatment success, adverse events, and patient satisfaction. All seven economic studies concluded that office hysteroscopy (range 97–1258 USD) is substantially less expensive than hysteroscopy completed in the operating room (range 258–3144 USD) (13). The success of hysteroscopic myomectomy performed in the operating room is dependent on the type of fibroid. Overall success rates are quite high for fibroids of which at least 50% are within the endometrial cavity. Staged resection may sometimes be required. Success rates of hysteroscopic lysis of adhesions, performed in either the office or operating room, are also high, ranging from 88% to 95%. Reformation of adhesions is possible but does not tend to occur with serial evaluation of the endometrial cavity (3).

26.2.3 See-and-Treat Approach

Office hysteroscopy is not only a diagnostic modality but it also allows for an opportunity of immediate and directed treatment via introduction of a hysteroscopic resectoscope, scissors, and graspers. Under direct visualization, intrauterine pathology is not often missed as it can be with blind endometrial biopsy (14). The see-and-treat approach is preferable to patients as it allows patients to leave the facility immediately after office hysteroscopy and does not require general anesthesia (9). It allows for a seamless transition between diagnostic and operative hysteroscopy if abnormal pathology is noted and the patient continues to tolerate the procedure (3). The see-and-treat approach has been shown to be effective and satisfactory in addressing a variety of intrauterine pathologies. Hysteroscopic endometrial sampling can be performed quickly, involving only mucosa without stimulating myometrial wall (5). In a retrospective study of 68 women who underwent office hysteroscopy after failed endometrial biopsy, 97% of polyps diagnosed were able to be successfully removed in office. Operating room–based procedures were avoided in 90% of overall cases (8).

Electrosurgical hysteroscopic treatment has also been completed successfully in the office setting. Treatment of intrauterine adhesions consists of cutting the adhesions with mechanical shears or an electrical knife and can be completed in most cases in the office with a see-and-treat approach (5). In an observational study of 501 women, benign intrauterine pathology was treated with see-and-treat office hysteroscopy using a bipolar probe and with no analgesia or anesthesia given. Treatment was noted to be efficacious on second-look hysteroscopy 3 months later, and patient acceptance was satisfactory (15).

A see-and-treat approach for management of retained products of conception was initially described by Jimenez et al. in 2009. In a retrospective study of 119 women comparing a see-and-treat office hysteroscopy approach with operating room–based hysteroscopic removal of retained products of conception equal to or smaller than 2 centimeters, office hysteroscopy was as effective as operating room–based hysteroscopy with similar operative time. Operating room–based hysteroscopy was associated with higher total procedure and assistant time and a higher proportion of cases complicated by excessive bleeding, cervical tear, or uterine perforation. The rate of failure to complete the procedure was similar between the two groups. Thus, office hysteroscopy with see-and-treat approach for treatment of retained products of conception smaller than 2 centimeters appears as effective as operating room–based hysteroscopy and has fewer complications (9).

26.3 Surgical Aspects

26.3.1 Office Hysteroscopy Setup

Patient selection and preparation. Appropriate patient selection for operative office hysteroscopy is critical with a clear understanding of the intrauterine pathology and knowledge of its size and depth of penetration (16). Adequate counseling before starting office hysteroscopy is a mandatory first step, allowing the patient to ask all questions to clarify potential doubts and fears about the procedure (17). Similar to hysteroscopy completed in the operating room, informed consent must be obtained before starting the procedure (18). Contraindications to hysteroscopy include known pregnancy, genital tract infection, pelvic inflammatory disease, pyometra, and active herpetic or HPV infections (6). Patients with significant anxiety or with a history of a failed office procedure in the past may not be good candidates for an office approach (18). A preprocedure pregnancy test is the only diagnostic workup recommended. Timing of office hysteroscopy during the early proliferative phase of the menstrual cycle, shortly after menstruation, is optimal for visualization, as the endometrial lining is thin and blood is not obstructing the operator's view. Small to moderate amounts of bleeding can be irrigated away with saline (11). In patients where menstrual timing is challenging, performing the procedure after a progesterone withdrawal or after 3 weeks of continuous progestin therapy is also an effective approach (3).

Need for antibiotic prophylaxis. Recommendations given by the American College of Obstetrics and Gynecology do not indicate a need for antibiotic prophylaxis prior to operative or diagnostic hysteroscopy (16). A prospective, multicenter observational study of 42,934 women who underwent office hysteroscopy between 2015 and 2017 showed that 25 of the 42,934 patients exhibited symptoms of infection within 3 weeks of hysteroscopy for an overall infection rate of 0.06%. In five patients with fever and pelvic pain, clinical examination and transvaginal ultrasound revealed unilateral or bilateral tubo-ovarian abscess (TOA). In these patients, histological examination from surgical specimens revealed the presence of endometriosis lesions. This suggests that in the presence of damaged tubes owing to pelvic adhesions or endometriosis, fluid related to the distension medium may remain in the tubes and trigger or reactivate a latent infection. Routine antibiotic prophylaxis is not necessary before office hysteroscopy because the prevalence of infection following office hysteroscopy is low (19).

26.3.2 Pain Management

The greatest barrier to delivering office hysteroscopy is patient experience, which is significantly impacted by pain arising from genital tract instrumentation, uterine cavity distention, and trauma to the endometrium (20). Pain is the primary reason for failure to complete hysteroscopies in an outpatient setting, with 84% of failed office hysteroscopy attributed to pain and discomfort (1, 21). Distension of the uterine myometrial wall by saline leads to contractile activity making patients report colicky pain of moderate to severe intensity (1). The innervation of the cervical canal and lower uterine segment comes from the uterovaginal plexus, which originates from the largest part of the parasympathetic sacral S1 to S4 nerve roots,

meanwhile the upper half of the uterine body's innervation is derived from the thoracic nerves, commonly derived from T8–T10 and L1 roots, which are composed of sympathetic fibers of the superior hypogastric plexus (17). Patient factors contributing to higher pain scores include cervical stenosis, menopausal state, anxiety, chronic pelvic pain, nulliparity, and previous cesarean section (5).

Historically, pain levels during office hysteroscopy are not high. Sensory innervation is largely absent in polyps, endometrium, myomas, and adhesions. Sensitive innervation of the uterus starts from myometrium outward (15). Mean pain scores on an 11-point visual analog scale (VAS) during office hysteroscopy have been reported at 3.57 (18). Vaginoscopy and use of smaller diameter scopes have been shown to decrease pain scores (1). A systematic review of five randomized controlled trials showed that 3.5 mm diameter scopes were less painful than 5 mm scopes when used in office hysteroscopy (5). The lowering of intrauterine pressure has been proven to decrease pain scores during office hysteroscopy but can sometimes result in reduced ability to obtain clear images (1). Higher pain scores have been associated with larger pathology greater than 2 centimeters and increased procedure time over 15 minutes (5).

The patient should be properly positioned to minimize discomfort during the procedure. Staff should welcome the patient, creating a warm and familiar environment. Staff should assist the patient before, during, and after the procedure (17).

Anxiety. Patient anxiety can exacerbate the painful experience and decrease patient satisfaction (17, 22). Although office hysteroscopy is considered to be a minimally invasive approach that increases patient convenience, 65% of women report preoperative anxiety before office hysteroscopy. Patient average state anxiety scores on validated tools such as Spielberger State-Trait Anxiety Index (STAI) or Hospital Anxiety and Depression Scale (HADS) were similar or greater for patients undergoing office hysteroscopy than for patients undergoing operating room–based hysteroscopy under general anesthesia. Factors such as trait anxiety, age, indication for hysteroscopy, and inefficiency of the clinic are correlated with higher state anxiety before office hysteroscopy (22).

Music. Promising nonpharmacological interventions to reduce anxiety during office hysteroscopy include patient education, communication via traditional or multimedia approach, interaction and support during procedure, and listening to music (22). Music reduces activity of the sympathetic nervous system and causes relaxation response and a feeling of well-being. The most commonly accepted theory is that music is a distracter, taking focus away from pain stimuli to something pleasant and comforting (23). A study of virtual reality during office hysteroscopy showed that 80% of patients found music calming (24). A randomized controlled trial in 356 patients was conducted to evaluate the effects of music on anxiety or the perception of pain during office hysteroscopy. STAI and VAS assessments were used. During office hysteroscopy, systolic blood pressure and heart rate were significantly lower in the music group. Women in the music group experienced significantly lower anxiety and less pain during office hysteroscopy. Postop STAI and VAS scores significantly lower in the music group. Music can be useful as a complementary method to control anxiety and reduce perception of pain during office hysteroscopy (23).

Nonsteroidal anti-inflammatory drugs (NSAIDs). A systematic review and meta-analysis published in 2020 was done to identify the most effective analgesia for women undergoing office hysteroscopy. Analgesics included agents acting on the peripheral and/or central nervous system(s) to reduce pain without affecting sensation. Twenty-two studies were selected for systematic review with 16 eligible for meta-analysis. Statistically significant reduction in pain during and after office hysteroscopy was noted with administration of NSAIDs, oral antispasmodics, and transcutaneous electrical nerve stimulation (TENS). Statistically significant reduction in pain after office hysteroscopy was noted with NSAIDs, oral antispasmodics, and TENS. Statistically significant reduction in pain during and after office hysteroscopy was noted with NSAIDs administered orally compared with other routes. Significantly more adverse events were noted with opioids and oral antispasmodics compared with oral NSAIDs or TENS. This review recommended oral NSAIDs before office hysteroscopy and noted that TENS could be an alternative in people with contraindications to NSAIDs (25).

Specifically, seven studies comprising 781 patients investigated pain control with NSAIDs versus control groups during office hysteroscopy, and a meta-analysis showed significant reduction in intraprocedure pain. A meta-analysis of six studies (711 patients) investigating NSAID use showed reduced post-procedure pain (25). We use premedication with 800 mg of ibuprofen 2 hours prior to office hysteroscopy.

Opioids. Opioids showed a significant reduction in pain compared with control groups both during (four studies, 234 patients) and after (two studies, 190 patients) office hysteroscopy. Opioids were given 40–60 minutes prior to the start of the procedure. The route of administration was heterogeneous, including intravenous, intramuscular, sublingual, and oral routes. There was a significantly increased risk of adverse events with use of opioids (25).

Oral antispasmodics. A meta-analysis of two studies (166 patients) investigating the use of oral antispasmodics versus controls for pain management during office hysteroscopy showed significant reduction in pain both during and after office hysteroscopy. Oral antispasmodics were given 1 hour before office hysteroscopy in both studies. There was a significantly increased risk of adverse events with use of oral antispasmodics (25).

Transcutaneous electrical nerve stimulation (TENS). A meta-analysis of TENS versus controls for pain management during office hysteroscopy showed significant reduction in pain both during (two studies, 234 patients) and after (one study, 92 patients) office hysteroscopy (25).

Warming of distension media. A systematic review and meta-analysis of randomized controlled trials was done to evaluate the impact of warm vs room temperature saline distention media on pain control in patients undergoing office hysteroscopy. The primary outcome was VAS during and after the procedure. Five randomized controlled trials were included with a total of 441 patients. Warm saline was linked to significant reduction in VAS during and after the procedure. More patients were significantly satisfied with warm vs room temperature distension media. This makes some physiologic sense if one considers that local heat is used for treatment of muscle spasm. It improves the flow of blood, relaxes muscles, reduces pain, and is effective, rapid, and safe for management of acute pelvic pain (1).

Local anesthesia. Local anesthesia is less relevant for office hysteroscopy given the advent of miniaturized hysteroscopes (25). Paracervical block decreased pain with tenaculum use

and with cervical dilation but was not necessary if vaginoscopy was completed. Anesthetic sprays have not been shown to be effective for pain control during office hysteroscopy (1).

Cervical ripening. There is currently insufficient evidence to recommend routine cervical ripening. Misoprostol is a prostaglandin E1 analog, and various doses have been studied (3). Misoprostol has been shown to minimize pain during office hysteroscopy when the procedure was done within 12 hours of administration (1). A systematic review and meta-analysis including 25 randomized controlled trials and 2203 women evaluating the effects of misoprostol use on cervical priming prior to hysteroscopy was completed. Compared with placebo or no medication, the use of misoprostol prior to hysteroscopy led to significant relief of the need for cervical dilation, resulted in greater cervical width, resulted in fewer hysteroscopy complications, and caused mild and insignificant side effects. Subgroup analysis revealed that a regimen of 200 or 400 micrograms administered vaginally may be a safe and effective method for cervical priming prior to hysteroscopy. Administration of misoprostol may decrease hysteroscopic complications including cervical laceration and creation of a false passage (26). These benefits were not seen with oral or sublingual dosing. The benefits of use of misoprostol must be balanced with the adverse effects of the medication, including abdominal cramping, increased body temperature, and vaginal bleeding. If a need for cervical dilation is expected, it may be reasonable to pretreat with vaginal misoprostol to improve patient comfort and lower complications (3).

Conscious sedation. Conscious sedation is defined by the American Association of Anesthesiologists as "drug-induced depression of consciousness during which patients respond purposefully to verbal commands, either alone or accompanied by light tactile stimulation" where "no interventions are required to maintain a patent airway" and "cardiovascular function is usually maintained." It is commonly employed in gastrointestinal endoscopy for pain relief and anxiolysis. A systematic review and meta-analysis of randomized controlled trials was completed investigating office hysteroscopy procedures with women allocated to either conscious sedation or a suitable comparator where the primary outcome was pain. Seven studies met criteria for inclusion. Intravenous conscious sedation compared with local anesthesia reduced pain during but not after office hysteroscopy with no significant difference in side effects. Intravenous conscious sedation, when compared with an oral analgesic and antispasmodic, was associated with increased pain both during and after office hysteroscopy and had significantly more side effects. Inhalational conscious sedation when compared with an oral analgesic and antispasmodic showed reduction in pain with office hysteroscopy but side effects were not reported. The routine use of conscious sedation should be avoided due to the absence of any clear reduction in pain and the higher risk of side effects (20).

Virtual reality. Studies have shown that virtual reality reduces pain in adults and children through active distraction. One main rationale is that attention is required for perception of pain and that attention is limited; diverting attention can reduce the body's available resources for processing pain. A randomized controlled trial comparing virtual reality to standard care in 50 patients showed no statistically significant difference in pain scores or change in heart rate prior to, during, or after hysteroscopic procedures. The virtual reality intervention consisted of guided meditation through an Oculus Go headset. Patients reported high levels of satisfaction with the intervention (24).

26.3.3 Office Hysteroscopy Equipment

The five key components of an office hysteroscopy setup (Figure 26.1) are the hysteroscope, endocamera, monitor, light source, and light cable (3).

Hysteroscope. Hysteroscopes come in a variety of models. They can be reusable or disposable. Within these categories, hysteroscopes can further be divided into flexible hysteroscopes, hystero-fiberscopes or rigid rod lens hysteroscopes. Hystero-fiberscopes are rarely used because they are costly, not durable, and difficult to sterilize. We will focus on flexible and rigid rod lens hysteroscopes in this discussion (3).

Rigid rod lens hysteroscopes are the most commonly used type overall in hysteroscopy. The rigid direct optical hysteroscope was derived from the cystoscope. A system of lenses and prisms gives the viewer excellent contrast and resolution. These hysteroscope widths range from 1.9 to 4 mm. Hysteroscopes are made with different viewing angles ranging 0–70 degrees (4). The 12° hysteroscope allows for the working instrument to be kept in the view and the 30° hysteroscope is more advantageous for diagnostic procedures as it allows for small rotational movements to visualize the entire uterine cavity (21, 27).

Flexible fiberoptic hysteroscopes are single channel scopes that are 3.2 to 3.5 mm in diameter with a tip capable of deflecting 90° to 120°. They are reported to make insertion easier and less painful. They do not require cervical dilation; however, they are more costly and less durable (21). The image quality of the fiberoptic scope is not yet matched in quality to that of the lens-based scope, and a 0° lens is used. The flat rather than fluted instrument tip does not facilitate penetration, and introduction through a stenotic cervical os may be more difficult. In 3.6% of patients, office hysteroscopy was not able to be completed due to cervical stenosis, intractable pain during dilation, or poor visualization of the endometrial cavity (5).

Currently, office hysteroscopy is performed with 5 mm or smaller instruments. Reduction of the diameter size by 1–2 mm is significant in that it reduces the section area by 50%–75%, with obvious advantages in ease of insertion and reduction of pain. The 3.5 mm scope has been shown to be superior in pain control and patient acceptability. Pain and vasovagal reactions were noted to be significantly less with the 3.5 vs 5 mm hysteroscope. A randomized controlled trial involving 480 patients undergoing diagnostic office hysteroscopy and randomized to the 5 mm or 3.5 mm hysteroscope demonstrated that surgeon experience is not as important a factor in pain management if a 3.5 mm instrument is used (5).

Sheath. The diagnostic hysteroscope sheath has a diameter of 2.5–5.5 mm while the operative hysteroscope sheath has a diameter of 5.5–9.0 mm. The hysteroscope sheath is fitted with dual ports for continuous laminar flow of distension media. Inflow and outflow are regulated by separate stopcocks. Innovation in hysteroscope sheaths is a balance between decreasing sheath diameter and obstructing hysteroscope view with operative instruments (4).

Endocamera. A camera is attached to the proximal end of the hysteroscope to broadcast the image onto a video monitor. A light cord and light source are also critical equipment components (5).

Operative instruments. Hysteroscopic operative instruments can be reusable or disposable and can be rigid or semi-rigid. They are inserted through the operative channel which can

FIGURE 26.1 Office hysteroscopy room setup.

also be the inflow. Examples of these instruments are shown in Figure 26.2. Scissors are commonly used for undermining or lysing tissue in polypectomy, lysis of adhesions, metroplasty, and retained products of conception. Grasping forceps are used to grasp and remove intrauterine lesions such as intrauterine devices and retained products of conception or for directed biopsies. A hysteroscopic tenaculum allows for intact removal of large polyps as it provides a better grip than grasping forceps. Polyp snares can also be useful in tissue extraction (3, 27).

Monopolar and bipolar wire tip electrodes are available for office use; however, there is a higher risk of complications such as perforation and injury to nearby structures (27). Use of these electrodes requires a radiofrequency generator, appropriate distention media, and a formal fluid management system. The electrodes come in a variety of forms, including loop or needle electrode, roller ball, and button tip. The benefits of using a bipolar electrode with saline irrigant versus a monopolar electrode with glycine irrigant are limited cervical dilation and reduced pain and avoidance of perceived hazards of glycine irrigant. Disadvantages include reduced speed of tissue removal, vaporization of tissue with associated difficulties in histological assessment, increased equipment cost, and fragility of equipment. A feasibility study in 118 women where a monopolar resectoscope was used during office hysteroscopy showed a 90% success rate and low glycine absorption (28). Polypectomy performed during office hysteroscopy has been shown to be feasible with both mechanical and electrical instruments. There was no difference seen in the rate of polyp excision, surgical time, or induced pelvic discomfort (5).

The hysteroscopic resectoscope is a modification of the urologic resectoscope. The outer diameter is 7–9 mm with inflow and outflow tracts. Resectoscopes can be monopolar or bipolar. Bipolar resectoscopes are currently favored due to the safety profile of saline distention media. The formation of gas bubbles occurs more frequently with the bipolar resectoscope, and these bubbles can disturb visibility (4). More recently, a 5 mm bipolar office resectoscope allows for the use of 15 Fr loop, wire, and coagulation tips for true resectoscopic surgery often without cervical dilation (3).

Multiple hysteroscopic tissue morcellator models have been developed that mechanically shave tissue with no energy required. Removed tissue is discharged through the device. A randomized controlled trial conducted among resident trainees showed faster operating time using the hysteroscopic morcellator. A disadvantage of the morcellator is that the shaving mechanism is suboptimal for extraction of fibroids with a portion embedded within the myometrium. The resectoscope loop better allows this tissue to be shelled out (4). Small-gauge models have been developed that can be used without cervical dilation in selected patients (3).

Instrument choice can have an impact on procedural pain. A systematic review of randomized controlled trials evaluating

FIGURE 26.2 Office hysteroscopy prep table.

the effect of hysteroscopic devices on pain experienced by women undergoing office hysteroscopy was conducted. Ten studies were included for review. A significant reduction in pain was found using morcellators rather than miniature bipolar electrosurgical devices, 22 Fr rather than 26 Fr resectoscopes, and 3.5 mm fiberoptic hysteroscopes with 7 Fr forceps rather than 5 mm lens-based hysteroscopes with 5 Fr forceps. One study investigating septoplasty found that there was a significant reduction in pain when cold mini-scissors rather than a miniature bipolar electrode were used (20).

26.3.4 Distention Media

There are several types of distension media used for hysteroscopy, including high-viscosity fluid, low-viscosity fluid, and gas. These media types are described as follows.

Dextran 70. Dextran 70 is a high-viscosity distention medium that is rarely used at present in hysteroscopy. It is a hyperosmolar solution of 32% dextran 70 in 10% glucose. Advantages include that it is immiscible with blood, providing better visualization in a bleeding endometrial cavity. Intravasation as little as 300 cc of fluid is associated with adverse events such as cardiovascular events and pulmonary edema. An incidence of anaphylaxis of 1:821 was shown in a population of 5745 patients. Instruments must be cleaned immediately to prevent fluid caramelization; this precludes its use with flexible hysteroscopes (29).

Saline. The most commonly used distention medium in office hysteroscopy is normal saline (27). It is a relatively safe solution that does not cause electrolyte imbalance but can cause fluid overload and pulmonary edema if absorbed in very large quantities. This risk is extremely low in short office procedures (3). Normal saline is associated with improvement in image clarity and reduction in episodes of vasovagal attacks compared to carbon dioxide (1). With this distention media, one can use bipolar energy and mechanical morcellation but not monopolar energy. The upper limit of the fluid deficit is 2500 mL. It is important to monitor the fluid deficit and treat excessive intravasation with diuretics (e.g., Furosemide 20 mg) (4).

Lactated ringers. Lactated ringers is a low-viscosity solution presumed to be similar in quality to normal saline. However, it has not been specifically tested in the office hysteroscopy setting (3).

Electrolyte-free low-viscosity solutions: Glycine 1.5%, Mannitol 5%, Sorbitol 3%–5%. These distention media are preferred only when monopolar electrosurgery will be used. Volume overload with disturbance in sodium balance is the major concern with these fluids which can cause water intoxication, pulmonary edema, hyponatremia, hypo-osmolarity, and cerebral edema. These side effects would be rare in office hysteroscopy, given that those procedures are typically shorter and less complex than hysteroscopy undertaken in the operating room. Theoretically, mannitol because of its near isotonic composition is a safer choice than glycine or sorbitol (4).

Carbon dioxide gas. Carbon dioxide gas is generally well tolerated and provides clear visualization for hysteroscopy, although there is no way to clear blood from the scope or flush blood and debris from the operative field. It can cause uterine spasm, subdiaphragmatic irritation, and air embolism (4). Because of the risk of embolism, this distention media is recommended for use for diagnostic hysteroscopy only. Two randomized controlled trials (263 patients) comparing carbon dioxide gas to normal saline showed the normal saline group to have a lower incidence of vasovagal reaction, a shorter operative time, less analgesic requirement, and better patient satisfaction (29). Saline has lower costs than carbon dioxide gas and allows for use of bipolar instruments (3).

26.3.5 Distention Media Delivery Systems

Atmospheric pressure. With this system, the fluid bag or container is hung on an IV pole above the patient's uterus. This creates an intrauterine pressure just below the patient's mean

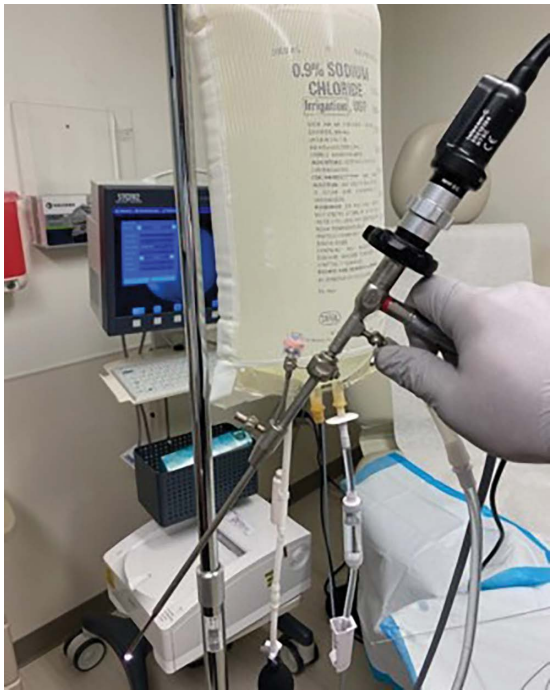


FIGURE 26.3 Rigid hysteroscope with pressure bag.

arterial pressure. It is the simplest distention media delivery system. Fluid flow rate cannot be controlled in this system (29).

Squeeze bag system. In this system, a pressure cuff is positioned around the bag containing distention media. It is an economical system that is best for short cases, as inflow and outflow cannot be precisely measured. Fluid can leave the uterus by the outflow channel, leakage from the cervix or fallopian tubes, or extravasation. The primary mechanism of systemic fluid absorption during hysteroscopy is through extravasation via venous sinuses in the endometrium and myometrium (3). While the inability to precisely measure fluid outflow is a limitation, absorption of clinically relevant volumes of fluid distention media is a rare occurrence during office hysteroscopy, particularly when mechanical or radiofrequency resectoscopic procedures are not being undertaken. In addition, it is possible to conservatively limit fluid intake by using a 1 L fluid bag for the procedure (3). The squeeze bag system is the distention media delivery system that we prefer at our institution (25) (Figure 26.3).

Electronically controlled fluid management system. This system uses electronic pumps and can accurately control inflow and record outflow. For diagnostic and minor operative office hysteroscopy, an electronic fluid management system is not as important because the risk of fluid intravasation is low in procedures that take only minutes to perform (4). For advanced resectoscopic techniques, a fluid management system is a necessity (3).

26.3.6 Hysteroscopy Equipment Maintenance

Although both disposable and reusable hysteroscopy equipment is used in the office, this section will focus on the maintenance of reusable hysteroscopic equipment.

The risk for serious infection during office hysteroscopy can be avoided by strictly following guidelines for decontamination, disinfection, and sterilization of all reusable equipment. There are three major steps for equipment cleaning and sterilization: decontamination, disinfection, and sterilization. Decontamination eliminates, kills, or inhibits microorganisms. Disinfection kills all recognized pathogenic microorganisms and viruses, but not necessarily all types of microorganisms such as bacterial endospores that might be present on inanimate objects (3). Sterilization destroys all microorganisms and viruses. Decontamination and disinfection processes are the same for rigid and flexible hysteroscopes, while sterilization processes differ between the two. Sterilization can be performed in a well-equipped clinic or at an off-site facility using a medical equipment transport service. Types of equipment sterilization processes are reviewed as follows (30).

Steam sterilization. Steam sterilization, or autoclaving, is most suitable for rigid hysteroscopes and is performed at 134°C. Ancillary instruments (e.g., hysteroscopic scissors) need to be sterilized as well and can be sterilized via this method (30). Scrub and rinse steps must be completed prior to autoclaving (3).

Gas sterilization. Ethylene oxide gas or vaporized hydrogen peroxide gas plasma is used for this sterilization process, which can be completed at a well-equipped clinic or off-site facility. This process can be used with both rigid and flexible hysteroscopes. Hydrogen peroxide gas plasma sterilization is a low-temperature sterilization technique for rigid hysteroscopes, with a sterilization cycle that lasts 60 minutes (30). If gas sterilization is performed, the scrub and rinse steps should be completed first (3).

High-level disinfection. Flexible hysteroscopes cannot withstand autoclaving and can be high-level disinfected by soaking in an enzymatic solution for a time period noted by the manufacturer. Several enzymatic solutions are on the market including Steris Prolystica and 2% glutaraldehyde solution (Cidex OPA) (3). This process can be performed at most clinics and does not necessitate a significant capital investment. However, specific institutional sterilization requirements should be considered before committing to this methodology (30).

Steps for cleaning and sterilization. Hysteroscopes can be cleaned and sterilized manually or via an automatic cleaning process. Lenses should be buffed immediately after use. Steps are as follows:

1. *Take apart the hysteroscope.* Any working channel inserts need to be disconnected and removed and stopcocks disassembled.
2. *Wipe down any soiled areas.*
3. *Clean with hot water and flush lumens with distilled water.* Under 32°–40°C water, the hysteroscope and disassembled components are rinsed to remove blood and debris. The lumen of the hysteroscope and the lumen of the working channel are flushed with distilled water. The hysteroscope and disassembled components are immersed in an enzymatic bath for a time length as dictated by the enzymatic solution manufacturer. Several types of lumens are primed with detergent and flushed. The hysteroscope and disassembled components are scrubbed under hot water with a soft nylon brush.
4. *Wipe lenses with gauze pad soaked in tap water.*
5. *Rinse with hot and then purified water.*
6. *Dry with medical grade compressed air.*
7. *Package carefully to ensure sterility.*

For an automatic cleaning process, equipment is still cleaned, but rather than using an enzymatic bath, equipment is sterilized by machine, following the instructions of that device (31).

26.3.7 Office Hysteroscopy Surgical Technique

Vaginoscopy. Rather than utilizing a speculum and tenaculum to place the hysteroscope within the cervical canal, we routinely practice vaginoscopy. This "no-touch" approach decreases the need for genital tract instrumentation or local anesthesia and is less painful and tenaculum-free (24, 25). Vaginoscopy was first described in 1996 (8). A randomized controlled trial compared no-touch vaginoscopy for diagnostic office hysteroscopy with the traditional speculum and tenaculum approach in 83 women and found mean pain scores during and after office hysteroscopy were significantly lower in the vaginoscopy group (5). The steps for performing vaginal hysteroscopy are as follows and are illustrated in Video 26.1:

1. Patients are most comfortable when asked to void prior to the procedure. Place the patient in the lithotomy position taking care to avoid any unnecessary pressure that may contribute to nerve injury. It can be helpful to perform a bimanual exam prior to the procedure to assess the position of the uterus.
2. Set up the hysteroscope; white-balance and focus the camera. Prime the inflow tract.
3. Use betadine swabs with a water-based lubricating gel to prep the cervix and vagina.
4. Place your index finger into the posterior vaginal fornix to guide the hysteroscope.
5. Introduce the hysteroscope with saline flowing into the posterior vaginal fornix by guiding it over your index finger. Remove your finger.
6. Pull back the hysteroscope while maintaining the upward angle until the cervix is in view. Find the external cervical os.
7. Place the hysteroscope within the external cervical os and drive the camera following the cervical canal until it is within the uterine cavity. Orient your camera with the light cord pointing down on a 30° hysteroscope and with the opening of the cervical canal in the lower section of your screen to prevent inadvertently causing trauma to endocervical and endometrial tissue. If entry is challenging, the uterus can be brought to a more axial position by applying pressure above the pubic symphysis or anterior pressure distally through the rectum (3).
8. Confirm intrauterine positioning by visualizing both tubal ostia and proceed with the remainder of the procedure.

Cervical stenosis is a common hysteroscopic finding in postmenopausal women, particularly those with a history of cervical procedures such as cone biopsy. It presents a challenge to even experienced gynecologists. In a patient with cervical stenosis, a few tips and tricks can be utilized to find the cervical os. In the case where the cervix appears flush with the vaginal mucosa, decreasing the pressure of fluid during vaginoscopy will cause the cervix to protrude into the vagina and facilitate visual identification of the cervical os. Another trick is to look for the "blue behind the white" sign, which indicates a patent canal opening behind an area of white scar tissue. Hysteroscopic graspers or scissors can be used to dilate the external cervical os (32). Placement of the speculum for dilation of the external cervical os followed by removal of the speculum before placement of the hysteroscope can often be sufficient to allow utilization of vaginoscopy (3).

Operative office hysteroscopy. We routinely excise polyps and small fibroids and lyse intrauterine adhesions in the office. Intrauterine devices can also be clearly visualized and removed if malpositioned. We use cold instruments such as hysteroscopic scissors and graspers to eliminate the need for an electrosurgical setup. We benefit from the use of a 30° scope as this allows us to optimize visualization of both the pathology and the surgical instrument while minimizing side-to-side movement of the hysteroscope and patient discomfort. It is important to remember that movement of the instruments to and away from the intrauterine pathology is best achieved with movement of the hysteroscope, as these delicate semi-rigid instruments can be easily bent and broken when excessive torque is applied.

Post-procedure care. Following office hysteroscopy, patients can immediately resume normal activities if no sedatives were administered for the procedure. Otherwise, patients should be driven home by a family member or support person and refrain from activities requiring physical strain or mental alertness (4).

26.4 Economics of Office Hysteroscopy

As illustrated in this chapter, office hysteroscopy affords numerous economic benefits to patients and providers. These include:

1. Lower costs to patients and the healthcare system, due to lower anesthesia and facility fees (13).
2. Faster recovery time for patients (5, 33).
3. Less time away from work for patients resulting in less lost income from medical procedural visits (5, 33).
4. Greater cost efficacy to do same procedure in office rather than the operating room, which is related primarily to decreased staff costs (5). A meta-analysis of seven economic studies concluded that office hysteroscopy cost range was 97–1258 USD, which was substantially less expensive than hysteroscopy completed in the operating room, with a cost range of 258–3144 USD (13).
5. Cost-effectiveness of office hysteroscopy has been recognized in the past several years, and reimbursement for these procedures has increased (3).

A couple of cost challenges impede widespread implementation of office hysteroscopy. First, reimbursement differences are not uniform. The reimbursement difference in performance of a polypectomy in the office versus the operating room significantly favors performance of the procedure in the office, with an additional reimbursement rate of around 1100 USD. However, in the case of hysteroscopic lysis of adhesions and hysteroscopic myomectomies, that reimbursement incentive is not as pronounced with a less than 10 USD difference in reimbursement between office and operating room–based procedures. There is a moderate difference in reimbursement for diagnostic hysteroscopy performed in office, with a 115 USD difference in reimbursement. It is important to note that when an office practice charges a facility fee, reimbursement may be decreased even if this procedure is not performed in the operating room (3).

In addition, the decision to invest in reusable hysteroscopic equipment can present a significant capital cost. Disposable instruments (Table 26.2) are convenient and do not require the same capital investment from the practice or creation of reliable sterilization protocols. However, the high cost of these disposable instruments can significantly cut into reimbursement fees. The decision whether to invest in reusable equipment

VIDEO 26.1 Vaginoscopy. (See Support Material at www.routledge.com/9781032319407)

depends on the office hysteroscopy volume of a particular practice; capital investments for reusable equipment can typically be recouped after 50 procedures (3).

Key Points

1. Hysteroscopy is the gold standard for evaluation of abnormal uterine bleeding and intrauterine pathology. Technological advances in hysteroscope size and operative instruments have made the office approach more accessible to patients and gynecologists.
2. Vaginoscopy is an important technique for introduction of the hysteroscope that decreases pain levels compared with the traditional approach. It does not require a speculum or tenaculum.
3. Many different types of hysteroscopic instruments and sterilization methods are available for use in office hysteroscopy. Each has a unique cost-to-benefit ratio.
4. Office hysteroscopy costs less than operating room–based hysteroscopy, although some reimbursement challenges exist.

References

1. Baradwan S et al. Warm saline effectiveness for pain relief in office hysteroscopy: a systematic review and meta-analysis of randomized controlled trials. *J Obstet Gynaecol Res*. 2022;48(7):1523–1530.
2. Moore JF et al. Hysteroscopy [Updated 2021 Dec 5]. In: *StatPearls* [Internet]. Treasure Island, FL: StatPearls Publishing; 2022.
3. Zelivianskaia et al. Office hysteroscopy: setting up your practice for success. *Obstet Gynecol Clin N Am*. 2022;49:315–327.
4. Emanuel MH. New developments in hysteroscopy. *Best Pract Res Clin Obstet Gynaecol*. 2013;27(3):421–429.
5. Cicinelli E. Hysteroscopy without anesthesia: review of recent literature. *J Minim Invasive Gynecol*. 2010;17(6):703–708.
6. Yen CF et al. Effectiveness and appropriateness in the application of office hysteroscopy. *J Formos Med Assoc*. 2019;118(11):1480–1487.
7. Centini G et al. Modern operative hysteroscopy. *Minerva Ginecol*. 2016;68(2):126–132.
8. Nguyen DB et al. Outpatient hysteroscopy is effective for uterine cavity evaluation following failed office-based endometrial biopsy. *J Obstet Gynaecol Res*. 2022 Sep;48(9):2452–2458.
9. Raz N et al. See-and-treat in-office hysteroscopy versus operative hysteroscopy for the treatment of retained products of conception: a retrospective study. *J Obstet Gynaecol Res*. 2022;48(9):2459–2465.
10. Robinson JK et al. Postoperative adhesiolysis therapy for intrauterine adhesions (Asherman's syndrome). *Fertil Steril*. 2008;90(2):409–414.
11. Brooks PG. The management of abnormal uterine bleeding, is office hysteroscopy preferable to sonography? The case for hysteroscopy. *J Minim Invasive Gynecol*. 2007;14(1):12–14.
12. Kelekci S et al. Comparison of transvaginal sonography, saline infusion sonography, and office hysteroscopy in reproductive-aged women with or without abnormal uterine bleeding. *Fertil Steril*. 2005;84(3):682–686.
13. Bennett A et al. Effectiveness of outpatient versus operating room hysteroscopy for the diagnosis and treatment of uterine conditions: a systematic review and meta-analysis. *J Obstet Gynaecol Can*. 2019;41(7):930–941.
14. Wortman M. "See-and-Treat" hysteroscopy in the management of endometrial polyps. *Surg Technol Int*. 2016;28:177–184.

15. Bettocchi S et al. Advanced operative office hysteroscopy without anaesthesia: analysis of 501 cases treated with a 5 Fr. bipolar electrode. *Hum Reprod*. 2002;17(9):2435–2438.
16. ACOG Committee Opinion 800. The use of hysteroscopy for the diagnosis and treatment of intrauterine pathology. *Obstet Gynecol*. 2020;135:e138–e148.
17. Vitale SG et al. Pain management for in-office hysteroscopy. A practical decalogue for the operator. *J Gynecol Obstet Hum Reprod*. 2021;50(1):101976.
18. Florio P et al. Prevalence of infections after in-office hysteroscopy in premenopausal and postmenopausal women. *J Minim Invasive Gynecol*. 2019;26(4):733–739.
19. De Silva PM et al. Pain and operative technologies used in office hysteroscopy: a systematic review of randomized controlled trials. *J Minim Invasive Gynecol*. 2021;28(10):1699–1711.
20. Salazar CA et al. Office operative hysteroscopy: an update. *J Minim Invasive Gynecol*. 2018;25(2):199–208.
21. Gambadauro P et al. Anxiety at outpatient hysteroscopy. *Gynecol Surg*. 2015;12(3):189–196.
22. Angioli R et al. Use of music to reduce anxiety during office hysteroscopy: prospective randomized trial. *J Minim Invasive Gynecol*. 2014;21(3):454–459.
23. Brunn E et al. Virtual reality effects on acute pain during office hysteroscopy: a randomized control trial. *J Gyncol Surg*. 2022;38(3):214–220.
24. De Silva PM et al. Analgesia for office hysteroscopy: a systematic review and meta-analysis. *J Minim Invasive Gynecol*. 2020;27(5):1034–1047.
25. Hua Y et al. The use of misoprostol for cervical priming prior to hysteroscopy: a systematic review and analysis. *Drug Des Devel Ther*. 2016;10:2789–2801.
26. Wright KN et al. Getting started with office hysteroscopy. *Contemp OB/GYN J*. 2021;66(9):28–32.
27. Penketh RJ et al. Feasibility of resectoscopic operative hysteroscopy in a UK outpatient clinic using local anesthetic and traditional reusable equipment, with patient experiences and comparative cost analysis. *J Minim Invasive Gynecol*. 2014;21(5):830–836.
28. Munro MG et al. AAGL practice report: practice guidelines for the management of hysteroscopic distending media. *J Minim Invasive Gynecol*. 2013;20(2):137–148.
29. Marty R. Decontamination, disinfection and sterilization of the hysteroscopes. In: Blanc R, ed. *Office and Operative Hysteroscopy*. Paris: Springer; 2002.
30. TruClear system elite hysteroscopes cleaning and sterilization guide. *Medtronic*, 2020. Available at: https://asiapac.medtronic.com/content/dam/covidien/library/us/en/product/gynecology-products/truclear-system-elite-hysteroscope-sterilization-guide.pdf (Accessed Oct 2021).
31. Di Spiezio Sardo A et al. The invisible external cervical os. tips and tricks to overcome this challenge during in-office hysteroscopy. *J Minim Invasive Gynecol*. 2021;28(2):172–173.
32. Marsh FA et al. A randomised controlled trial comparing outpatient versus daycase endometrial polypectomy. *BJOG*. 2006;113(8):896–901.

27 HYSTEROSCOPY FOR ABNORMAL UTERINE BLEEDING (DIAGNOSTIC, POLYPS, VISUALLY GUIDED BIOPSY, MYOMECTOMY)

Salvatore Giovanni Vitale, Gilda Sicilia, Antonio Succu, Stefano Angioni, and Jose Carugno

27.1 Introduction

Any change in menstrual volume, flow duration, rhythm, and frequency in premenopausal women falls within the definition of abnormal uterine bleeding (AUB) (1). Up to 30% of women of reproductive age experience at least one episode of AUB, and evidence shows that this can negatively impact their quality of life (2). The bleeding could be acute, requiring immediate intervention, or chronic, with changes in terms of quantity, regularity, and frequency, which can persist even for 6 months or more. Both acute and chronic AUB represent a significant cause of morbidity in premenopausal women, negatively impacting their quality of life (3). Traditionally, many terms were used to describe AUB, such as menorrhagia, metrorrhagia, intermenstrual bleeding, dysfunctional uterine bleeding, and polymenorrhagia, among others. However, such a variety of definitions and inconsistency of the nomenclature is now considered outdated and confusing. In order to provide a more standardized method of investigation and improve the accuracy of the diagnosis, new classification methods have been proposed over time. In 2011, the International Federation of Gynecology and Obstetrics (FIGO) proposed the PALM-COEIN classification to standardize the diagnostic approach of AUBs and improve communicative effectiveness among specialists (4–6). The PALM-COEIN classification system highlights the possible etiologies of AUB in nongravid women of reproductive age. PALM-COEIN is an acronym for polyp, adenomyosis, leiomyoma, malignancy, coagulopathy, ovulatory dysfunction, endometrial, iatrogenic, and not yet classified. The first part of the acronym (PALM) encompasses structural entities that can be diagnosed using imaging/physical exam or histopathological confirmation. The second part (COEIN), on the contrary, defines nonstructural entities (7). In 2018, a revision of the 2011 PALM-COEIN classification was published (8) (Table 27.1).

Hysteroscopy is the gold standard procedure for the evaluation and management of the patient with intrauterine pathology, which can be the underlying cause of AUB. The hysteroscopic approach allows treating intracavitary pathologies such as polyps or submucous myomas at the time of diagnosis, or "see and treat" (9).

TABLE 27.1 Classification of Causes of Abnormal Uterine Bleeding According to the PALM-COEIN System

Structural Anomalies	Functional Anomalies
Polyp	**C**oagulopathy
Adenomyosis	**O**vulatory dysfunction
Leiomyoma	**E**ndometrial
Malignancy	**I**atrogenic
	Not yet classified

27.2 The Management of the Patient with AUB: Workup of the Nonpregnant Patient with AUB?

AUB is a common complaint of women of all ages representing a leading cause (approximately 30%) of gynecological visits, particularly in the perimenopausal period (10–12). It is estimated that approximately 80% of women will have at least three episodes of AUB during their transition to menopause (10). Several factors may contribute to the onset of AUB. Coexisting conditions (such as uterine fibroids, endometrial polyps, adenomyosis) may be present but not responsible for the symptomatology. Therefore, the evaluation of patients with AUB must be approached rationally, ensuring reasonable use of the available resources (7).

A detailed anamnesis, a thorough physical examination, and transvaginal ultrasound (TVUS) are crucial in the diagnostic workup of women with AUB (8, 13). However, the accuracy of TVUS in the diagnosis of benign uterine conditions is suboptimal, although it is of big help in ruling out endometrial cancer in postmenopausal women when endometrial thickness at the US evaluation is less than 5 mm, providing a negative predictive value of > 99% (1, 14). Saline infusion sonohysterography (SIS) offers a higher detection rate of benign lesions than TVS does. Nevertheless, it is more expensive and less well tolerated (15).

Hysteroscopy is considered the gold standard for the diagnosis and treatment of intrauterine pathologies. Hysteroscopy can be performed in the office setting without anesthesia or just mild sedation or under general or peripheral anesthesia in the operating room (16). Office hysteroscopy carries fewer anesthetic risks, offers greater time and cost efficiency, and improves patient satisfaction (17). Modern gynecology has witnessed a rapid evolution and a widespread application of endoscopic techniques over the past 20 years, particularly in the hysteroscopic field, due to improved technological developments of instrumentations and improvement of surgical techniques. With the miniaturization of hysteroscopes, working channels provided with a continuous flow system, and newer instruments such as 5 Fr bipolar devices, 5 Fr diode laser fiber, mini-resectoscopes, and hysteroscopic tissue removal systems (morcellators), outpatient hysteroscopy is now also used for the treatment on intrauterine pathology and no longer as a diagnostic tool only. Using the "see-and-treat" approach, when AUB is due to polyps, small submucous fibroids, or other endometrial causes, it can be diagnosed and treated, in many cases, in only one intervention (18, 19). This leads to an expedited resolution of the symptomatology, improving patient satisfaction (9, 20).

DOI: 10.1201/9781003312109-27

27.3 Structural Causes of Abnormal Uterine Bleeding: Polyps, Adenomyosis, Leiomyomas, Malignancy/Hyperplasia (PALM)

27.3.1 Endometrial and Cervical Polyps (AUB-P)

Polyps are benign uterine lesions caused by epithelial proliferation with a variable percentage of fibromuscular, glandular, and connective tissue. Polyps can grow from the endometrial mucosa of the uterine body or the cervix. The vascularization pattern of a polyp can be typical or atypical (Figures 27.1 and 27.2). It is a common finding in women of reproductive age, although the exact epidemiology remains unclear and difficult to estimate. The prevalence of uterine polyps range from 7.8% to 50% (21, 22). Clark et al. found a prevalence of 10% in a population with no AUB. However, in women with AUB, the prevalence of endometrial polyps rises from up to 34.9% (23). Polyps are mostly asymptomatic. However, sometimes their presence may cause symptoms and signs, such as AUB, postcoital spotting, and infertility, which mostly do not correlate with the lesions' number, size, or locations (24). Endometrial polyps are a frequent cause of AUB, most likely because of vascular fragility and little areas of surface erosion. A small minority among them may show atypical or malignant features: evidence data estimated that the prevalence of premalignant and malignant lesions in patients with endometrial polyps is between 3.4% and 4.9% in postmenopausal women and 1.1% in women of reproductive age (25–27).

Transvaginal ultrasound with color Doppler and 3D evaluation and saline infusion sonohysterography are the best diagnostic tools for the diagnosis of endometrial polyps. However, the hysteroscopic approach with a hysteroscopic-guided biopsy/removal is the gold standard for polyp diagnosis and treatment (28). Robust evidence shows that hysteroscopic resection of endometrial polyps under direct vision is a safe procedure to be performed in the office setting and superior to blind polypectomy techniques (29–32). Hysteroscopic polypectomy is effective for the treatment of AUB symptoms in most patients (75%–100%) with high patient satisfaction. Moreover, it also allows the histopathological confirmation of the disease and the exclusion of the malignant potential of the lesion (33, 34). Especially when also causing postmenopausal bleeding, it is noteworthy that AUB after menopause is associated with the highest risk of precancerous and malignant lesions and, although infrequent, both cancer and atypical hyperplasia can originate from endometrial polyps; hence, histopathological exclusion of more serious disease is crucial (35, 36).

FIGURE 27.1 Endometrial polyp with irregular surface and marked vascularity, presenting denuded vascular bridges and vessels.

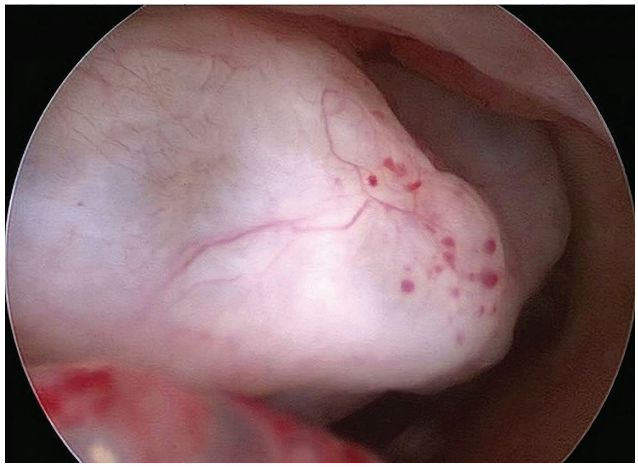


FIGURE 27.2 Multiple polyps in the uterine cavity. Note a sessile polyp of the right lateral uterine wall.

Endometrial polypectomy is one of the most commonly performed procedures in modern gynecological practice. The rationale for endometrial polypectomy is dual: the first aim is to treat the symptomatology, and the second is to exclude any potential neoplastic transformation (37). A small, glandular polyp can be hysteroscopically removed in the office setting, with a direct vision excision using miniaturized instruments (scissors, grasping forceps, or a bipolar twizzle electrode) (Figure 27.3). Also, the 15 Fr bipolar office resectoscope (also known as "mini-resectoscope") and smaller tissue removal devices (TRDs) are a suitable option for in-office polypectomy. However, patients with larger and more fibrous polyps require the procedure to be performed in the operating room. Hysteroscopic resectoscopes are frequently used for hysteroscopic polypectomy (9). Another viable option for hysteroscopic polypectomy is the use of TRDs (intrauterine morcellation), characterized by their unique feature of combining cutting and aspiration, maintaining a clear view of the uterine cavity throughout the procedure (9).

27.3.2 Adenomyosis (AUB-A)

Adenomyosis is a clinical condition defined by the presence of ectopic endometrial tissue (both glands and stroma) within the myometrium (38). The association between AUB and adenomyosis still needs further investigation. Nevertheless, adenomyosis is recognized as a structural cause of AUB and

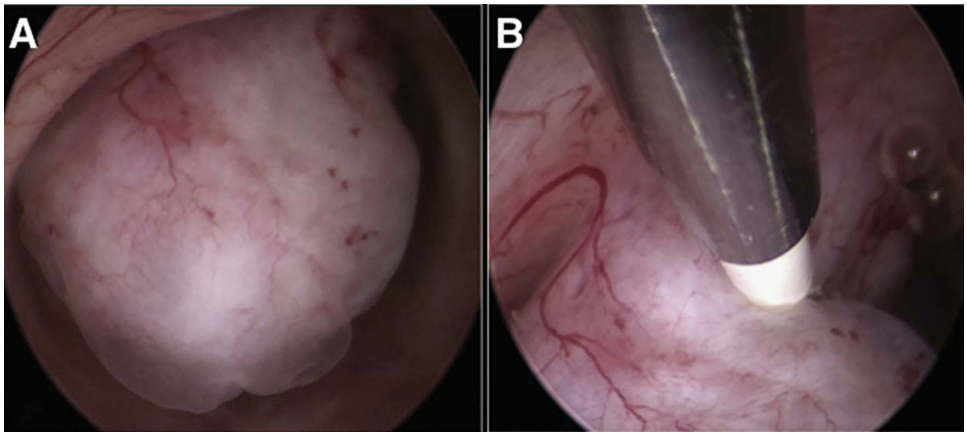


FIGURE 27.3 Polypectomy technique using a 5 Fr bipolar twizzle electrode (Gynecare Versapoint™, Ethicon EndoSurgery Inc.) for an endometrial polyp larger than the internal cervical os.

included as such in the PALM-COEIN classification (8). The current literature shows that the prevalence varies (depending on selected diagnostic criteria) from 10% to 35% of hysterectomy specimens, appearing more frequently in multiparous women in their fourth or fifth decade of life (39). Imaging has an important role in the diagnosis of adenomyosis. US evaluation and MRI can confirm the clinical suspicion (40–42). Adenomyosis is frequently found as an incidental finding during US evaluation. However, more recently, the improvement of diagnostic imaging and the development of new hysteroscopic techniques have increased the accuracy of diagnosing the pathology (39). Hysteroscopy allows the direct visualization of the surface of the endometrial mucosa facilitating the detection of any lesion suggestive of the presence of adenomyosis (hypervascularization, the typical strawberry pattern, endometrial defects, and submucosal hemorrhagic cysts) (Figures 27.4 and 27.5). Although not pathognomonic, these findings have good predictive value for diagnosing adenomyosis. When the clinical suspicion is strong, hysteroscopic evaluation should not be limited to the visualization of the anomalous areas but should also include the performance of a biopsy sample of internal and external myometrial structures (39, 43, 44). However, diagnosing adenomyosis can be challenging.

Hysteroscopy is not the first-line treatment in women with adenomyosis. However, it can be a suitable option in selected cases (in the presence of focal lesions or diffuse superficial adenomyotic patterns). In a study by Di Spiezio Sardo et al., in-office hysteroscopy was a feasible treatment of superficial focal adenomyomas or evacuating hemorrhagic cystic lesions smaller than 1.5 cm in diameter. In the case of diffuse superficial adenomyosis and small superficial focal adenomyotic nodules (> 1.5 cm) in a patient with AUB, resectoscopic treatment by endometrial ablation is indicated (43). It is important to highlight that hysteroscopic treatment is not indicated in the case of deep and/or diffuse adenomyosis. Some studies show that it does not improve the symptoms and can mask deep adenomyosis below the endometrial scar tissue, which may consecutively be prone to malignant transformation (45).

FIGURE 27.4 Hysteroscopic image of adenomyosis. During hysteroscopy small openings on the endometrial surface are visualized.

27.3.3 Leiomyomas (AUB-L)

Uterine leiomyomas (also known as uterine fibroids or myomas) are one of the most common benign pathologies of the female genital tract (46, 47). They are estimated to affect up to 70% of women of reproductive age, and prevalence seems to be markedly influenced by factors such as age, race, and body mass index (BMI) (48, 49). The high prevalence of myomas necessitates a cautious approach when diagnosing them as the cause of AUB: a careful differential diagnosis must be conducted, particularly when the fibroids do not protrude into the uterine cavity. Myomas can even be completely asymptomatic or the underlying cause of several bothersome symptoms, which can strongly negatively impact patients' quality of life (50). In 30% of cases, they cause severe clinical symptoms, including AUB and iron deficiency that can lead to anemia. Approximately 40% of premenopausal patients who seek medical care for heavy menstrual bleeding are found to have intrauterine lesions, including submucous myomas (51). Presurgical evaluation and characterization of submucous myoma is pivotal in improving

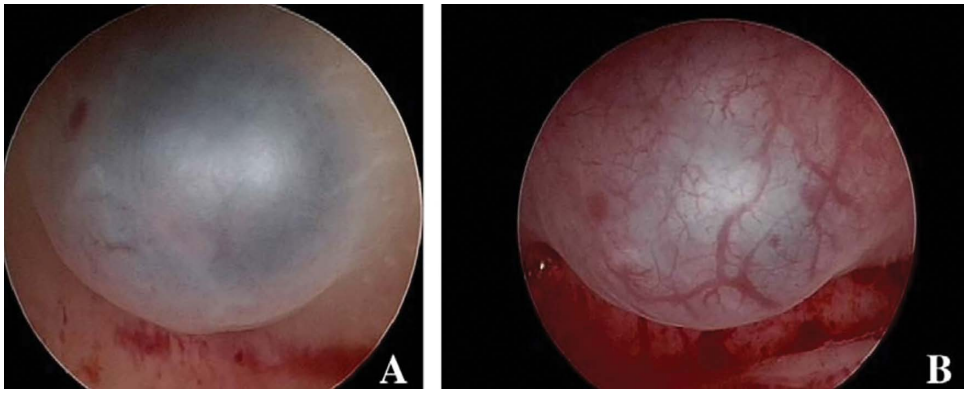


FIGURE 27.5 Hysteroscopy image of adenomyosis. (A) Cystic lesions with a dark blue color originate from the accumulation of blood inside the lesion. (B) In the same lesions, superficial vascularization is seen when the intracavitary pressure is decreased.

surgical outcomes and decreasing the risk of complications. The classification of Lasmar et al., the *STEP-W* classification, considers five important features of the submucous myomas: size, topography, extension of the base, penetration, and lateral wall position (52).

In the past, hysterectomy was considered the first-choice treatment for uterine fibroids. However, hysterectomy is major surgery and should be avoided when possible. Moreover, an increasing number of patients desire uterine-sparing therapeutic options (53). Hysteroscopic myomectomy is the gold standard treatment for women with symptomatic submucosal myomas who want to preserve their fertility (50). Hysteroscopic myomectomy is a safe procedure with low complication risk; however, it can sometimes be a complex procedure. New instruments such as bipolar resectoscopes, mini-resectoscopes, and hysteroscopic mechanical morcellators allow the treatment of patients with small type 0 and 1 myomas in the office setting (54, 55). Different techniques are applicable for hysteroscopic myomectomy: slicing, morcellation, and pedicle-cut (56). Available data in the literature do not allow for establishing the superiority of one technique over the others, even if the slicing technique is the most commonly used for type 0 myomas (54). Slicing consists of a repeated and progressive passage of the cutting loop (bipolar or monopolar), starting behind the lesion and gradually working toward its base. This technique allows the partial and progressive removal of the myoma in fragments. In the case of larger submucosal fibroids with partial intramural component (type 1 or 2 myomas, with a diameter of more than 1.5 mm), although the slicing technique is feasible and provides reproducible results, there is a lack of high-quality evidence indicating the most appropriate technique and instruments for hysteroscopic myomectomy (57) (Figure 27.6). In these patients, it is possible to use a double-step technique called office preparation of partially intramural myomas (OPPIuM). This technique aims to "prepare" the myomas with an intramural component to facilitate subsequent resectoscopic myomectomy (58, 59). In the first step, performed in-office setting, using a 5 Fr bipolar electrode (e.g., twizzle) or 5 Fr scissors, with an incision on the endometrium surrounding the myoma, the plane of cleavage between the fibroid and its pseudo capsule is identified. This induces the migration of the intramural portion of the myoma into the uterine cavity during the subsequent menstrual cycles. In the second step, the resectoscopic myomectomy can be easily performed since the myoma, as a result of the previous treatment, is expected to be totally intracavitary or intramural just in a minimal part (59).

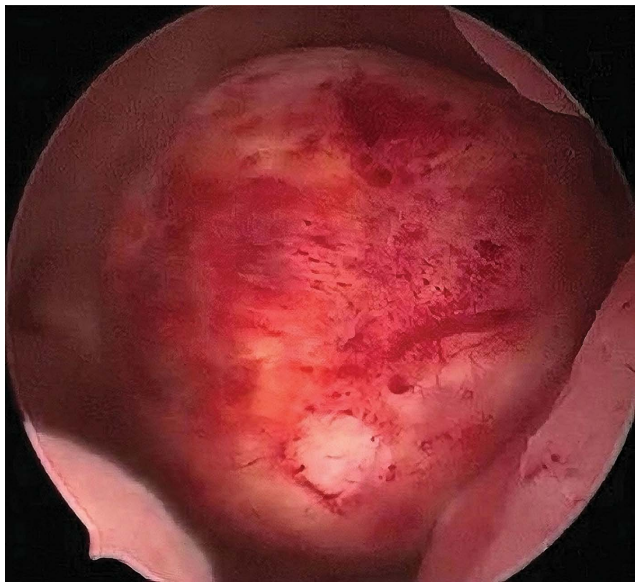


FIGURE 27.6 Submucosal myoma with its larger portion (> 50%) inside the uterine cavity (Type 1 submucous fibroid).

Another technique to improve the ease of the myomectomy is the stimulation of the myoma through the "massaging" of the fibroid with the aid of a cold loop or hydro massage. This technique relies on using electronic fluid management systems for irrigation and suction: it provides rapid changes in intrauterine pressure, stimulating uterine contractions and promoting the migration of the intramural component of the myoma (60).

When dealing with a submucous (type 1 or 2) fibroid up to 40 mm in diameter, another feasible option is a single- or two-step in-office hysteroscopic myomectomy using a diode laser. The application of a laser will lead to myolysis with the destruction of the myoma or a late expulsion after volume reduction and ischemia. This device uses a 5 Fr fiber, mixing two different wavelengths (980 nm and 1470 nm). The 980 nm wavelength

causes a higher coagulation effect; at 1470 nm, a higher vaporization effect will be predominant. This flexible capacity allows combined effects that can be adjusted for each tissue and surgical procedure (61).

Another hysteroscopic instrument considered effective for the treatment of fibroids is the hysteroscopic tissue removal systems, also known as hysteroscopic mechanical morcellators (62). The guidelines of the International Society for Gynecologic Endoscopy (ISGE) recommend using morcellators for type 0 myoma because it is faster and shows a shorter learning curve when compared to the resectoscope. However, the slicing technique is recommended for type 1 and 2 leiomyomas (57). Several types of morcellators are available on the market, and all of them share the fundamental mechanism consisting of a cylindrical blade and suction system that, by acting simultaneously, allows sequential morcellation of the tissue without restricting vision and preventing the retention of the material (53, 63).

Hysteroscopic myomectomy is the most challenging and complex hysteroscopic surgery, with potential risks for complications. Nevertheless, it is well established that its performance can be safe and efficient for treating intrauterine diseases, being the best therapeutic option for submucous myoma, with a high success rate in managing AUB.

27.3.4 Malignancy and Hyperplasia (AUB-M)

Endometrial hyperplasia is defined as an increased presence of proliferating endometrial glands of varying size and shape and with a greater gland-to-stroma ratio than normal (64). Endometrial hyperplasia is most likely due to unopposed chronic estrogen stimulation of the endometrium. In 2014, the old classification of endometrial hyperplasia (as simple or complex, with or without atypia) was abandoned. Since then, only the presence of atypia has been considered in characterizing endometrial hyperplasia (65). Evidence shows that endometrial hyperplasia with atypia has a 10%–30% risk of progression to endometrial adenocarcinoma if not treated (66–68). What distinguishes a hyperplasic endometrium with atypia from invasive adenocarcinoma is the absence of stromal invasion. Malignancy is not a common cause of AUB in women of reproductive age. Still, it is mandatory to take it into account, considering its impact and implications.

The diagnosis can be suspected during the hysteroscopic evaluation (starting from the patient's familial and personal history and clinical and imaging findings). However, histopathological confirmation is mandatory.

Several techniques are available to obtain an endometrial sample for histopathological examination, including simple blind aspiration (aspiration biopsy), blind dilation and curettage (D&C), or directed hysteroscopic guided biopsies (performed in an office setting) (69). The traditional procedure of D&C has now become obsolete and should no longer be used as the primary modality for endometrial disease investigation. D&C is inaccurate because of the probability of a missed diagnosis and incomplete removal of the intracavitary pathology, carrying a high false-negative rate (70). Moreover, this procedure is burdened by more frequent complications, including uterine perforation, intrauterine adhesion formation, and cervical lacerations, among others (71). Bettocchi et al. have shown the inadequacy of D&C in detecting intrauterine disorders with a sensitivity of 46%, a specificity of 100%, a positive predictive value of 100%, and a negative predictive value of only 7.1%: a substantial number of the focal lesions (polyps, myomas, hyperplasia, and cancer) is missed by this old technique (72,73). Even other blind sampling techniques have been questioned, and similarly to D&C, they showed poor diagnostic accuracy in evaluating patients with suspected endometrial disease (74).

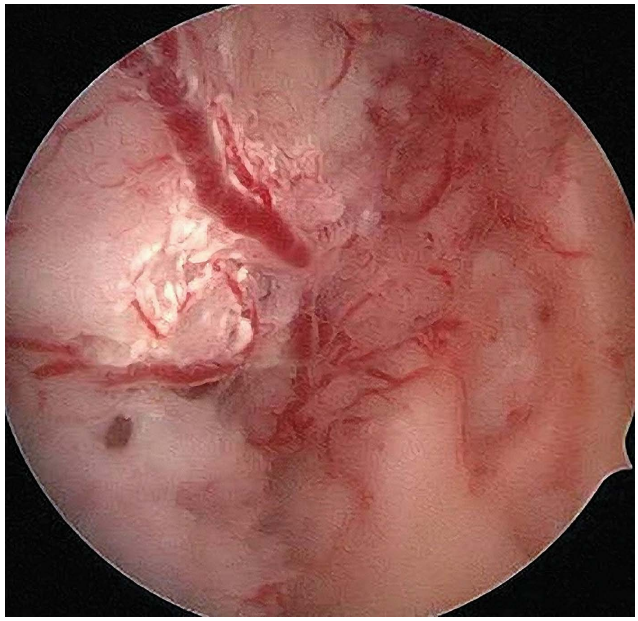


FIGURE 27.7 Endometrial adenocarcinoma with a distinctive atypical vascularization and irregular surface.

Diagnostic hysteroscopy with endometrial biopsy is currently the method of choice for diagnosing endometrial hyperplasia or endometrial cancer (75) (Figure 27.7). Continuous technological progress has provided numerous devices that allow adequate biopsy sampling. The most commonly used are forceps with spoon-shaped tips, sharp-edge jaws (spoon forceps), and serrated or toothed-edge jaws (alligator forceps). More recently, an innovative tool that allows one to grasp and cut simultaneously (the biopsy snake grasper) has been developed (76, 77).

There are several techniques for performing endometrial biopsy. The standard technique is the "punch biopsy," which is performed with the "spoon" forceps. According to this technique, the instrument's jaws grasp the endometrium and are then closed. The closed forceps are then retracted through the working channel of the hysteroscope, still maintaining the hysteroscope in the uterine cavity. However, this technique makes the jaw extension relatively small compared to other biopsy forceps. Hence the collected tissue volume is often insufficient for an adequate histopathological diagnosis (76). To remove a larger and adequate amount of tissue for adequate histopathological analysis, in 2002, Bettocchi et al. introduced another biopsy technique named the "grasp biopsy" technique using the so-called alligator forceps (toothed grasping forceps) (76). These forceps are characterized by gentle double-length toothed jaws and a pin that protrudes from the inner surface of the jaws, allowing an adequate biopsy sampling (78). When performing this technique, the alligator forceps are placed in close contact with the target area that was selected for the biopsy. Then, with its jaws widely opened, the forceps are pushed forward for about 0.5–1 cm in the endometrial mucosa,

avoiding the underlying myometrium, in order to not stimulate myometrial nerve fibers and to make the procedure painless (79). Subsequently, the jaws are closed, grasping the fragment of endometrial tissue to excise, then retrieving it alongside the hysteroscope from the uterine cavity. The biggest limitation is that when multiple biopsies are necessary, the operator must repeatedly enter and exit the cavity multiple times causing discomfort to the patient (80).

In 2020, a new "pick-up biopsy" technique was designed to obtain more tissue during the procedure, especially for patients with atrophic endometrium in whom both the spoon and the alligator forceps have shown several limitations. This technique involves the use of a new innovative miniaturized instrument: the biopsy "snake" forceps sec. VITALE (Centrel Srl, Ponte San Nicolo, Italy) (77). The pick-up biopsy allows one to easily obtain a suitable biopsy sample, even in the case of a thin endometrium (e.g., an atrophic postmenopausal endometrium), since the tip of the forceps avoids the loss of material, and the sharp edges can cut a flat surface (56).

In 2021 a multicenter, single-blind randomized clinical trial (HYGREB-1) compared these three aforementioned types of endometrial biopsy in postmenopausal women. As a result, the duration of the biopsy was comparable between the three groups, while the alligator and snake forceps reported wider biopsy specimens than the spoon forceps ($p < 0.0001$). Therefore, snake and alligator forceps should be preferred for endometrial biopsy, especially in women with an atrophic endometrium (e.g., postmenopausal women) (81).

To date, the possibility of using electrosurgery in the office setting allows for performing endometrial biopsies using bipolar electrodes (82). The most frequently used instruments are the "twizzle" bipolar electrode and the 16 Fr mini-resectoscope (Karl Storz SE & Co. KG, Tuttlingen, Germany). The standard technique requires "cutting" the selected area of the endometrium to excise it by creating a "chip" of tissue ("chip biopsy" technique) (Figure 27.8). This technique allows for performing deeper biopsies, especially in the case of perimenopausal and postmenopausal women with hypertrophic or atrophic endometrium, where an appropriate tissue sample is required. Conversely, "chipping" the endometrium allows the sampling of the superficial myometrial surface (e.g., in women with suspected premalignant or malignant endometrial pathology). The most significant limitations are represented by the possible specimen alteration due to thermal damage and the high cost compared to reusable mechanical graspers.

The tissue retrieval system, also known as a hysteroscopic morcellator, allows the sampling of a large portion of the uterine cavity under direct visualization using mechanical energy. This technique is known as the "visual D&C." This innovative technique also has some limitations; the main one is the inability to coagulate active bleeding vessels when visualized (83).

Clark et al. (84) and De Franciscis et al. (85) demonstrated how in-office hysteroscopy is highly accurate for the diagnosis of endometrial hyperplasia and cancer. Collecting an adequate biopsy sampling is crucial to ensure an accurate endometrial evaluation, including collecting an adequate amount of tissue from the areas that are morphologically suspicious (86). Sugimoto et al. first categorized the hysteroscopic morphological criteria of endometrial carcinomas, describing it as a whitish or grayish color pattern, atypical vascularization, ulcerated and irregular surface, friable, and sessile/nodular and polypoid structures (87). Moreover, Di Spiezio Sardo et al. revealed that preoperative hysteroscopy-guided endometrial biopsy using the grasp forceps provides a more accurate diagnosis of

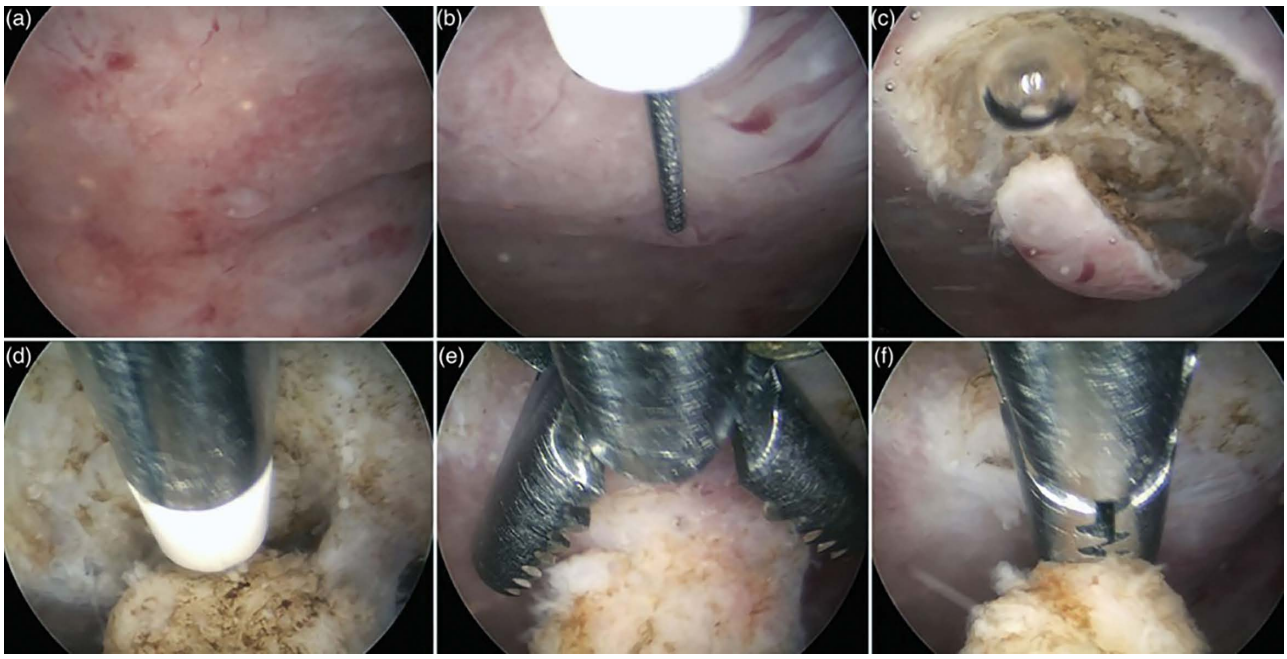


FIGURE 27.8 Chip biopsy technique using the bipolar electrode: the bipolar electrode is positioned parallel to the area to be excised (a, b), then the endometrial tissue to be sampled is separated from the underlying myometrium creating a chip of tissue (c, d). Subsequently, the chip is grabbed and retrieved from the uterine cavity using the alligator forceps without retracting the forceps into the operating channel of the hysteroscope (e, f).

endometrial carcinoma histology type and tumor grade in case of an endometrioid tumor when compared to blind endometrial sampling (88).

Each instrument and technique used for hysteroscopic endometrial biopsy has strengths and limitations. To date, there is no evidence to determine the best tool for biopsy: the operator's experience and comfort level with the different available options must guide the choice when approaching patients with endometrial pathology.

Interestingly, many patients with atypical endometrial hyperplasia or endometrial cancer are still in their reproductive age with a desire to preserve fertility; hence fertility-sparing management, whenever feasible, is highly recommended. Hysteroscopy permits, in selected patients, to perform focal resections, avoiding the hysterectomy and allowing future fertility (89).

27.4 Functional Causes of Abnormal Uterine Bleeding: Coagulopathy, Ovulatory Dysfunction, Endometrial, Iatrogenic, Not Yet Classified (COEIN)

27.4.1 Coagulopathy (AUB-C)

The term "coagulopathy" indicates a series of coagulation disorders that may be associated with AUB. There is strong evidence supporting that 13% of women with heavy menstrual bleeding have disorders of hemostasis, mostly von Willebrand disease (90). Especially among adolescents, up to 10% of them can present with AUB due to coagulation disorders. There is no consensus about the frequency in which these alterations may be the cause or may be involved in the genesis of AUB and how often they remain asymptomatic or with only minimal symptoms. Nevertheless, it is important to include these disorders as potential causes of AUB and consider them in the differential diagnosis. To date, scientific evidence indicates that only a few clinicians consider systemic hemostasis disorders in the differential diagnosis of women with heavy menstrual bleeding (91).

27.4.2 Ovulatory Dysfunction (AUB-O)

Ovulatory dysfunction is one of the most common "nonstructural" causes of AUB, especially at the extremes of reproductive age (postmenarchal adolescents and perimenopausal women). Clinical endocrinological conditions which can impact the hypothalamic–pituitary–ovarian (HPO) axis, such as polycystic ovary syndrome (PCOS), hyperprolactinemia, and thyroid diseases, can lead to ovulation disorders, often resulting in AUB (92, 93). Also, obesity, eating disorders, and excessive exercise (frequently seen in athletes) can cause AUB (94). Menstrual alteration in case of ovulatory dysfunction may vary from amenorrhea, spotting, and episodes of unpredictable and severe heavy bleeding for which emergency care may be necessary. Anovulatory bleeding mostly results from estrogen breakthrough bleeding caused by the focal breakdown of an endometrium that has received continuous estrogen stimulation without progesterone stimulation. An endometrium chronically exposed to unopposed estrogens proliferates and becomes overgrown and structurally fragile. Without progesterone's growth-limiting and stabilizing effects, the stromal support structure is lacking: the endometrium focally breaks down, causing AUB (95).

27.4.3 Endometrial (AUB-E)

In patients with regular ovulatory cycles and cyclic menstrual bleeding, particularly when no other causes have been identified, the mechanism seems to be referred to as a primary disorder of the endometrium. If the primary symptom is an increased amount of bleeding, a primary disorder of the mechanism regulating local endometrial "hemostasis" should be investigated. In this context, there is emerging evidence demonstrating that the cause may be related to the lack of the endometrial production of vasoconstrictors (endothelin-1 and prostaglandin F2α) as well as to the high rate of lysis of endometrial clot due to the high-level production of lysis factors (plasminogen activator) (96). In addition, the increased local production of vasodilating factors, such as prostaglandin E2 and prostacyclin, may represent another cause of AUB (97, 98). Other primary endometrial disorders may contribute to prolonged bleeding by endometrial factors. It has been suggested that it may be the result of the alteration of molecular mechanisms, which negatively impact the endometrial capacity to repair after endometrial infective manifestations, alterations in the local inflammatory response, or aberration in the endometrial genesis of the local vascular system. However, the role of infection and inflammatory disorders in the genesis of AUB is not yet well defined, and it can be misinterpreted by the common presence of inflammatory cells in the endometrium. Newer evidence indicates a relationship between subclinical infection by chlamydia trachomatis and AUB (99), although consistent evidence demonstrating a histopathological validation is still lacking (100, 101).

27.4.4 Iatrogenic (AUB-I)

Causes of AUB may be related to several mechanisms, including iatrogenic causes such as medical devices (e.g., medicated or inert intrauterine systems and interventions or medications which directly damage the endometrium, interfering with blood coagulation or with the systemic ovulation control) (102). Unscheduled endometrial bleeding can occur during gonadal steroid therapy (breakthrough bleeding). Systemically administered single-agent or combined gonadal steroids (including estrogens, progestogens, and androgens) impact the HPO axis and control ovarian steroidogenesis. Moreover, this has a direct effect on the endometrium. Specifically, with a cyclic administration of estrogen–progestin combination, the scheduled uterine bleeding normally coincides with the periodic withdrawal of the steroidal agents. However, episodes of unscheduled bleeding may happen even during cyclic administration. When combined estrogen–progestin preparations are continuously administered to obtain amenorrhea, any bleeding is considered unscheduled and may be classified as AUB-I (103). However, several episodes of unscheduled bleeding may be related to decreasing circulating gonadal steroid levels due to low patient compliance (missed, delayed, or erratic use of pills) or erroneous use of transdermal patches or vaginal rings. In women using the levonorgestrel intrauterine system (LNG-IUS), it is not infrequent to experience at least one episode of vaginal spotting in the first 3–6 months after the placement of the device (104, 105).

Among the systemic agents that can lead to episodes of AUB, the ones interfering with dopamine metabolism (such as tricyclic antidepressants and phenothiazine) are frequently identified (106). The process is related to the resulting reduced inhibition of prolactin release, causing prolactin-related

disruption in the HPO axis and consequent ovulation disorders, including anovulation.

Anticoagulant drugs may also cause AUB by interfering with clotting formation within the endometrial vessels' lumen (107).

27.4.5 Not Yet Classified (AUB-N)

It has been suggested that several uterine entities, which are still poorly defined (such as chronic endometritis or arteriovenous malformation), can be the leading cause of AUB (108). In addition, other not yet identified disorders may be defined only by future biochemical or molecular biology assays. Therefore, these entities are placed in the "not yet classified" category. It is worth highlighting that the evaluation of a patient with AUB cannot disregard the personal history of the patient (e.g., abnormal postmenstrual spotting recurs in a woman with a history of a previous cesarean section, suggesting the presence of an isthmocele; abnormal bleeding in a patient who was recently pregnant can suggest the retention of products of conception [RPOC]) (109–112). Only a thorough evaluation of the patient ensures the best management of this clinical condition and optimizes the efficiency of the treatment, improving the quality of care.

27.5 Conclusion

Hysteroscopy has impressively progressed over time, evolving from being only an ancillary diagnostic tool complementing the traditional D&C to an unmissable technique for the diagnosis and treatment of most causes of AUB. Moreover, the extraordinary progress in outpatient hysteroscopy has made it possible to treat more and more patients in an ambulatory setting, avoiding the risk of general anesthesia, improving the efficiency of care, and making hysteroscopy and patients' satisfaction. Thanks to the direct visual approach to the uterine cavity, hysteroscopy permits confirming or even excluding the diagnostic hypotheses and provides an accurate assessment and treatment of the majority of structural intracavitary pathologies which can cause AUB, such as polyps and submucous myomas. Furthermore, hysteroscopic evaluation of the uterine cavity is a key component in the diagnostic path of women with premalignant or malignant endometrial lesions. Thanks to the direct visualization, it has totally overcome the diagnostic inaccuracy of the old blind techniques, ensuring a more accurate assessment of the uterine cavity, thus allowing to perform directed biopsies on suspicious areas, hence improving the thoroughness of the diagnostic path and the reliability and effectiveness of care.

References

1. Committee on Practice Bulletins – Gynecology. Practice bulletin no. 128: diagnosis of abnormal uterine bleeding in reproductive-aged women. *Obstet Gynecol*. 2012;120(1):197–206.
2. Kuppermann M et al. Effect of hysterectomy vs. medical treatment on health-related quality of life and sexual functioning: the medicine or surgery (Ms) randomized trial. *JAMA*. 2004;291(12):1447–1455.
3. Marjoribanks J et al. Surgery versus medical therapy for heavy menstrual bleeding. *Cochrane Database Syst Rev*. 2016;2016(1):CD003855.
4. Madhra M et al. Abnormal uterine bleeding: advantages of formal classification to patients, clinicians, and researchers. *Acta Obstet Gynecol Scand*. 2014;93(7):619–625.
5. Töz E et al. Comparison of classic terminology with the FIGO PALM-COEIN system for classification of the underlying causes of abnormal uterine bleeding. *Int J Gynaecol Obstet*. 2016;133(3):325–328.
6. Shubham D et al. Critical evaluation of the PALM-COEIN classification system among women with abnormal uterine bleeding in low-resource settings. *Int J Gynaecol Obstet*. 2018;141(2):217–221.
7. Munro MG et al. FIGO classification system (PALM-COEIN) for causes of abnormal uterine bleeding in nongravid women of reproductive age. *Int J Gynaecol Obstet*. 2011;113(1):3–13.
8. Munro MG et al. The two FIGO systems for normal and abnormal uterine bleeding symptoms and classification of causes of abnormal uterine bleeding in the reproductive years: 2018 revisions. *Int J Gynaecol Obstet*. 2018;143(3):393–408. Erratum in: *Int J Gynaecol Obstet*. 2019;144(2):237.
9. Cooper NA et al. Ambulatory hysteroscopy and its role in the management of abnormal uterine bleeding. *J Fam Plann Reprod Health Care*. 2015;41(4):284–291.
10. Paramsothy P et al. Bleeding patterns during the menopausal transition in the multi-ethnic Study of Women's Health Across the Nation (SWAN): a prospective cohort study. *BJOG*. 2014;121(12):1564–1573.
11. Carugno J. Clinical management of vaginal bleeding in postmenopausal women. *Climacteric*. 2020;23(4):343–349.
12. Goldstein SR. Appropriate evaluation of postmenopausal bleeding. *Menopause*. 2018;25(12):1476–1478.
13. Van Den Bosch T et al. Typical ultrasound features of various endometrial pathologies described using International Endometrial Tumor Analysis (IETA) terminology in women with abnormal uterine bleeding. *Ultrasound Obstet Gynecol*. 2021;57(1):164–172.
14. Vitale SG et al. Hysteroscopic endometrial biopsy: from indications to instrumentation and techniques. A call to action. *Minim Invasive Ther Allied Technol*. 2021;30(5):251–262.
15. Vroom AJ et al. Diagnostic accuracy of saline contrast sonohysterography in detecting endometrial polyps in women with postmenopausal bleeding: systematic review and meta-analysis. *Ultrasound Obstet Gynecol*. 2019;54(1):28–34.
16. Di Spiezio Sardo A et al. Hysteroscopy: a technique for all? Analysis of 5,000 outpatient hysteroscopies. *Fertil Steril*. 2008;89(2):438–443.
17. Nagele F et al. 2500 Outpatient diagnostic hysteroscopies. *Obstet Gynecol*. 1996;88(1):87–92.
18. Vitale SG et al. Hysteroscopic endometrial resection vs. hysterectomy for abnormal uterine bleeding: impact on quality of life and sexuality. Evidence from a systematic review of randomized controlled trials. *Curr Opin Obstet Gynecol*. 2020;32(2):159–165.
19. Angioni S et al. Detection of benign intracavitary lesions in postmenopausal women with abnormal uterine bleeding: a prospective comparative study on outpatient hysteroscopy and blind biopsy. *J Minim Invasive Gynecol*. 2008;15(1):87–91.
20. Di Spiezio Sardo A et al. Review of new office-based hysteroscopic procedures 2003–2009. *J Minim Invasive Gynecol*. 2010;17(4):436–448.
21. Dreisler E et al. Prevalence of endometrial polyps and abnormal uterine bleeding in a Danish population aged 20–74 years. *Ultrasound Obstet Gynecol*. 2009;33(1):102–108.
22. de Azevedo JM et al. Endometrial polyps: when to resect? *Arch Gynecol Obstet*. 2016;293(3):639–643.
23. Clark TJ et al. A randomized controlled trial of Outpatient versus inpatient Polyp Treatment (OPT) for abnormal uterine bleeding. *Health Technol Assess*. 2015;19(61):1–194.
24. Levy-Zauberman Y et al. Update on the management of abnormal uterine bleeding. *J Gynecol Obstet Hum Reprod*. 2017;46(8):613–622.
25. Anastasiadis PG et al. Endometrial polyps: prevalence, detection, and malignant potential in women with abnormal uterine bleeding. *Eur J Gynaecol Oncol*. 2000;21(2):180–183.
26. Shushan A et al. How often are endometrial polyps malignant? *Gynecol Obstet Invest*. 2004;58(4):212–215.

27. Uglietti A et al. The risk of malignancy in uterine polyps: a systematic review and meta-analysis. *Eur J Obstet Gynecol Reprod Biol*. 2019;237:48–56.
28. Henriquez DD et al. Polypectomy in premenopausal women with abnormal uterine bleeding: effectiveness of hysteroscopic removal. *J Minim Invasive Gynecol*. 2007;14(1):59–63.
29. Vitale SG et al. Endometrial polyps. An evidence-based diagnosis and management guide. *Eur J Obstet Gynecol Reprod Biol*. 2021;260:70–77.
30. Raz N et al. Endometrial polyps: diagnosis and treatment options – a review of literature. *Minim Invasive Ther Allied Technol*. 2021;30(5):278–287.
31. Ceci O et al. Office treatment of large endometrial polyps using nuclear 5C: feasibility and acceptability. *J Obstet Gynaecol Res*. 2019;45(3):626–633.
32. Rovira Pamplona J et al. Outpatient hysteroscopic polypectomy: bipolar energy system (Versapoint®) versus mechanical energy system (TRUCLEAR System®) – preliminary results. *Gynecol Obstet Invest*. 2015;80(1):3–9.
33. Céspedes Martínez MA et al. Effectiveness and patient satisfaction with office hysteroscopic polypectomy in patients with symptomatic endometrial polyps. *Facts Views Vis Obgyn*. 2022;14(4):325–329.
34. Nathani F et al. Uterine polypectomy in the management of abnormal uterine bleeding: a systematic review. *J Minim Invasive Gynecol*. 2006;13(4):260–268.
35. ACOG committee opinion 557: Management of acute abnormal uterine bleeding in nonpregnant reproductive-aged women. *Obstet Gynecol*. 2013;121(4):891–896.
36. Wang JH et al. Opportunities and risk factors for premalignant and malignant transformation of endometrial polyps: management strategies. *J Minim Invasive Gynecol*. 2010;17(1):53–58.
37. Clark TJ et al. Endometrial Polyps, and Abnormal Uterine Bleeding (AUB-P): What is the relationship, how are they diagnosed, and how are they treated? *Best Pract Res Clin Obstet Gynaecol*. 2017;40:89–104.
38. Gordts S et al. Uterine adenomyosis: a need for uniform terminology and consensus classification. *Reprod Biomed Online*. 2008;17(2):244–248.
39. Molinas CR et al. Office hysteroscopy and adenomyosis. *Best Pract Res Clin Obstet Gynaecol*. 2006;20(4):557–567.
40. Brosens JJ et al. Endovaginal ultrasonography in the diagnosis of adenomyosis uteri: identifying the predictive characteristics. *Br J Obstet Gynaecol*. 1995;102(6):471–474.
41. Mark AS et al. Adenomyosis and leiomyoma: differential diagnosis with MR imaging. *Radiology*. 1987;163(2):527–529.
42. Togashi K et al. Adenomyosis: diagnosis with MR imaging. *Radiology*. 1988;166(1 Pt 1):111–114.
43. Di Spiezio Sardo A et al. The role of hysteroscopy in the diagnosis and treatment of adenomyosis. *Biomed Res Int*. 2017;2017:2518396.
44. Puttemans P et al. Hysteroscopic images of an isolated lesion of unknown origin in a young infertile patient. *J Minim Invasive Gynecol*. 2005;12(2):104–105.
45. McCausland V et al. The response of adenomyosis to endometrial ablation/resection. *Hum Reprod Update*. 1998;4(4):350–359.
46. Stewart EA et al. Uterine fibroids. *Nat Rev Dis Primers*. 2016;2:16043.
47. AAGL practice report: practice guidelines for the diagnosis and management of submucous leiomyomas. *J Minim Invasive Gynecol*. 2012;19(2):152–171.
48. Day Baird D et al. High cumulative incidence of uterine leiomyoma in black and white women: ultrasound evidence. *Am J Obstet Gynecol*. 2003;188:100–107.
49. Sparic R et al. Epidemiology of uterine myomas: a review. *Int J Fertil Steril*. 2016;9(4):424–435.
50. Maheux-Lacroix S et al. The need for further surgical intervention following primary hysteroscopic morcellation of submucosal leiomyomas in women with abnormal uterine bleeding. *Aust NZ J Obstet Gynaecol*. 2018;58(5):570–575.
51. Donnez J et al. Fibroid management in premenopausal women. *Climacteric*. 2019;22(1):27–33.
52. Lasmar RB et al. Submucous myomas: a new presurgical classification to evaluate the viability of hysteroscopic surgical treatment – preliminary report. *J Minim Invasive Gynecol*. 2005;12(4):308–311.
53. Vitale SG et al. Hysteroscopic treatment of submucosal fibroids in perimenopausal women: when, why, and how? *Climacteric*. 2020;23(4):355–359.
54. Friedman JA et al. Hysteroscopic myomectomy: a comparison of techniques and review of current evidence in the management of abnormal uterine bleeding. *Curr Opin Obstet Gynecol*. 2018;30(4):243–251.
55. Vitale SG et al. Innovations in hysteroscopic surgery: expanding the meaning of "in-office." *Minim Invasive Ther Allied Technol*. 2021;30(3):125–132.
56. Laganà AS et al. Management of asymptomatic submucous myomas in women of reproductive age: a consensus statement from the global congress on hysteroscopy scientific committee. *J Minim Invasive Gynecol*. 2019;26(3):381–383.
57. Loddo A et al. Hysteroscopic myomectomy: the guidelines of the International Society for Gynecologic Endoscopy (ISGE). *Eur J Obstet Gynecol Reprod Biol*. 2022;268:121–128.
58. Bettocchi S et al. A new hysteroscopic technique for the preparation of partially intramural myomas in office setting (OPPIuM technique): a pilot study. *J Minim Invasive Gynecol*. 2009;16(6):748–754.
59. Cicinelli E et al. The OPPIuM technique: office hysteroscopic technique for the preparation of partially intramural leiomyomas. *Minerva Ginecol*. 2016;68(3):328–333.
60. Capmas P et al. Surgical techniques and outcome in the management of submucous fibroids. *Curr Opin Obstet Gynecol*. 2013;25(4):332–338.
61. Lasmar RB et al. Hysteroscopic myomectomy. *Medicina*. 2022;58(11):1627.
62. Vitale SG et al. Hysteroscopic morcellation of submucous myomas: a systematic review. *Biomed Res Int*. 2017:6848250.
63. Valentine LN et al. Hysteroscopy for abnormal uterine bleeding and fibroids. *Clin Obstet Gynecol*. 2017;60(2):231–244.
64. Singh G et al. Endometrial hyperplasia. In: *StatPearls* [Internet]. Treasure Island, FL: StatPearls Publishing; 2023.
65. Emons G et al. New WHO classification of endometrial hyperplasias. *Geburtshilfe Frauenheilkd*. 2015;75(2):135–136.
66. Kurman RJ et al. The behavior of endometrial hyperplasia. A long-term study of "untreated" hyperplasia in 170 patients. *Cancer*. 1985;56(2):403–412.
67. Vitale SG et al. Risk of endometrial malignancy in women treated for breast cancer: the BLUSH prediction model – evidence from a comprehensive multicentric retrospective cohort study. *Climacteric*. 2024. https://doi.org/10.1080/13697137.2024.2376189. Epub ahead of print.
68. Tabata T et al. Natural history of endometrial hyperplasia. Study of 77 patients. *Arch Gynecol Obstet*. 2001;265(2):85–88.
69. Kolhe S. Management of abnormal uterine bleeding – focus on ambulatory hysteroscopy. *Int J Womens Health*. 2018;10:127–136.
70. Stock RJ et al. Prehysterectomy curettage. *Obstet Gynecol*. 1975;45(5):537–541.
71. Urman B et al. Fertility and anatomical outcomes following hysteroscopic adhesiolysis: an 11-year retrospective cohort study to validate a new classification system for intrauterine adhesions (Urman-Vitale Classification System). *Int J Gynaecol Obstet*. 2024;165(2):644–654.
72. Epstein E et al. Dilatation and curettage fail to detect most focal lesions in the uterine cavity in women with postmenopausal bleeding. *Acta Obstet Gynecol Scand*. 2001;80(12):1131–1136.
73. Bettocchi S et al. Diagnostic inadequacy of dilatation and curettage. *Fertil Steril*. 2001;75(4):803–805.
74. Demirkiran F et al. Which is the best technique for endometrial sampling? Aspiration (pipelle) versus dilatation and curettage (D&C). *Arch Gynecol Obstet*. 2012;286(5):1277–1282.

75. Vitale SG et al. Endometrial biopsy: indications, techniques and recommendations. An evidence-based guideline for clinical practice. *J Gynecol Obstet Hum Reprod*. 2023;52(6):102588.
76. Bettocchi S et al. Endometrial biopsies using small-diameter hysteroscopes and 5F instruments: how can we obtain enough material for a correct histologic diagnosis? *J Am Assoc Gynecol Laparosc*. 2002;9(3):290–292.
77. Vitale SG. The biopsy snake grasper sec. VITALE: a new tool for office hysteroscopy. *J Minim Invasive Gynecol*. 2020;27(6):1414–1416.
78. Bettocchi S et al. Office hysteroscopy. *Obstet Gynecol Clin North Am*. 2004;31(3):641–54, xi.
79. Hinckley MD et al. 1000 office-based hysteroscopies prior to in vitro fertilization: feasibility and findings. *JSLS*. 2004;8(2):103–107.
80. Vitale SG et al. Pain management for in-office hysteroscopy. A practical decalogue for the operator. *J Gynecol Obstet Hum Reprod*. 2021;50(1):101976.
81. Vitale SG et al. Comparison of three biopsy forceps for hysteroscopic endometrial biopsy in postmenopausal patients (HYGREB-1): a multicenter, single-blind randomized clinical trial. *Int J Gynaecol Obstet*. 2021;155(3):425–432.
82. Bradley LD. Diagnosis of abnormal uterine bleeding with biopsy or hysteroscopy. *Menopause*. 2011;18(4):425–433.
83. Georgiou D et al. Hysteroscopic tissue removal system (MyoSure) for the resection of polyps, sub-mucosal leiomyomas and retained products of conception in an outpatient setting: a single UK institution experience. *Eur J Obstet Gynecol Reprod Biol*. 2018;231:147–151.
84. Clark TJ et al. Accuracy of hysteroscopy in diagnosing endometrial cancer and hyperplasia: a systematic quantitative review. *JAMA*. 2002;288(13):1610–1621.
85. De Franciscis P et al. Concordance between the hysteroscopic diagnosis of endometrial hyperplasia and histopathological examination. *Diagnostics*. 2019;9(4):142.
86. Lécuru F et al. Performance of office hysteroscopy and endometrial biopsy for detecting endometrial disease in women at risk of human non-polyposis colon cancer: a prospective study. *Int J Gynecol Cancer*. 2008;18(6):1326–1331.
87. Sugimoto O. Hysteroscopic diagnosis of endometrial carcinoma. A report of fifty-three cases was examined at the Women's Clinic of Kyoto University Hospital. *Am J Obstet Gynecol*. 1975;121(1):105–113.
88. Di Spiezio Sardo A et al. Should endometrial biopsy under direct hysteroscopic visualization using the grasping technique become the new gold standard for the preoperative evaluation of the patient with endometrial cancer? *Gynecol Oncol*. 2020;158(2):347–353.
89. Vitale SG et al. Hysteroscopy in the management of endometrial hyperplasia and cancer in reproductive-aged women: new developments and current perspectives. *Transl Cancer Res*. 2020;9(12):7767–7777.
90. Shankar M et al. von Willebrand disease in women with menorrhagia: a systematic review. *BJOG*. 2004;111(7):734–740.
91. Dilley A et al. A survey of gynecologists concerning menorrhagia: perceptions of bleeding disorders as a possible cause. *J Womens Health Gend Based Med*. 2002;11(1):39–44.
92. Munro MG. Dysfunctional uterine bleeding: advances in diagnosis and treatment. *Curr Opin Obstet Gynecol*. 2001;13(5): 475–489.
93. American College of Obstetricians and Gynecologists. ACOG releases guidelines on the management of abnormal uterine bleeding associated with ovulatory dysfunction. *J Am Fam Physician*. 2014;89(12):987–988.
94. Wen Z et al. Clinical changes of leptin/ghrelin and PAI-1 levels in adolescent girls with abnormal uterine bleeding-ovulatory dysfunction. *Gynecol Endocrinol*. 2022;38(4):345–349.
95. Sweet MG et al. Evaluation and management of abnormal uterine bleeding in premenopausal women. *Am Fam Physician*. 2012;85(1):35–43.
96. Gleeson NC. Cyclic changes in endometrial tissue plasminogen activator and plasminogen activator inhibitor type 1 in women with normal menstruation and essential menorrhagia. *Am J Obstet Gynecol*. 1994;171(1):178–183.
97. Smith SK et al. A role for prostacyclin (PGi2) in excessive menstrual bleeding. *Lancet*. 1981;1(8219):522–524.
98. Smith SK et al. Prostaglandin synthesis in the endometrium of women with ovular dysfunctional uterine bleeding. *Br J Obstet Gynaecol*. 1981;88(4):434–442.
99. Toth M et al. Association between Chlamydia trachomatis and abnormal uterine bleeding. *Am J Reprod Immunol*. 2007;57(5):361–366.
100. Pitsos M et al. Association of pathologic diagnoses with clinical findings in chronic endometritis. *J Reprod Med*. 2009;54(6):373–377.
101. Heatley MK. The association between clinical and pathological features in histologically identified chronic endometritis. *J Obstet Gynaecol*. 2004;24(7):801–803.
102. Achanna KS et al. Evaluation and management of abnormal uterine bleeding. *Med J Malaysia*. 2022;77(3):374–383.
103. Hickey M et al. Iatrogenic unscheduled (breakthrough) endometrial bleeding. *Rev Endocr Metab Disord*. 2012;13(4): 301–308.
104. Backman T et al. Length of use and symptoms associated with premature removal of the levonorgestrel intrauterine system: a nation-wide study of 17,360 users. *BJOG*. 2000;107(3):335–339.
105. Cox M et al. Clinical performance of the levonorgestrel intrauterine system in routine use by the UK Family Planning and Reproductive Health Research Network: 5-year report. *J Fam Plann Reprod Health Care*. 2002;28(2):73–77.
106. Lohr PA et al. Oral contraceptives and breakthrough bleeding: what patients need to know. *J Fam Pract*. 2006;55(10):872–880.
107. Samuelson Bannow B et al. Menstruation, anticoagulation, and contraception: VTE and uterine bleeding. *Res Pract Thromb Haemost*. 2021;5(5):e12570.
108. Riemma G et al. Hysteroscopic criteria for the diagnosis of chronic endometritis: a systematic review and diagnostic test accuracy meta-analysis. *Am J Obstet Gynecol*. 2025;233(1):12–24.e4.
109. Kremer TG et al. Isthmocele: an overview of diagnosis and treatment. *Rev Assoc Med Bras* (1992). 2019;65(5):714–721.
110. Vitale SG et al. Surgical and reproductive outcomes after hysteroscopic removal of retained products of conception: a systematic review and meta-analysis. *J Minim Invasive Gynecol*. 2021;28(2):204–217.
111. Vitale SG et al. Virtual sonographic hysteroscopy in assisted reproduction: a retrospective cost-effectiveness analysis. *Int J Gynaecol Obstet*. 2022;156(1):112–118.
112. Chiofalo B et al. Reproductive outcomes of infertile women undergoing "see and treat" office hysteroscopy: a retrospective observational study. *Minim Invasive Ther Allied Technol*. 2021;30(3):147–153.

28 HYSTEROSCOPY AND MÜLLERIAN ANOMALIES

Maria Chiara De Angelis, Virginia Foreste, Alfonso Manzi, Alessandra Gallo, Serena Guerra, Brunella Zizolfi, and Attilio Di Spiezio Sardo

28.1 Introduction

Congenital anomalies of the female genital tract are alterations in embryonic development due to an interruption or deviation in the ontogenesis of individual organs of the reproductive tract, or of any part thereof (1, 2). The etiology of these anomalies is unknown (2). Various hypotheses have been proposed, related to genetic alterations, hereditary factors, and exposure to exogenous noxae including environmental pathogens (3). The prevalence of congenital anomalies of the female genital tract, whether in the general population, in the infertile patient group, or in women with recurrent pregnancy loss, is difficult to establish with certainty. Their diagnosis involves the use of various modalities based on different technical equipment and nonspecific clinical criteria, which also makes it difficult to compare data from different centers (4, 5).

28.2 Classification of Müllerian Anomalies

The first international classification of congenital anomalies of the uterus was done in 1979 by Buttram and Gibbons, based on their ontogenetic and morphological appearance (6). This system was revised in 1983 and again in 1988 by the American Fertility Society (AFS) (7). The AFS classification system distinguishes between seven classes that are based on the degree of uterine anomalies and grouped according to reproductive prognosis and therapeutic options. One of the limitations of the AFS classification is that it does not specify diagnostic modalities or the criteria that should be applied to assign a uterine anomaly to a specific class. Apart from that, the classification system does not include all uterine anomalies diagnosed to date. For this reason, the classification of the AFS serves merely as a first step for describing the anomalies in question, rather than being considered an exhaustive list of all possible existing anomalies.

Consequently, the clinician faced with a complex or combined uterine abnormality should describe it based on individual components, rather than trying to assign it to a specific category. This concept has been developed further into another classification system, proposed by Oppelt et al. (8): the "VCUAM" classification. This new system allows for the description of a complex anomaly by referring to its individual components, based on the structure involved, such as vagina (V), cervix (C), uterus (U), adnexa (A), or an associated malformation of other organs (M).

In 2013, a joint task force, the Congenital Uterine Anomalies (CONUTA) working group of the European Society of Human Reproduction and Embryology (ESHRE) and the European Society of Gynecological Endoscopy (ESGE), issued a new classification system for female genital tract congenital anomalies, which is primarily based on uterine anatomy with cervical and vaginal anomalies being independently addressed in supplementary subcategories (9).

In this chapter we will refer to the 2013 ESHRE/ESGE classification (10), which, to date, is the one most widely used in clinical practice.

28.3 Clinical Implications

The diagnosis of Müllerian anomalies is often coincidental. They may be identified in the course of an examination for infertility or during investigations performed in patients with endometriosis, either suspected or whose presence has recently been established (11). Occasionally, the diagnosis is established in an emergency, when a patient presents with both pelvic pain and cryptomenorrhea (the apparent absence of menstruation, which occurs but cannot drain out). With a certain frequency, diagnosis of genital anomalies may be established during a primary clinical examination or on an ultrasound examination done in early pregnancy (12).

28.3.1 Uterine Anomalies

Anomalies of the uterine corpus, taken as a whole, are associated with pathologies and/or obstetrical complications of great clinical importance, such as miscarriage and preterm labor, abnormal presentation, perinatal mortality, toxemia in pregnancy, growth retardation, and cervical incontinence. According to a recent study investigating pregnancy in patients with uterine anomalies, they are burdened with an increased risk of gestational hypertension, probably resulting from abnormal vascularization (4, 13).

Class U1 encompasses a variety of symptoms including dysmenorrhea, pelvic pain, and obstetric complications such as miscarriage and preterm delivery, depending on the type of malformation and its subentity.

Class U2, among all others, is associated with the highest rate of gestational complications, such as miscarriage in the first and second trimester, preterm delivery, fetal anomalies, and impaired intrauterine fetal growth with increased rate of cesarean sections. The incidence of miscarriage ranges from 60% to 90% in all pregnancies depending on case history, with spontaneous abortion commonly occurring between the 8th and 16th week of gestation. Class U2 anomalies are also associated with an elevated rate of primary infertility. Some recent studies have found endometrial alterations in women with septate uterus, both at a structural and ultrastructural level, as well as vascular compromise at the site of embryo implantation, particularly when occurring at the septal level.

Class U3 is associated with a high rate of miscarriage and preterm delivery.

Class U4 is characterized by a low reproductive performance as well as an elevated rate of miscarriage and preterm delivery. However, the reproductive performance of the different types of hemiuterus is variable and determined by the degree of vascularization of the uterine horn, the extent to which the musculature of its walls is reduced, and the degree of cervical incompetence and concomitant pathologies. In some cases, the U4 uterine malformation is accompanied by symptoms of hematometra, pelvic pain, menstrual irregularities, and/or dysmenorrhea.

Class U5 includes mostly asymptomatic or mildly symptomatic cases and is often diagnosed after examinations performed

DOI: 10.1201/9781003312109-28

for primary amenorrhea or following diagnostic clarification of associated diseases, frequently affecting the urinary tract.

28.3.2 Anomalies of the Uterine Cervix

The absence of a functioning cervix in the presence of a normal uterus gives rise to a symptomatology related to retained menstrual blood resulting from an obstructed outflow: absence of menarche with concomitant cyclic pelvic pain (4).

28.3.3 Vaginal Anomalies

The double vagina, or the presence of longitudinal septa, whether complete, partial, or partially transverse, often constitutes a random finding made during a gynecological examination scheduled for other disorders or performed during pregnancy. In some cases, such anomalies are associated with leucorrhea, cryptomenorrhea, recurrent vaginal infections, dyspareunia, or postcoital bleeding (4).

28.4 Diagnosis

28.4.1 General Overview

For definitive diagnosis of Müllerian anomalies, it is necessary to visualize both the internal and external uterine contour. Various diagnostic modalities have been utilized for uterine anomalies, each one having its own advantages and limitations (14–19).

If faced with the suspicion of uterine anomalies, double vagina, or longitudinal vaginal septa, it is also useful to examine the urinary tract, given their common embryological origin. Depending on the type and severity of the anomaly, 5% to 55% of affected women have a coexisting anomaly of the urinary tract. In general, it can be said that the more serious the anomaly of the uterovaginal tract, the more frequent the finding of concomitant urinary tract anomalies.

28.4.1.1 Hysterosalpingography (HSG)

Hysterosalpingography is a cost-effective technique of evaluating the uterine cavity for diagnosis of uterine anomalies. The advantage of hysterosalpingography is that it provides additional information of fallopian tube patency. The drawback of HSG is that it does not give any information about external uterine contour. To overcome this, additional modalities, such as 3D ultrasound, may be required for making a definitive diagnosis (Figure 28.1) (19).

28.4.1.2 Transvaginal Sonography (TVS), Three-Dimensional Ultrasound Imaging (3D US)

According to several authors, TVS is the first-line diagnostic modality in the assessment of uterine morphology and function and is also used for intraoperative monitoring during surgical treatment. Similarly to HSG, transvaginal sonography can diagnose uterine anomalies of classes U4 and U5. Moreover, in the case of a "double" uterus, it provides more information as compared to HSG, allowing to examine the morphology of the fundus and adnexa. With its high sensitivity and reproducibility, 3D US has become the current gold standard for diagnosis of uterine malformations (Figure 28.2).

It has been estimated that 3D US has a diagnostic accuracy greater than 90%, particularly for the diagnosis of a septate

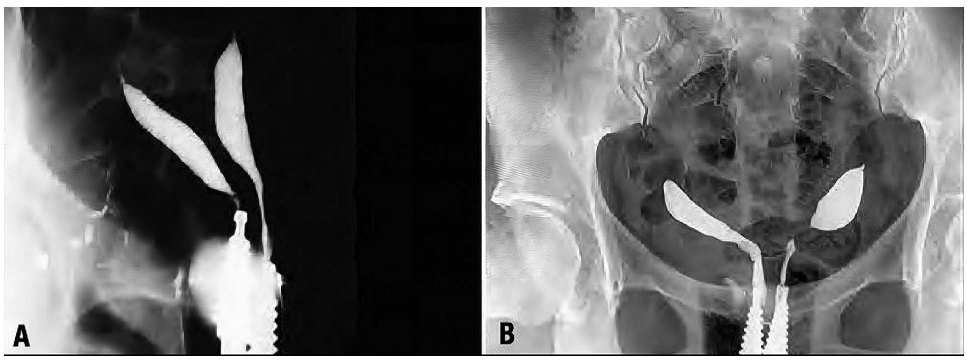


FIGURE 28.1 Hysterosalpingography: a complete septate uterus (A) and a bicorporeal uterus (B).

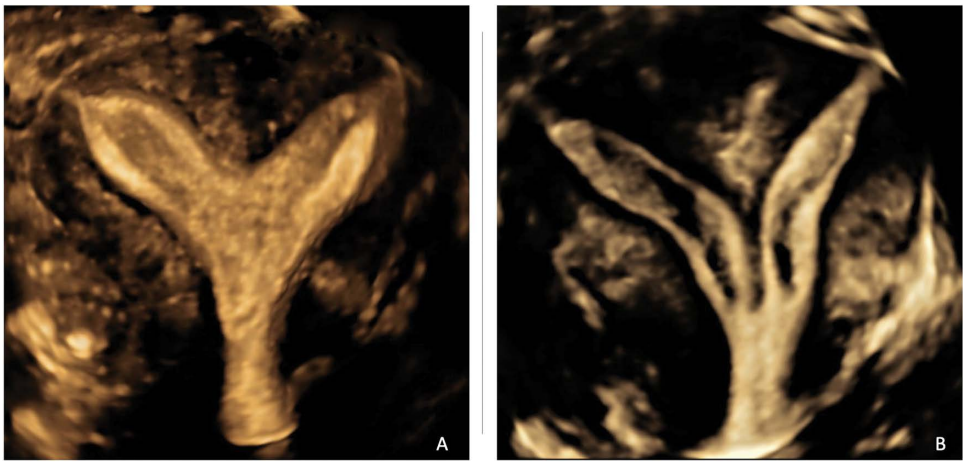


FIGURE 28.2 3D ultrasound images. Partial septate uterus (Class U2a) (A) and complete septate uterus (Class U2b) (B).

uterus. Three-dimensional ultrasound also allows for the measurement of length and thickness of a suspected septate uterus, or even to quantify the cavitary volume. The introduction of appropriate and widely accepted criteria bears the potential of enhancing the precision of ultrasound diagnosis (17, 18).

28.4.1.3 Sonohysterography (SHG)

Sonohysterography provides a good view of the uterine cavity and is associated with only moderate costs. This diagnostic modality has recently become even more widely accepted owing to excellent results related to the use of 3D ultrasound (virtual hysteroscopy), particularly when performed with a gel that promotes a longer deposition of the ultrasound contrast fluid in the uterine cavity (15).

28.4.1.4 Magnetic Resonance Imaging (MRI)

Among all third-level examinations, MRI not only allows for the effective establishment of an accurate classification of the anomaly, but also for the identification of any possible concomitant gynecological and extragenital pathology. MRI, however, is still not a primary diagnostic modality used on a routine basis because of its high costs and the fact that it is not readily available in the daily clinical practice (16).

28.4.2 Hysteroscopic Diagnosis

Hysteroscopic examination in the presence of suspected anomalies must always be performed in the first phase of the menstrual cycle; indeed, a thickened endometrium can make it difficult to visualize the entire uterine cavity, and, in the case of a double cavity, it is hard to identify the median septum and its main features in terms of texture, color, and vascularity. Moreover, access to both hemicavities can be extremely challenging. A thickened endometrium may also disguise any communication with a rudimentary accessory horn. The hysteroscopic examination can be divided into three stages: vaginoscopy, examination of the uterine cervix, and examination of the uterine cavity (4).

- *Stage I*: Inspection of the vaginal canal through a vaginoscopic approach is of crucial importance in cases of suspected congenital anomalies of the genital tract; it allows for the investigation of the morphology and size of the vaginal canal, along with an identification of any septa (Figure 28.3).

FIGURE 28.3 Partial longitudinal vaginal septum under hysteroscopic examination performed using liquid distension medium.

- *Stage II*: The second stage of hysteroscopic examination includes a detailed assessment of the position, morphology, and size of the uterine cervix (Figure 28.4).

The four vaginal fornices are identified by use of a panoramic view of the cervix. In case of doubling of the uterine cervix, the two cervices are visualized at a certain distance from each other, allowing for the identification of their contours. When faced with two clearly distinguishable cervical canals, in the differential diagnosis between single cervix with a cervical septum versus the presence of a double cervix, the anatomic criteria described previously are valuable (double cervix, both cervices are competent and spread apart; hemicervices that are ipsilaterally deflected, or presenting with contours that cannot be readily identified as a whole). Hysteroscopy, in these cases, may only provide a tentative diagnosis of cervical anomalies, prompting referral of the patient for MRI evaluation or more invasive diagnostic procedures. However, cervical anomalies, in the presence of a uterine cavity with intact physiological function, are extremely rare finds.

- *Stage III*: Beyond the internal uterine ostium, in the uterine cavity, hysteroscopic evaluation is focused on morphology, size, and shape of the fundus, as well as on the number and characteristics of the tubal ostia. A reduced intertubal distance is suggestive of a uterine cavity with "tubular" or hypoplastic morphology; conversely, an extended intertubal distance in the longitudinal uterine axis may be a clue to a T-shaped uterus, while a more or less pronounced fundus should raise the suspicion of a subseptate. Failure to visualize a tubal ostium should prompt the tentative diagnosis of hemiuterus. In such cases, at the level of the uterine isthmus, the operator should search for a rudimentary horn that is communicating with the main cavity. Moreover, in the presence of this finding, a detailed ultrasound examination of the uterine cavity is indicated accessorily to complement the hysteroscopic findings. In fact, a suspected hemiuterus could actually prove to be a "double" uterus, since in some cases of dual cavities, it has shown to be very difficult to gain access to one of them. In such cases, a panoramic view should permit the quantification of the dimensions of septation by comparing its length with the longitudinal diameter of the uterus, e.g., estimated as less than 0.5 cm or equal to about 1/3, 2/3, or 3/3 of the cavity (Figure 28.5).

28.5 Treatment

28.5.1 General Overview

The treatment of Müllerian anomalies certainly involves a surgical approach. Already in 1974, the endoscopic technique proposed by Edstrom revolutionized the approach to this pathology (20). This type of surgery still today attracts the greatest surgical interest since with a minimally invasive procedure performed via the transcervical route, it is possible to obtain excellent results. In fact, the treatment of most of Müllerian anomalies is the most accessible surgical interventions for hysteroscopic approach, which therefore represents today the gold standard in the treatment of Müllerian anomalies amenable to surgical correction (21–23). Over time, different methods and instruments have been used for the hysteroscopic management of Müllerian anomalies, associated with greater benefits than

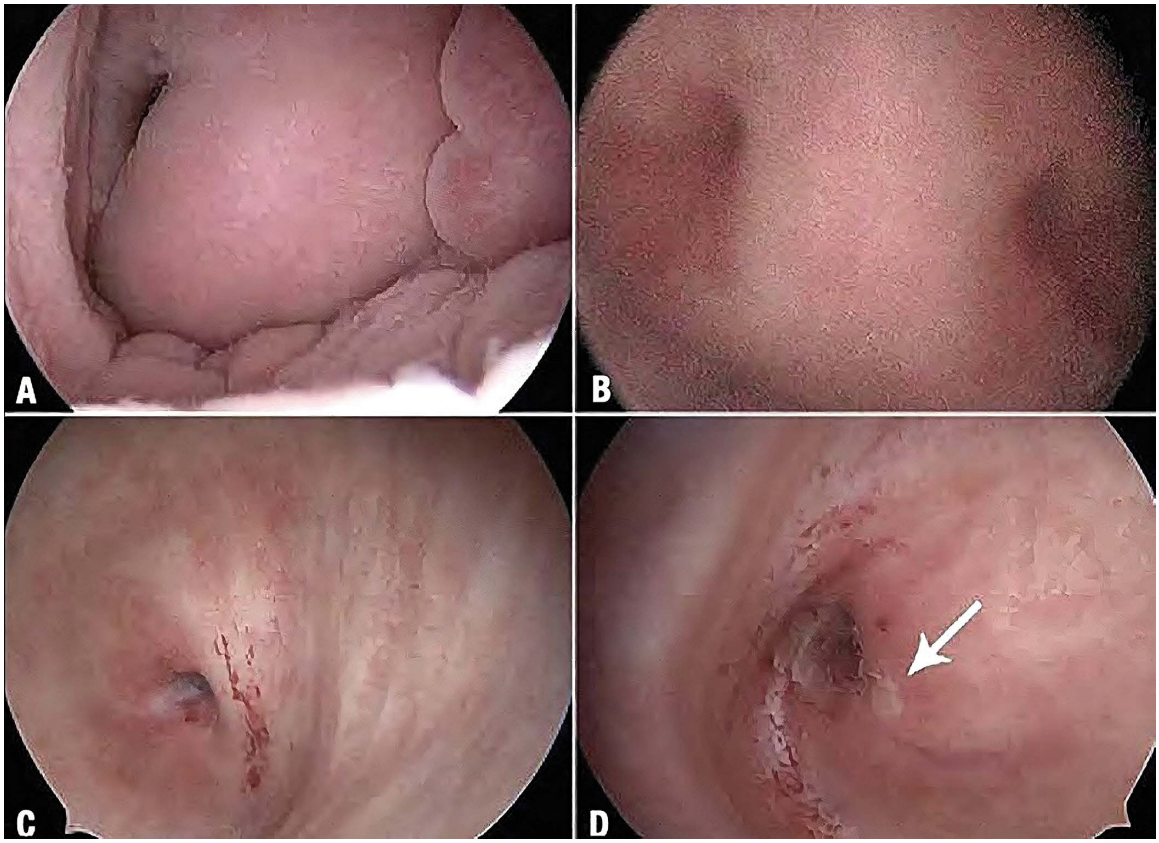


FIGURE 28.4 Uterine cervix under hysteroscopic examination using a liquid distension medium. Single incompetent cervix, laterodeviated toward the right (A). Single cervix, or normal volume, presenting with well-defined contours and a thick central septation (B). Longitudinal vaginal septum with two hemicervices (C–D); visibility of an identification mark (arrow) placed on the exocervical surface with a bipolar electrode allows for the confirmation of the presence of two distinct cervical canals.

those yielded via laparoscopy or laparotomy. Some authors have reported an effective and safe treatment for this pathology even in an office setting (24, 25). In any case, whether it is performed in the operating room or in an outpatient setting, the success of the treatment depends on accurate diagnosis and the choice of the best technique.

28.5.2 Uterine Anomalies

Not all congenital uterine anomalies require treatment. While a unicornuate uterus does not always justify surgery, in case of malformations due to fusion or unification defects, such as a septate or dysmorphic uterus, surgery becomes useful. However, despite remaining a highly controversial topic, many studies have confirmed the benefits of the hysteroscopic treatment of class U1 and U2, according to the ESHRE/ESGE classification system, to improve reproductive outcomes (26, 27).

The procedure is usually performed in the early proliferative phase, without any pharmacological preparation of the endometrium. Nevertheless, we often have to deal with a dysmorphic uterus with a very small volume or with a septate uterus where the two hemicavities are very narrow spaces and therefore every movement is much more complicated. In these situations, the presence of a thickened endometrium or profuse bleeding can represent a further obstacle to a clear vision, not allowing correct identification of the median plane in the case of a septum (4). For this reason, some surgeons recommend a preoperative treatment with GnRH analogues, estrogen progestin or progestogen alone, to obtain a significant decrease in both endometrial thickness and intraoperative blood loss.

New studies are demonstrating the possibility that some benefit may also be related to microscopic changes in the endometrium, such as the expression of endometrial receptivity genes. However, what is certain is that hysteroscopic metroplasty leads to an increase in uterine volume and the optimization of uterine morphology (28).

Starting from this consideration, we provide next a description of all the possible surgical techniques with the related instrumentation used in the treatment of the different uterine malformations.

28.5.2.1 Class U1 Anomalies: Dysmorphic Uterus

Over time, different methods and techniques for achieving surgical correction of dysmorphic uterus have been developed. Recent surgical innovations in hysteroscopic surgery have allowed the treatment of this malformation, thus avoiding laparotomy and resulting in lower morbidity. The technique is the same, whatever the tool used. Longitudinal lateral incisions are performed on the fibrotic or fibromuscular stenotic rings in the isthmic area, along the main axis of the uterine cavity, with a 5 Fr bipolar electrode, scissors, or a 15 Fr bipolar electrode (4). The aim is to decrease the centripetal force of muscle fibers and of fibromuscular rings that lead to stenosis.

The advances of this minimally invasive technique, making it less painful and less invasive, have increased the safety

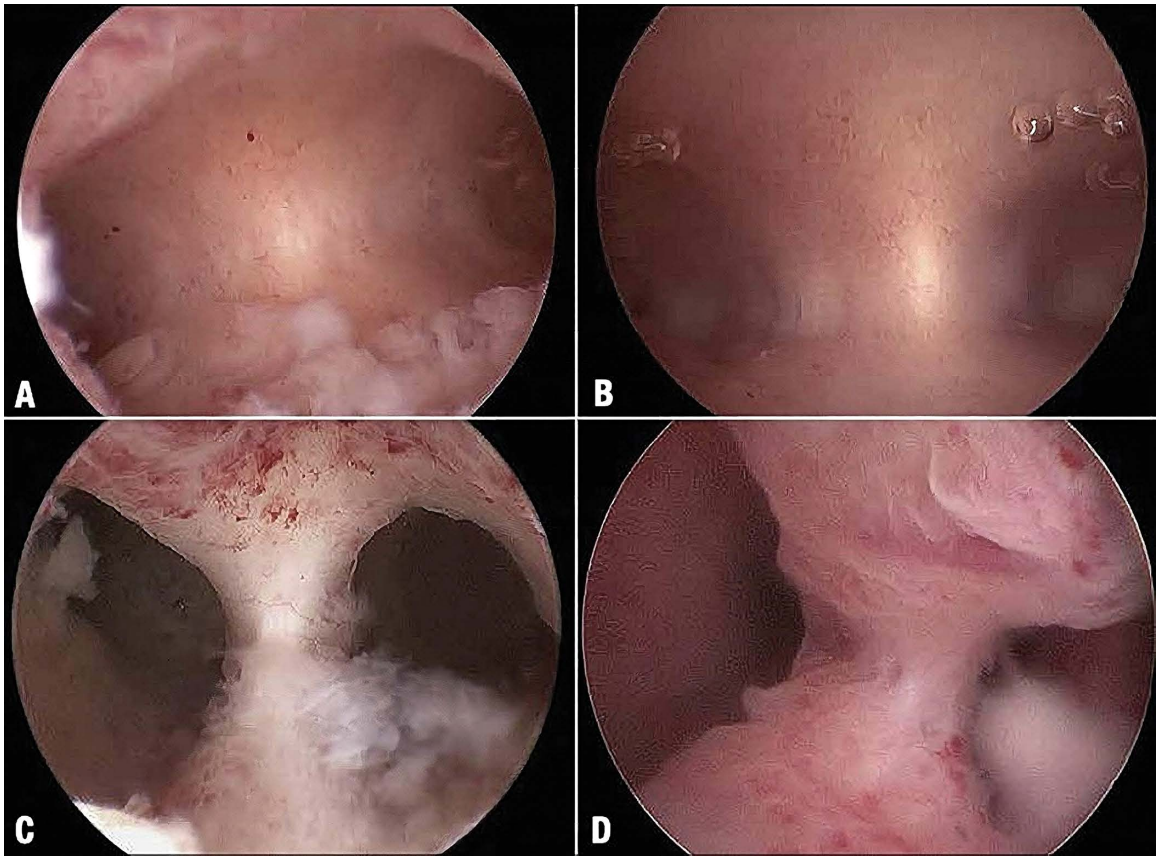


FIGURE 28.5 A double uterine cavity of < 0.5 cm (A), 1/3 (B), 2/3 (C), and 3/3 (D) of its length under hysteroscopic examination using a liquid distension medium; the endocervical mucosa presented in (D) serves as a clue that one tract of the endocervical canal is involved in the septation. 3D ultrasound, in this case, furnished evidence of a subseptate uterus (A–C) and complete septate uterus with involvement of the cervix (D).

and efficacy of also treating this kind of pathology outside the operating room. Indeed, in 2014 Di Spiezio et al. described an outpatient technique for dysmorphic uteri, the HOME-DU technique: hysteroscopic outpatient metroplasty to expand dysmorphic uteri (29). The procedure was performed under conscious sedation, on day 6–10 of the menstrual cycle. With a 30° fore-oblique hysteroscope, using a vaginoscopic approach and a stable intrauterine pressure of about 40 mmHg, the surgeon made two incisions 3–4 mm in depth, placing a 5 Fr bipolar electrode parallel to the lateral uterine walls. Other symmetrical incisions were made on the anterior and posterior wall, from the fundus up to the isthmus, without exceeding 5–6 mm in depth. At the end of all the procedures, an antiadhesive gel is applied into the uterine cavity, through the inflow channel of the hysteroscope, to minimize postoperative intrauterine adhesions.

Currently, another treatment option is available for dysmorphic uteri, which involves the use of a mini-resectoscope (15 or 16 Fr) (25). Using both a pointed electrode and a cutting loop, meticulously orienting them against the lateral wall, the surgeon performs longitudinal incisions along the main axis of the uterine cavity, starting from the caudal part until the isthmus (Figure 28.6).

Using the cutting loop, it is possible not only to incise the isthmic stenotic rings but also to resect all fibrotic or fibromuscular tissue (Figure 28.7B–D).

When faced with a Y-shaped uterus, the procedure is the same; the surgeon will add the section of the septum to the incisions on the lateral wall.

A study conducted by Bilgori et al. described hysteroscopic metroplasty for dysmorphic T- or Y-shaped uterus performed under general anesthesia in an ambulatory setting, using diode laser (30). They demonstrated that hysteroscopic metroplasty using diode laser is a safe, simple, and effective procedure, improving reproductive outcomes in cases of T-shaped or Y-shaped dysmorphic uterus, but longer follow-up and larger controlled studies are needed to confirm its impact on reproductive outcomes.

28.5.2.2 Class U2 Anomalies: Septate Uterus

Although septate uterus is associated with the highest rate of infertility, the indication for surgical treatment of this uterine malformation is still a matter of debate, mainly due to the lack of randomized controlled trials for which it is not possible to draw up guidelines (31).

According to most authors, given the minimally invasive nature and effective simplicity of the procedure, together with the significant improvement in reproductive outcomes it may provide, metroplasty could be considered as a treatment option even in the absence of negative reproductive history. Besides, the presence of uterine anomalies is often associated with symptoms such as dysmenorrhea which seem to reduce when a metroplasty is performed.

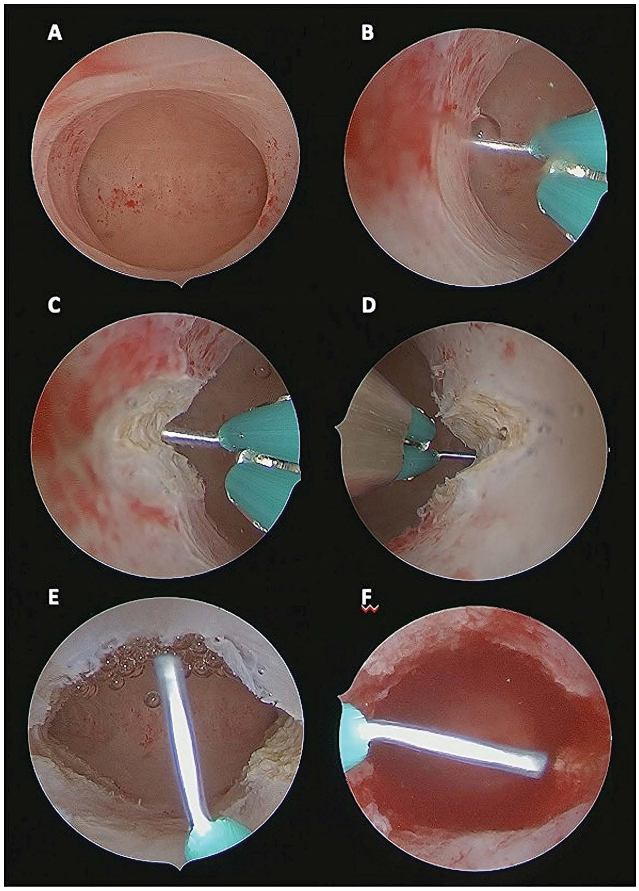


FIGURE 28.6 Hysteroscopic view of a T-shaped uterus with stenotic isthmic rings (A); with a 15 Fr bipolar resectoscope, using a pointed electrode (KARL STORZ, Germany), a longitudinal incision of fibrotic tissue is performed (B, C); the same maneuver is performed on the contralateral wall (D). At the end of procedure, positioning the hysteroscope at uterine isthmus, both tubal ostia are now visible (E); finally, auto-cross-linked hyaluronic acid gel is inserted under direct visualization into the uterine cavity (F).

Before hysteroscopy became the gold standard technique, treatment of the uterine septum was performed by abdominal surgical approach. To date, the hysteroscopic technique has allowed for a vaginal approach to correct a septum, providing several advantages such as simple and short surgery with a shorter hospitalization time, a shorter interval before conception (3–6 months), a lower risk of uterine rupture during future pregnancies, and the possibility of planning a vaginal birth.

Currently there are different tools and different techniques available to treat septate uterus (32). The surgical technique consists in incision of the septum, staying at the middle plane of the septum itself. It is the only hysteroscopic procedure in which an anterograde movement is performed, therefore starting from the apex and proceeding gradually towards the fundus.

The hysteroscopic approach to a septate uterus raises the major issue of deciding when to stop the incisions, to avoid any immediate or late complication such as perforation or subsequent uterine rupture, respectively. Generally, when both tubal ostia are clearly and simultaneously visible, or when the myometrial venous sinuses become visible, the procedure can be considered complete (33). However, basing only on these criteria, an undertreatment of the anomaly is possible. A surgeon's subjective assessment of the completeness of resection and a lack of standardized pre- and postoperative evaluation of the uterine cavity are the main causes of the persistence of a residual septum. Starting from this consideration, Di Spiezio et al. demonstrated that presurgical 3D transvaginal ultrasonography in combination with a novel, graduated intrauterine palpator introduced through the working channel of the hysteroscope, improves the accuracy of hysteroscopic metroplasty, allowing complete removal of a uterine septum in one surgical step. Introducing objective intraoperative criteria, they suggested that the metroplasty should be stopped and considered optimal when the resected septum ([Z + Y] – 1.0 cm) corresponds to the presurgical ultrasonographic measurements and a fundal notch measuring no more than 10 mm is obtained (34).

28.5.2.2.1 Resectoscopic Treatment

The traditional resectoscopic treatment with a 26 Fr resectoscope can be applied, using a straight cutting loop or a Collins electrode, starting to remove the septum from the medial portion and continuing with well-directed smooth lateromedial movements of the cutting loop, with the hook oriented perpendicular to the septum.

Then, during the anterograde movements, in case of a thick septum, the resection proceeds in a laterolateral direction, from one uterotubal horn towards the other. In proximity of the base of the septum, it may be helpful to engage the fibrotic tissue with the pointed electrode and to continue retrograde resection.

Resectoscopic metroplasty was once performed under laparoscopic guidance; performed primarily to evaluate the morphology of the uterine fundus; laparoscopy is also used during surgery with the flawed idea that is it possible to control the depth of resection using the varying intensity of the transilluminated spot while advancing the hysteroscope toward the fundus.

To date, modern ultrasound has well replaced laparoscopy. By studying the morphology of the uterine fundus, US allows for the obtaining of an accurate preoperative diagnosis, as well as guides the surgeon during the procedure. However, laparoscopy remains useful in case it is necessary to evaluate associated pelvic pathologies.

28.5.2.2.2 Treatment with Miniaturized Instruments

The possibility of performing a metroplasty with miniaturized instruments, such as bipolar electrodes, scissors, and mini-resectoscope, both under general anesthesia and in an outpatient setting, represents an effective alternative to the traditional resectoscope, especially as it avoids the need for cervical dilatation.

The same rules are applied in case of treatment of uterine septa using miniaturized instruments. The bipolar electrode is operated in pulsed mode, from the apex to base along the median plane of the septum and proceeding from one side of the septum to the other with laterolateral movement, to gradually obtain a smooth outcome of resection. When the removal of 3/4 of the septum has been achieved, miniaturized scissors are introduced through the operative channel, replacing the bipolar electrode and allowing a neat finish of resection (Figure 28.8).

The 15 Fr resectoscope allows for the use of the same classic surgical maneuvers, substantially simplifying the technique, with no loss in effectiveness as offered by a classic resectoscope

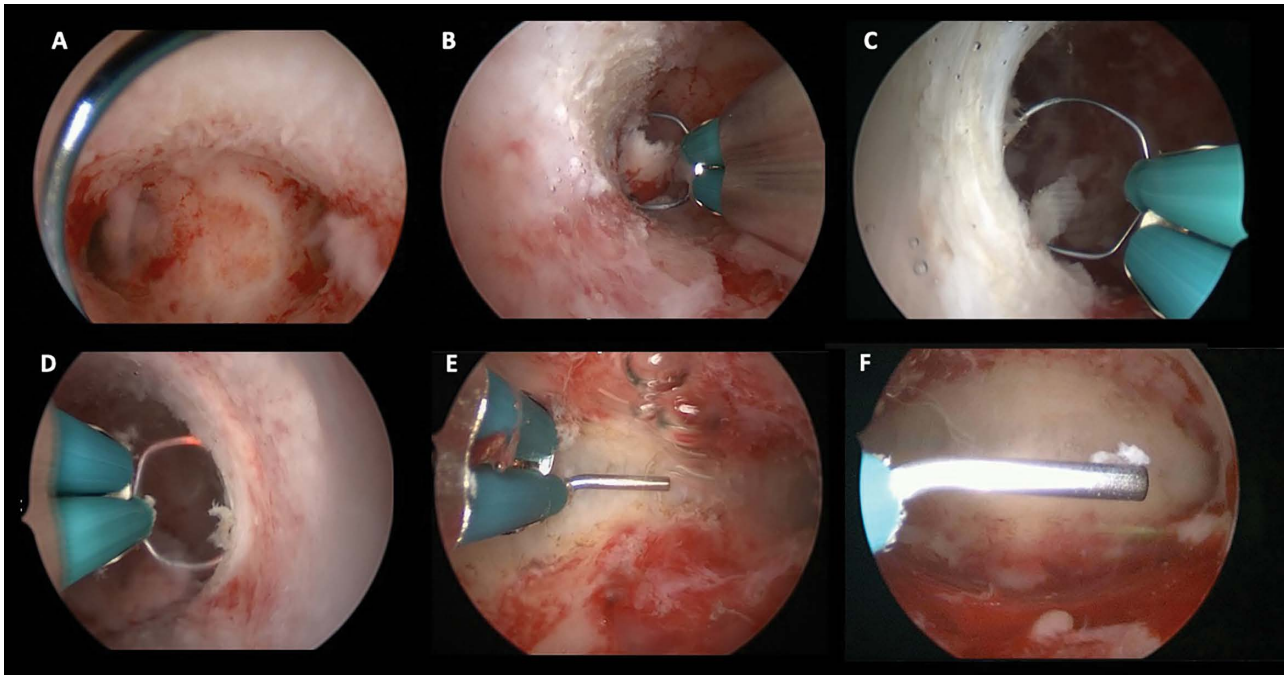


FIGURE 28.7 Hysteroscopic examination demonstrating a Y-shaped uterus, stenotic isthmic rings with the combined presence of a partial uterine septum (A); using a 15 Fr resectoscope with angle cutting loop (KARL STORZ, Germany), the fibrotic tissue on right lateral walls is removed through the standard slicing technique (B, C); the same procedure is performed on the contralateral wall (D); switching to pointed electrode, a section of the septum on the midline is performed, proceeding from the apex to the base (E); at the end of procedure, both tubal ostia are easily visible (F).

and offering significant savings in surgical time. Using a pointed electrode, dissection of the uterine septum is gradually performed from the apex up to the fundus, always keeping a symmetric distance between the anterior and the posterior wall.

Thanks to its small caliber offering more ergonomic movements, a mini-resectoscope may be used as well for the outpatient treatment of some septa without using anesthesia. Another strength of this device is the possibilities of adapting a bridge with a working channel to the hysteroscope; in this way, it gives the option of introducing 5 Fr miniaturized scissors in final stages, facilitating thickness trimming of the remaining fundal tissue and allowing for precise finishing of the resection.

Considering the recent histological studies on the composition of septum, using a mini-resectoscope it is possible to perform a modified technique of hysteroscopic metroplasty, as proposed by Fascilla et al. (35) When the entire septum has been dissected, the pointed electrode is replaced with angle cutting loop to resect the anterior and posterior fibrotic tissue (Figure 28.8E).

The large and growing diffusion of tissue removal devices has also prompted their use in the field of uterine malformations. However, very few cases are reported in the literature; therefore, it is not possible to define their effectiveness in metroplasty procedures (36).

There is yet another type of hysteroscopic metroplasty using diode laser. Tissue vaporization and coagulation obtained using this technique allows for the rapid elimination of the uterine septum without affecting the underlying myometrium, thus demonstrating extreme precision of cutting, precise control of tissue vaporization, controlled penetration power, a high capacity of hemostasis, and high safety. Optimal patient compliance was associated with metroplasty performed by laser, thanks to the possibility of being performed in an office setting without the need for cervical dilatation. Nappi et al. highlighted that the very high precision of laser vaporization allowed the surgeon to remove the septum while avoiding the stimulation of sensitive nerves inside the myometrium (37). This resulted in exceptionally low patient-reported pain scores and therefore good patient compliance during the surgery.

Another great advantage of using the laser in metroplasty is the reduced formation of adhesions and therefore the consequent reduction of the persistence of the septum after the procedure. In 2022 Manchado et al. concluded that office hysteroscopic metroplasty for septate uterus using diode laser appears to be a feasible and safe alternative to other techniques and has sufficient efficacy in terms of reproductive outcomes to be considered for further investigations (38).

There is a consensus among experts that hysteroscopic follow-up should be scheduled between the first and second month after surgery. There is controversy about the management of a residual septum detected on hysteroscopic follow-up. Some authors suggest that women of advanced reproductive age with recurrent pregnancy loss may benefit from a removal of smaller residual spurs of tissue, while others maintain that a remnant spur <1 cm in size does not affect reproductive outcomes. According to recent study, a remodeling of the uterine fundus with modifications of its external and internal profiles can be observed after metroplasty. Therefore, Casadio et al. propose to always perform a second ultrasound look at least 3 months after the metroplasty to identify cases that require a second-step metroplasty (39). Although the available evidence suggests that the uterine cavity is healed by 2 months postoperatively, there is insufficient evidence to advocate a specific length of time before a woman should conceive.

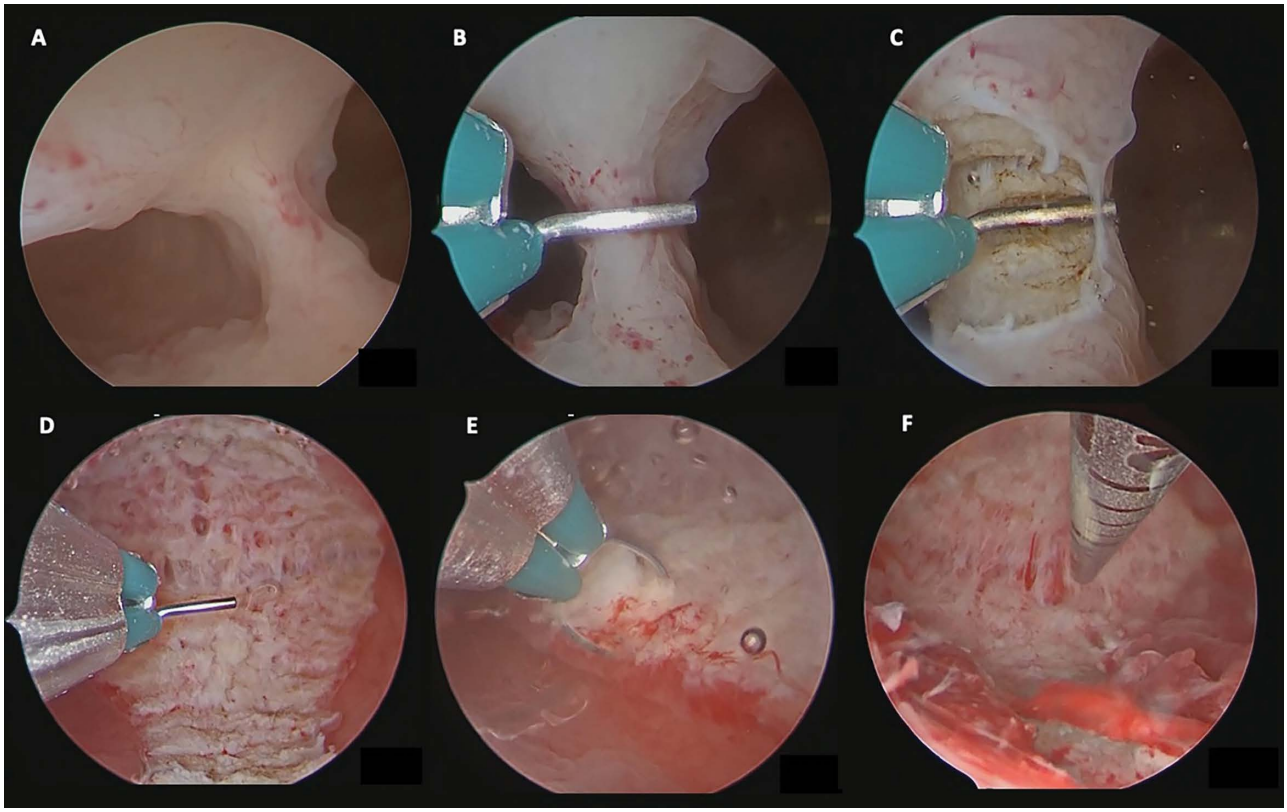


FIGURE 28.8 At diagnostic hysteroscopy, a complete uterine septum is observed (A). With 15 Fr bipolar resectoscope, using a pointed electrode (KARL STORZ, Germany), a gradual section of the septum is performed on the midline, from the apex of the septum to the fundus (B–D). Then, the pointed electrode is replaced with a classical angled cutting loop to remove residual fibrotic tissue on anterior and posterior wall by performing a slicing technique (E). In the final stage, by replacing the inner sheath of the resectoscope with a telescope bridge (KARL STORZ, Germany), an intrauterine palpator is inserted through the operative channel of the telescope bridge itself to objectively measure the length of the septum removed (F).

Metroplasty is one of the most adhesiogenic procedures (40). For this reason, there is broad consensus regarding the routine use of intrauterine barrier devices, such as antiadhesive gel applied into the uterine cavity through the inflow channel of the hysteroscope and antibiotics or hormone therapies to minimize the risk of postoperative intrauterine adhesions and/or to promote rapid endometrial reepithelialization. Synechiae can usually be easily removed during a routine office follow-up examination.

28.5.3 Cervical Anomalies

Currently, there is no consensus on the best treatment in case of a complete uterine septum associated with cervical anomalies (41, 42). While hysteroscopic uterine septum resection in symptomatic patients has been widely adopted due to well-recognized surgical and reproductive outcomes, doubts still exist regarding whether to treat a cervical septum. Indeed, a traditional approach calls for excluding the cervical canal from any resection to reduce the risk of secondary cervical incompetence, thus initiating resection from the isthmic portion of the septum, as will be described in the last paragraph. On the other hand, some authors suggest resecting both the intrauterine and the cervical septum in a single procedure, also facilitating corporeal metroplasty. This approach provides for a resectoscopic removal of the cervical septum, which is resected together with the uterine septum using the classic technique, without any increase in cervical incompetence associated with the treatment (43).

Nowadays, only few reports describing the treatment of cervical septum and double cervix associated with complete uterine septum are available in the literature, and there is still a lack of data regarding reproductive outcomes related to any treatment. For these reasons, the presence and subsequent management of cervical anomalies is still to be investigated.

28.5.4 Vaginal Anomalies

Although most vaginal anomalies are surgically corrected via the traditional laparoscopic or laparotomic approach, some recent studies have shown that some vaginal anomalies can be effectively and safely treated via hysteroscopic approach. The enlarged video and the distended vaginal cavity allow for a greater level of safety during the resection of the septum, avoiding iatrogenic injury of the rectum and bladder.

28.5.4.1 Longitudinal Septum: Classes V1–V2

Several surgical techniques using the vaginal route have been proposed to correct this anomaly (44). However, they require the introduction of large surgical instruments inside the vagina, which is often unacceptable mostly in virgin patients. Starting from this consideration, some authors have presented innovative minimally invasive hysteroscopic approach that resulted in successful restoration of the vaginal anatomy. First, the application of Kelly or Kocher forceps is essential to obtain adequate distension of the vagina. Once vaginal septum is identified, operative vaginoscopy is performed. As for the uterine septum, as well as for the vaginal one, the surgical technique is similar, what changes is the instrument that can be used. The resectoscopic approach involves serial meticulous resection of the

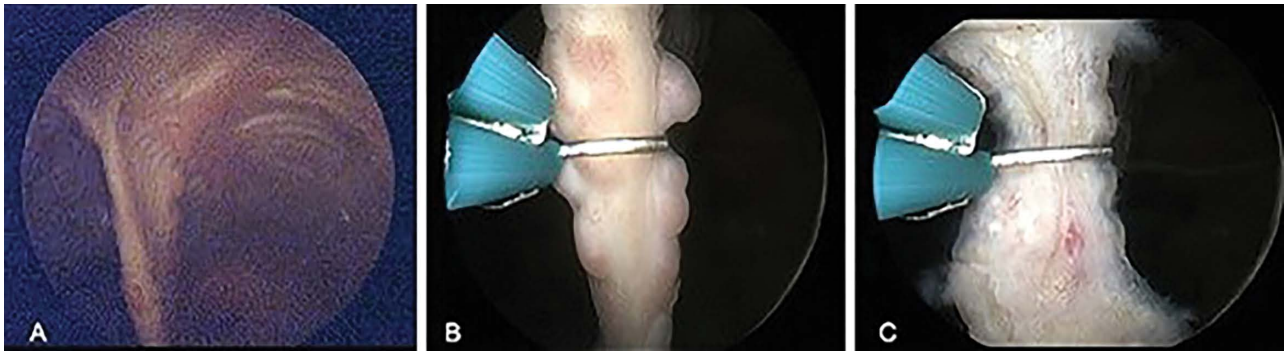


FIGURE 28.9 Complete longitudinal vaginal septum (A). Using a 15 Fr resectoscope and pointed electrode (KARL STORZ, Germany), after adequate distention of the vagina, the same technique used for the removal of the uterine septum is applied, along the median plane of the septum, from the apex to the base of the septum itself (B, C).

septum using a straight loop or pointed electrode, in anterograde direction, starting from the apex (Figure 28.9).

However, it could be challenging, due to very limited spaces and the mandatory use of general anesthesia. The introduction of 15 Fr bipolar resectoscope has partially solved these problems.

Another option is the resection of the vaginal septum using a bipolar electrode. Always in a pulsed mode, moving in anterograde direction, lateral movements of the electrode are made, taking care to follow the median plane of the septum.

However, whatever tool is used, the crucial part of this surgery is to maintain a proper view by ensuring adequate distension of the vagina to allow for the resection of the septum precisely in the transverse plane, avoiding consequent perforation on the anterior or posterior wall. As proof of the efficacy of the hysteroscopic treatment of vaginal anomalies, a subsequent follow-up revealed normal re-epithelialization at the site of the previous septum.

28.5.4.2 Imperforated Hemivagina with Bicorporeal Uterus

The standard approach consists of an incision of the vaginal wall with scissors and drainage of the hematocolpos (45). Unfortunately, there are many disadvantages associated with this surgical technique, such as the need for general anesthesia, the painful distension of the vagina with a speculum, and the inevitable disruption of the hymen. To date, hysteroscopic treatment using miniaturized instruments represents a valid alternative to this kind of surgery. Thanks to a needle inserted through the working channel of the hysteroscope, a local analgetic infiltration of the vaginal wall is performed. Then, a radial incision on the vaginal wall is obtained using bipolar electrode or scissors, always under control, without incurring the risk of iatrogenic damage to nearby anatomical structures.

28.5.5 Complex Müllerian Anomalies

Multiple coexisting malformations of the uterus, cervix, and/or vagina can be found. In these cases, it is essential to have a correct diagnosis to choose the best possible treatment, tailored to the patient, that matches the needs of each patient. Indeed, the treatment of complex Müllerian anomalies does not always involve only a hysteroscopic approach, but sometimes requires a laparoscopic or abdominal approach or often a combined approach (46).

An example is the case of a complete uterine septum, with double "normal" cervix and nonobstructive longitudinal vaginal septum, class U2bC2V1 according to ESHRE/ESGE classification (43). The first step consists in the resection of the vaginal septum with 15 Fr resectoscope using Collin's loop. The surgeons cuts in the middle plane of the septum, maintaining a high intravaginal fluid pressure to clearly visualize all the septum, until the visualization of the two cervices is obtained. To better identify the best location to perforate the uterine septum, at isthmic level, a Hegar dilator is inserted into the cervical canal of the left cervix. In the next step, the septum is incised and fenestrated until revealing the Hegar in the opposite hemicavity, followed by gradual resection toward the fundus always on the middle plane, using the classical technique (Figure 28.10). Also in this case, the anterior and posterior fibrotic tissue of septum is resected with an angle cutting loop.

The possibilities of using miniaturized instruments such as the 15 Fr bipolar resectoscope allows the surgeon to overcome difficulties in maneuvering in some constricted conditions such as complex Müllerian anomalies.

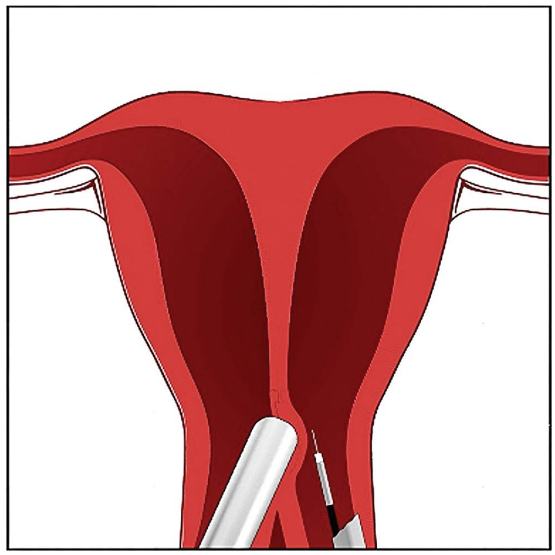


FIGURE 28.10 A schematic representation of the approach for metroplasty in case of complete uterine septum and double cervix: an Hegar dilator is inserted into one cervix, pushing towards the opposite side, to evidence the isthmic portion of the uterine septum to cut. In the opposite cervix, a hysteroscope is inserted to perform a section of the septum at the isthmic level using a pointed electrode; then, the surgeon proceeds performing a classic section of the septum on the midline.

References

1. Byrne J et al. Prevalence of Mullerian duct anomalies detected at ultrasound. *Am J Med Genet*. 2000;94:9–12.
2. Jayaprakasan K et al. Prevalence of uterine anomalies and their impact on early pregnancy in women conceiving after assisted reproduction treatment. *Ultrasound Obstet Gynecol*. 2011;37(6):727–732.
3. Green L et al. Uterine anomalies. Frequency of diagnosis and associated obstetrics complications. *Obstet Gynecol*. 1976;47:427–429.
4. Di Spiezio Sardo A et al. *State-of-the-Art Hysteroscopic Approaches to Pathologies of the Genital Tract, Version 2.0*. EndoPress; 2022.
5. Pellerito JS et al. Diagnosis of uterine anomalies: relative accuracy of MR imaging, endovaginal sonography, and hysterosalpingography. *Radiol*. 1992;183(3):795–800.
6. Buttram VC, Jr. et al. Mullerian anomalies: a proposed classification (An analysis of 144 cases). *Fertil Steril*. 1979;32(1):40–46.
7. The American Fertility Society classifications of adnexal adhesions, distal tubal occlusion, tubal occlusion secondary to tubal ligation, tubal pregnancies, müllerian anomalies and intrauterine adhesions. *Fertil Steril*. 1988;49(6):944–955.
8. Oppelt P et al. The VCUAM (Vagina Cervix Uterus Adnex-associated Malformation) classification: a new classification for genital malformations. *Fertil Steril*. 2005;84(5):1493–1497.
9. Grimbizis GF et al. Clinical approach for the classification of congenital uterine malformations. *Gynecol Surg*. 2012;9(2):119–129.
10. Grimbizis GF et al. The ESHRE/ESGE consensus on the classification of female genital tract congenital anomalies. *Hum Reprod*. 2013;28(8):2032–2044.
11. Hassan MA et al. Congenital uterine anomalies and their impact on fertility. *Womens Health*. 2010;6(3):443–461.
12. Akhtar MA et al. Reproductive implications and management of congenital uterine anomalies: scientific impact paper 62, 2019. *BJOG*. 2020;127(5):e1–e13.
13. Sugi MD et al. Müllerian duct anomalies: role in fertility and pregnancy. *Radiographics*. 2021;41(6):1857–1875.
14. Saravelos SH et al. Prevalence and diagnosis of congenital uterine anomalies in women with reproductive failure: a critical appraisal. *Hum Reprod Update*. 2008;14(5):415–429.
15. Alonso L et al. Diagnostic accuracy of hysteroscopy, ultrasound and magnetic resonance imaging in detecting congenital uterine anomalies. *Minerva Obstet Gynecol*. 2022;74(1):12–23.
16. Brown MA. MR imaging of benign uterine disease. *Magnetic Resonance Imaging Clin N Am*. 2006;14(4):439–453.
17. Faivre E et al. Accuracy of three-dimensional ultrasonography in differential diagnosis of septate and bicornuate uterus compared with office hysteroscopy and pelvic magnetic resonance imaging. *J Minim Invasive Gynecol*. 2012;19(1):101–106.
18. Ghi T et al. Accuracy of three-dimensional ultrasound in diagnosis and classification of congenital uterine anomalies. *Fertil Steril*. 2009;92(2):808–813.
19. Midan MF et al. Comparative study between three-dimensional ultrasonography and office hysteroscopy in infertile women with uterine cavity abnormalities. *Middle East Fertil Soc J*. 2017;22:329–332.
20. Edström K. Intrauterine surgical procedures during hysteroscopy. *Endoscopy*. 1974;6:175–181.
21. Grimbizis GF et al. Clinical implications of uterine malformations and hysteroscopic treatment results. *Hum Reprod Update*. 2001;7(1):161–174.
22. Colacurci N et al. The significance of hysteroscopic treatment of congenital uterine malformations. *Reprod Biomed Online*. 2002;4:52–54.
23. Di Spiezio Sardo A et al. Hysteroscopic treatment of Müllerian duct anomalies. *Minerva Ginecol*. 2016;68(2):175–185.
24. Bettocchi S et al. Advanced operative office hysteroscopy without anaesthesia: analysis of 501 cases treated with a 5 Fr. Bipolar electrode. *Hum Reprod*. 2002;17(9):2435–2438.
25. Catena U et al. New approach for T-shaped uterus: metroplasty with resection of lateral fibromuscular tissue using a 15 Fr mini-resectoscope. A step-by-step technique. *Facts Views Vis Obgyn*. 2021;13(1):67–71.
26. Di Spiezio Sardo A et al. Long-term reproductive outcomes after hysteroscopic treatment of dysmorphic uteri in women with reproductive failure: an European multicenter study. *J Minim Invasive Gynecol*. 2020;27(3):755–762.
27. Ban-Frangez H et al. The outcome of singleton pregnancies after IVF/ICSI in women before and after hysteroscopic resection of a uterine septum compared to normal controls. *Eur J Obstet Gynecol Reprod Biol*. 2009;146(2):184–187.
28. Unlu C et al. Expression of endometrial receptivity genes increase after myomectomy of intramural leiomyomas not distorting the endometrial cavity. *Reprod Sci*. 2016;23(1):31–41.
29. Di Spiezio Sardo A et al. Hysteroscopic outpatient metroplasty to expand dysmorphic uteri (HOME-DU technique): a pilot study. *J Minim Invasive Gynecol*. 2012;19(6):S61–S62.
30. Bilgory A et al. Diode laser hysteroscopic metroplasty for dysmorphic uterus: a pilot study. *Reprod Sci*. 2022;29(2):506–512.
31. Practice Committee of the American Society for Reproductive Medicine. Uterine septum: a guideline. *Fertil Steril*. 2016;106(3):530–540.
32. Colacurci N et al. Small diameter hysteroscope with versapoint vs resectoscope with unipolar knife for the treatment of septate uterus: a prospective randomized study. *J Minim Invasive Gynecol*. 2007;14(5):622–627.
33. Bettocchi S et al. Office hysteroscopic metroplasty: three "diagnostic criteria" to differentiate between septate and bicornuate uteri. *J Minim Invasive Gynecol*. 2007;14(3):324–328.
34. Di Spiezio Sardo A et al. Accuracy of hysteroscopic metroplasty with the combination of presurgical 3-dimensional ultrasonography and a novel graduated intrauterine palpator: a randomized controlled trial. *J Minim Invasive Gynecol*. 2016;23(4):557–566.
35. Fascilla FD et al. Resectoscopic metroplasty with uterine septum excision: a histologic analysis of the uterine septum. *J Minim Invasive Gynecol*. 2020;27(6):1287–1294.
36. Simons M et al. Hysteroscopic morcellator system can be used for removal of a uterine septum. *Fertil Steril*. 2011;96(2):e118–e121.
37. Nappi L et al. Hysteroscopic metroplasty for the septate uterus with diode laser: a pilot study. *Eur J Obstet Gynecol Reprod Biol*. 2016;206:32–35.
38. Esteban Manchado B et al. Office hysteroscopic metroplasty with diode laser for septate uterus: a multicenter cohort study. *Minim Invasive Ther Allied Technol*. 2022;31(3):441–447.
39. Casadio P et al. Uterine fundus remodeling after hysteroscopic metroplasty: a prospective pilot study. *J Clin Med*. 2021;10(2):260.
40. Healy MW et al. Intrauterine adhesion prevention after hysteroscopy: a systematic review and meta-analysis. *Am J Obstet Gynecol*. 2016;215(3):267–275.e7.
41. Chang AS et al. Septate uterus with cervical duplication and longitudinal vaginal septum: a report of five new cases. *Fertil Steril*. 2004;81(4):1133–1136.
42. Wang J et al. Hysteroscopic septum resection of complete septate uterus with cervical duplication, sparing the double cervix in patients with recurrent spontaneous abortions or infertility. *Fertil Steril*. 2009;91(6):2643–2649.
43. Di Spiezio Sardo A et al. The step-by-step hysteroscopic treatment of patients with vaginal and complete uterine septum with double cervix (U2bC2V1). *Fertil Steril*. 2021;116(2):602–604.
44. Montevecchi L et al. Resectoscopic treatment of complete longitudinal vaginal septum. *Int J Gynaecol Obstet*. 2004;84(1):65–70.
45. Fedele L et al. Double uterus with obstructed hemivagina and ipsilateral renal agenesis: pelvic anatomic variants in 87 cases. *Hum Reprod*. 2013;28(6):1580–1583.
46. Di Spiezio Sardo A et al. An exceptional case of complete septate uterus with unilateral cervical aplasia (class U2bC3V0/ESHRE/ESGE classification) and isolated mullerian remnants: combined hysteroscopic and laparoscopic treatment. *J Minim Invasive Gynecol*. 2016;23(1):16–17.

29 HYSTEROSCOPY AND EARLY PREGNANCY LOSS (MISSED AB, RPOC, TISSUE REMOVAL SYSTEMS)

Salvatore Giovanni Vitale, Gilda Sicilia, Stefania Saponara, Jose Carugno, and Stefano Angioni

29.1 Introduction

Early pregnancy loss (EPL), defined as the unintended loss of an intrauterine pregnancy within the first 10–12 weeks of gestation, is an ever-present medical issue affecting millions of women annually. It is the most common complication during pregnancy, resulting in miscarriage approximately 15%–20% of all first-trimester gestations (1).

Most early losses result from chromosomic anomalies, autosomal trisomy being the most frequent of all (1). Many demographic, lifestyle, and environmental factors may be involved in the pathogenesis of an EPL, with maternal age and a history of previous early miscarriages being the most strongly correlated ones (2). Symptoms may range from a completely asymptomatic status to an even life-threatening condition in the worst cases (3). EPL is a topic of impactful social relevance, and its psychological and social repercussions must not be undervalued (4).

The evolving clinical scenarios of an EPL are many. In the case of *complete* abortion, the product of conception is spontaneously fully expelled. However, it can be retained either in part (*incomplete* abortion) or in full (*missed* abortion) in the uterine cavity: this is called retained products of conception (RPOC).

Based on the patient's symptoms, the clinical picture, and the diagnostic findings, EPL management has traditionally rested on three pillars: expectant care, medical treatment with uterotonic agents, and surgical evacuation of the uterine cavity through blind removal via blunt, sharp, or suction curettage after dilation (D&C).

The improper management of an EPL can lead to catastrophic reproductive outcomes. Surgical management with blind D&C undeniably raises the risk of postoperative intrauterine adhesions and uterine perforation (5). Plus, due to the blindness of the technique, RPOC can remain in the uterine cavity even after uterine curettage, hence requiring, on some occasions, a second intervention and causing additional iatrogenic trauma.

Due to its safety and efficacy, the use of hysteroscopy in EPL management is gaining more ground, appearing to be the most suitable surgical alternative. The direct visual check of the uterine cavity improves the percentage of complete treatment, operating on a limited area of the uterine cavity and thus decreasing the iatrogenic adhesion rate. Moreover, endoscopic direct visualization of the uterine cavity provides great help in the identification of previously undetected congenital uterine anomalies, which may be the underlying reason for the early pregnancy demise (6).

Whether it is about missed abortion, incomplete abortion, or even incomplete surgical evacuation after D&C, the hysteroscopy approach not only manages to alleviate the current acute patient's symptoms but also best optimizes the patient's future outcomes.

29.2 RPOC after an Early Pregnancy Loss: A Challenging Issue

29.2.1 Generalities and Clinical Manifestations

Retained products of conception is a common pregnancy complication. Estimates of incidence quote a 1%–6.3% rate of RPOC following all pregnancies and 0.5%–19% prevalence (6, 7). Placental and fetal tissue can remain inside the uterine cavity either after a full-term or preterm vaginal/cesarean delivery or after a spontaneous/elective abortion. However, it is thought to be more frequent after miscarriage or termination of pregnancy (8) (Figure 29.1).

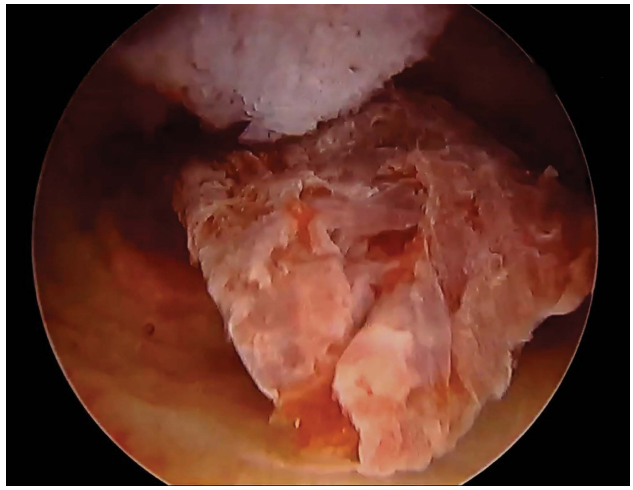


FIGURE 29.1 Hysteroscopic view of retained product of conception.

When a pregnancy stops during the early stages, RPOC seems to be more frequent when conservative or medical management is chosen (9).

The most frequent clinical finding in women with RPOC is vaginal bleeding, which can range from light to even life-threatening hemorrhage. Symptoms' severity and clinical appearance depend on the features of the retained tissue in terms of dimensions, the presence of vascularization, and the time frame in which tissue has been retained in the uterine cavity (10). When pregnancy is over, any vaginal bleeding which is abnormal, either in quantity or in length, must make one suspect RPOC, and further diagnostic insights become mandatory. RPOC can seldom present with complete amenorrhea for a long time after pregnancy. Moreover, abdominal or pelvic pain, uterine tenderness, unpleasant smell, and fever may occur.

29.2.2 Diagnosis

RPOC diagnosis is often challenging since light bleeding and nonspecific discomfort are common findings after an abortion or a delivery. Diagnosis is achieved thanks to a combination of clinical and sonographic criteria (11).

Hysteroscopy is considered the gold standard for RPOC diagnosis and treatment, but other diagnostic approaches can help.

- *Physical examination*: Bimanual exam allows for assessing the extent of vaginal bleeding and uterine dimension and tenderness, which are usually larger than expected

DOI: 10.1201/9781003312109-29

if RPOC is present. The cervical canal can also be valued through physical evaluation, assessing its degree of dilation and the possible presence of either clots or products of conception protruding through the cervix, which can, on some occasions, be removed with the aid of ring forceps (12).

- *Beta-hCG*: Retained trophoblastic tissue can keep endocrine activity for a very long time, continuing to deliver albeit small amounts of human chorionic gonadotropin (hCG) into the bloodstream. However, low hCG levels (> 5 mIU/mL) can be dosed in blood flow even after regular labor. Besides, a negative hCG value does not exclude for sure the persistence of trophoblastic tissue *in utero*. For this reason, quantitative hCG blood values have limited relevance in RPOC diagnosis (13).
- *Transvaginal sonography (TVS)/color Doppler ultrasound transvaginal sonography*: This is the most valid imaging test for RPOC diagnosis. Endometrial appearance changes over time after the end of a pregnancy, looking like a thin regular echogenic line 8 weeks after delivery and 1 week after an early miscarriage (14). Suggestive US findings for RPOC are a hyperechoic irregular focal mass in the uterine cavity (with or without a vascular flow), a thickened and inhomogeneous endometrium that may also contain a small fluid collection in its context, and a sparsely defined endometrium/myometrium interface (15). Establishing a cutoff value for endometrial thickness as a diagnostic criterion for RPOC is challenging. Many authors tried to set a cutoff value in the past with no little difficulties and with wide differences between studies, with a median cutoff set at 8 mm (16). Diagnostic accuracy and specificity of TVS can be significantly improved by using *color Doppler*. Color Doppler allows us to evaluate the vascularization of the placental retained tissue (which is typically intense) to study the RPOC implantation area better and to differentiate retained trophoblastic tissue from clots. Color Doppler US detection of any vascularity within a thickened endometrium or echogenic mass increases the positive predictive value (PPV) for diagnosis of RPOC to 96% (17) (Figure 29.2).
- *Sonohysterography (SHG)/3D Sonography*: Even though TVS and color Doppler are the imaging modalities of choice to best detect RPOC in the pre-hysteroscopic evaluation, sonohysterography and 3D sonography can be used as complementary diagnostic methods since they can increase US specificity, enhancing and better identifying a possible floating mass in the uterine cavity and better characterizing its size, morphology, and implantation area.
- *MRI*: RPOC can also be detected with magnetic resonance imaging, having the appearance of a soft-tissue mass inside the uterine cavity with varying degrees of signal intensity on T1- and T2-weighted images. The myometrial layer can appear thinner, and the junctional zone may be obliterated in the RPOC implantation area (18). However, MRI is an expensive diagnostic procedure that does not add anything to the US and color Doppler findings. Consequently, it is not routinely used in the RPOC diagnostic path, although RPOC can be an incidental finding in an RM scan adopted for other diagnostic purposes.

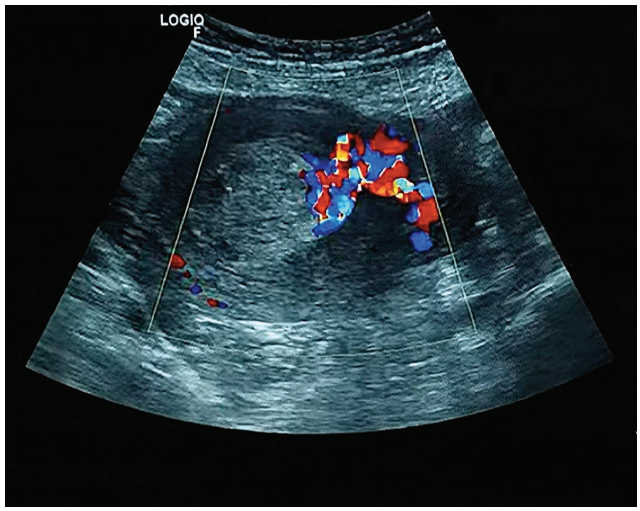


FIGURE 29.2 Ultrasonographic finding of RPOC: color Doppler shows the vascularization of the placental retained tissue and highlights the implantation area.

29.2.3 Classification Systems

In 2009 Kamaya et al., for the first time, tried to classify RPOC based on color Doppler US findings. They examined sonographic images of patients with suspicion of RPOC and classified them into four groups based on color Doppler analysis. The degree of vascularity within the endometrial mass compared with myometrial vascularity is graded as type 0, 1, 2, or 3 (17). Type 0 is defined by no detectable vascularity within the thickened endometrium or intrauterine hyperechogenic mass and may suggest a blood clot presence rather than RPOC. Type 3 is defined by intense vascularization, higher in the endometrium than in the myometrium.

In 2018, a new and more complete classification system, the *Gutenberg classification*, was proposed (10). The Gutenberg classification tries to compare ultrasonographic images to the hysteroscopic appearance of RPOC. In Gutenberg classification, US findings are described for what concerns vascularization pattern and the echogenicity of the retained tissue (Figures 29.3 and 29.4).

29.2.4 Differential Diagnosis

The differential diagnosis of RPOC can be complex. In the differential diagnosis, it is crucial to consider some medical issues such as placental site trophoblastic tumor, choriocarcinoma, and acquired arteriovenous malformation (AVM), which may have some diagnostic features in common with RPOC, still requiring their own care and management.

- *Placental site trophoblastic tumor (PSTT)* is a rare gestational trophoblastic disease (GTD). It stems from intermediate trophoblastic cells, which incur some degree of neoplastic transformation. Laboratory studies that may help in the diagnosis are beta-hCG (which continues to be produced in small amounts) and human placental lactogen (hPL). In most cases, it is restricted to the uterus, but metastatic cases have also been reported. PSTT has in common some clinical and diagnostic features with RPOC: both may occur with vaginal bleeding and may have a

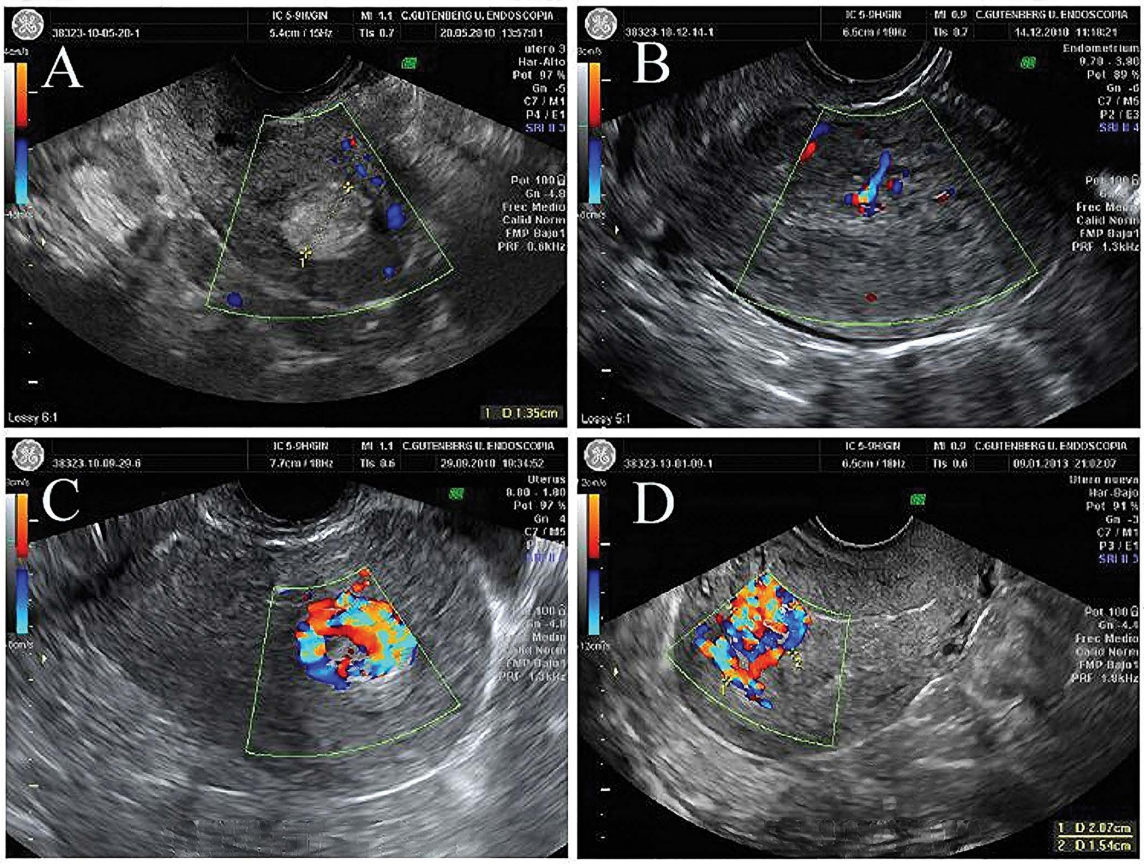


FIGURE 29.3 Ultrasonographic patterns of RPOC. Gutenberg classification. (A) Type 0: hyperechogenic avascular mass. (B) Type 1: different echoes with minimal or no vascularization. (C) Type 2: highly vascularized mass confined to the uterine cavity. (D) Type 3: highly vascularized mass with highly vascularized endometrium. (From Ref. 10 with permission.)

similar ultrasonographic pattern. Histopathological diagnostic confirmation is crucial (19).

- *Choriocarcinoma* is a very invasive tumor with high metastatic potential. In most cases, it occurs after molar pregnancies but can also develop from regular delivery, spontaneous miscarriage, or even ectopic pregnancy. Quantitative values of beta-hCG are typically very high and may help with the diagnosis, while ultrasonographic findings can be tough to read. A histopathological diagnosis for an official diagnosis is needed (20).
- *Acquired uterine arteriovenous malformation* can stem from iatrogenic uterine trauma, with D&C being one of the most common causes. Ultrasonographic analysis can be challenging since RPOC and AVM may have a similar look at imaging. However, on closer inspection, AVM is characterized by a distinctive turbulent flow with a more intramyometrial development. Arterial embolization is the recommended treatment (21).

29.2.5 Possible Consequences of RPOC

Early consequences of RPOC are infection and abnormal uterine bleeding. Long-term complications that may stem from an improper treatment or RPOC persistence are intrauterine adhesions (IUAs). IUAs can cause menstrual disturbances, infertility, miscarriage, ectopic pregnancy, abnormal placentation, intrauterine growth restriction, or preterm delivery. IUAs have significant bad outcomes on future reproductive ability and are often a result of RPOC and its treatment (22).

29.2.6 Current Management Strategies

29.2.6.1 Nonsurgical

Expectant management may be offered to the stable patient without evidence of infection and is reported to be successful in up to 81% of patients. However, after 4 weeks of expectant management, one in five still have RPOC (23).

When opting for medical therapy, uterotonic agents and misoprostol are the choice. Misoprostol is the most widely used medication for RPOC management, even if there is no consensus on the most adequate dose and posology.

A 2016 Cochrane review determined no differences in rates of complete miscarriage between expectant management and vaginal misoprostol. However, misoprostol, compared to the surgical approach, had lower rates of complete evacuation, higher rates of unplanned secondary surgical intervention, and longer duration of bleeding (24).

In first-trimester miscarriage, misoprostol use yields an 84% success rate of RPOC removal compared to 97% with surgical vacuum aspiration. However, after medical termination of pregnancy, about 1.5% of patients still have RPOC after 24 hours (23).

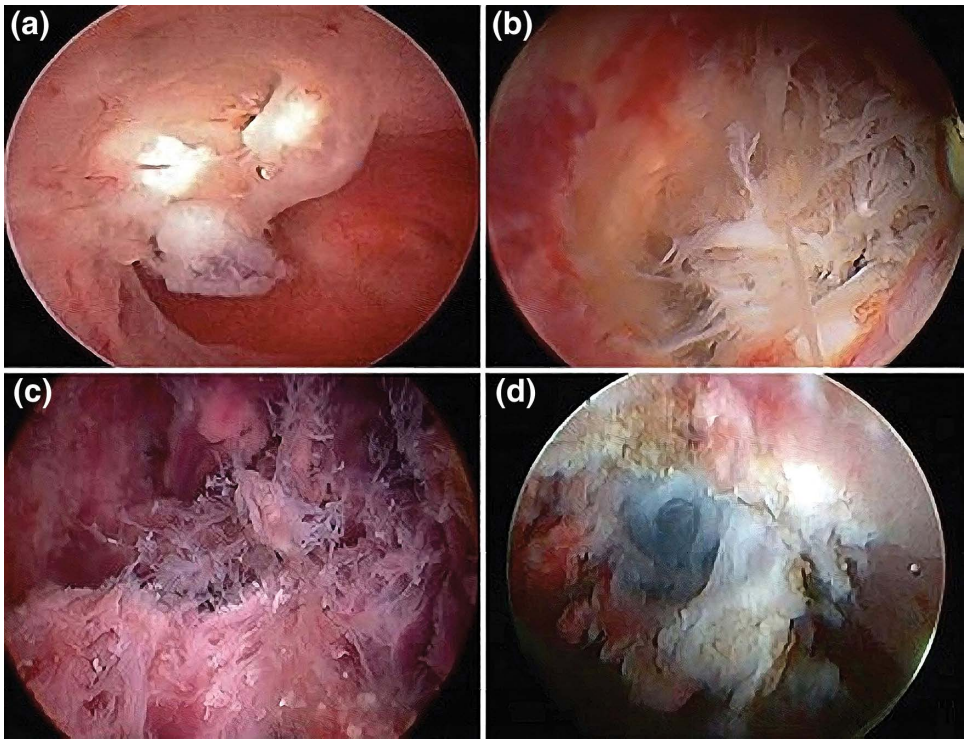


FIGURE 29.4 Hysteroscopic patterns of RPOC. Gutenberg classification. (a) Type 0: white mass with no clear structures. (b) Type 1: well-defined avascular chorionic villi. (c) Type 2: well-vascularized chorionic villi. (d) Type 3: aneurism over myometrium in the implantation area (From ref 10 with permission).

These nonsurgical choices are safe and feasible in the appropriately selected and counseled patient. However, there is still a very limited number of studies investigating IUAs' development and reproductive outcomes after medical or expectant management of RPOC (6).

29.2.6.2 Surgical

Traditionally, the most widespread treatment for RPOC is blind dilation and curettage (D&C) with a blunt, sharp, or suction curette (6). This approach exposes the endometrium to further iatrogenic trauma as well as to several postoperative complications, including incomplete evacuation, persistent uterine bleeding, uterine perforation, infection (pelvic inflammatory disease, endometritis), IUAs, and infertility (15, 25, 26). Although blind D&C has more efficacy in fully evacuating RPOC when compared to expectant or medical management, this technique has a 3% risk of uterine perforation, and up to 20.8% of patients have incomplete curettage, necessitating a second surgical procedure. Furthermore, only 50% of specimens collected by D&C result in histological confirmation of RPOC (7). The rate of IUAs' formation after just one D&C is 19%, and severe IUAs are seen in 0.5%–30% of women undergoing a second curettage for RPOC (27). The risk and severity of IUAs worsen with the number of intrauterine interventions, rising to 32% in women who underwent three interventions, with more than 50% of adhesions being severe (25).

Therefore, despite being a generally accessible procedure to treat RPOC, blind D&C leads to an alarmingly high rate of IUAs and incomplete curettage.

An increasingly emerging alternative surgical approach for RPOC treatment is hysteroscopic resection of the retained tissue. Hysteroscopic resection of RPOC is the best alternative regarding safety and efficacy, improving complete resection rate and reproductive outcomes while exposing the patients to fewer risks of the development of IUAs and uterine perforation.

29.3 Role of Hysteroscopy in RPOC Management

Hysteroscopy is the gold standard for the diagnosis and treatment of intrauterine pathologies. Thus, opting for this technique for RPOC management is a natural step in the evolution of the treatment paradigm.

In 1984, Tchabo first resorted to diagnostic hysteroscopy to view RPOC directly in women with incomplete miscarriages or with suspicion of RPOC after delivery. With the aid of the endoscopic view, he made an official diagnosis, took out the retained tissue with polyp forceps, and took a second look to ensure the complete resection of the pathology (28).

In 1997 Goldenberg first performed cold loop hysteroscopic resection of RPOC (29). This first attempt increased attention to this innovative approach to the disease. The unique advantage of hysteroscopy over blind D&C is that the hysteroscopic approach allows one to visualize the pathology directly and to operate in a limited area of the uterine cavity where the disease is located. Therefore, accurate removal of RPOC through hysteroscopic view permits a complete evacuation of the uterine cavity and, at the same time, spares the healthy endometrium from additional unnecessary trauma (25, 30). This leads to less postoperative inflammation and a lower rate of IUAs, hence improving patients' reproductive outcomes.

29.3.1 Instruments and Techniques

29.3.1.1 Office Treatment with Miniaturized Instruments

On some occasions, RPOC can be approached in an outpatient setting. Especially if retained tissue is not vascularized and if the implantation area is small, RPOC removal can be performed with the aid of a 5 Fr miniaturized instrument (e.g., "alligator forceps," "snake grasper") (31, 32). The small diameter of the miniaturized instruments allows physicians to execute hysteroscopy, avoiding cervical dilation and without general anesthesia (33). If tissue is small and not supplied by vascular vessels, a simple repeated open/close mechanism can be sufficient to complete remotion, separating it from the underlying myometrium (34, 35). Electrosurgery via bipolar instruments may be necessary for more strongly attached tissue.

29.3.1.2 Resectoscopic and Mini-Resectoscopic Removal Technique

The efficacy of a cutting loop application for selective retained trophoblastic tissue removal is well established. The classical resectoscopes approach requires the 25–27 Fr resectoscope to be introduced into the cavity with a previous cervical dilation (using Hegar dilators) and under general anesthesia (36).

However, in many patients (especially the most symptomatic ones, in which the cervical canal may be found opened), the resectoscope may be introduced directly without cervical dilation and in an outpatient setting.

Moreover, the increasingly widespread use of the new 15/16 Fr so-called "mini-resectoscope" is making the outpatient setting ever more accessible for hysteroscopic treatment, thus becoming a valid option for retained tissue removal (37).

The classical *slicing* technique requires the loop to be advanced up to the uterine fundus until a cleavage plane between the pathology and the healthy myometrial tissue is identified. After that, the loop is moved in a retrograde direction in order to detach the residual trophoblastic tissue, paying great attention to the healthy underlying myometrium (25) (Figure 29.5).

A resectoscope loop is preferably used without electrical energy (*cold* loop) to spare healthy myometrium from unintended trauma. Occasionally, the pathology might be more firmly attached to the uterine wall, or a clear cleavage plan is undetectable, making it necessary to resort to an *activated* loop operation (with an electrical current).

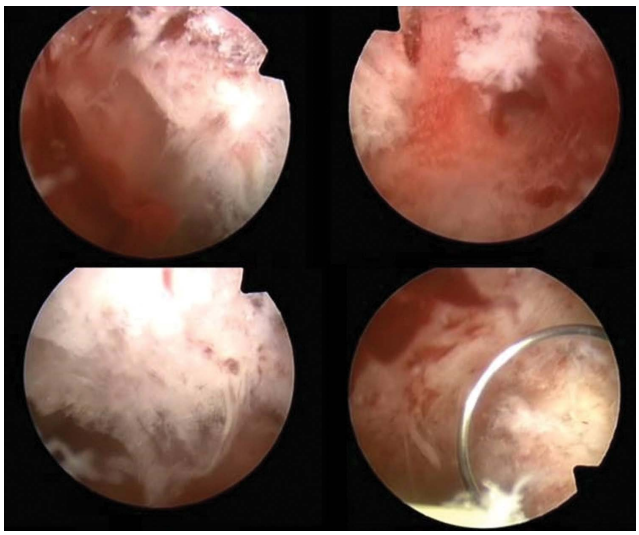


FIGURE 29.5 Resectoscopic removal of RPOC using a *cold* (inactive) cutting loop.

29.3.1.3 Tissue Removal Systems

The hysteroscopic morcellator (*tissue removal system*) is a mechanical alternative to the cold loop technique. Its benefits over loop resection are thought to be due to more accessible adaptation to office-based surgery, closed-loop irrigation, and the unique suction system, which allows simultaneous excision and removal of retained tissue (38). Morcellators may lower the risk of perforation due to the instrument's closed blunted tip and the need for fewer insertions of the instrument in the uterine cavity compared with the loop resectoscope. On the other hand, bleeding management can be complex with the morcellator system because of its mechanical property of action. Thus, it should be preferred when the pathology seems to be not highly vascularized at the pre-hysteroscopic US evaluation and with hysteroscopic direct visualization (36).

Some studies compared mechanical morcellator to resectoscope application in retained tissue removal. In 2016, Hamerlynck et al. found significant differences between the two methods regarding median operating time and the number of hysteroscope insertions in the uterine cavity through the cervical canal. The median operative time for morcellation was 6.2 minutes versus 10 minutes for the resectoscope. The number of hysteroscope insertions was one with morcellation versus three with the resectoscope. Complete removal of the retained tissue was 93% without significant differences between the two techniques. When perforation occurred, it was in patients who had recent term deliveries and was unrelated to instrument insertion. Adequate tissue samples were collected in 95% of patients, of which 70% had positive histologic findings of RPOC. Of enrolled patients, 82% underwent a second-look hysteroscopic check, and the rate of IUAs was 3% for both groups (27). The same cohort from the 2016 RCT was examined in a 2-year follow-up study to assess reproductive and obstetric outcomes. No differences in conception, live birth rates, and time to reach conception were found between the morcellation and resectoscope groups. Additionally, the two techniques had comparable rates of abnormal placentation, retained placenta, or persistent RPOC (39).

The shorter operative time and the smaller number of insertions may yield the use of a morcellator even more suitable for office-based settings. Morcellation also provides a constant blood aspiration, and it is provided with a system of simultaneous excision and removal of retained tissue, ensuring a better visualization of the uterine cavity during the entire procedure (Figure 29.6). On the other hand, loop resection always requires the removal of the hysteroscope to clear the operating field and to pick up samples for histopathological analysis.

Nevertheless, the loop resectoscope may be necessary to thoroughly remove particularly firmly attached RPOC and manage bleeding through coagulation (27).

Since current evidence shows no significant difference in each method's capacity to achieve complete removal with minimal complication rate and comparable reproductive outcomes, the decision of the hysteroscopic approach needs to be based on the preoperative evaluation of the vascularity and size of the pathology, as well as on the gynecologist's preference.

29.3.2 Efficacy and Outcomes

If compared with traditional blind D&C, the use of hysteroscopy for the management of RPOC is superior in terms

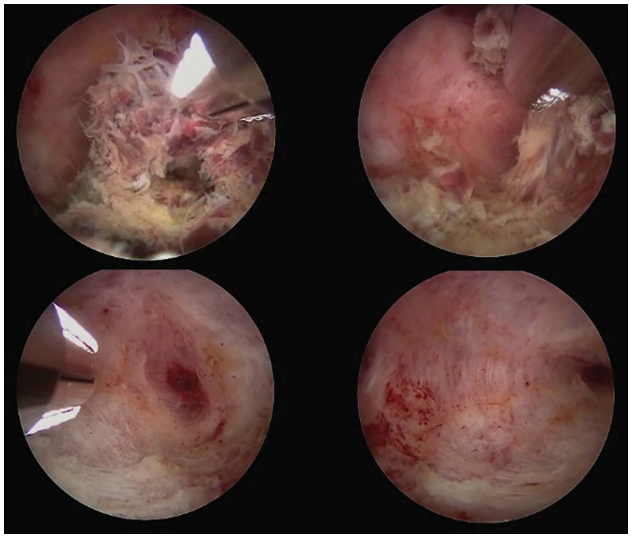


FIGURE 29.6 Hysteroscopic treatment of retained tissue using a hysteroscopic tissue removal device (hysteroscopic morcellator).

of rate of complete resection, a higher chance of pathologic confirmation of the disease, easier visualization of previously unknown uterine anomalies, lower risk of postoperative adhesions, shorter time interval until conception, and better clinical pregnancy outcomes (15).

29.3.2.1 Resection Rate

The complete resection rate depends on the total volume of RPOC, tissue adherence to the uterine wall, the chance of proper visibility due to potential bleeding, and the patient's compliance. Smaller RPOC size has been noticed to be more likely to undergo complete resection (30). Interestingly, the hysteroscopically assessed size was more punctual in predicting complete resection rates than the ultrasonographic pre-hysteroscopic estimated size (7).

29.3.2.2 Pathology Confirmation

Histopathological analysis of RPOC can help suggest the etiology of a pregnancy loss. It is also crucial to differentiate true cases of RPOC from other pathological conditions such as placental site trophoblastic tumour (PTSS), choriocarcinoma, and placenta accreta spectrum (PAS) related issues. Evidence shows that RPOC histopathologic confirmation is obtained much more when achieved by hysteroscopic resection rather than from D&C (65.2%–97% against 58.3%) (36).

29.3.2.3 Congenital Uterine Anomalies

On some occasions, hysteroscopic management of RPOC allows for diagnosing previously unidentified uterine anomalies. Congenital uterine anomalies cause a higher rate of early pregnancy loss. They may also be responsible for incomplete uterine evacuation after a spontaneous abortion, a standard delivery, or even a previous D&C for RPOC itself. The direct visualization provides an additional value, facilitating the detection of previously unrecognized uterine anomalies while ensuring complete evacuation of the RPOC (6).

29.3.2.4 Intrauterine Adhesions

Intrauterine adhesions can have a catastrophic impact on future patients' fertility and reproductive outcomes, leading to a high rate of secondary infertility. Evidence shows that hysteroscopic management is superior to D&C in preventing severe intracavitary adhesions, being the first line of RPOC management, especially in patients seeking pregnancy. Rein et al. compared the IUA formation rate after hysteroscopic RPOC resection with one after D&C. Based on their results, patients who underwent US-guided D&C had significantly more mild adhesions (30.8%) when compared with those who had hysteroscopically managed RPOC (4.2%) (40, 41).

29.3.2.5 Reproductive Outcomes

Fertility is often a priority in patients with RPOC, who frequently raise concerns about their future reproductive health. It is crucial for gynecologists who perform hysteroscopy to be in line with patients' demands, to give them priority, and to be aware of the intrinsic risks and consequences of the surgical procedures they deal with.

As already mentioned, blind D&C causes a higher rate of IUAs which can lead to even severe adhesive conditions (Asherman's syndrome). Hysteroscopy guarantees a lower rate of intracavitary adhesions after RPOC removal and a lower risk of complications, and it can even help to visualize and recognize previously undiagnosed intracavitary pathology.

Some studies compared fertility and reproductive outcomes after hysteroscopy or D&C, demonstrating a far lower IUA rate in the patients who underwent hysteroscopy than in those who underwent uterine curettage. Plus, post-hysteroscopy adhesions seem thinner and milder. In contrast, more cases of thick, dense, and extensive adhesions occurred in patients after D&C (38–40). Moreover, the conception rate emerged to be higher, and the time until conception was shorter after hysteroscopic RPOC removal (36, 40).

A higher rate of newly diagnosed infertility after uterine curettage (24.5%) than hysteroscopic treatment (12%) has been noted (43). Not surprisingly, the primary etiology for infertility was mechanical tubal occlusion or IUAs.

29.3.3 Complications

Overall complications of RPOC surgical management include mild to heavy uterine bleeding, vasovagal reaction, the formation of intrauterine adhesions, uterine perforation, fluid overload risk, cervical laceration (with or without the creation of a *falsa via*), postoperative fever, and abdominal pain (43).

Hooker's systematic review cited a pooled complication rate of 1% after surgery, but none occurred in the cohort (63/205) who underwent a hysteroscopic procedure (6).

Uterine perforation occurred in about 1.2% and seemed more usually associated with RPOC removal after full-term delivery, cesarean section, or manually removed placenta (28).

29.4 Missed Abortion and Hysteroscopy

Despite not being common in clinical and surgical practice, hysteroscopy may be applied, even in case of missed abortion, to perform the diagnostic procedure on the product of conception before uterine evacuation. The endoscopic approach can provide the ability to perform embryoscopy after a loss of fetal heart tone is proven or when a blighted ovum pregnancy has been confirmed. Hysteroembryoscopy can be a beneficial opportunity in evaluating first-trimester missed abortions, 60%–70% of which are due to chromosomal abnormalities. The direct visualization of the product of conception, which is still

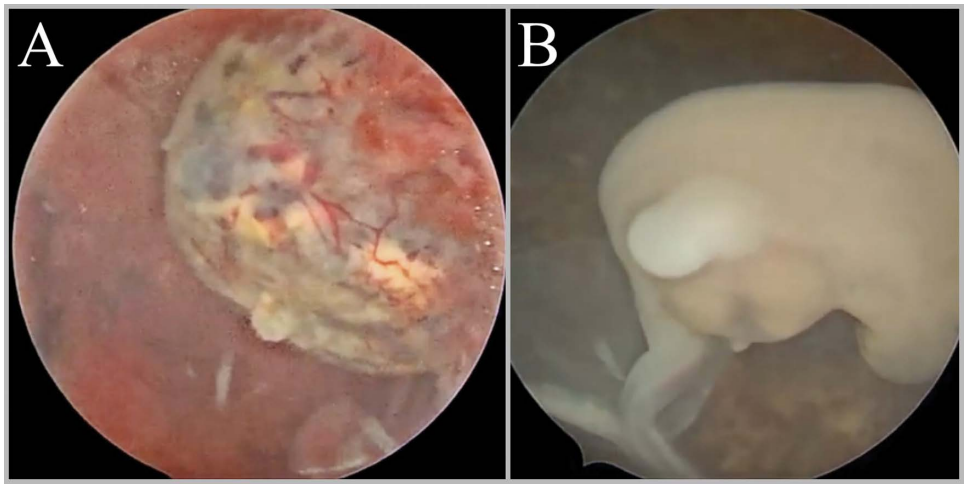


FIGURE 29.7 Embryoscopy. (A) Hysteroscopic appearance of a gestational sac. (B) After the incision of the gestational sac, a 7-week embryo, compatible with estimated gestational age, is visualized.

retained *in utero* after a miscarriage, allows us to recognize better embryonic or fetal macroscopic abnormalities thanks to the visual evaluation of early gestational structures. Moreover, due to the possibility of doing selected direct biopsies of embryonic and chorionic tissue, the endoscopic approach provides an accurate sample collection, which increases the accuracy of cytogenetic evaluation by reducing maternal tissue contamination (44) (Figure 29.7).

A study of 233 women who underwent embryoscopic directed biopsy yielded karyotypes in 99.1%. Half of the 31 patients thought to have normal fetal morphology had an abnormal karyotype instead. Abnormal fetal morphologies noted during embryoscopy were growth disorganization and isolated and combined defects; 60%–86% of these were associated with abnormal karyotypes. Three cases were noted to have amniotic band syndrome (45).

Other studies demonstrated that karyotypes obtained from direct hysteroembryoscopic biopsies are likely more accurate than those obtained from the curettage material (44).

Therefore, hysteroembryoscopy not only increases the yield of fetal chromosomes for cytogenetic evaluation but also provides information on possible morphologic or environmental causes of pregnancy loss which may be critical to reducing risks to a subsequent pregnancy, hence showing great potential in the management of early pregnancy loss, especially in recurring cases.

29.5 Conclusion

The safety and feasibility of hysteroscopy in EPL management are well established. The endoscopic "see-and-treat" approach allows for selective treatment pathology while sparing underlying myometrial and surrounding endometrium from unintended iatrogenic trauma.

The benefits of utilizing the hysteroscopic approach for the treatment of EPL-related issues are clear: it is a readily available technology familiar to gynecologists, succeeding in high rates of complete resection and allowing accurate tissue analysis, as well as providing the opportunity to diagnose previously unrecognized uterine anomalies, contributing valuable insight into the causes of miscarriage. Hysteroscopy also seems to better match the needs of the pregnancy-seeking population of patients by lowering IUA development and improving clinical pregnancy rates.

For all these reasons, hysteroscopy appears to be the best surgical alternative for treating EPL-related issues, and its evermore widespread use may be decisive in definitively changing the paradigm of EPL management.

References

1. Sonalkar S et al. Management of early pregnancy loss with mifepristone and misoprostol: clinical predictors of treatment success from a randomized trial. *Am J Obstet Gynecol*. 2020 Oct;223(4):551.e1–551.e7.
2. Quenby S et al. Miscarriage matters: the epidemiological, physical, psychological, and economic costs of early pregnancy loss. *The Lancet*. 2021;397:1658–1667.
3. Sapra KJ et al. Signs and symptoms of early pregnancy loss: a systematic review. *Reprod Sci*. 2017;24:502–513.
4. Brier N. Clinical commentary understanding and managing the emotional reactions to a miscarriage. *Obstet Gynecol*. 1999;93(1):151–155.
5. Hooker AB et al. Asherman's syndrome after removal of placenta remnants: a serious clinical problem. *Gynecol Surg*. 2011;8(4):449–453.
6. Hooker AB et al. Long-term complications and reproductive outcome after the management of retained products of conception: a systematic review. *Fertil Steril*. 2016;105(1):156–164.e2.
7. Cohen A et al. Office hysteroscopy for removal of retained products of conception: can we predict treatment outcome? *Clin Exp Obstet Gynecol*. 2017;44(5):683–685.
8. Smorgick N et al. Hysteroscopic management of retained products of conception: meta-analysis and literature review. *Eur J Obstet Gynecol Reprod Biol*. 2014;173(1):19–22.
9. Say L et al. Medical versus surgical methods for first trimester termination of pregnancy. *Cochrane Database of Systematic Reviews*. 2002;2010(3).
10. Pacheco LA et al. Hysteroscopy and retained products of conception. In: Tinelli A et al., eds. *Hysteroscopy*. Springer International Publishing; 2018:181–191.
11. Ganer HH et al. Pregnancies following hysteroscopic removal of retained products of conception after delivery versus abortion. *Gynecol Obstet Invest*. 2018;83(6):586–592.

12. Hoffman BL et al. First-trimester abortion. In: Hoffman BL et al., eds. *Williams Gynecology*, 4th edn. New York: McGraw-Hill; 2020.
13. Smorgick N et al. Serum β-HCG level in women diagnosed as having retained products of conception: a prospective cohort study. *J Minim Invasive Gynecol*. 2022;29(3):424–428.
14. Mulic-Lutvica A et al. Ultrasonic evaluation of the uterus and uterine cavity after normal, vaginal delivery. *Ultrasound Obstet Gynecol*. 2001;18(5):491–498.
15. Cholkeri-Singh A et al. Hysteroscopy for infertile women: a review. *J Minim Invasive Gynecol*. 2015;22(3):353–362.
16. Ustunyurt E et al. Role of transvaginal sonography in the diagnosis of retained products of conception. *Arch Gynecol Obstet*. 2008;277(2):151–154.
17. Kamaya A et al. Retained products of conception: spectrum of color Doppler findings. *J Ultrasound Med*. 2009;28(8):1031–1041.
18. Noonan JB et al. MR imaging of retained products of conception. *AJR*. 2003;181(2):435–439.
19. Kim SJ. Placental site trophoblastic tumour. *Bailliere's Best Practice Res Clin Obstet Gynaecol*. 2003;17(6):969–984.
20. Jauniaux E. Ultrasound diagnosis and follow-up of gestational trophoblastic disease. *Ultrasound Obstet Gynecol*. 1998;11:367–377.
21. Timmerman D et al. Color Doppler imaging is a valuable tool for the diagnosis and management of uterine vascular malformations. *Ultrasound Obstet Gynecol*. 2003;21(6):570–577.
22. Hooker AB et al. Reproductive performance of women with and without intrauterine adhesions following recurrent dilatation and curettage for miscarriage: long-term follow-up of a randomized controlled trial. *Hum Reprod*. 2021;36(1):70–81.
23. Hamerlynck TWO et al. An alternative approach for removal of placental remnants: hysteroscopic morcellation. *J Minim Invasive Gynecol*. 2013;20(6):796–802.
24. Kim C et al. Medical treatments for incomplete miscarriage. *Cochrane Database Syst Rev*. 2017;1(1).
25. Golan A et al. Operative hysteroscopy to remove retained products of conception: novel treatment of an old problem. *J Minim Invasive Gynecol*. 2011;18(1):100–103.
26. Riemma G et al. Hysteroscopic criteria for the diagnosis of chronic endometritis: a systematic review and diagnostic test accuracy meta-analysis. *Am J Obstet Gynecol*. 2025;233(1):12–24.e4.
27. Hamerlynck TWO et al. Hysteroscopic morcellation versus loop resection for removal of placental remnants: a randomized trial. *J Minim Invasive Gynecol*. 2016;23(7):1172–1180.
28. Tchabo JG. Use of contact hysteroscopy in evaluating postpartum bleeding and incomplete abortion. *J Reprod Med*. 1984;29(10):749–751.
29. Goldenberg M et al. Managing residual trophoblastic tissue: hysteroscopy for directing curettage. *J Reprod Med*. 1997;42(1):26–28.
30. Jakopič Maček K et al. Office hysteroscopy in removing retained products of conception – a highly successful approach with minimal complications. *J Obstet Gynaecol*. 2020;40(8):1122–1126.
31. Vitale SG. The biopsy snake grasper sec. VITALE: a new tool for office hysteroscopy. *J Minim Invasive Gynecol*. 2020;27(6):1414–1416.
32. Chiofalo B et al. Reproductive outcomes of infertile women undergoing "see and treat" office hysteroscopy: a retrospective observational study. *Minim Invasive Ther Allied Technol*. 2021;30(3):147–153.
33. Di Spiezio Sardo A et al. Review of new office-based hysteroscopic procedures 2003–2009. *J Minim Invasive Gynecol*. 2010;17(4):436–448.
34. Vitale SG et al. Comparison of three biopsy forceps for hysteroscopic endometrial biopsy in postmenopausal patients (HYGREB-1): a multicenter, single-blind randomized clinical trial. *Int J Gynaecol Obstet*. 2021;155(3):425–432.
35. Vitale SG et al. Risk of endometrial malignancy in women treated for breast cancer: the BLUSH prediction model – evidence from a comprehensive multicentric retrospective cohort study. *Climacteric*. 2024;27(5):482–488.
36. Cohen SB et al. Hysteroscopy may be the method of choice for management of residual trophoblastic tissue. *J Am Ass Gynecol Laparoscop*. 2001;8:199–202.
37. Dealberti D et al. New mini-resectoscope: analysis of preliminary quality results in outpatient hysteroscopic polypectomy. *Arch Gynecol Obstet*. 2013;288(2):349–353.
38. Georgiou D et al. Hysteroscopic tissue removal system (MyoSure) for the resection of polyps, sub-mucosal leiomyomas and retained products of conception in an out-patient setting: a single UK institution experience. *Eur J Obstet Gynecol Reprod Biol*. 2018;231:147–151.
39. van Wessel S et al. Reproductive and obstetric outcomes after hysteroscopic removal of retained products of conception. *J Minim Invas Gynecol*. 2020;27(4):840–846.
40. Rein DT et al. Hysteroscopic management of residual trophoblastic tissue is superior to ultrasound-guided curettage. *J Minim Invas Gynecol*. 2011;18(6):774–778.
41. Urman B et al. Fertility and anatomical outcomes following hysteroscopic adhesiolysis: an 11-year retrospective cohort study to validate a new classification system for intrauterine adhesions (Urman-Vitale Classification System). *Int J Gynaecol Obstet*. 2024;165(2):644–654.
42. Vitale SG et al. Virtual sonographic hysteroscopy in assisted reproduction: a retrospective cost-effectiveness analysis. *Int J Gynaecol Obstet*. 2022;156(1):112–118.
43. Vitale SG et al. Surgical and reproductive outcomes after hysteroscopic removal of retained products of conception: a systematic review and meta-analysis. *J Minim Invas Gynecol*. 2021;28:204–217.
44. Ferro J et al. Improved accuracy of hysteroembryoscopic biopsies for karyotyping early missed abortions. *Fertil Steril*. 2003;80(5).
45. Philipp T et al. Embryoscopic and cytogenetic analysis of 233 missed abortions: factors involved in the pathogenesis of developmental defects of early failed pregnancies. *Hum Reprod*. 2003;18(8):1724–1732.

30 ASHERMAN SYNDROME; HYSTEROSCOPICALLY DIAGNOSED INTRAUTERINE ADHESIONS

Miriam M.F. Hanstede and Esther A.M. Kuijper

30.1 Introduction

Intrauterine adhesions (IUAs), also known as synechiae or Asherman syndrome (AS), have been recognized for over a century. The earliest case reports trace back to the late 19th century, and Joseph Asherman provided a detailed description of adhesions linked to symptoms, forming the foundation of what is now known as Asherman syndrome (1–3). Intrauterine adhesions can develop due to trauma from procedures, infections, or hypoxia of the endometrium, leading to symptoms such as infertility, menstrual irregularities, and recurrent pregnancy loss (4, 5). AS is defined by hysteroscopically diagnosed intrauterine adhesions combined with one or more clinical features.

30.2 Prevalence

The prevalence of IUA varies significantly across different populations and over time, with reports ranging from as low as 1.5%–2.8% in unselected populations to nearly 50% in high-risk groups (6–8). In Europe, AS has a prevalence of four per 10,000, classifying it as a rare disease (9). Global variation is influenced by factors such as endemic infections like genital tuberculosis (10, 11) and schistosomiasis (12), as well as the management of miscarriage.

One year after a miscarriage, approximately 20% of women are diagnosed with IUA, regardless of the type of management (expectant, medication, or curettage). Prevalence increases with the number of miscarriages, likely due to the number of curettages (6). Similar prevalence rates are observed after termination of pregnancy and for retained products of conception (13–15). Up to 40% prevalence rates are observed in patients primarily treated with curettage, regardless of whether it was a first, repeated, or postpartum procedure (5, 16, 17).

30.3 Etiology

The formation of adhesion varies based on pregnancy stage at the time of miscarriage, repeated surgical procedures, and timing of surgery postpartum. Increased risks are found for miscarriage in advanced gestational age (31%) compared to early pregnancy loss (6%) (18), repeated (up to almost 50%) (19) versus one curettage (16%) (6, 20), postpartum versus first trimester (21), and a few weeks (2–4) after birth (23%) versus directly postpartum (4%) (22, 23). Uncomplicated cesarean sections may result in IUAs in 2%–3% of patients. Management of abundant bleeding after birth by means of compressing sutures (B-Lynch 18.5%) or (temporarily) blocking the uterine artery (embolization 14%) might induce adhesion formation due to reduced vascularization and suppression of endometrial regeneration (15, 24). The basal layer seems to be most susceptible to damage in the first month after birth or miscarriage. A possible explanation is the hypoestrogenic state of the uterus which makes regeneration more difficult (16). Intrauterine procedures, such as hysteroscopic surgeries for fibroids, polyps, or septa, result in adhesions in 8%–24% of patients (15). The type of surgery and the number of myoma removed may influence the likelihood of adhesion formation (25, 26). Women with congenital uterine anomalies are at higher risk due to an increased likelihood of miscarriage and subsequent curettage (27). Moreover, correction of Müllerian duct abnormalities itself can also result in IUA formation. (15, 26, 28). However, most women undergoing intrauterine surgery do not develop adhesions, suggesting that predisposing factors determine susceptibility to adhesion formation. Infections like genital tuberculosis and schistosomiasis can cause severe adhesions, completely obliterating the uterine cavity (29, 30). Impaired vascularization of the endometrium and myometrium is shown in AS (31). Fibrotic tissue contains fewer blood vessels and is therefore less susceptible to hormonal stimulation and tissue regeneration. In conclusion, all intrauterine processes with the ability to damage the endometrial basal layer are risk factors for adhesion formation in women susceptible to this problem (Figure 30.1). However, whether women are susceptible to developing IUAs depends on their genetic predisposition (9).

30.4 Symptomatology

The presence of symptoms is a key feature in AS and includes one or more of the following: reduced blood flow (amenorrhea or hypomenorrhea in ovulatory women), subfertility or recurrent pregnancy loss (RPL), history of abnormal invasive placentation (AIP; placenta previa, accreta, increta, or percreta) or cyclic abdominal pain.

Symptoms can vary between patients but most (70%–95%) of them experience changed menstrual blood flow (37% amenorrhea, 31% hypomenorrhea, 1% menorrhagia, 6% normal menses) (8, 32, 33). The original hypothesis by Asherman for the reduced blood flow focused on inhibition of nerves originating in the internal cervical os, resulting in reduced endometrial response to hormonal stimulation (2). Reduced functional endometrial surface area in combination with unresponsiveness of the residual endometrium might explain why no hematometrium is found in these patients (34). Subfertility is reported in 7%–43% of women with AS, and proposed mechanisms are hampered sperm transport and reduced implantation capability (8, 32, 33), which could result in recurrent pregnancy loss. A small percentage of patients report cyclic pain (3%–4%) mostly in cases of amenorrhea (8), which might be due to small parts of functional endometrium unable to expel blood from the uterine cavity (35).

30.5 Adhesion Detection

Before the advent of hysteroscopy, hysterosalpingography (HSG) was the primary diagnostic test for identifying occluded areas in the uterine cavity. HSG is still valuable because it outlines specific filling defects, which can indicate intrauterine adhesions and serve as a guidance method. On transvaginal ultrasound (TVUS), an echogenic area in the endometrial cavity or an asymmetric endometrial thickness is suggestive of

DOI: 10.1201/9781003312109-30

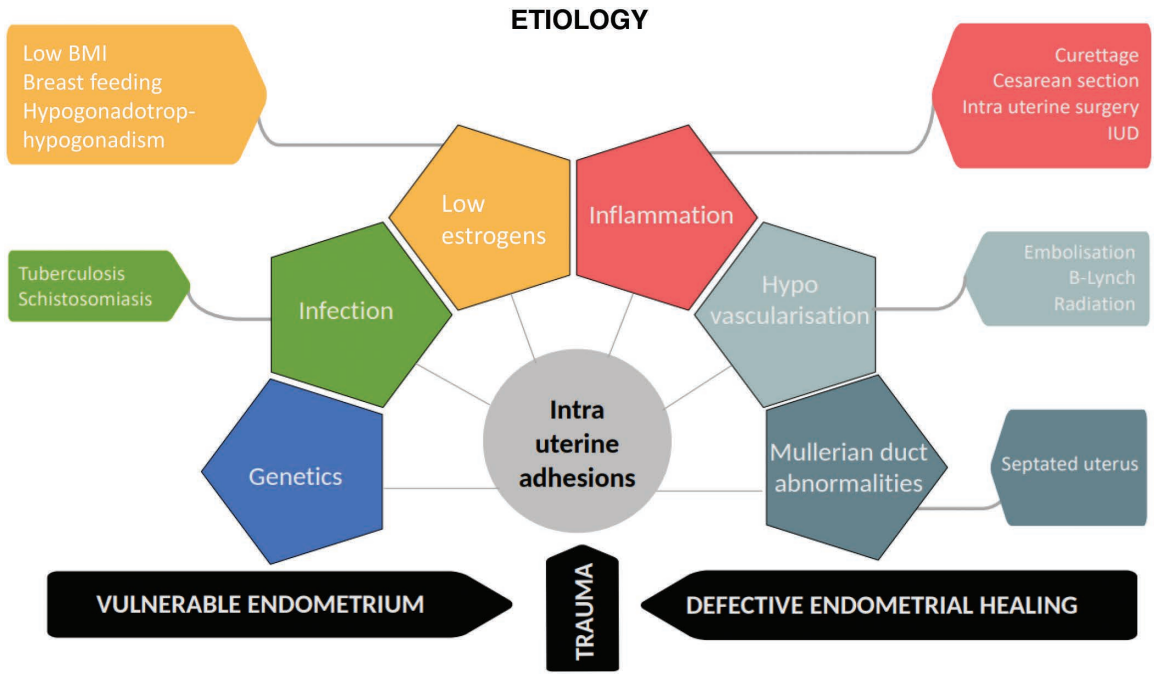


FIGURE 30.1 Etiology of Asherman syndrome.

IUA; however, the sensitivity (52%) (36) and specificity (11%) (37) for diagnosing intrauterine adhesions are notably low. Three-dimensional (3D) offers a more accurate diagnostic approach, particularly in differentiating between severe IUA and lower uterine segment outflow obstructions. It has demonstrated higher sensitivity (100% vs 66.7%) compared to HSG for classifying adhesion severity (37). MRI is useful for assessing residual functional endometrium. In women with IUA, the endometrium may exhibit reduced signal intensity, with fibrous bands appearing as areas of low signal intensity (38, 39).

Hysteroscopy is the gold standard for the detection of IUA, as it allows for direct visualization of the uterine cavity. It can accurately confirm the presence, extent, and severity of adhesions, as well as assess the quality of the residual endometrium (Figure 30.2). Importantly, hysteroscopy has the added benefit of immediate treatment following the diagnostic procedure.

30.6 Classification Systems

To assess the severity of intrauterine adhesions, identify the most appropriate treatment, and predict treatment outcomes, several classification systems have been proposed using various diagnostic techniques. However, none of these systems gained universal acceptance or underwent full validation. One of the key classification systems is the American Fertility Society (AFS) classification, which categorizes IUA into four grades based on the extent of adhesions and the severity of the uterine cavity obliteration. This system, though useful, has its limitations in terms of universal applicability. The European Society of Gynecological Endoscopy (ESGE) classification provides a more comprehensive approach. It includes five categories based on the extent, type, and location of adhesions. The ESGE classification incorporates a more detailed description of specific anatomical areas affected by adhesions (Figure 30.3), which is advantageous for tailoring treatment strategies. Despite the availability of multiple classifications, the lack of a universally accepted system continues to pose a challenge in standardizing IUA treatment and reporting on outcomes.

30.7 Treatment

The primary goal of adhesiolysis is removing IUAs and restoring the normal anatomy of the uterine cavity. All treatment options are summarized in Figure 30.4. Hysteroscopy is the gold standard due to its minimally invasive nature and the ability to directly visualize the uterine cavity. Distention of the uterine cavity not only provides vision but also helps in separating the adhesions. In case of filmy adhesions sometimes distention alone or slight manipulation with the hysteroscope is enough to remove them (40), but in most cases additional actions are needed. A variety of surgical techniques can be employed during hysteroscopy, including the use of lasers, monopolar or bipolar instruments, electrosurgery, and conventional dissection. However, while techniques like laser and electrosurgery are effective in reconstructing the uterine cavity, they carry the risk of damaging any remaining healthy endometrial tissue, which can negatively impact fertility outcomes and are therefore not recommended (21). Care must be taken to preserve as much functional endometrium as possible to optimize future reproductive potential.

The most common complications during hysteroscopic adhesiolysis in Asherman syndrome include uterine wall perforation. The risk of perforation varies based on the severity of the adhesions, with low-grade adhesions posing a 2% perforation risk and severe adhesions raising the risk to 9% (41). The risk of infection is small, and antibiotic prophylaxis is generally not required (42), unless a perforation occurs.

To minimize the risk of complications, several guidance techniques have been developed. Ultrasound guidance is widely used due to its accessibility and noninvasive nature,

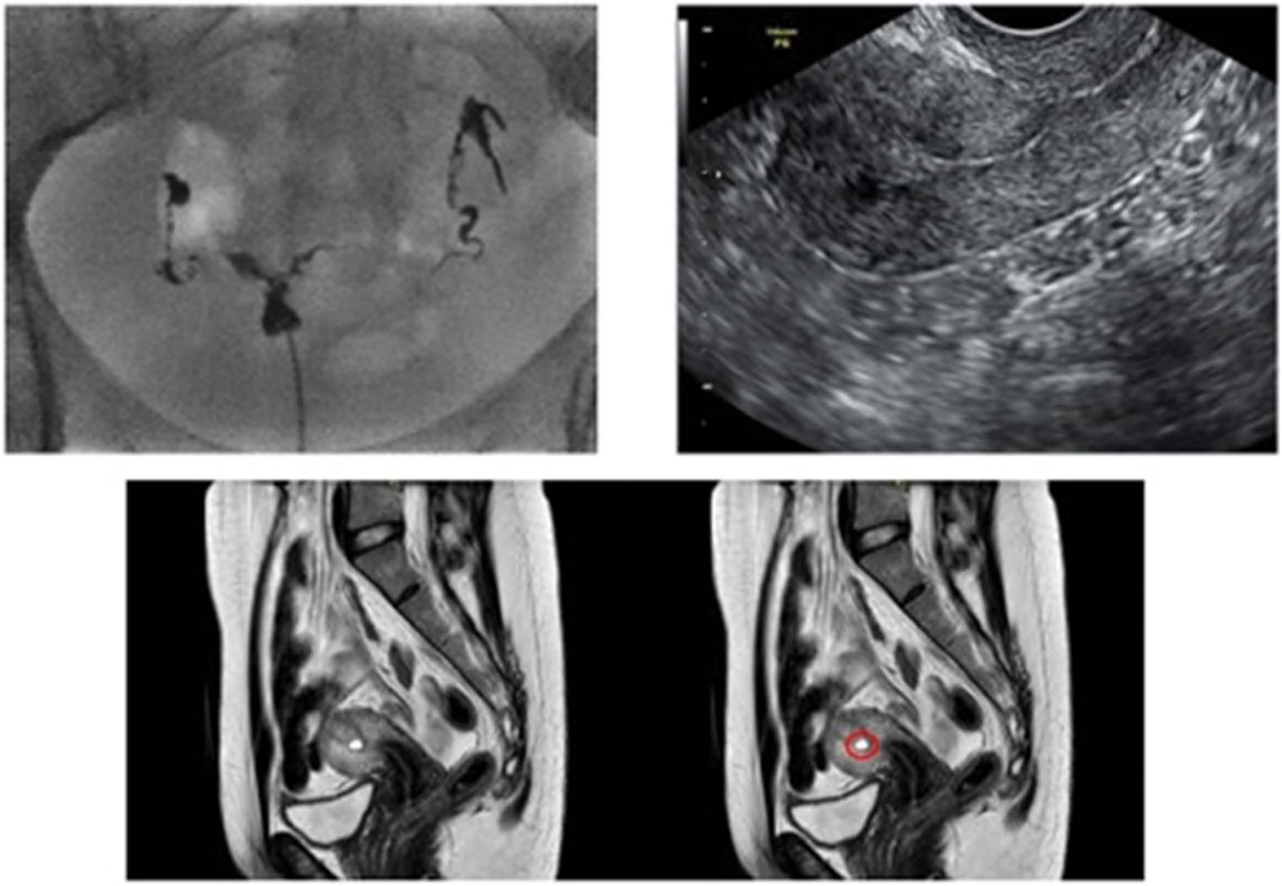


FIGURE 30.2 Adhesions on HSG, TVUS, and remaining functional endometrium on MRI (within the red circle).

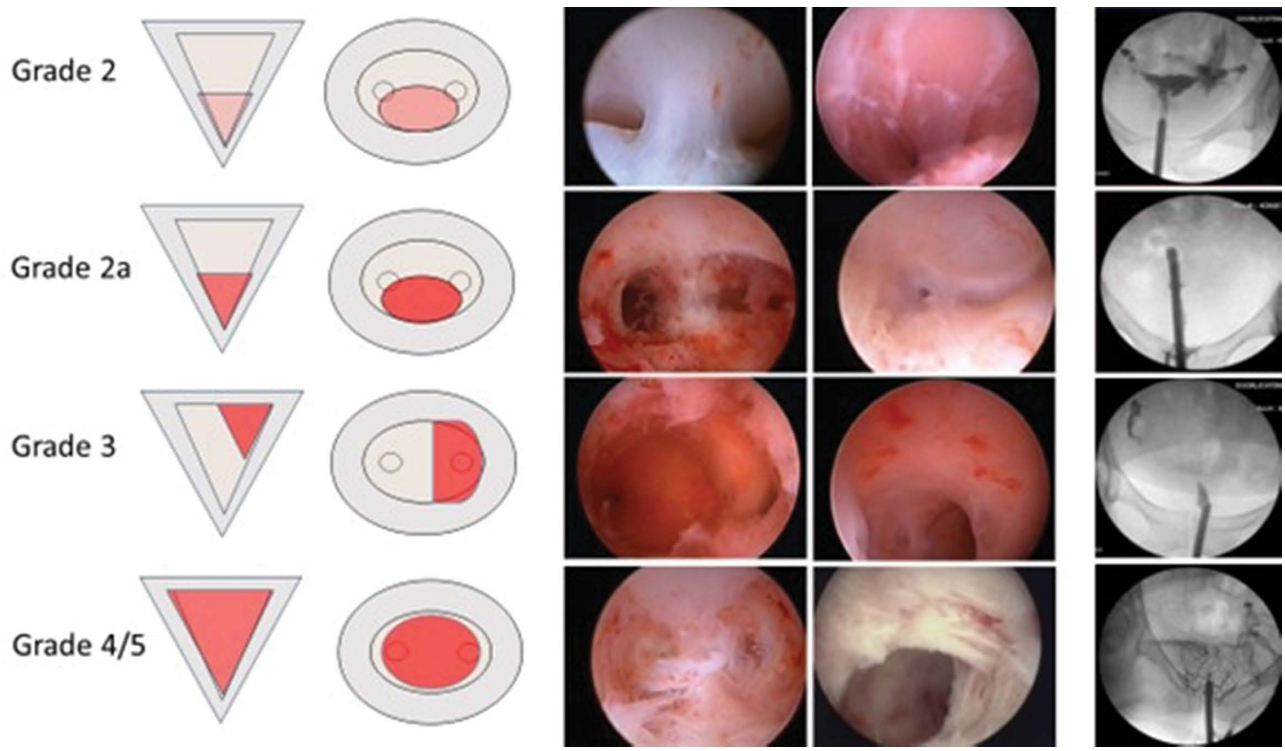


FIGURE 30.3 Grades of adhesions in the ESGE classification, shown in the form of a diagram, hysteroscopy, and fluoroscopy.

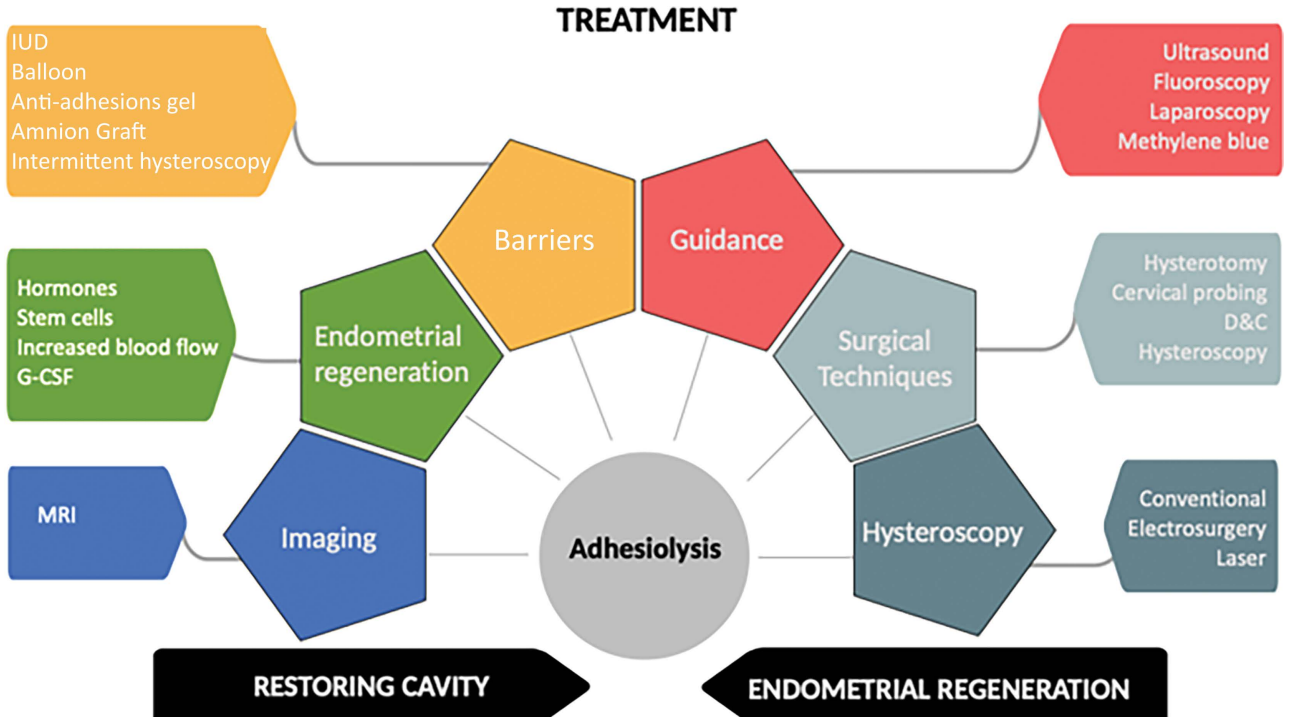


FIGURE 30.4 Overview of treatment options.

although it still presents a perforation risk of around 5% (32). Laparoscopy can also be employed by visualizing light transmission through the uterine wall, though it is more effective at recognizing perforations and limiting damage to surrounding organs than preventing them. Fluoroscopy provides additional visual guidance, particularly in identifying hidden endometrial pockets and the fallopian tubes, which serve as landmarks during dissection and reduce the risk of creating false passages or perforations (21, 43). These techniques have been developed to improve the safety and efficacy of the procedure, especially in cases involving firm or severe adhesions where surgery is more challenging. Hysteroscopic transcervical adhesiolysis (TCA) with fluoroscopy (Figure 30.5) has been performed since the early 1990s. This technique combines hysteroscopy with conventional instruments and fluoroscopic guidance (43, 44).

A three-way tap is connected to the inflow channel of the hysteroscope, allowing for the simultaneous management of fluid infusion and the administration of contrast dye. This tap is attached to a syringe containing 20 cc of radiopaque dye, which is used to enhance visualization of the uterine cavity during the procedure. The dye is typically a water-soluble iodine-based contrast medium that facilitates fluoroscopic imaging by creating clear differentiation between anatomical structures. To locate blocked areas of endometrium or occluded regions within the uterine cavity, a small perforation is made through the dense adhesions using a forceps or scissors. This perforation creates a passage through the scar tissue, enabling the introduction of contrast dye directly into the otherwise inaccessible portions of the uterine cavity. The next step involves creating a continuous fluoroscopic image using the C-arm while simultaneously flushing the dye through the hysteroscope. As the dye flows through the cavity, it highlights any previously obstructed or nonvisible areas, including endometrial pockets or regions blocked by adhesions. The dye outlines the uterine cavity's true borders, enabling precise identification of remaining adhesions, blocked regions, or anatomical abnormalities. This process provides critical visual feedback during the procedure, allowing the surgeon to distinguish between normal uterine tissue and adhesions, reducing the risk of creating false passages or causing unintended damage to healthy tissue. Additionally, this method allows for more accurate and complete removal of adhesions, increasing the overall success rate of the adhesiolysis procedure (Figure 30.5).

30.8 Postoperative Management

Spontaneous recurrence of adhesions is a significant issue in women with AS, with reported recurrence rates reaching up to 70% (21, 45). Various approaches have been developed to prevent recurrence and promote endometrial recovery post-adhesiolysis, involving mechanical barriers, hormonal therapies, and regenerative techniques.

30.8.1 Mechanical Barriers

One of the most common approaches to prevent adhesion reformation involves the use of intrauterine devices (IUDs) or intrauterine balloons (8, 41, 46). Copper- and hormone-free IUDs are preferred to avoid inflammatory responses or hypoestrogenic effects, which could hinder endometrial recovery. Special intrauterine balloons or catheter balloons can be placed immediately after surgery and typically remain in the uterine cavity for 3 to 10 days (47–49). Both IUDs and balloons help maintain uterine cavity patency during the healing process and have shown similar efficacy in preventing adhesion reformation after hysteroscopic adhesiolysis (50). Some reports on the use of **amniografts** or **gels** placed over the balloon have shown modest improvements in reducing adhesion recurrence, though fertility outcomes were not assessed and recurrence rates were initially very high (51, 52).

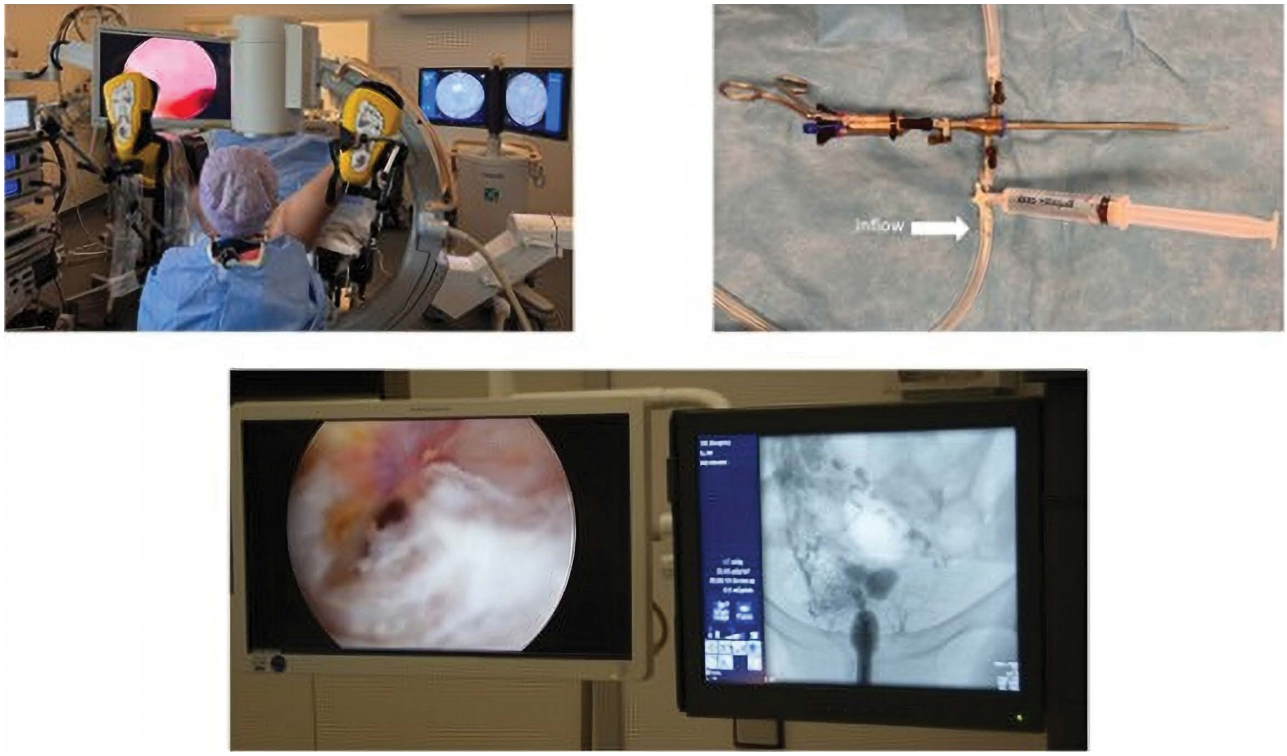


FIGURE 30.5 TCA in operating theatre; a combination of hysteroscopic view and fluoroscopy.

Hyaluronic acid (HA) gel has been explored as a barrier therapy for prevention of adhesion formation (53). Some studies suggest that HA gel significantly reduces the formation of primary adhesions compared to no treatment, though there are conflicting results regarding its use in reducing recurrence rates (54, 55).

30.8.2 Hormonal Therapy

Estrogen therapy is commonly employed to stimulate the regeneration of any remaining functional endometrium (56). However, evidence of the direct role of estrogens in regenerating damaged endometrium remains limited. While hormonal therapy alone has limited impact on preventing readhesions, it appears to be beneficial when combined with mechanical barriers such as IUDs or balloons (49, 57).

30.8.3 Stem Cell Therapy

Regeneration of the endometrium by stem cells was tested but despite some positive outcomes this still needs further evaluation (58–60).

Although various methods show potential in preventing adhesion recurrence, further studies are needed to determine the most effective strategy or combination of treatments. The development of innovative therapies, including regenerative medicine, is a promising direction for improving outcomes in women with AS.

30.9 Postoperative Outcome

Success rates of adhesiolysis largely depend on the severity of the adhesions and the likelihood of recurrence. In most cases, between 67.7% and 97.8% of patients experience the restoration of blood flow (21, 32, 45, 61, 62). Studies show that while adhesiolysis can improve reproductive potential, the overall live birth rates remain less consistent compared to blood flow restoration (63).

30.10 Fertility and AS

Fecundity in patients with IUA is significantly reduced, even after successful treatment, due to a combination of mechanical and physiological factors. If the internal cervical os, the cavity, or both tubal ostia are blocked completely by adhesions, it is easy to understand why sperm cells are not able to reach the oocyte. Cervical adhesions alone result in a reduction of mucosal folds, channel formation, and an unresponsive mucosa which reduces sperm transport through the cervix (64, 65).

Movement of the subendometrial layer, which enhances sperm cells on their way to the fallopian tubes, might be impaired by IUA as well. Reduced speed of transport through the cervix and uterine cavity leaves sperm cells more susceptible to immunologic reactions, reducing their fertilizing potential. In addition, the endometrium in patients with AS often exhibits reduced responsiveness to hormonal stimulation due to the presence of avascular and fibrotic tissue, leading to a thin endometrial lining. Even when endometrial thickness and subsequently menstrual blood flow improves after adhesiolysis, the arterial impedance remains high, which negatively impacts endometrial receptivity (66).

Moreover, the impaired interaction between the embryo and the endometrium, both mechanically and at the molecular level, contributes to the reduced fecundity (67). Endometrial glands function in early pregnancy as a source of nutrition before the placenta takes over. The reduced number of functional glands might be related to the increased miscarriage rate in AS (68). Thus, even with successful treatment, the long-term

TABLE 30.1 Review of Literature Reporting Life Birth Rates in Women with IUA after Surgery

Year	Author	Number of Cases (N)	Life Birth Rate after Surgery (%)
1978	March 1978 (50)	65	70
1978	Sugimoto 1978 (40)	143	31
1983	Hamou 1983 (69)	59	38
1986	Fedele 1986 (70)	22	41
1986	Friedman 1986 (71)	33	96
1988	Lancet 1988 (72)	120	64
1988	Valle 1988 (45)	187	80
1996	Katz 1996 (73)	90	69
1996	Pistofidis 1996 (74)	86	15
1997	McComb 1997 (75)	6	67
1997	Pabuccu 2008 (76)	71	24
1998	Protopapas 1998 (77)	7	14
1999	Capella-Allouc 1999 (78)	31	32
2006	Fernandez 2006 (79)	71	33
2010	Deans 2010 (32)	154	64
2015	Hanstede 2021 (33)	500	67
Pooled data			
1982	Schenker 1982 (8)	1052	51
2008	Yu 2008 (41)	666	79

outcomes for women with IUA remain challenging due to these complex factors.

30.11 Pregnancy Rates and Live Birth Rates

Pregnancy rates and live birth rates following hysteroscopic treatment of IUA vary significantly, ranging from 14% to 96% (Table 30.1). This wide variation reflects the heterogeneity of the data and the differing severity of adhesions among patients. Women with lower-grade IUA generally have more favorable outcomes, with mean pregnancy rates as high as 81%, whereas those with higher-grade IUA face more challenges, with mean pregnancy rates dropping to around 32%. Live birth rates in severe cases of IUA remain consistently low, with a reported rate of approximately 30% after treatment.

30.12 Complications in Pregnancies after Adhesiolysis

Women with treated AS face an increased risk of pregnancy-related complications, including a 40%–50% chance of premature delivery, with some cases linked to premature rupture of membranes and others to cervical insufficiency, which may occur after repeated hysteroscopies. Endometrial deficiency may also contribute to intrauterine growth restriction (IUGR) (32) and complications such as placenta accreta spectrum (PAS) (45, 64, 68, 78, 80, 81). Uterine rupture may occur and is postulated to be related to the weakened and scarred uterine wall resulting from hysteroscopic surgery, especially in cases in which a perforation occurred in the index procedure (82, 83). The problem with establishing pregnancy-related complication rates is that data are collected from case reports and retrospective studies and reporting bias may be substantial. In the absence of prospective studies, women who have had treatment for AS should be counseled about the potential risks of obstetric complications, and their pregnancies should be managed in a high-risk obstetric setting (69–77).

References

1. Asherman JG. Amenorrhoea traumatica (atretica). *BJOG*. 1948;55(1):23–30.
2. Asherman JG. Traumatic intra-uterine adhesions. *BJOG*. 1950;57(6):892–896.
3. Asherman J. Traumatic intrauterine adhesions and their effects on fertility. *Int J Fertil*. 1957;2(1):49–61.
4. Hanstede M et al. Reproductive outcomes of 10 years asherman's surgery. *J Minima Invas Gynecol*. 2015;22(6S):S14.
5. Dreisler E et al. Asherman's syndrome: current perspectives on diagnosis and management. *Int J Women's Health*. 2019;11:191–198.
6. Hooker AB et al. Systematic review and meta-analysis of intrauterine adhesions after miscarriage: prevalence, risk factors and long-term reproductive outcome. *Hum Reprod Update*. 2014;20(2):262–278.
7. March CM. Intrauterine adhesions. *Obstet Gynecol Clin N Am*. 1995;22(3):491–505.
8. Schenker JG et al. Intrauterine adhesions: an updated appraisal. *Fertil Steril*. 1982;37(5):593–610.
9. Santamaria X et al. Asherman's syndrome: it may not be all our fault. *Human Reprod*. 2018;33(8):1374–1380.
10. Sharma JB. Current diagnosis and management of female genital tuberculosis. *J Obstet Gynecol India*. 2015;65(6):362–371.
11. Sharma JB et al. Female genital tuberculosis: revisited. *Indian J Med Res*. 2018;148(Suppl):S71–S83.
12. Krolikowski A et al. Asherman syndrome caused by schistosomiasis. *Obstet Gynecol*. 1995;85(5 Pt 2):898–899.

13. Hooker AB et al. Long-term complications and reproductive outcome after the management of retained products of conception: a systematic review. *Fertili Steril*. 2016;105(1):156–164. e1–2.
14. Hooker A et al. Prevalence of intrauterine adhesions after termination of pregnancy: a systematic review. *Eur J Contracept Reprod Health Care*. 2016;21(4):329–335.
15. Doroftei B et al. Mini-review of the new therapeutic possibilities in Asherman syndrome-where are we after one hundred and twenty-six years? *Diagnost*. 2020;10(9):706.
16. Westendorp IC et al. Prevalence of asherman's syndrome after secondary removal of placental remnants or a repeat curettage for incomplete abortion. *Human Reprod*. 1998;13(12):3347–3350.
17. Salzani A et al. Prevalence of uterine synechia after abortion evacuation curettage. *Sao Paulo Med J*. 2007;125(5):261–264.
18. Adoni A et al. The incidence of intrauterine adhesions following spontaneous abortion. *Int J Fertil*. 1982;27(2):117–118.
19. Romer T. Post-abortion-hysteroscopy – a method for early diagnosis of congenital and acquired intrauterine causes of abortions. *Eur J Obstet Gynecol Reprod Biol*. 1994;57(3):171–173.
20. Friedler S et al. Incidence of post-abortion intra-uterine adhesions evaluated by hysteroscopy – a prospective study. *Human Reprod*. 1993;8(3):442–444.
21. Hanstede MM et al. Results of centralized asherman surgery, 2003–2013. *Fertili Steri*. 2015;104(6):1561–1568.e1.
22. Eriksen J et al. The incidence of uterine atresia after post-partum curettage. A follow-up examination of 141 patients. *Danish Med Bull*. 1960;7:50–51.
23. Bergman NP. Traumatic intra-uterine lesions. *Acta Obstet Gynecol Scand*. 1961;40(Suppl 4):1–39.
24. Poujade O et al. Risk of synechiae following uterine compression sutures in the management of major postpartum haemorrhage. *BJOG*. 2011;118(4):433–439.
25. Mazzon et al. Does cold loop hysteroscopic myomectomy reduce intrauterine adhesions? A retrospective study. *Fertil Steril*. 2014;101(1):294–298.e3.
26. Taskin O et al. Role of endometrial suppression on the frequency of intrauterine adhesions after resectoscopic surgery. *J Am Assoc Gynecol Laparosc*. 2000;7(3):351–354.
27. Stillman RJ et al. Association between Mullerian duct malformations and Asherman syndrome in infertile women. *Obstet Gynecol*. 1985;65(5):673–677.
28. Yu X et al. The incidence of post-operative adhesion following transection of uterine septum: a cohort study comparing three different adjuvant therapies. *Eur J Obstet, Gynecol Reprod Biol*. 2016;201:61–64.
29. Sharma JB et al. Genital tuberculosis: an important cause of asherman's syndrome in india. *Arch Gynecol Obstet*. 2008;277(1):37–41.
30. Bukulmez O et al. Total corporal synechiae due to tuberculosis carry a very poor prognosis following hysteroscopic synechialysis. *Human Reprod*. 1999;14(8):1960–1961.
31. Polishuk W et al. Intrauterine adhesions: diagnosis and therapy. *Obstet Gynecol Digest*. 1966;8:41.
32. Deans R et al. Review of intrauterine adhesions. *J Minim Invas Gynecol*. 2010;17(5):555–569.
33. Hanstede MMF et al. Live births after Asherman syndrome treatment. *Fertili Steril*. 2021;116(4):1181–1187.
34. Toaff R et al. Traumatic hypomenorrhea-amenorrhea (asherman's syndrome). *Fertil Steril*. 1978;30(4):379–387.
35. Kodaman PH et al. Intra-uterine adhesions and fertility outcome: how to optimize success? *Curr Opinion Obstet Gynecol*. 2007;19(3):207–214.
36. Salle B et al. Transvaginal sonohysterographic evaluation of intrauterine adhesions. *J Clin Ultrasound*. 1999;27(3):131–134.
37. Sylvestre C et al. A prospective study to evaluate the efficacy of two- and three-dimensional sonohysterography in women with intrauterine lesions. *Fertil Steril*. 2003;79(5):1222–1225.
38. Bacelar AC et al. The value of MRI in the assessment of traumatic intra-uterine adhesions (asherman's syndrome). *Clin Radiol*. 1995;50(2):80–83.
39. Letterie GS et al. Magnetic resonance imaging of intrauterine synechiae. *Gynecol Obstet Investig*. 1994;37(1):66–68.
40. Sugimoto O. Diagnostic and therapeutic hysteroscopy for traumatic intrauterine adhesions. *Am J Obstet Gynecol*. 1978;131(5):539–547.
41. Yu D et al. Asherman syndrome – one century later. *Fertil Steril*. 2008;89(4):759–779.
42. ACOG Committee on Practice Bulletins. ACOG practice bulletin no. 74. Antibiotic prophylaxis for gynecologic procedures. *Obstet Gynecol*. 2006;108(1):225–234.
43. Broome JD et al. Fluoroscopically guided hysteroscopic division of adhesions in severe Asherman syndrome. *Obstet Gynecol*. 1999;93(6):1041–1043.
44. Wamsteker K. *Intrauterine Adhesions (Synechiae). Diagnostic Imaging and Endoscopy in Gynecology: A Practical Guide*. London: WB Saunders; 1997:171–184.
45. Valle RF et al. Intrauterine adhesions: hysteroscopic diagnosis, classification, treatment, and reproductive outcome. *Am J Obstet Gynecol*. 1988;158(6 Pt 1):1459–1470.
46. Polishuk WZ et al. A syndrome of recurrent intrauterine adhesions. *Am J Obstet Gynecol*. 1975;123(2):151–158.
47. Klein SM et al. Asherman's syndrome: a critique and current review. *Fertil Steril*. 1973;24(9):722–735.
48. Amer MI et al. The role of intrauterine balloon after operative hysteroscopy in the prevention of intrauterine adhesions: a prospective controlled study. *Middle East Fertili Soc J*. 2005;10(2):125–129.
49. Orhue AAE et al. A comparison of two adjunctive treatments for intrauterine adhesions following lysis. *Int J Gynaecol Obstet*. 2003;82(1):49–56.
50. Lin XN et al. Randomized, controlled trial comparing the efficacy of intrauterine balloon and intrauterine contraceptive device in the prevention of adhesion reformation after hysteroscopic adhesiolysis. *Fertil Steril*. 2015;104(1):235–240.
51. Yan Y et al. The effect of adjuvant treatment to prevent and treat intrauterine adhesions: a network meta-analysis of randomized controlled trials. *J Minim Invasive Gynecol*. 2018;25(4):589–599.
52. Li C et al. The study on the safety and efficacy of amnion graft for preventing the recurrence of moderate to severe intrauterine adhesions. *Genes Dis*. 2019;7(2):266–271.
53. Hooker AB et al. Pregnancy and neonatal outcomes 42 months after application of hyaluronic acid gel following dilation and curettage for miscarriage in women who have experienced at least one previous curettage: follow-up of a randomized controlled trial. *Fertil Steril*. 2020;114(3):601–609.
54. Fei Z et al. Meta-analysis on the use of hyaluronic acid gel to prevent recurrence of intrauterine adhesion after hysteroscopic adhesiolysis. *Taiwanese J Obstet Gynecol*. 2019;58(6):731–736.
55. Lin X et al. A comparison of intrauterine balloon, intrauterine contraceptive device and hyaluronic acid gel in the prevention of adhesion reformation following hysteroscopic surgery for Asherman syndrome: a cohort study. *Eur J Obstet Gynecol Reprod Biol*. 2013;170(2):512–516.
56. Wood J et al. Treatment of traumatic uterine synechias. *Int J Fertil*. 1964;9:405–410.
57. March CM et al. Hysteroscopic management of intrauterine adhesions. *Am J Obstet Gynecol*. 1978;130(6):653–657.
58. Singh N et al. Autologous stem cell transplantation in refractory asherman's syndrome: a novel cell based therapy. *J Hum Reprod Sci*. 2014;7(2):93–98.
59. Tan J et al. Autologous menstrual blood-derived stromal cells transplantation for severe asherman's syndrome. *Hum Reprod*. 2016;31(12):2723–2729.
60. Santamaria X et al. Autologous cell therapy with CD133 bone marrow-derived stem cells for refractory asherman's syndrome and endometrial atrophy: a pilot cohort study. *Hum Reprod*. 2016;31(5):1087–1096.
61. Pabuccu R et al. Hysteroscopic treatment of intrauterine adhesions is safe and effective in the restoration of normal menstruation and fertility. *Fertil Steril*. 1997;68(6):1141–1143.
62. Fernandez H et al. Operative hysteroscopy for infertility using normal saline solution and a coaxial bipolar electrode: a pilot study. *Hum Reprod*. 2000;15(8):1773–1775.

63. Bosteels J et al. Anti-adhesion barrier gels following operative hysteroscopy for treating female infertility: a systematic review and meta-analysis. *Gynecol Surg*. 2014;11(2):113–127.
64. Magos A. Hysteroscopic treatment of asherman's syndrome. *Reprod Biomed Online*. 2002;4(Suppl 3):46–51.
65. Suarez SS et al. Sperm transport in the female reproductive tract. *Hum Reprod Update*. 2006;12(1):23–37.
66. Malhotra N et al. Changes in endometrial receptivity in women with asherman's syndrome undergoing hysteroscopic adhesiolysis. *Arch Gynecol Obstet*. 2012;286(2):525–530.
67. Revel A. Defective endometrial receptivity. *Fertil Steril*. 2012;97(5):1028–1032.
68. Hooker AB et al. The link between intrauterine adhesions and impaired reproductive performance: a systematic review of the literature. *BMC Pregnancy Childbirth*. 2022;22(1):837.
69. Hamou J et al. Diagnosis and treatment of intrauterine adhesions by microhysteroscopy. *Fertil Steril*. 1983;39(3): 321–326.
70. Fedele L et al. Intrauterine adhesions: current diagnostic and therapeutic trends. *Acta Eur Fertil*. 1986;17(1):31–37.
71. Friedman A et al. Severe obstetric complications after aggressive treatment of Asherman syndrome. *Obstet Gynecol*. 1986;67(6):864–867.
72. Lancet M et al. A review of asherman's syndrome, and results of modern treatment. *Int J Fertil*. 1988;33(1):14–24.
73. Katz Z et al. Reproductive outcome following hysteroscopic adhesiolysis in asherman's syndrome. *Int J Fertil Menopaus Stud*. 1996;41(5):462–465.
74. Pistofidis G et al. Comparison of operative and fertility outcome between groups of women with intrauterine adhesions after adhesiolysis. *J Am Ass Gynecol Laparosc*. 1996;3(4, Suppl):S40.
75. McComb PF et al. Simplified therapy for asherman's syndrome. *Fertil Steril*. 1997;68(6):1047–1050.
76. Pabuccu R et al. Efficiency and pregnancy outcome of serial intrauterine device-guided hysteroscopic adhesiolysis of intrauterine synechiae. *Fertil Steril*. 2008;90(5):1973–1977.
77. Protopapas A et al. Myometrial scoring: a new technique for the management of severe asherman's syndrome. *Fertil Steril*. 1998;69(5):860–864.
78. Capella-Allouc S et al. Hysteroscopic treatment of severe asherman's syndrome and subsequent fertility. *Human Reprod*. 1999;14(5):1230–1233.
79. Fernandez H et al. Fertility after treatment of asherman's syndrome stage 3 and 4. *J Minim Invas Gynecol*. 2006;13(5):398–402.
80. Zikopoulos KA et al. Live delivery rates in subfertile women with asherman's syndrome after hysteroscopic adhesiolysis using the resectoscope or the versapoint system. *Reprod Biomed Online*. 2004;8(6):720–725.
81. Tavcar J et al. Incidence and clinical implications of placenta accreta spectrum after treatment for asherman syndrome. *J Minim Invasive Gynecol*. 2023;30(3):192–198.
82. Deaton JL et al. Spontaneous uterine rupture during pregnancy after treatment of asherman's syndrome. *Am J Obstet Gynecol*. 1989;160(5 Pt 1):1053–1054.
83. Hulka JF. Uterine rupture after treatment of asherman's syndrome. *Am J Obstet Gynecol*. 1990;162(5):1352–1353.

31 CESAREAN SCAR DEFECT (ISTHMOCELE)

Sergio Haimovich and Noam Smorgick

31.1 Introduction

Isthmocele is a post-cesarean complication that can have significant consequences for women's reproductive health. Cesarean scar defects (CSDs) (1, 2), cesarean scar dehiscence (3–5), isthmocele (6–8), uterine transmural hernia (9), diverticulum (10), pouch formation (11), niche (12, 13), and uteroperitoneal fistula (14) are all used in the literature to describe this condition. CSDs occur when a defect or indentation develops at the site of a previous cesarean section scar in the lower segment of the uterus (Figure 31.1), often resulting from incomplete healing of the scar tissue. The term "isthmocele" was introduced by Morris in 1995 by examining the uterine specimens following hysterectomy in women with previous cesarean section (6).

In recent years, there has been a growing interest in understanding the etiology, prevalence, diagnosis, and management of isthmocele, especially given the rising rates of cesarean deliveries worldwide (15). As the rates of cesarean deliveries continue to rise, so does the importance of addressing isthmocele and its associated complications. The development of comprehensive guidelines for diagnosing and managing this condition, as well as increasing awareness among healthcare providers, can help ensure that women receive appropriate care and support. In addition, further investigation into the underlying factors contributing to the development of isthmocele may guide the development of effective prevention strategies, as well as refining diagnostic techniques and evaluating the long-term outcomes of different treatment approaches.

In this chapter we will discuss the significance, diagnosis, and management of isthmocele, as well as emphasize the diagnosis and approach to cesarean scar pregnancy (CSP).

31.2 Epidemiology

Cesarean sections (CSs) are among the most common surgical procedures performed worldwide. In the United States, the rate of CS has risen substantially in recent decades, with approximately 32% of all births delivered by CS in 2020 (16). Similar rates have been reported in many other regions of the world (15, 17). CS is associated with both short-term and long-term risks, resulting in higher rates of obstetrical sequelae in subsequent pregnancies (placenta accreta, scar dehiscence, ectopic scar pregnancy, and uterine rupture) (1). While cesarean deliveries can be lifesaving interventions for both mother and baby, they are not without risks, including the development of isthmocele (16).

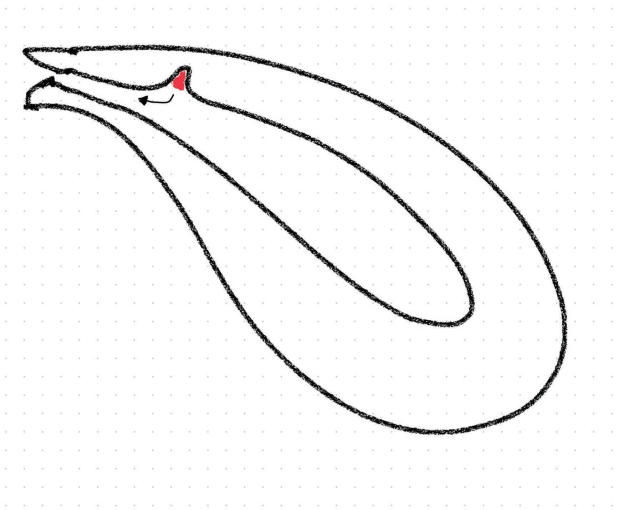


FIGURE 31.1 Cesarean scar defect or isthmocele.

The prevalence of isthmocele varies across studies, with reported rates ranging from 24% to 70% (11, 13). In particular, large CSD (defined as a scar with a depth of at least 50% or 80% of the anterior myometrium, or the remaining myometrial thickness < 2.2 mm evaluated by ultrasound) occurs with an incidence ranging from 11% to 45% (13, 18).

Several risk factors have been implicated in the development of isthmocele:

1. Factors related to the surgical technique: The suturing technique used to close the uterine incision is one of the primary factors affecting the development of isthmocele. Among the factors associated with the surgical techniques which have been investigated in association with isthmocele are single- versus double-layer closure, suture material, locked versus unlocked sutures, surgeon's experience, and intraoperative complications.
   a. Single- versus double-layer closure: Several studies have compared single- versus double-layer suturing in association with isthmocele prevalence. Bij de Vaate et al. (13) conducted a systematic review of the literature and found that single-layer closure was associated with a higher prevalence of isthmocele compared to double-layer closure. This increased risk may be attributed to insufficient tissue approximation and support, leading to deficient scar healing. In a meta-analysis, Roberge et al. (19) compared single- and double-layer closure techniques, concluding that double-layer closure was associated with a decreased risk of uterine rupture and isthmocele formation.
   b. Suture materials: The type of suture material used during the closure of the uterine incision can also influence the likelihood of isthmocele formation. Hosseini R et al. (20) compared the use of Vicryl and catgut sutures in a randomized controlled trial, finding that the risk of CSD was lower with the use of Vicryl. However, further research is necessary to establish the optimal suture material for minimizing isthmocele risk. In particular, the risk of isthmocele with the use of the barbed suture, which has become increasingly popular for closure of the uterus, has not been determined yet (21).
   c. Locked versus unlocked sutures: Bujold et al. (22) found that locked sutures were associated with an increased risk of isthmocele compared to unlocked

DOI: 10.1201/9781003312109-31

sutures. Locked sutures may lead to tissue ischemia and necrosis due to increased tension, thereby impairing the healing process and resulting in a higher likelihood of isthmocele formation.

d. Surgical experience and skill: The surgeon's experience and skill level can impact the quality of the uterine incision closure, which in turn may affect the risk of isthmocele. Gubbini et al. (23) emphasized the importance of surgical experience in minimizing the risk of isthmocele, suggesting that inexperienced surgeons may inadvertently cause tissue damage or use suboptimal suturing techniques, leading to an increased likelihood of isthmocele development.

e. Intraoperative factors: Intraoperative factors such as blood loss, tissue handling, and surgical time can influence the healing process and potentially contribute to isthmocele formation.

2. Number of prior cesarean deliveries: The number of previous cesarean deliveries may be associated with insufficient healing of the uterine scar, contributing to the development of isthmocele. In general, the risk of isthmocele increases with each subsequent cesarean delivery. Osser et al. reported a CSD incidence of 61% after one CS, reaching 81% after two surgeries and even 100% after three procedures (24). Similarly, Antila-Långsjö et al. observed that women with only one CS had a 35% chance of developing a CSD, while the risks were 76% and 88%, respectively, after two and three CSs (25). A systematic review also found that repeated trauma to the uterine wall from multiple cesarean deliveries might lead to a weakened myometrium and an increased likelihood of isthmocele formation (13).
3. Elective versus urgent CS and CS during active labor: The prevalence of isthmocele is higher when CS is performed during active labor. Furthermore, the risk of isthmocele increases significantly when labor lasts > 5 hours or when the cervical dilation is > 5 cm (26). Specifically, low hysterotomy (often performed for second stage of labor CS) is associated with a sixfold increased risk of large CSDs compared with high hysterotomy (27).
4. Infection: Postoperative infections after CS can compromise the healing process, potentially increasing the risk of developing isthmocele (28). Although direct evidence linking post-cesarean infection to the development of isthmocele is limited, it is reasonable to hypothesize that compromised healing due to infection may contribute to the formation of isthmocele. In a retrospective study, Wang et al. (29) found a higher prevalence of isthmocele among women with a history of post-cesarean infection compared to those without infection. Thus, prevention of post-CS infections may reduce the risk for isthmocele.

31.3 Symptoms of Isthmocele and Association with Infertility

Many cases of isthmocele are asymptomatic and diagnosed as incidental findings on ultrasound (30). When isthmocele is associated with specific symptoms (including abnormal uterine bleeding or postmenstrual spotting, pelvic pain or dysmenorrhea, and infertility), the condition is referred to as cesarean scar syndrome or disorder (31, 32). Symptomatic isthmocele may greatly impact a woman's quality of life, and as such, it is crucial for healthcare providers to be aware of these symptoms and their potential implications. A recent study using the Delphi methodology proposed the definition and criteria for diagnosing cesarean scar disorder (32). The proposed definition was that cesarean scar disorder would be diagnosed when the patient has at least one primary symptom or two secondary symptoms, in the presence of a sonographic finding of a niche (Table 31.1). For the diagnosis of cesarean scar disorder, other uterine intracavitary pathologies and other causes of postmenstrual spotting (such as oral contraceptive use, vaginal or uterine infections, and cervical dysplasia) must be excluded (32).

The pathophysiology of abnormal uterine bleeding, pelvic pain, and infertility in women with isthmocele has been hypothesized to be retention of menstrual blood inside the niche, possibly due to insufficient contractility of the myometrium of the isthmocele (caused by decreased muscular density of the isthmocele when compared to adjacent myometrium) (18, 33, 34). In addition, hypervascularization and abnormal blood vessels lining the niche could cause de novo localized bleeding (34).

A patient with CSD may present with the following symptoms:

1. *Abnormal uterine bleeding*: One of the most commonly reported symptoms of isthmocele is abnormal uterine bleeding, which may present as intermenstrual bleeding or heavy, prolonged menstrual bleeding (menorrhagia) and postmenstrual spotting. Bij de Vaate et al. (13) reported that 63% of women with isthmocele experienced abnormal uterine bleeding, while Fabres et al. (35) found that 76% of symptomatic women with isthmocele presented with intermenstrual bleeding. In a study by Tower and Frishman (34), the authors reported that abnormal uterine bleeding was the most common presenting symptom among women with isthmocele.
2. *Dysmenorrhea*: Dysmenorrhea, or painful menstruation, is another symptom associated with isthmocele (36). The pathophysiology behind the association between isthmocele and dysmenorrhea is not entirely understood, but several mechanisms have been proposed. One theory suggests that isthmocele may cause the accumulation and retention of menstrual blood, leading to increased intrauterine pressure and pain. Additionally, the presence of isthmocele may lead to inflammation or infection, further exacerbating pelvic pain and dysmenorrhea (34).
3. *Chronic pelvic pain*: In addition to dysmenorrhea, isthmocele can be associated with chronic pelvic pain, which may be persistent or intermittent and not limited to the menstrual period. A study by Gubbini et al. (7) found that women with isthmocele were more likely to experience chronic pelvic pain compared to those without isthmocele.
4. *Dyspareunia*: Dyspareunia, or painful sexual intercourse, is a prevalent gynecological issue that affects many women, causing considerable distress and negatively impacting their quality of life. Dyspareunia can be classified into superficial dyspareunia, which occurs upon penetration, and deep dyspareunia, which is pain experienced during deeper penetration. The etiology of dyspareunia can be complex, involving various

TABLE 31.1 Consensus-Based Definition of Primary and Secondary Symptoms of Cesarean Scar Disorder

Primary Symptoms	RoA %	Secondary Symptoms	RoA%
Postmenstrual spotting	80.6	Dyspareunia	72.7
Pain during uterine bleeding	84.2	Abnormal vaginal discharge	87.5
Technical issues with catheter insertion during embryo transfer	73.1	Chronic pelvic pain	87.1
Secondary unexplained infertility combined with intrauterine fluid	70.4	Avoiding sexual intercourse	90.3
		Odor associated with abnormal blood loss	83.4
		Secondary unexplained infertility	70.0
		Secondary infertility despite ART	72.4
		Negative self-image	88.0
		Discomfort during participation in leisure activities	77.3

Abbreviation: RoA – Rate of Agreement.

factors such as psychological, hormonal, anatomical, and structural issues. The pathophysiology behind the connection between isthmocele and dyspareunia is not entirely understood, but several mechanisms have been proposed, mainly due to the accumulation of blood and the distension of the wall leading to an increase on the intrauterine pressure that is translated into pain during intercourse. Florio et al. (8) reported that dyspareunia was a common symptom among women with isthmocele, and treatment of the isthmocele resulted in significant improvement in dyspareunia scores.

5. *Infertility and adverse reproductive outcomes*: The exact cause of infertility in patients with isthmocele remains unclear, but several theories have been proposed. One theory is that the defect leads to abnormal accumulation and retention of menstrual blood, which may interfere with normal sperm transport and implantation (37, 38). Another possibility is that isthmocele may be associated with inflammation or infection, which can affect endometrial receptivity and embryo implantation. Moreover, uterine synechiae or adhesions may form around the isthmocele, further contributing to infertility. The risk of infertility in women with isthmocele has been estimated to be from 4% to 19% (37, 38). A meta-analysis published in 2013 estimated that a previous cesarean section affects fertility by reducing the probability of subsequent pregnancy by an average of 10% when compared to vaginal delivery (37). In addition, in patients undergoing assisted reproductive techniques, the rate of clinical pregnancy is reduced in the presence of isthmocele (39). Nevertheless, although many studies have investigated the association between infertility and isthmocele, high-quality evidence of such an association is still lacking, and surgical treatment of isthmocele should be recommended in cases of symptomatic CSD without any other explanation for secondary infertility (40).
6. *Obstetrical complications*: Isthmocele may be associated with obstetrical complications including placenta accreta, placenta previa, dehiscence of the scar with or without uterine rupture, and ectopic pregnancy in cesarean scar defects (cesarean scar pregnancy) (40).

31.4 Assessment

Various diagnostic methods including ultrasonography, sonohysterography, magnetic resonance imaging (MRI) and hysteroscopy can be used to assess the anterior uterine wall and diagnose isthmocele. None of the diagnostic methods is considered as the "gold standard." The advantage of ultrasound and MRI over hysteroscopy is their ability to provide accurate measurements of the isthmocele's width, depth, and residual myometrial thickness (Figure 31.2 and section 31.4.1). On the other hand, hysteroscopy allows for a visual demonstration of the isthmocele, cervical canal, and uterine cavity. Thus, for the optimal assessment of the isthmocele, and particularly prior to planning any surgical intervention, both ultrasound and hysteroscopy are often used. The assessment for isthmocele by either ultrasound or hysteroscopy is typically performed in the nonpregnant patient. Furthermore, it is advisable to wait at least 3 months after cesarean section for the assessment of the niche (41).

31.4.1 Ultrasound and Sonohysterography

The most common imaging methods for the assessment of isthmocele are two-dimensional transvaginal ultrasound and saline-infusion ultrasound (sonohysterography). Ultrasound is usually widely available and is relatively low cost. According to a Delphi consensus published in 2018, the isthmocele is defined as an indentation at the site of a cesarean section with a depth of at least 2 mm (Figure 31.2) (41). Additional measurements including the residual and adjacent myometrial thickness are obtained in the sagittal plane, while the isthmocele's width is obtained in the transverse plane. The residual myometrial thickness (RMT), measured from the apex of the isthmocele to outer edge of myometrium, is particularly important because of its role in determining the appropriate surgical management and the theoretical risks for pregnancy complications (34). In addition to the measurements described earlier, the ultrasound assessment should also include a description and measurements of the isthmocele's branches (41).

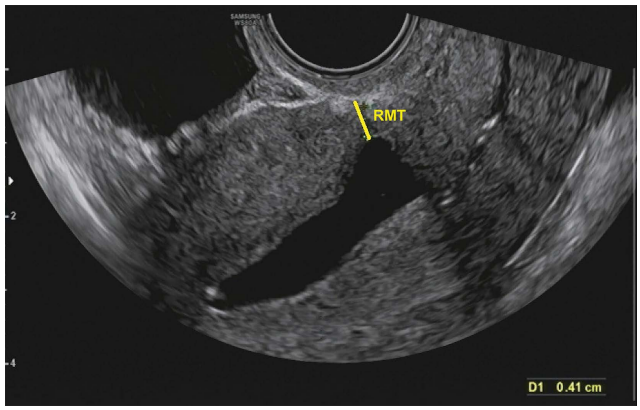


FIGURE 31.2 Appearance of the isthmocele on hydrosonography. The measurement of the residual myometrial thickness (RMT) is shown (yellow).

The isthmocele's measurements may be obtained by conventional two-dimensional ultrasound when free fluid is present in the uterine cavity. Otherwise, sonohysterography with infusion of gel or saline into the uterine cavity is necessary (33). Sonohysterography has the advantage of increased sensitivity and specificity for isthmocele detection over traditional ultrasound but is more invasive than the traditional ultrasound, may lead to overdiagnosis, and carries a small risk for post-procedure infection (42). The three-dimensional ultrasound, while allowing for diagnosis of concomitant uterine Müllerian anomalies, does not appear to have additional benefit for the evaluation of isthmocele over two-dimensional ultrasound (43).

31.4.2 Magnetic Resonance Imaging

The isthmocele and its measurements are clearly visualized on MRI using sagittal T2-weighted images with similar accuracy when compared to ultrasound, albeit at higher cost and with reduced availability (44). However, MRI may be useful for the comprehensive evaluation of patients with isthmocele and additional complex pathologies such as uterine fibroids and deep infiltrating endometriosis, especially for the planning of surgical interventions.

31.4.3 Hysteroscopy

Diagnostic office hysteroscopy using a "no-touch" vaginoscopic approach allows for visual inspection of the isthmocele's anatomy, including the main defect and all of its branches (Figure 31.3). An angled scope (i.e., a 12° or 30° optic) is preferable for these exams. At hysteroscopy, the isthmocele appears as a pouch or wedge on the anterior wall of the lower uterine segment, in proximity to the internal cervical os. Small vessels are often observed at the base of the defect, while blood-tinted secretions are often seen inside the isthmocele.

Although hysteroscopy cannot be used to obtain the isthmocele's measurements, it provides information on the anatomy of the niche, cervical canal, and uterine cavity which could be important for the comprehensive evaluation of the clinical disorders associated with the isthmocele, such as abnormal uterine bleeding and secondary infertility. For example, chronic endometritis and the presence of abnormal vessels at the base of the niche are pathologies easily diagnosed by hysteroscopy but missed by ultrasound. Thus, a combination of diagnostic hysteroscopy and ultrasound may allow for the optimal evaluation of patients with symptomatic isthmocele.

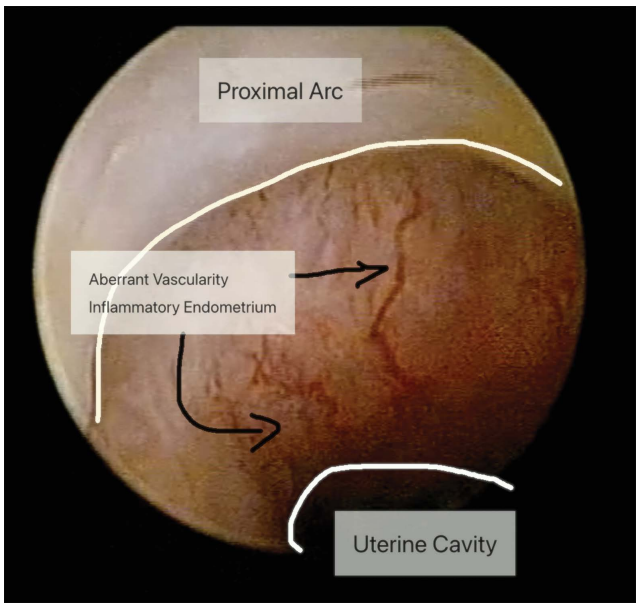


FIGURE 31.3 The hysteroscopic appearance of isthmocele.

31.5 Treatment

The treatment of isthmocele is reserved for symptomatic patients. The choice of conservative management, medical treatment, and surgical management depends on the patient's symptoms and her wish for future pregnancies. In general, symptoms of abnormal uterine bleeding and/or pelvic pain may be treated either medically or surgically, while secondary infertility and obstetrical concerns related to the isthmocele are usually treated surgically.

31.5.1 Medical Treatment

Medical treatment of isthmocele is aimed to address abnormal uterine bleeding and pelvic pain by administration of various hormonal combinations. These treatments have not been sufficiently investigated to date. Oral combined estrogen–progesterone formulations improved spotting symptoms in 10 of 11 women in a small study nonrandomized study (45). The levonorgestrel intrauterine system (LNG-IUS) achieved a 50% reduction in spotting in 78.4% of women after 6 months, and in 89.2% of women after 9 months, comparing favorably with hysteroscopic resection (46). However, hormone-related side effects were reported by ~10% of women (46). Another drawback to consider in this setting is the potentially more difficult insertion of the LNG-IUS in cases of large isthmocele causing significant anatomical distortion of the cervical canal and lower uterine segment. Other hormonal formulations such as progesterone-only pills and vaginal or transdermal combined estrogen–progesterone formulations could also be useful for treatment of niche-related spotting but have not been studied to date.

To conclude, despite the scarce available literature, it is reasonable to consider hormonal therapy for isthmocele-associated abnormal uterine bleeding in women without relevant contraindication and without immediate wish to conceive.

31.5.2 Surgical Management

The surgical management of isthmocele includes reconstruction of the cesarean scar defect by abdominal (mostly laparoscopic or robotic-assisted route) or vaginal approach and remodeling of the defect by hysteroscopy. The reconstructive procedures aim to completely excise the fibrotic tissue of the niche followed by reapproximation of the edges by suturing, creating a new and hopefully thicker scar. The non-reconstructive hysteroscopic procedure aims to "flatten" the niche by resecting its edges, combined with ablation or resection of the base of the niche. Alternatively, in women who have completed childbearing and do not wish to conserve their uterus, a total or subtotal hysterectomy may be offered.

31.5.2.1 Hysteroscopy

Hysteroscopy is the least invasive and shortest procedure for the surgical management of isthmocele. This procedure is offered to patients whose RMT is at least 2.5–3 mm, due to the (mostly theoretical) concerns for intraoperative uterine and bladder perforation and to the risk of uterine rupture in subsequent pregnancies. The procedure is performed using an electrosurgical bipolar or monopolar resectoscope loop, via a large-diameter (7 to 9 mm) or small-diameter (5 mm)

resectoscope. After inspection of the cervical canal, lower uterine segment and uterine cavity, the proximal edge of the niche is resected, and the base of the niche ablated or resected. The distal edge of the niche may also be resected in a similar fashion. Most studies reported on outpatient hysteroscopic procedures under general anesthesia.

The outcomes of hysteroscopic treatment for isthmocele have been extensively studied, albeit mostly in observational, retrospective, and noncontrolled studies. Favorable outcomes were reported for hysteroscopic treatment of isthmocele-associated abnormal uterine bleeding, with improvement of postmenstrual spotting in > 80% of women (47). Similarly, in a randomized trial comparing hysteroscopic and conservative management, Vervoot et al. found that the median duration of postmenstrual spotting decreased from 8 to 4 days in the hysteroscopy group (48). Regarding hysteroscopic treatment of isthmocele for patients with secondary infertility, a systematic meta-analysis reported pregnancy rates reaching ~80% after the procedure (47). These encouraging outcomes are applicable to women attempting natural conception as well as women conceiving via assisted reproductive techniques (49). Obviously, other causes of secondary infertility should be investigated and addressed prior to attempting hysteroscopic isthmoplasty.

Concerns have been raised regarding the risk of uterine rupture in pregnancies following hysteroscopic treatment for isthmocele, due to the possible thinning of the scar by the procedure. Although this outcome is difficult to accurately estimated in small, noncontrolled studies, a consensus statement from the Global Congress on Hysteroscopy in 2018 recommended a waiting period of 3 months prior to conception as well as delivery by scheduled cesarean section (50). These recommendations have been challenged since the RMT may increase following hysteroscopic remodeling of the niche (51).

To conclude, hysteroscopic repair of the niche appears to be the first-line surgical approach for women with symptomatic isthmocele in cases of RMT > 2.5–3 mm, in view of its favorable outcomes, low rates of complications, and minimally invasive approach.

31.5.2.2 Laparoscopic and Robotic-Assisted Reconstruction

An abdominal repair by laparoscopy or robotic-assisted approach may be offered to symptomatic patients whose RMT measures < 2.5–2 mm. This reconstructive surgery allows for complete removal of the "old" fibrotic cesarean section scar, and the creation of a "new," healthier, scar. Indeed, a prospective study has reported an increase in the median RMT from 1.2 mm to 5.3 mm after the surgery (52). However, this surgery requires advanced laparoscopic skills and probably has a considerable learning curve even for experienced surgeons.

The surgical steps of laparoscopic and robotic-assisted isthmocele repair are similar (53). First, the area of the isthmocele is identified and exposed, often requiring extensive adhesiolysis of the uterovesical pouch. This step is associated with the risk of bladder injury. A concomitant hysteroscopy may aid in the abdominal visualization of the isthmocele, while retrograde bladder filling may help to identify the bladder borders and avoid injury. Next, the fibrotic scar tissue is excised, preferably with cold scissors to avoid thermal injury to the remaining myometrium. Finally, the edges of the new scar are approximated by suturing. There is no consensus regarding the type of sutures (i.e., interrupted, mattress, or running), the number of layers, and the suturing material (i.e., multifilament, monofilament, or barbed). Administration of diluted vasopressin into the adjacent myometrium before excision of the scar may be helpful to reduce bleeding, improve visibility, and minimize the use of electrosurgery. In cases of retroverted uterus, a uteropexy procedure may be added to reduce the tension on the newly created scar (53). Application of antiadhesion barriers on the surgical field may be considered. Although the laparoscopic and robotic-assisted techniques have not yet been directly compared, the proponents of the robotic approach for this procedure claim it allows for easier suturing and precise adhesiolysis (54).

Overall, favorable outcomes have been reported for isthmocele repair by laparoscopy/robotic-assisted laparoscopy. A prospective nonrandomized study found that ~80% of patients experienced improvement or resolution of their main niche-related symptom (52), while a meta-analysis found that symptoms improved in ~90% of patients (47). Regarding laparoscopic/robotic isthmocele repair for treatment of secondary infertility, a recent meta-analysis found that only ~50% of women conceived after surgery (49). However, the relatively small number of included cases precluded forming a definite conclusion.

The most controversial indication regarding laparoscopic/robotic repair of isthmocele is prevention of obstetrical complications (including uterine rupture, cesarean scar pregnancy, and placenta accreta spectrum) in women who are otherwise asymptomatic. Although adverse outcomes have been associated with isthmocele, especially in cases of low or inexistent RMT, there is insufficient evidence to date to support the recommendation for routine repair of isthmocele in otherwise asymptomatic women. Thus, a multidisciplinary consultation involving obstetricians, infertility specialists, and surgeons is advised for reaching an individualized recommendation.

31.5.2.3 Vaginal Reconstruction of Isthmocele

The vaginal approach may be considered the least invasive approach for isthmocele repair. However, it has been used by relatively few surgeons. The largest series published to date reported the outcomes of 183 patients operated vaginally in a single center in China (55). Reduced number of postmenstrual spotting days, reduced prevalence of pelvic pain, and increased RMT were found after isthmocele correction. The postoperative pregnancy rate was ~66%, including two cases of cesarean scar pregnancy. The approach appears to be a good alternative to laparoscopic/robotic isthmocele repair, although its adoption outside China has been slow and relatively few surgeons have mastered it.

References

1. Donnez O et al. Gynecological and obstetrical outcomes after laparoscopic repair of a cesarean scar defect in a series of 38 women. *Fertil Steril*. 2017;107:289–296.
2. Osser OV et al. Cesarean section scar defects: agreement between transvaginal sonographic findings with and without saline contrast enhancement. *Ultrasound Obstet Gynecol*. 2010;35:75–83.
3. van Horenbeeck A et al. Cesarean scar dehiscence and irregular uterine bleeding. *Obstet Gynecol*. 2003;102:1137–1139.
4. Klemm P et al. Laparoscopic and vaginal repair of uterine scar dehiscence following cesarean section as detected by ultrasound. *J Perinat Med*. 2005;33:324–331.
5. Donnez O et al. Laparoscopic repair of wide and deep uterine scar dehiscence after cesarean section. *Fertil Steril*. 2008;89:974–980.
6. Morris H. Surgical pathology of the lower uterine segment caesarean section scar: is the scar a source of clinical symptoms? *Int J Gynecol Pathol*. 1995;14:16–20.
7. Gubbini G et al. Resectoscopic correction of the "isthmocele" in women with postmenstrual abnormal uterine bleeding and secondary infertility. *J Minim Invasive Gynecol*. 2008;15:172–175.

8. Florio P et al. Hysteroscopic treatment of the cesarean-induced isthmocele in restoring infertility. *Curr Opin Obstet Gynecol*. 2012;24:180–186.
9. Jeremy B et al. Uterine isthmique transmural hernia: results of its repair on symptoms and fertility. *Gynecol Obstet Fertil*. 2013;41:588–596.
10. Luo L et al. Vaginal repair of cesarean section scar diverticula. *J Minim Invasive Gynecol*. 2012;19:454–458.
11. Fabres C et al. The cesarean delivery scar pouch: clinical implications and diagnostic correlation between transvaginal sonography and hysteroscopy. *J Ultrasound Med*. 2003;22:695–700.
12. Monteagudo A et al. Saline infusion sonohysterography in nonpregnant women with previous cesarean delivery: the "niche" in the scar. *J Ultrasound Med*. 2001;20:1105–1115.
13. Bij de Vaate AJ et al. Prevalence, potential risk factors for development and symptoms related to the presence of uterine niches following Cesarean section: systematic review. *Ultrasound Obstet Gynecol*. 2014;43:372–382.
14. Jacobson MT et al. Laparoscopic repair of a uteroperitoneal fistula. *JSLS*. 2003;7:367–369.
15. Osterman M et al. Births: final data for 2020. *Natl Vital Stat Rep*. 2021;70:1–50.
16. Dahlke JD et al. Evidence-based surgery for cesarean delivery: an updated systematic review. *Am J Obstet Gynecol*. 2013;209:294–306.
17. Betrán AP et al. The increasing trend in caesarean section rates: global, regional and national estimates: 1990–2014. *PLoS One*. 2016;11:e0148343.
18. Van der Voet LF et al. Long-term complications of caesarean section. The niche in the scar: a prospective cohort study on niche prevalence and its relation to abnormal uterine bleeding. *BJOG*. 2014;121:236–244.
19. Roberge S et al. Impact of single- vs double-layer closure on adverse outcomes and uterine scar defect: a systematic review and metaanalysis. *Am J Obstet Gynecol*. 2014;211:453–460.
20. Hosseini R et al. A comparison of the effects of Two suture materials on isthmocele formation: a cohort study. *J Gynecol Obstet Hum Reprod*. 2021;50:101933.
21. Raischer HB et al. Knotless barbed versus conventional suture for closure of the uterine incision at cesarean delivery: a systematic review and meta-analysis. *J Minim Invasive Gynecol*. 2022;29:832–839.
22. Bujold E et al. The role of uterine closure in the risk of uterine rupture. *Obstet Gynecol*. 2010;116:43–50.
23. Gubbini G et al. Surgical hysteroscopic treatment of cesarean-induced isthmocele in restoring fertility: prospective study. *J Minim Invasive Gynecol*. 2011;18:234–237.
24. Osser OV et al. High prevalence of defects in Cesarean section scars at transvaginal ultrasound examination. *Ultrasound Obstet Gynecol*. 2009;34:90–97.
25. Antila-Långsjö RM et al. Cesarean scar defect: a prospective study on risk factors. *Am J Obstet Gynecol*. 2018;219:458.e1–458.e8.
26. Vikhareva Osser O et al. Risk factors for incomplete healing of the uterine incision after caesarean section. *BJOG*. 2010;117:1119–1126.
27. Vikhareva O et al. Hysterotomy level at Cesarean section and occurrence of large scar defects: a randomized single-blind trial. *Ultrasound Obstet Gynecol*. 2019;53:438–442.
28. Nisenblat V et al. Maternal complications associated with multiple cesarean deliveries. *Obstet Gynecol*. 2006;108:21–26.
29. Wang CB et al. Cesarean scar defect: correlation between Cesarean section number, defect size, clinical symptoms and uterine position. *Ultrasound Obstet Gynecol*. 2009;34:85–89.
30. Sipahi S et al. The minimally invasive approach to the symptomatic isthmocele – what does the literature say? A step-by-step primer on laparoscopic isthmocele – excision and repair. *Curr Opin Obstet Gynecol*. 2017;29:257–265.
31. Morris H. Cesarean scar syndrome. *S Afr Med J*. 1996;86:1558.
32. Klein Meuleman SJM et al. Definition and criteria for diagnosing cesarean scar disorder. *JAMA Netw Open*. 2023;6:e235321.
33. Bij de Vaate AJ et al. Ultrasound evaluation of the cesarean scar: relation between a niche and postmenstrual spotting. *Ultrasound Obstet Gynecol*. 2011;37:93–99.
34. Tower AM et al. Cesarean scar defects: an underrecognized cause of abnormal uterine bleeding and other gynecologic complications. *J Minim Invasive Gynecol*. 2013;20:562–572.
35. Fabres C et al. Surgical treatment and follow-up of women with intermenstrual bleeding due to cesarean section scar defect. *J Minim Invasive Gynecol*. 2005;12:25–28.
36. Marotta ML et al. Laparoscopic repair of post-cesarean section uterine scar defects diagnosed in nonpregnant women. *J Minim Invasive Gynecol*. 2013;20:386–391.
37. Gurol-Urganci I et al. Impact of Caesarean section on subsequent fertility: a systematic review and meta-analysis. *Hum Reprod*. 2013;28:1943–1952.
38. Gurol-Urganci I et al. A population-based cohort study of the effect of Caesarean section on subsequent fertility. *Hum Reprod*. 2014;29:1320–1326.
39. Vissers J et al. Reduced pregnancy and live birth rates after in vitro fertilization in women with previous Caesarean section: a retrospective cohort study. *Hum Reprod*. 2020;35:595–604.
40. Dominguez JA et al. Diagnosis and management of isthmocele: a SWOT analysis. *Ultrasound Obstet Gynecol*. 2023;62(3):336–344.
41. Jordans IPM et al. Sonographic examination of uterine isthmocele in non-pregnant women: a modified Delphi procedure. *Ultrasound Obstet Gynecol*. 2019;53:107–115.
42. Rasheedy R et al. Agreement between transvaginal ultrasound and saline contrast sonohysterography in evaluation of cesarean scar defect. *J Gynecol Obstet Hum Reprod*. 2019;48:827–831.
43. Marjolein Bij de Vaate AJ et al. Reproducibility of three-dimensional ultrasound for the measurement of a niche in a caesarean scar and assessment of its shape. *Eur J Obstet Gynecol Reprod Biol*. 2015;188:39–44.
44. Rosa F et al. Imaging findings of cesarean delivery complications: cesarean scar disease and much more. *Insights Imaging*. 2019;10:98.
45. Tahara M et al. Preliminary report of treatment with oral contraceptive pills for intermenstrual vaginal bleeding secondary to a cesarean section scar. *Fertil Steril*. 2006;86:477–479.
46. Zhang J, Zhu C, Yan L, Wang Y, Zhu Q, He C, He X, Ji S, Tian Y, Xie L, Liang Y, Xia W, Mol BW, Huirne JAF. Comparing levonorgestrel intrauterine system with hysteroscopic niche resection in women with postmenstrual spotting related to a niche in the uterine cesarean scar: a randomized, open-label, controlled trial. *Am J Obstet Gynecol*. 2023 Jun;228(6):712.e1-712.e16. doi: 10.1016/j.ajog.2023.03.020. Epub 2023 Mar 17. PMID: 36935068.
47. Vitale SG et al. From hysteroscopy to laparoendoscopic surgery: what is the best surgical approach for symptomatic isthmocele? A systematic review and meta-analysis. *Arch Gynecol Obstet*. 2020;301:33–52.
48. Vervoort A et al. Hysteroscopic resection of a uterine caesarean scar defect (niche) in women with postmenstrual spotting: a randomised controlled trial. *BJOG*. 2018;125(3):326–334.
49. Harjee R et al. Reproductive outcomes following surgical management for isthmoceles: a systematic review. *J Minim Invasive Gynecol*. 2021;28:1291–1302.e2.
50. Laganà AS et al. Optimal timing and recommended route of delivery after hysteroscopic management of isthmocele? A consensus statement from the global congress on hysteroscopy scientific committee. *J Minim Invasive Gynecol*. 2018;25:558.
51. Tsuji S et al. Pregnancy outcomes after hysteroscopic surgery in women with cesarean scar syndrome. *PLoS One*. 2020;15:e0243421.
52. Vervoort A et al. The effect of laparoscopic resection of large niches in the uterine caesarean scar on symptoms, ultrasound findings and quality of life: a prospective cohort study. *BJOG*. 2018;125:317–325.
53. Huirne JAF et al. Technical aspects of the laparoscopic niche resection, a step-by-step tutorial. *Eur J Obstet Gynecol Reprod Biol*. 2017;219:106–112.
54. Cardaillac C et al. Robot-assisted laparoscopy repair of uterine isthmocele: a two-center observational study. *Int J Gynaecol Obstet*. 2023;160:244–248.
55. Deng K et al. Obstetric and gynecologic outcomes after the transvaginal repair of cesarean scar defect in a series of 183 women. *J Minim Invasive Gynecol*. 2021;28:1051–1059.

32 TUBAL STERILIZATION

Nicole Afuape and Danielle Dukes

32.1 Brief History of Tubal Sterilization

Tubal sterilization is a procedure which aims to physically prevent ovum fertilization and pregnancy conception. Evidence of the idea of tubal sterilization as a form of contraception dates back to the early 1800s. The first tubal sterilization was performed in 1880 by Samuel Smith Lungren at the time of a repeat cesarean section (1, 2). The fallopian tubes were each tied with silk ligatures in an effort to prevent the patient from undergoing a second repeat of what was then considered to be a life-threatening procedure. Abdominal incision and colpotomy were utilized as routes to access the fallopian tubes for this procedure early on. Due to the extreme risk of open surgery at the time, laparotomy for the sole purpose of sterilization was seldom performed. This remained the popular opinion until the 1970s when the world saw a dramatic increase in the frequency of this procedure. This boom was fueled by the rise of two alternative surgical approaches: the minilaparotomy and laparoscopy. The first laparoscopic tubal sterilization procedure was achieved in Switzerland by gynecologist Boesch in the early 1900s. Refinement of this procedure was continued over time. Decades later came the introduction of hysteroscopy, which eliminated the need for any incisions (3, 4).

32.2 Fallopian Tube Anatomy

The fallopian tube, also known as the oviduct, is a seromuscular organ which arises bilaterally from the uterus at the level of the fundus. It can be identified within the upper layer of the broad ligament, between the round ligament and the uteroovarian ligament (Figures 32.1 and 32.2). The fallopian tube is generally composed of three layers – the outer serosal layer, a smooth muscle layer, and an inner mucosal layer. The serosal layer is contiguous with the fallopian tubal mesentery, the mesosalpinx. The smooth muscle layer can be further divided into an internal oblique layer, a middle circular, and an outer longitudinal layer (5). The fallopian tube serves as a conduit for sperm and ovum, and it is the site for potential fertilization.

The fallopian tube is typically 9 to 11 cm in length and can be divided into four parts. The interstitium is the intramural portion that traverses the uterine cornua. The tube continues with the isthmic portion, characterized by a muscular wall with a narrow lumen. The lumen expands as it transitions into the ampulla, the largest portion of the tube where fertilization typically occurs. The lumen expands further as the tube transitions to the infundibulum. The infundibulum terminates with a fimbriated end, a collection of approximately 25 finger-like projections which facilitate ovum pickup from the ovary. A smooth muscle band called the fimbria ovarica connects the distal tube to the ovary – it brings the two structures closer together at the time of ovulation. The blood supply for the lateral fallopian tube arises from ovarian artery collaterals, and the supply for the medial tube comes from the uterine artery (1, 2, 5).

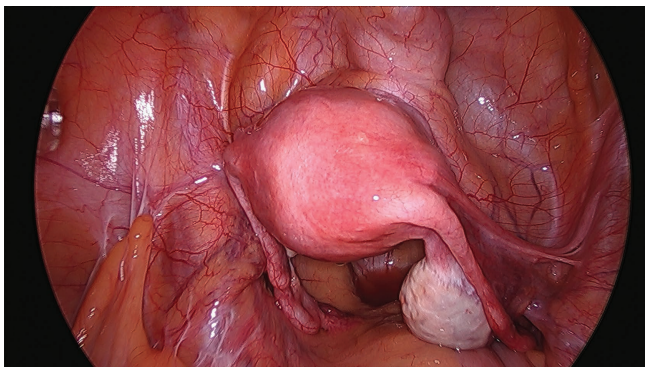


FIGURE 32.1 Normal pelvic anatomy.

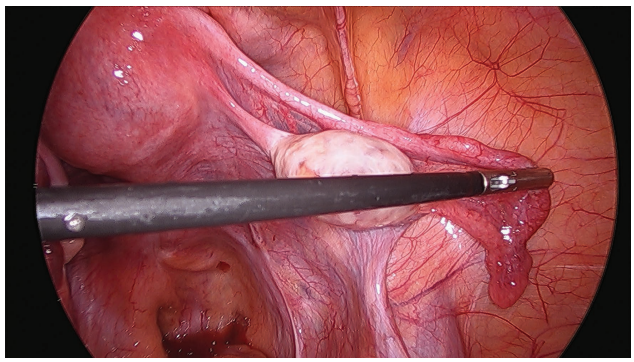


FIGURE 32.2 Fallopian tube anatomy.

32.3 General Considerations

Tubal sterilization is typically considered to be a permanent contraceptive intervention with emphasis placed on thorough preprocedure patient counseling. Patient capacity for medical decision making must be confirmed and any requirements set by local laws must be addressed prior to proceeding. The patient should be thoroughly counseled on procedure risks and alternatives, including partner vasectomy. Risk of sterilization failure should also be reviewed, including the associated increased risk of ectopic pregnancy should sterilization failure occur at any point in the future. Medical and gynecologic comorbidities should also be considered to confirm that the patient is appropriate for elective surgery and to confirm that the correct procedure is being performed. For example, a patient with abnormal uterine bleeding and workup consistent with either fibroid uterus or endometrial hyperplasia may be more appropriate for a hysterectomy (1, 2, 6, 7).

About half of the tubal sterilizations done in the United States are interval sterilization procedures, which are performed at a time unrelated to pregnancy (7, 8). Postpartum tubal sterilization occurs shortly after childbirth, either at the time of cesarean section or within 24 to 48 hours following vaginal delivery. Postpartum sterilization is typically performed via a subumbilical minilaparotomy as the uterus remains well outside of the pelvis and within centimeters of the umbilicus.

DOI: 10.1201/9781003312109-32

All of the tubal sterilization techniques described later can be performed utilizing general anesthesia, conscious intravenous sedation, and/or local anesthetic. Spinal anesthesia has also been described (2, 7, 9, 10). General anesthesia is typically considered by both patients and surgeons to be more acceptable, however in the United States the mortality rate of 1 to 2 deaths per 100,000 sterilization procedures is in large part related to general anesthetic complications (7, 11, 12). Local analgesia is achieved by infiltration of a fast-acting anesthetic such as lidocaine into the skin and fascial layers at each incision site. Our authors have also previously described transcervical instillation of local anesthetic (10 mL carbocaine + lidocaine) through the uterine manipulator with an additional 10 mL of lidocaine dripped over the length of the fallopian tube at the start of the case (13). Lower insufflation pressures (8–10 mmHg) may also be considered. For hysteroscopic techniques, a paracervical block using local anesthetic can be performed.

32.4 Opportunistic Salpingectomy

Ovarian cancer remains the leader in mortality among gynecologic cancers, and we are also still lacking a reliable screening tool. Epithelial ovarian carcinomas are the most common form, making up 90% of cases, and they are also considered to be the most aggressive (7, 14). Molecular data on the origin and pathogenesis of ovarian cancer suggests that serous, endometrioid, and clear cell carcinomas are derived from the fallopian tube and the endometrium, rather than the ovary itself. In 2013 the Society of Gynecologic Oncology released a practice statement advising that women at population risk of developing ovarian cancer who are completed with childbearing be considered for salpingectomy at the time of pelvic surgery for any indication. Complete salpingectomy is preferred over fimbriectomy as cancer precursors can be found throughout the fallopian tube. Salpingectomy as a means of sterilization is not associated with any increase in perioperative complications. Salpingectomy may also be the preferred approach in the setting of fallopian tube pathology, such as hydrosalpinx, or following failure of prior sterilization attempt (2, 15). Although long-term data on the efficacy of bilateral salpingectomy is not available, failure with development of spontaneous intrauterine pregnancy has only been published in a few case reports (16).

Salpingectomy should involve complete removal of the fallopian tube excluding the interstitium. Any fimbria attachments to the ovary should also be removed or cauterized to optimize this intervention (Figure 32.3). The fallopian tube can be elevated with an atraumatic clamp or grasper and the mesosalpinx sequentially transected just below the tube, moving from lateral to medial or medial to lateral as access to the anatomy allows (Figure 32.4). Electrocautery or ultrasonic energy can be utilized. Any blood vessels encountered within the mesosalpinx along the way should be sealed prior to transection (Figure 32.5). The fallopian tube itself should be sealed and transected at the level of the cornua, taking care to avoid leaving behind any tubal stump. If utilizing laparoscopic approach, extraction of the fallopian tube can generally be achieved through a 5 mm port by grasping the tube at the isthmic end, parallel to the length of the tube, and utilizing a twisting or corkscrew motion. Both fallopian tube specimens should be forwarded to pathology for evaluation.

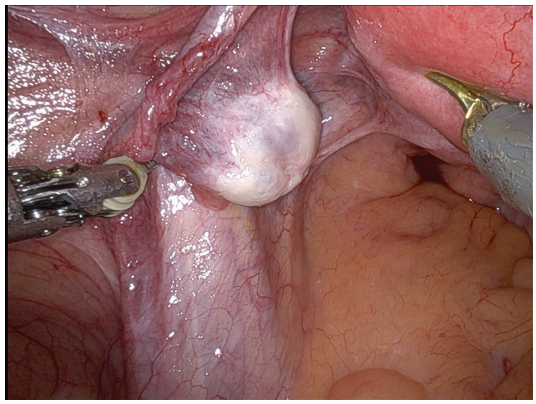


FIGURE 32.3 Residual fimbria found at the time of follow-up procedure.

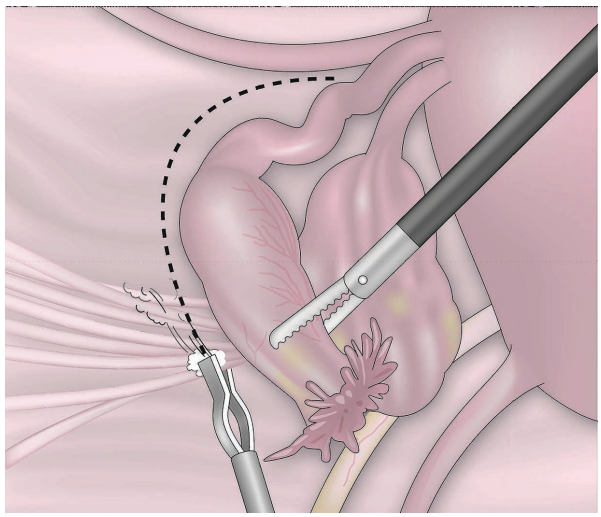


FIGURE 32.4 Laparoscopic salpingectomy. (From Ref. 13 with permission.)

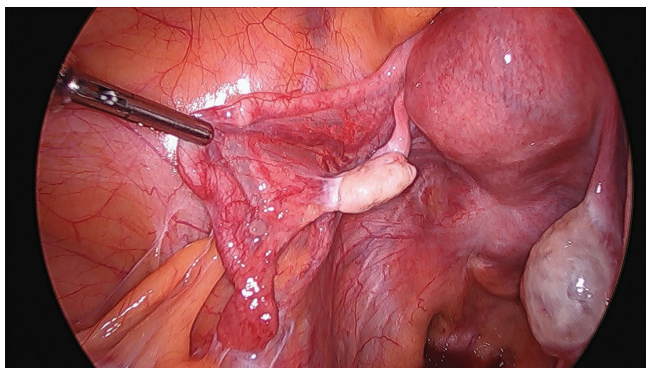


FIGURE 32.5 Large blood vessel traversing the mesosalpinx.

32.5 Abdominal Access: Minilaparotomy

Interval tubal sterilization utilizing minilaparotomy is less common in the United States. This approach is a useful tool in low-resource settings and for patients who may not be able to

tolerate peritoneal cavity insufflation required for laparoscopic approach. A 2004 Cochrane review reflected that operating time was approximately 5 minutes longer for minilaparotomy in comparison to laparoscopy. There was a lack of difference in major morbidity between the two groups (17).

Interval tubal sterilization via minilaparotomy typically requires suprapubic abdominal access as the uterine fundus is anticipated to be below the level of the pubic bone. By definition, a minilaparotomy involves an incision of 5 cm or less, with incisions typically kept at 2 to 3 cm. The patient may be positioned in dorsal lithotomy and a uterine manipulator may be placed to assist with elevation, access, and positioning of the uterus during the procedure. The abdomen is accessed in the usual fashion, by incising the skin and dissecting down to the level of the fascia, which is then elevated and opened. The peritoneum may be entered bluntly or sharply. Once the pelvis is accessed, Army–Navy retractors may be used to manipulate the incision for cavity exploration. Trendelenburg position and airplane tilt of the operating table towards either side may also help to expose the anatomy. These steps will be made more difficult in the obese patient, who thus may not be an ideal candidate for this approach. Once the fallopian tube is identified, a Babcock clamp(s) can be used to grasp the tube and progressively walk it down to the fimbria for confirmation. This step should not be omitted, as a common cause of failure in tubal ligation techniques is tubal misidentification for the nearby round ligament or the utero-ovarian ligament (Figure 32.2). Salpingectomy can be achieved utilizing ultrasonic energy, advanced bipolar energy, or monopolar energy with suture ligation of any larger vessels traversing the mesosalpinx.

Prior to salpingectomy, the Parkland and Pomeroy methods became the most commonly used in the United States for minilaparotomy and laparotomy approach. The Pomeroy method is initiated by placing a Babcock clamp at mid-tube and elevating the anatomy. A loop of tube is created and tied off using rapid-absorbable suture (1–0 or 0 plain catgut for the modified technique) and ligating the fallopian tube and its blood supply simultaneously. A second tie may be placed. A cross-section of fallopian tube of at least 2 cm is subsequently resected above the suture and sent for pathology confirmation. The lumen should be visible at each tubal stump, confirming a full cross-section of the fallopian tube. If the loop is made too small, a complete transection may not be achieved. The use of rapid-absorbable suture is key for this technique as once the suture is absorbed, the proximal and distal tubes are separated and returned to their anatomical positions.

The Parkland method allows for immediate separation of the tubal segments. This method involves identifying an avascular section within the mesosalpinx at the level of the isthmus and creating a window. Two rapid-absorbable sutures are subsequently introduced and used to tie off a 2 to 3 cm segment of fallopian tube. It is important that each suture is tied securely with blanching at the segment. The tubal segment is then resected between the two sutures using Metzenbaum scissors. The tubal segment should be sent to pathology to confirm that an appropriate cross-section of the fallopian tube was obtained. For the Parkland and Pomeroy methods, failure rate is 1 per 1000 procedures by year 1 and 7.5 per 1000 procedures by year 10 (18).

The laparoscopic techniques described next may also be modified for utilization with minilaparotomy approach. Once the sterilization procedure is completed and hemostasis confirmed, a delayed-absorbable suture should be used to close the fascia in a running fashion followed by skin closure utilizing the surgeon's preferred technique.

32.6 Abdominal Access: Laparoscopy

Laparoscopic approach has remained the most common minimally invasive technique for achieving interval tubal sterilization. Absolute contraindications are limited to patient tolerance of general anesthesia and clinical readiness for elective surgery. The patient is positioned in dorsal lithotomy with placement of a uterine manipulator to assist with positioning and access of the bilateral adnexa. Trendelenburg positioning is implemented after the abdomen is accessed to displace the bowel out of the pelvis. The most common entry site is at the umbilicus, with incision size dependent on a combination of abdominal entry technique and the sterilization technique being performed. Laparoscopy generally requires a camera port at the midline and one to two accessory ports, placed either at the midline or laterally based on surgeon preference, the system being used (e.g., straight stick vs robotics), and the sterilization technique. A single-site system may alternatively be used. Laparoscopic approach optimizes visualization and offers the ability to perform complete assessment of the abdomen and pelvis at the time of surgery.

32.6.1 Salpingectomy

Bilateral salpingectomy may be performed as described previously by sealing and transecting the mesosalpinx and the fallopian tube using monopolar energy, bipolar energy, or ultrasonic energy. Although not typically used solely for this indication, robotic platforms offer monopolar and bipolar instruments, which may also be used.

32.6.2 Modified Pomeroy

A modified Pomeroy technique may be achieved laparoscopically using two accessory access points. The principle of utilizing a rapid-absorbable suture should be maintained. A plain gut suture with an endoscopic slip knot or Roeder loop can be utilized. The suture should be introduced, a Babcock clamp or grasper passed through the suture loop, and the fallopian tube grasped at its midportion. The fallopian tube is elevated initiating a loop and the slip knot subsequently tightened at the base to complete the tubal loop. The loop should contain at least 2 cm of fallopian tube length. Elevation of the tube is maintained and laparoscopic scissors are introduced for transection of the tissue within the loop. A complete cross-section of the fallopian tube should be confirmed by pathology.

32.6.3 Surgical Electrocautery

Monopolar coagulation was the first form of surgical electrocautery used for tubal sterilization. This method was associated with an unacceptable level of risk due to wide thermal spread and association with capacitive coupling and bowel injury (4, 7, 13). The introduction of bipolar electrocautery in the 1970s produced a safer alternative. Bipolar electrocautery offered a decrease in thermal spread at 1.5 to 3 cm compared to the 5.5 cm associated with monopolar electrocautery. Bipolar energy also eliminated concerns regarding capacitive coupling. For this technique, the Kleppinger bipolar forceps were classically used, potentially with one accessory access point. The fallopian tube is grasped along the midportion with the bipolar forceps, at least 2 cm from the level of the cornua to minimize the risk of uteroperitoneal fistula formation. The tube should be completely encircled, ideally including a small portion of

mesosalpinx. The tube is lifted toward the abdominal wall away from other pelvic organ structures and electrocautery is activated. Dr. Richard Soderstrom reported that failures could be minimized by utilizing a cutting waveform at a power of at least 25 watts to facilitate full thickness tube desiccation. Two additional contiguous areas should be desiccated to a total length of at least 3 cm. The failure rate at 10 years for this procedure is 2.48% (18).

32.6.4 Mechanical Devices

Mechanical devices for tubal sterilization also became available in the 1970s as safer alternatives to monopolar electrocautery. Mechanical devices offer an option for tubal occlusion without the use of any form of electrocautery. These devices are typically placed with a device specific applicator which often requires a larger 8 mm accessory trocar. They perform best with normal fallopian tube anatomy and mobility without the presence of tubal adhesions, tubal thickening, or tubal dilation. Normal anatomy optimizes ease of correct placement and subsequent efficacy (4, 7, 19).

The spring clip was first introduced by Hulka in 1973. This initial model was a gold-plated spring clip manufactured to minimize tubal and peritoneal irritation. With the fallopian tube elevated for stretch, the clip was placed along the isthmic portion of the tube in a perpendicular orientation. The Hulka clip offered tubal occlusion with only a 3 mm range of tissue damage (1, 4).

The Filshie clip (CooperSurgical, Trumbull, Connecticut) was also introduced in Europe in the 1970s but not approved in the United States until the 1990s. The Filshie clip is a silicone-lined titanium clip. The silicone rubber lining offers additional expansion which results in avascular necrosis and subsequent fibrosis of a 3 to 5 mm segment of fallopian tube. The Filshie clip applicator offers easier placement in comparison to that of the Hulka. The applicator uses a finger bar which is released for clip opening and squeezed for closure. When placed, the clip should again be perpendicular to the course of the fallopian tube with the longer jaw oriented below the tube for optimized visualization. When closed, the clip should completely envelope the tube from the level of the hinge with the longer jaw extending to the mesosalpinx (Figure 32.6). Prior to deployment the clip can be opened and closed to readjust position. Once deployed, the clip can no longer be adjusted, however a second clip can be placed if the first is found to be misapplied (13). If the tube is transected by closing the clip too rapidly, a second clip can be placed on the free end of tube. The Filshie clip was not included in the original CREST study but has been found to have a relatively low 10-year failure rate at 0.41% to 2.3% when positioned correctly (19, 20).

The Falope-ring (Olympus Corporation of the Americas, Center Valley, Pennsylvania) is a silicone rubber band initially developed in the early 1970s by Dr. Yoon and associates. The silastic radiopaque ring containing an inner loop of 1 mm is loaded to the device applicator tip immediately prior to use to avoid persistent dilation of the inner ring. The original applicator was made of two concentric cylinders, an inner cylinder containing thongs for grasping the tube and an outer one which assisted with deployment of the silicone band.

Once positioned over the fallopian tube at approximately 3 cm from the uterine cornua, the grasping thongs are exposed from the inner cylinder of the applicator and used to lift a knuckle of the fallopian tube. The tube must be completely encircled in order to ensure appropriate placement of the silicone band around two separate portions of fallopian tube lumen. The thongs are then retracted, pulling the loop of fallopian tube up into the barrel. The silicone band is subsequently slid off of the applicator to the base of the loop by the outer cylinder (Figure 32.7). Any excessive traction during these steps can result in tissue shearing and hemorrhage. Constriction and devascularization results in destruction of the tubal loop by avascular necrosis. This may be associated with increased postoperative pain following this technique (6, 21). The 10-year failure rate for the Falope ring is 1.77% (18).

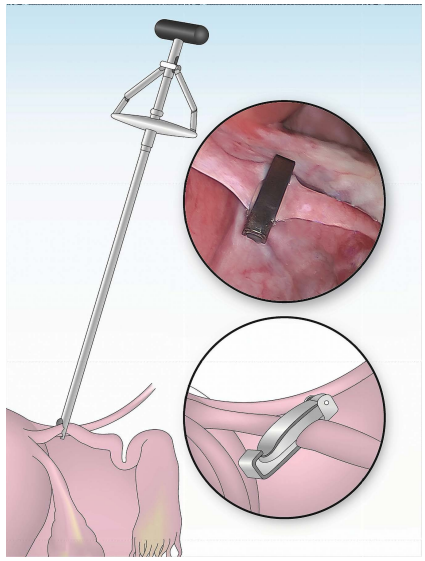


FIGURE 32.6 Correct Filshie clip placement. (From ref 13 with permission.)

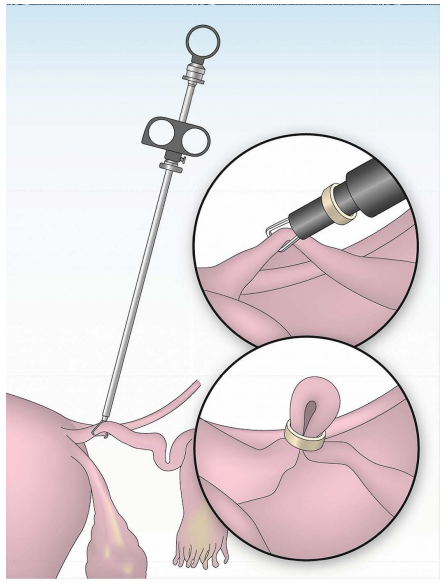


FIGURE 32.7 Correct silicone ring placement. (From ref 13 with permission.)

32.7 Avoiding the Abdomen: Transcervical Techniques

Transcervical approach to tubal sterilization offers optimization of the benefits of minimally invasive surgery and cost.

This approach, typically achieved by utilizing the hysteroscope, eliminates the need for any abdominal incisions, minimizing procedure risk and postoperative pain. Hysteroscopic sterilization can typically be performed without general anesthesia, further optimizing risk and anticipated patient recovery. This approach also offers the opportunity to complete sterilization in the office setting. It is the optimal approach for patients who have clinical factors which may increase their perioperative risk, such as medical comorbidities, obesity, and pelvic adhesions. Available data reflect clear benefits with respect to both patient pain and satisfaction as well as significant cost savings with hysteroscopic approach in the outpatient setting (22, 23).

The earliest reported attempt to achieve transcervical sterilization dates back to 1849 when a German physician, Friorep, attempted to achieve sterilization by infusion of a silver nitrate solution into the uterine cavity. Hysteroscopic attempts were made as early as 1934 using electrocautery to occlude the intramural portion of the tube. This approach was further developed in the 1970s by Quinones and colleagues who created a protocol which used a silicone-tip electrode to deliver 25 watts of electrocautery for 8 to 10 seconds to a zone of 6 mm into the tube. A temporary contraceptive was encouraged until 12 weeks when successful tubal occlusion was confirmed with hysterosalpingogram. Efficacy of this technique did ultimately come into question with a 35.5% failure rate. There were additional safety concerns regarding tubal perforation and potential for thermal injury to the bowel. Cryocoagulation, radiofrequency ablation, neodymium:yttrium-aluminum-garnet (Nd:YAG) laser, and hysteroscopic chemical sterilization using quinacrine (JOSHI PHARMA, Maharashtra State, India) were subsequently trialed with limited follow-up on efficacy and technique development. Tubal blockage using various forms of inserted devices such as silicone-based plugs was also attempted (3, 4, 11).

The Essure system (Bayer Healthcare Pharmaceuticals, Leverkusen, Germany) was approved by the Food and Drug Administration (FDA) in 2002. This tubal insert was 4 cm in length and 0.8 mm in diameter prior to insertion. It was made up of a stainless-steel inner coil wrapped in a layer of polyethylene terephthalate (PET) fibers, with an additional nitinol (nickel–titanium alloy) outer coil. When the insert was released into the fallopian tube, the outer coil expanded to a diameter of 1.5 to 2.0 mm and conformed itself to the diameter and shape of the fallopian tube. Tubal occlusion was achieved by this space-filling design and PET fiber stimulation of an inflammatory reaction which resulted in tissue in-growth into and around the insert (24). The Essure system carried a 94.6% to 99% successful placement rate, and an effectiveness of 99.85%. Immediate risks were those intrinsic to hysteroscopy and potential for tubal perforation with forceful insertion. By 2013, the number of medical device reports and patient submitted complaints increased, including reports of persistent post-procedure pain, hypersensitivity reactions, and interval insert perforation with migration into the abdominal cavity. In 2016 the FDA added a black box warning to the device and a "Patient Decision Checklist" for completion prior to insertion. The Essure system was ultimately removed from the United States market at year-end 2018 (7, 25, 26).

For patients with Essure devices remaining in place, if asymptomatic, the consensus is that the benefits of leaving the device in place outweigh any potential risks (7). For patients with symptoms that are believed to be Essure related, removal can be discussed. Hysteroscopic removal is unfortunately limited to the first 12 weeks following insertion, prior to the PET fiber–induced tissue in-growth to the device. Laparoscopic or robotic bilateral salpingectomy can be performed with consideration of cornuectomy to reduce the likelihood of leaving residual PET fibers behind. The surgeon must also confirm that any insert coils trailing into the uterine cavity are removed with each tube at the time of salpingectomy. Hysteroscopy and/or X-ray may be utilized for confirmation that all insert coils are extracted. Hysterectomy with bilateral salpingectomy is not required for Essure device removal but may be considered for the typical indications (7, 25–30).

A similar hysteroscopic device, Adiana (Hologic Inc., Marlborough, MA), was introduced to the market by Hologic following FDA approval in 2009. This device utilized radiofrequency energy to desiccate a segment of fallopian tube in the interstitium, followed by insertion of a silicone plug which stimulated an inflammatory reaction. The device was taken off the market in 2012.

References

1. Rock JA et al., eds. *Te Linde's Operative Gynecology*, 10th edn. Philadelphia: Wolters Kluwer/Lippincott Williams & Wilkins; 2008.
2. Handa VL et al., eds. *Te Linde's Operative Gynecology*, 12th edn. Philadelphia: Wolters Kluwer; 2020.
3. Zurawin RK et al. Tubal sterilization [Internet]. *Medscape*, 2021. Available at: https://emedicine.medscape.com/article/266799-printemedicine.medscape.com.
4. Chapman L et al. Currently available devices for female sterilization. *Expert Rev Med Devices*. 2005;2(5):623–634.
5. Ezzati M et al. Tubal transport of gametes and embryos: a review of physiology and pathophysiology. *J Assist Reprod Genet*. 2014;31:1337–1347.
6. Sanders BH. Laparoscopic sterilization: clinical aspects [Internet]. *Global Library of Women's Medicine*, 2008. https://doi.org/10.3843/GLOWM.10404.
7. American College of Obstetricians and Gynecologists. Benefits and risks of sterilization. ACOG practice bulletin 208. *Obstet Gynecol*. 2019;133:e194–e207.
8. Mackay AP et al. Tubal sterilization in the United States, 1994–1996. *Fam Plann Perspect*. 2001;33:161–165.
9. Bajwa SJS et al. Anaesthesia for laparoscopic surgery: general vs regional anaesthesia. *J Minimal Access Surg*. 2016;12:4–9.
10. Rosati M et al. Operative gynecological laparoscopy under conscious sedation. *J Soc Laparoendoscop Surg*. 2020;24(2):1–9.
11. Bartz D et al. Sterilization in the United States. *Rev Obstet Gynecol*. 2008;1.
12. Jamieson DJ et al. Complications of interval laparoscopic tubal sterilization: findings from the United States collaborative review of sterilization. *Obstet Gynecol*. 2000;96(6):997–1002.
13. Levine R et al. Laparoscopic tubal sterilization. In: Pasic R et al., eds. *Practical Manual of Minimally Invasive Gynecologic and Robotic Surgery*, 3rd edn. CRC Press; 2018:79–85.
14. Society of Gynecologic Oncology clinical practice statement: salpingoectomy for ovarian cancer prevention [Internet]. *SGO*, 2013. Available at: www.sgo.org/resources/sgo-clinical-practice-statement-salpingectomy-for-ovarian-cancer-prevention/.
15. American College of Obstetricians and Gynecologists. Opportunistic salpingectomy as a strategy for epithelial ovarian cancer prevention. Committee opinion 774. *Obstet Gynecol*. 2019;133: e279–e284.
16. Baltus T et al. Spontaneous pregnancy after total bilateral salpingectomy: a systematic review of literature. *J Minim Invas Gynecol*. 2022;29:213–218.
17. Kulier R et al. Minilaparotomy and endoscopic techniques for tubal sterilisation. *Cochrane Database Syst Rev*. 2004;3:CD001328.

18. Peterson HB et al. The risk of pregnancy after tubal sterilization: findings from the U.S. collaborative review of sterilization. *Am J Obstet Gynecol*. 1996;174(4):1161–1168; discussion 1168–1170.
19. Dominik R et al. Two randomized controlled trials comparing the Hulka and Filshie clips for tubal sterilization. *Contraception*. 2000;62:169–175.
20. Walhof KA et al. Long-term failure rates of interval Filshie clips as a method of permanent contraception. *Women's Health Rep*. 2021;2(1):279–284.
21. Schmidt EO et al. Surgical procedures for tubal sterilization [Internet]. *Global Library of Women's Medicine*, 2014. https://doi.org/10.3843/GLOWM.10400.
22. Levie MD et al. Office hysteroscopic sterilization compared with laparoscopic sterilization: a critical cost analysis. *J Minim Invasive Gynecol*. 2005;12(4):318–322.
23. Levie M et al. Analysis of pain and satisfaction with office-based hysteroscopic sterilization. *Fertil Steril*. 2010;94(4):1189–1194.
24. Hurskainen R et al. Hysteroscopic tubal sterilization: a systematic review of the Essure system. *Fertil Steril*. 2010; 94(1):16–19.
25. Walter JR et al. Hysteroscopic sterilization with Essure. *Obstet Gynecol*. 2017;129:10–19.
26. Clark NV et al. Essure removal for the treatment of device-attributed symptoms: an expanded case series and follow-up survey. *J Minim Invasive Gynecol*. 2017;24(6):971–976.
27. Thiel L et al. Laparoscopic cornuectomy as a technique for removal of Essure microinserts. *J Minim Invasive Gynecol*. 2017;24(1):10.
28. Maassen LW et al. Removal of Essure sterilization devices: a retrospective cohort study in the Netherlands. *J Minim Invasive Gynecol*. 2019;26(6):1056–1062.
29. Bhagavath B et al. Removal of Essure. *Fertil Steril*. 2020;114:81.
30. Gracia M et al. Essure removal: comparison of two minimally invasive approaches. *Fertil Steril*. 2020;114(1):187–188.

33 TUBOPLASTY

William Nolan and Naomi Whittaker

33.1 Introduction

Tuboplasty was the main therapeutic option for tubal infertility before assisted reproductive technologies (ART). Initially, surgical management of tubal disease was limited by postoperative adhesions as well as the drawbacks of open surgery. These limitations were improved upon by implementation of microsurgical techniques (1). Microsurgical techniques were initially applied via an open approach and with the development of laparoscopy, moved to a minimally invasive approach. The shift to minimally invasive surgery offered benefits such as same-day surgery, improved cosmesis, and decreased complications and pain (1).

Fallopian tube disorders amenable to surgery management include proximal tubal occlusions, adhesive disease, hydrosalpinx, tubal ligation, and tubal endometriosis. In the 1990s and early 2000s, success rates with IVF improved and infertility training focused on these techniques (1). This coincided with significant technological improvement in laparoscopic surgery. Because of IVF-focused fertility treatments, surgical training in microsurgical techniques for tubal repair suffered, although the technology to allow for tuboplasty improved. Despite ASRM recommendations favoring tubal surgery in certain instances, IVF is often the first or only option discussed with patients. Advantages of tubal repair include cost-effectiveness, ability to conceive multiple times without further medical intervention, avoidance of pregnancy risks associated with IVF, a more natural approach to fertility, and access to fertility care for patients who refuse IVF for religious or ethical reasons.

With continued innovation in minimally invasive surgery, laparoscopic and robotic-assisted surgery has allowed for tubal reconstruction with improved ease. However, while the access to minimally invasive surgery has expanded, the access to tuboplasty has not. This is likely due to a lack of training. For example, tuboplasty is not a requirement in training for the ACGME for general OB/GYN residency, minimally invasive gynecology fellowships, or even reproductive endocrinology fellowship programs. Despite its effectiveness, there is evidence for decline in surgical training for tubal anastomosis (2). This chapter outlines the indications and approaches to tuboplasty in minimally invasive surgery.

33.2 Gynecologic Aspects

Fallopian tube disorders are of interest during the workup for infertility and subfertility. However, disorders of the fallopian tube may be encountered in many clinical contexts which are important to the minimally invasive gynecologic surgeon. In these instances, the minimally invasive gynecologic surgeon should be equipped with the ability to generate a differential diagnosis and treatment plan for disorders of the fallopian tube. Additionally, the surgeon should be able to predict and be prepared to care for these disorders at the time of diagnostic laparoscopy or other scheduled procedures. Disorders of the fallopian can present in a variety of ways.

One common cause of fallopian tube distortion and adhesions is encountered in the patient with a history of pelvic inflammatory disease and/or tubo-ovarian abscess. In response to infection, adhesions can also form throughout the peritoneal cavity. One pathognomonic presentation of this is Fitz-Hugh–Curtis syndrome, demonstrated by violin string adhesions between the liver and anterior abdominal wall (Figure 33.1). Common pelvic manifestations include diffuse filmy adhesions which can drape the fallopian tubes, blunting or clubbing of the fimbriated end of the fallopian tubes, and in some cases, dense adhesions at the fimbria (Figure 33.1). This can lead to infertility, likely through physical barriers to conception (3). Another suggested mechanism is that adhesions facilitate the accumulation of cytotoxic peritoneal fluid which can include microorganisms and endotoxins, leading to oxidative stress and lack of nutrients (3, 4). The rate of tubal infertility is known to increase with the number of previous episodes of pelvic inflammatory disease (PID), reaching up to 54% with three prior infections (3). Other causes of tubal adhesions and damage include previous ectopic pregnancy, prior surgery, and endometriosis.

Tubal adhesions at the fimbriated end of the tube can lead to narrowing of the tube called fimbrial phimosis. In more severe cases, complete tubal blockage can occur, called hydrosalpinx (Figure 33.1). With hydrosalpinx, the tube fills with fluid and the distension can compound the tubal damage. The severity of tubal damage has direct implications to the fertility prognosis after surgery (5). Hydrosalpinx can be diagnosed with ultrasound and hysterosalpingogram. However, the gold standard for diagnosis remains combined tubal evaluation at the time of laparoscopy as both proximal and distal tubal disease can be evaluated simultaneously (Figure 33.1).

The presence of hydrosalpinx is known to decrease fertility in both spontaneous conception and with assisted reproductive technologies. This likely affects spontaneous conception by being a physical barrier and by harboring cytotoxic peritoneal fluid (3, 4). Due to the potential for an infectious component, we favor obtaining endocervical and endometrial cultures for patients in which hydrosalpinx is identified.

Fimbrioplasty to repair phimosis and salpingostomy to repair hydrosalpinx have been shown to improve spontaneous conception rates as well as conception rates with ART in the case of hydrosalpinx (5). In addition, salpingectomy has been shown to improve conception rates with IVF (6). Per ASRM, while salpingectomy combined with IVF remains the preferred approach in older women, those with other infertility factors, and those with male factor infertility, tuboplasty allows for attempts for spontaneous conception as well as improves success with IVF (5).

Unfortunately, there are no head-to-head studies available of fertility rates of irreversible salpingectomy versus corrective tubal surgery for IVF cycles. So, one may want to consider more conservative approaches and trials of natural conception before committing the patient to IVF or making a definitive treatment decision of salpingectomy.

Hydrosalpinx can be noninfectious and related to other sources of inflammation and adhesions, such as endometriosis. Endometriosis affects 6%–11% of asymptomatic women and as much as 50% of women with infertility (7). Theories for

DOI: 10.1201/9781003312109-33

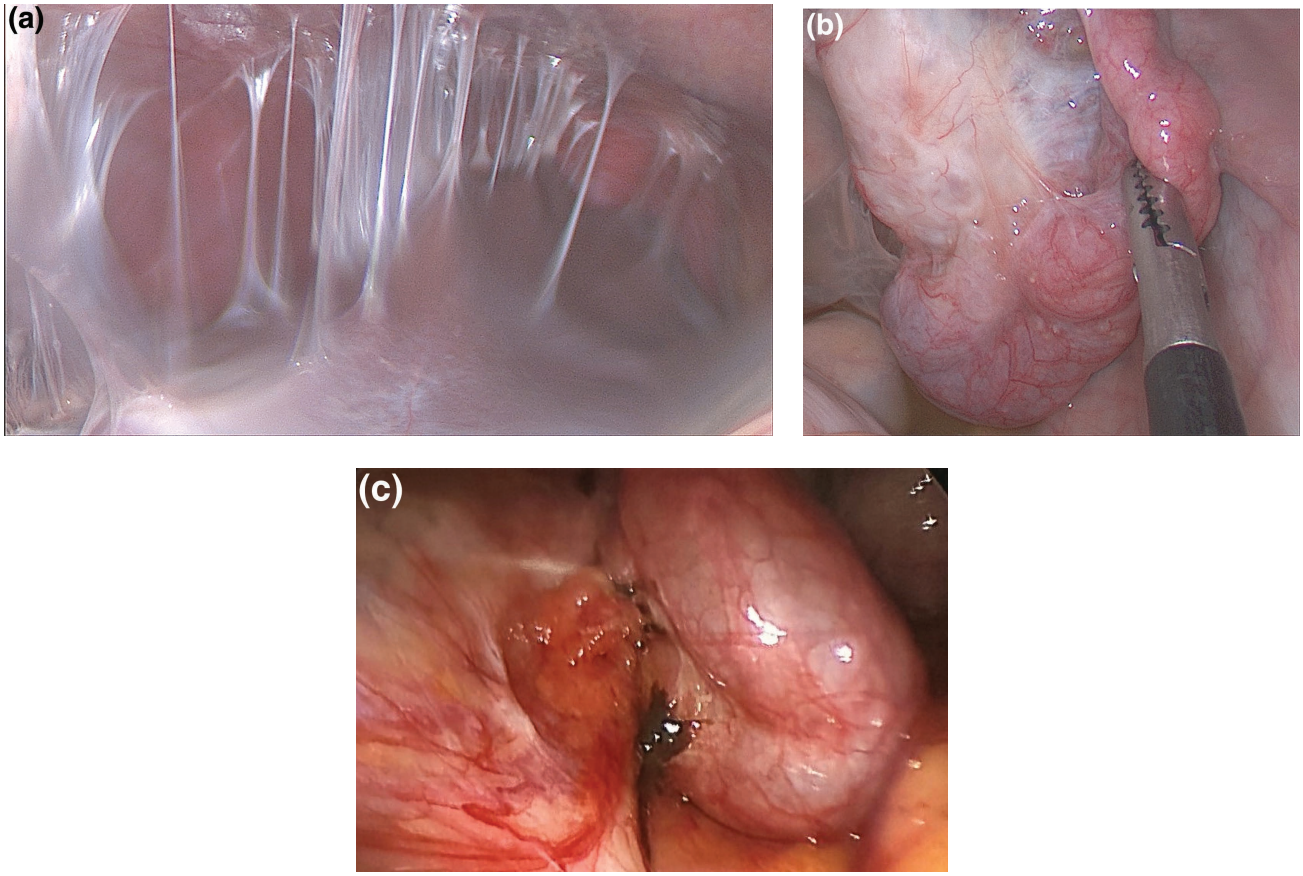


FIGURE 33.1 (a) Fitz-Hugh–Curtis syndrome with violin string adhesions of the liver to the anterior abdominal wall. (b) The fallopian tubes from the same patient are demonstrated. Both clinical findings are hypothesized to have one origin, namely intra-abdominal infection. (c) Combined HSG with laparoscopy. In this case, the fallopian tube was found to have severe adhesive disease at the mid- and distal portions at time of laparoscopy with concomitant normal findings on selective HSG.

the direct cause of infertility include structural changes and inflammatory cytokines affecting conception and implantation. Approximately 5% of patients with endometriosis will have tubal endometriosis and up to 28% will have endometriosis-related adhesions directly affecting the tube (8). Beyond this, adhesions from endometriosis can further affect the tube. With that, the minimally invasive gynecological surgeon should be adept at carefully removing endometriosis from the tube while preserving the tubal integrity and preventing adhesive disease. Surgery alone has been shown to improve spontaneous conception rates (9).

There are also iatrogenic causes of tubal pathology and infertility. Examples include adhesions from prior surgery and previous tubal sterilization. Hysteroscopic tubal sterilization is a known cause of sterility, pelvic pain, and other clinical issues (10). Tubal ligations are primarily associated with tubal infertility, and some patients, particularly younger patients, are at risk for regret and desire for future fertility (11).

Proximal tubal occlusion is a known cause of infertility which is amenable to minimally invasive surgery. Salpingitis isthmica nodosa is a little understood inflammatory condition that causes nodular thickening (up to a few centimeters in diameter) predominantly at the isthmus and is known to cause tubal infertility (3). Procedures include selective hysterosalpingogram with tubal cannulation, hysteroscopic tubal cannulation, and in cases refractory to cannulation, cornual resection and tubal reimplantation.

There are multiple approaches to the diagnosis of tubal pathology. The diagnosis of tubal occlusion can be complex in nature. Techniques for diagnosis include hysterosalpingogram (HSG), MR tubal patency studies, virtual CT HSG, and sonohysterography. HSG and ultrasound studies are favored for their accessibility, low cost, and effectiveness while chromopertubation with laparoscopy is considered the gold standard and confirmatory test (12). Selective HSG provides direct testing of individual fallopian tubes and is less susceptible to false positive results from tubal debris or spasm. Additionally, selective HSG allows for tubal cannulation, therefore can offer immediate treatment, and is more than a diagnostic procedure (13).

33.3 Surgical Aspects

At its conception, surgery for the fallopian tube was performed as an open abdominal procedure and was complicated by its high risk for adhesions (14). With the implementation of microsurgical techniques, more success was encountered with anatomical reconstruction and limiting adhesive disease. Microsurgical techniques include meticulous atraumatic tissue handling, judicious energy use, frequent and complete

irrigation, use of warm fluid, and use of anti-inflammatory medications (14). Specifically, for tubal handling, we avoid grasping the tube and prefer gentle retraction, and we avoid the use of lap sponges and techniques that lead to bleeding and abrasions. These techniques were initially developed for open surgery but were amenable to the advent of laparoscopic surgery, for which benefits such as decreased postoperative pain, decreased analgesic requirements, improved cosmesis, shorter hospital stay, reduced blood loss, and reduced costs are well documented (1, 14). In addition to these, there are suspected benefits from limiting insufflation pressure and using humidified CO_2 (15). Although high-quality evidence for adhesion barriers is limited, there is some evidence to support their use in gynecologic surgery, and various barriers are currently being investigated further (15). In combination, these microsurgical techniques serve to minimize tissue trauma, inflammation, residual blood, and denuded surfaces during the healing process, allowing for repair of tissue and avoidance of persistent or newly formed adhesive disease. To prevent tubal damage and adhesion formation, limiting thermal damage to the tubal lumen and muscularis are crucial for maintaining anatomy and function of the tube. The CO_2 laser is of particular benefit in this regard as there is minimal tissue penetration (16). With the variety of settings, one can cut the tissue cleanly, similar to a scalpel, and focus on excising or even vaporizing superficial disease on the serosal layer – with minimal lateral thermal spread – therefore preserving the integrity of the muscularis and lumen. Preventing adhesions and maintaining tubal anatomy and function is of the utmost importance when considering tuboplasty.

In addition to the development of microsurgical techniques, technological advances in laparoscopy continue to improve accessibility for surgeons. One major advancement in laparoscopy is the development of robotic-assisted surgery, which is useful for laparoscopic application of microsurgical principles. Robotic-assisted surgery retains the aforementioned benefits of traditional laparoscopy while providing 3D visualization, stable camera, wristed instruments with seven degrees of freedom, elimination of tremor, and motion scaling, as well as instrumentation especially designed for microsurgery (17). Unfortunately, many of the advances in laparoscopy have coincided with the increased frequency of ART use for tubal disease, and there has been limited published research regarding tuboplasty. With that said, we feel these advantages allow for fine dissection, gentle tissue handling, and precise repair during tubal surgery, increasing feasibility of tuboplasty.

33.4 Proximal Tubal Occlusion

Proximal tubal occlusion is not well studied but is thought to arise most commonly from past infection. Other causes may include endometriosis and salpingitis isthmica nodosa (SIN), inflammation, or idiopathic causes. Proximal tubal occlusion can be diagnosed with HSG, chromopertubation, or sonographic tubal studies. However, we prefer selective HSG as it gives objective data about location and significance of proximal tubal occlusion. In addition, it is simultaneously a therapeutic option. Proximal tubal occlusion is amenable to cannulation, with similar success rates noted fluoroscopically and hysteroscopically. Fluoroscopic tubal cannulation is successful in 71%–92% of patients, and pregnancy rates range from 30%–40% after cannulation (13). Similar success has been shown for fluoroscopic-guided hysteroscopic tubal cannulation (18).

Fluoroscopic tubal cannulation is performed at the time of HSG. An Echosight Jansen-Anderson Intratubal Transfer Set (Cook Medical, Bloomington, IN) catheter attached to a pressure gauge (Encore 26, Boston Scientific, Alpharetta, GA) is placed at the tubal ostia and radiopaque dye is injected into the tube. If fill and spill of dye is not appreciated or noted at elevated pressures, greater than 0.7 mmHg, the tube may be amenable to cannulation. Cannulation is performed with several passes of a gentle guidewire under fluoroscopic visualization. After cannulation, dye can be injected again to evaluate spill and new pressures (Figure 33.2a–c). Hysteroscopically, this can be achieved in a similar fashion, using a Fallopian Tube Catheterization Set (Cook Medical, Bloomington, IN) with a pressure gauge (Encore 26, Boston Scientific, Alpharetta, GA) attached to guidewire placed through a hysteroscopic cannula (Figure 33.2d). In cases in which a firmer guide wire is required, a Sensor guide wire (Boston Scientific, Alpharetta, GA) can be used for cannulation.

Success rates are lower for repeat tubal cannulation (13). However, repeat tubal cannulation can be offered with proper patient counseling and, in our experience, this has been successful on occasion. Historically, microsurgical tubocornual resection and anastomosis (TCA) was an approach for SIN or recurrent obstruction. In this procedure, the abnormal portion of the tube is identified and excised laparoscopically. Next, a stent is placed through the fallopian tube and cornual portion of the uterus with hysteroscopic guidance. Following this, the anastomosis is performed with double-layer suturing, reattaching the proximal end of the tubal submucosa and muscularis to the intramural portion of the uterine submucosal muscular layer (19). Next, the uterine defect is repaired. Throughout the process, tubal patency is confirmed with methylene blue. Following surgery, patency can be confirmed with HSG. Several series revealed spontaneous pregnancy rates greater than 50% following tubocornual anastomosis (1). These studies were performed without laparoscopy. However, a tubal patency rate of 64.2% was demonstrated after laparoscopic TCA without robotic assistance (19). We feel that with current technology, outcomes from an abdominal microsurgical approach can likely be replicated by surgeons with appropriate training. Currently, ASRM prefers IVF to tubocornual anastomosis but states that microsurgical anastomosis may be considered for patients if IVF is not an option and that it should only be attempted by surgeons with appropriate training (5). As previously stated, there is limited current evidence regarding these procedures and robotic approaches.

33.5 Distal Tubal Occlusion

Distal tubal occlusion is most often encountered with adhesive disease. Common causes of adhesive disease are pelvic infection, prior surgery, and endometriosis. Removal of scar tissue has the benefit of restoring anatomy and fertility. Outcomes typically depend on the degree of tubal damage. The minimally invasive surgeon should be equipped to counsel patients on the likelihood of success with tuboplasty as well as that of assisted reproductive procedures so the patient can make an informed decision prior to tubal surgery.

To perform salpingo-ovariolysis, the surgeon must first identify the adhesions of the ovary and fallopian tube. Once identified, the adhesions must be placed on tension and then transected, with the goal of remaining 1 mm away from the tubal or ovarian surface, thus preventing damage to these

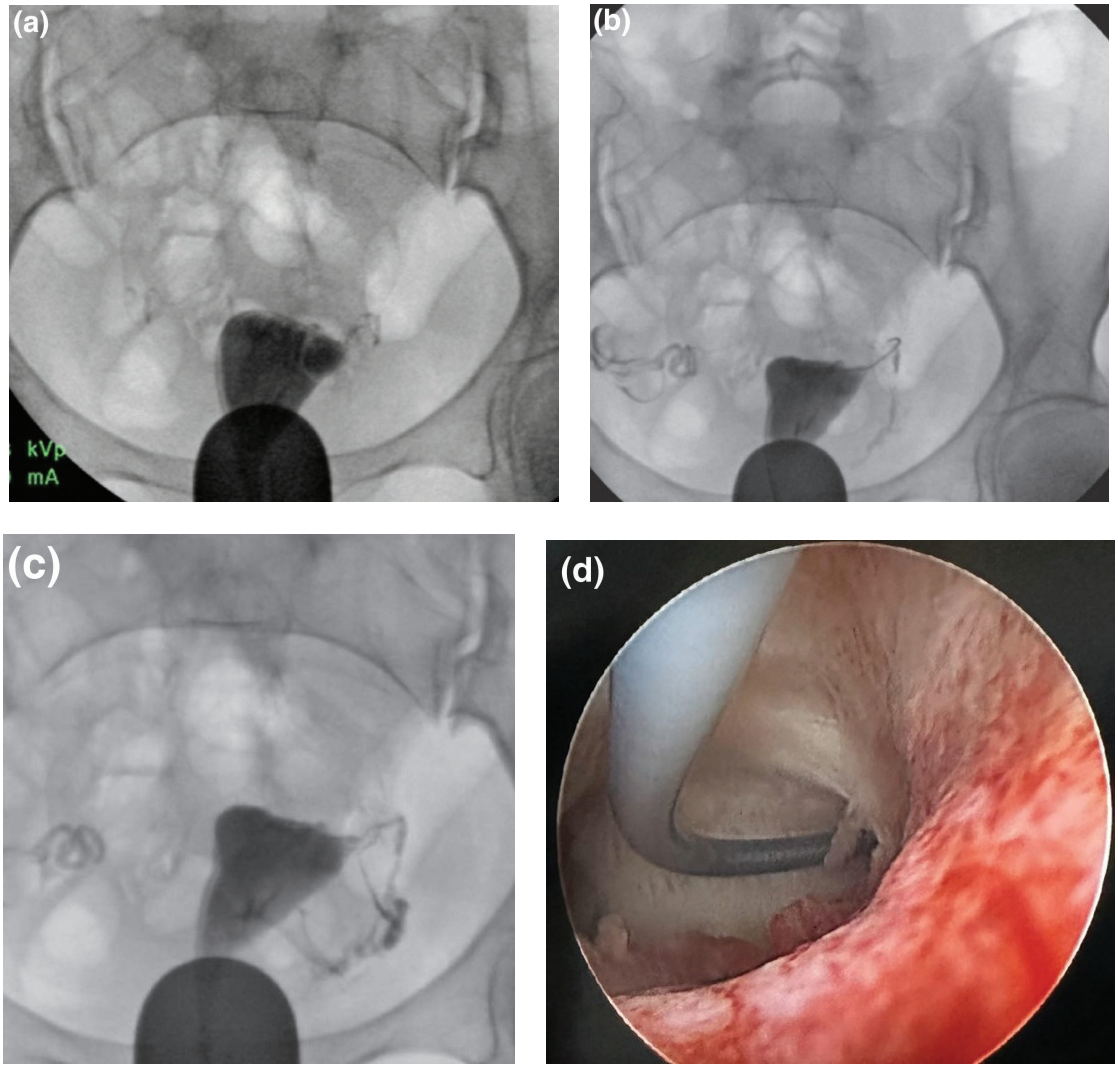


FIGURE 33.2 (a) Proximal occlusion of the fallopian tube on selective HSG. (b) The passage of a guidewire through the tubal ostia under fluoroscopic guidance to clear the tube. (c) Fill and spill of contrast dye after the tube has been cannulated, representing a patent fallopian tube. (d) Selective HSG being performed with hysteroscopic assistance. In this case, fluoroscopy is used with a pressure gauge just as done with fluoroscopy only.

structures. Gentle handling of the tube is advised to prevent iatrogenic damage to the tube as well as abrasions which can ultimately lead to further scarring and anatomical distortion. Filmy adhesions can simply be lysed, while more dense adhesions should be excised in their entirety. Additionally, incision may be necessary to begin the dissection of dense adhesions. Use of microsurgical techniques is essential for meticulous dissection and prevention of adhesion recurrence. Additionally, we favor the use of CO_2 laser given its advantage of atraumatic cutting with hemostasis and ability to vaporize lesions with minimal tissue penetration and thermal spread (16). Live birth rates range from 37% to 57% with lysis of adhesions, and with ectopic pregnancy from 5% to 8% (14).

If the fimbriae are partially enclosed in scar tissue, fimbrioplasty can be performed. If the fimbriae are completely encased in scar tissue forming a hydrosalpinx, salpingostomy can be performed. At times, a significant amount of scar tissue must be resected prior to encountering healthy fimbriae. Results of these procedures are dependent on the extent of tubal damage, particularly the fimbriae. Birth rates are as high as 40%–60% when tubal disease is characterized as mild but falls to less than 20% when disease is characterized as severe (14). These rates are important for patient counseling as IVF success is reported in live birth rate per embryo transfer, making the alternatives difficult to compare side by side.

To perform fimbrioplasty or salpingostomy, salpingo-ovariolysis is typically necessary for initial anatomical restoration. Following this, chromopertubation is performed, distending the tube and often highlighting the fimbriated end where avascular scar tissue needs to be incised. Ideally, fimbriae are encountered and can be tacked backwards onto the tube with permanent, non-adhesiogenic suture such as 5–0 polypropylene. However, if severe blunting is present with little to no healthy fimbriae, once the distal end of the tube is identified, a Y-shaped incision is made along the avascular adhesions covering the fimbria. The scar tissue is then everted to

expose the fimbria and tubal ostium. At this time, dye can be injected again to confirm adequate exposure of the fimbriated end. Once confirmed, a permanent suture is used to secure the previous scar tissue to the proximal tubal serosa, allowing for continued tubal patency. In a large meta-analysis, pregnancy rates after salpingostomy for hydrosalpinx was 27% with an ectopic pregnancy rate of 10% (20).

33.6 Endometriosis of the Fallopian Tube

Endometriosis can affect the fallopian tubes directly or by disease-related adhesions. In either case, clinical implications are typically pain and infertility. In removing tubal endometriosis or tubal adhesions, microsurgical techniques are of the utmost importance as thermal damage and postoperative adhesions can defeat the purpose of surgical intervention. Laser surgery is helpful in treating tubal endometriosis as a noncontact cutting device, allowing for meticulous, atraumatic, and hemostatic dissection with minimal thermal spread. CO_2 laser can have a depth of penetration as little as 0.1 mm (16). This is especially helpful for tubal disease to prevent thermal damage from compromising the tube. CO_2 laser is also favored for removing small amounts of endometriosis from the ovary, as limited thermal spread has been shown to benefit ovarian reserve (21). For this reason, we prefer the laser for vaporization of superficial endometriosis implants on the tube, bowel, and diaphragm. A typical approach to tubal endometriosis would begin with lysis of adhesions and restoration of anatomy (Figure 33.3). Following this, if discrete endometriosis lesions are identified, the overlying serosa can be outlined with the laser (Figure 33.4a). The serosa is then placed on tension while the underlying tissue is dissected away, leaving behind healthy tissue (Figure 33.4b). Once completely resected, the tube needs to be repaired in a fashion to restore its functional anatomy. Ideally, damage to the muscularis is limited to prevent narrowing of the lumen. Once the lesion is resected, the serosa is closed perpendicular to the long axis of the tube (Figure 33.4c).

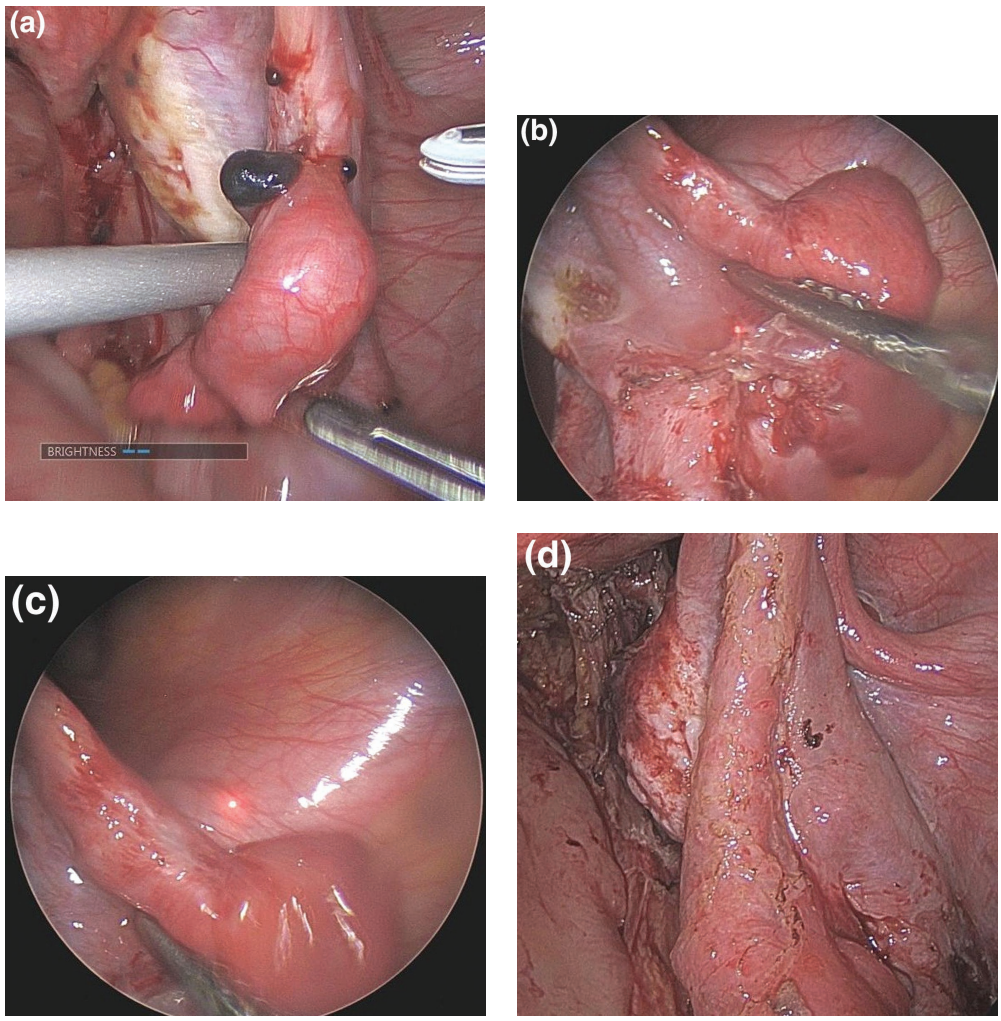


FIGURE 33.3 Excision of tubal endometriosis. (a) The fallopian tube is distorted with blebs of endometriosis and adhesions. (b) Lysis of adhesions has been performed to restore tubal length and anatomy. (c) Superficial endometriosis in the ampullary portion has been excised with the CO_2 laser. (d) The tubal anatomy has been restored and all visible endometriosis has been excised (by courtesy of Patrick Yeung, MD).

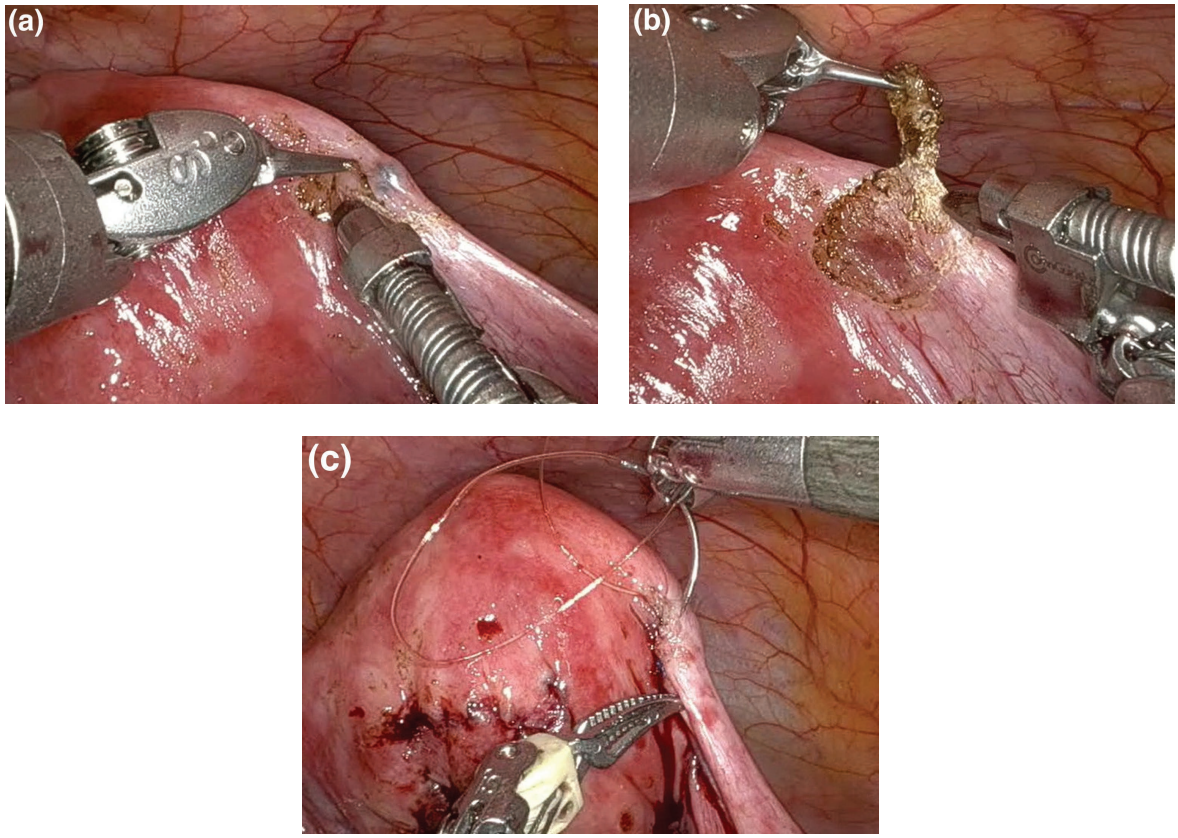


FIGURE 33.4 Removal of endometriosis nodule from proximal fallopian tube. (a) A nodule of endometriosis is noted on the proximal fallopian tube. (b) The nodule is outlined with the CO_2 laser, placed on tension, and excised in its entirety. (c) The muscularis and serosa have been repaired.

33.7 Tubal Anastomosis

Tubal reconstruction is at times desired secondary to pathology, such as endometriosis, prior surgery for ectopic pregnancy, or in the context of previous tubal sterilization. Tubal sterilization is the most common form of contraception in the United States, however, 20% of patients ultimately express regret after sterilization (11, 22). A 2012 committee opinion from the American Society of Reproductive Medicine states there is good evidence to support tubal reversal surgery (5). There are multiple factors that play a part in the counseling of patients in deciding between tubal reversal and IVF including age, type of previous ligation, and residual length of healthy tube, as well as a desire for multiple subsequent pregnancies. A large meta-analysis of tubal reversal revealed pregnancy rates range from 42% to 49% and ectopic pregnancy rates range from 4% to 8% after tubal reversal (23).

To perform the procedure, lysis of adhesion is often performed. Once anatomy is restored, the mesosalpinx can be injected with a diluted solution of vasopressin (0.2 IU/mL) to maintain hemostasis during dissection. The mesosalpinx is transected to mobilize the ligated ends of the fallopian tube. The ligated ends of the tube are then transected distally and proximally to expose the lumen. The patency of the proximal portion of the fallopian tubes is confirmed via chromopertubation. The mesosalpinx is then reapproximated with suture until the separated tubal lumen are in close proximity to reduce tension. A small catheter can be inserted as a stent in between both free ends of the fallopian tubes to aid in anastomosis. Examples include a 3 French pediatric whistle-tip ureteral catheter or 1–0 polypropylene suture. Anastomosis of the tubal mucosa and muscularis is performed via at minimum three interrupted sutures of 7–0 polydioxanone at 2, 6, and 10 o'clock positions, beginning at 6 o'clock position in order to maintain visualization of the tubal lumen. Suturing is performed such that knots are tied outside of the tubal lumen. Superficial muscularis and serosa are approximated using interrupted sutures of 7–0 polydioxanone. Chromopertubation is performed at the end to confirm patency of the anastomotic sites.

Given the use of small sutures and needles, the procedure can be technically challenging. Challenges include broken sutures and increased time of intracorporeal knot tying (23). However, the procedure can be completed laparoscopically by facile surgeons. Robot assistance offers minimally invasive microsurgical benefits in this area as wristed instruments can improve the ease of knot tying. Smaller robotic microsurgical instruments can be of significant technical benefit as well. The 7–0 gauge suture can be difficult to visualize when placed into the abdomen. Passing needles on small cut fabric can improve efficiency and safety of needle transfer.

33.8 Embryologic Abnormalities

The embryologic remnant of the paramesonephric Müllerian duct or mesonephric Wolffian duct appear as cysts at the fimbrial end of the fallopian tube (24). There is evidence that these

embryological remnants may contribute to unexplained infertility and that removal may improve fertility (25). It is hypothesized that the mechanism whereby paratubal cysts affect fertility is through ovum pickup through tubal distortion or by placing weight on the fimbrial end of the tube, increasing its distance from the ovary (25). It is our practice to remove paratubal cysts when the size distorts fallopian tube anatomy, are larger than 2 cm, or appear to be weight bearing at the time of laparoscopy. In addition, we remove pedunculated paratubal cysts which lead to minimal tubal damage. The surgeon must judge whether removing the cyst may cause damage to the tube beyond what is caused by anatomical distortion as there are no strong recommendations regarding their removal at this time.

For removal, pedunculated paratubal cysts can be amputated at their base, taking care not to injure fimbria. If a paratubal cyst is large and incorporated into the body of the tube, a small incision is made into the exposed thinnest portion of the serosa, and the cyst can be shelled out in a similar fashion to an ovarian cyst. Care should be taken during the dissection as a vascular stalk is often encountered and can be controlled with suture ligation to prevent thermal damage to the tube. Once removed, repair of the tube can be performed with 4–0 poliglecaprone 25 suture in a running, imbricating fashion with an effort to not narrow the lumen.

Various other abnormalities of the fallopian tubes have been described including accessory fallopian tubes, accessory tubal ostia, and patterns of tubal agenesis (24). These presentations are uncommon and their individual clinical relevance is unclear. Due to their rarity, recommendations regarding surgical intervention are unlikely. We recommend discussing risks and outlining that potential benefits of tubal surgery are unknown. When tubal repair is elected, principles of anatomical restoration with the use of microsurgical and adhesion prevention techniques are recommended.

33.9 Conclusion

In the last two decades, there have been significant advancements in laparoscopic surgery. During the same time period, there has been a trend towards ART for tubal disease. Despite the widespread implementation of IVF, tuboplasty offers benefits such as anatomical restoration, treatment of endometriosis, cost-effectiveness, ability to conceive multiple times without further medical intervention, avoidance of pregnancy risks associated with IVF, natural approach to fertility, and access to fertility care for patients who refuse IVF for religious or ethical reasons. For this reason, further training in tubal surgery, microsurgical techniques, and adhesion prevention is crucial for surgical trainees entering gynecologic subspecialties.

References

1. Gomel V. The place of reconstructive tubal surgery in the era of assisted reproductive techniques. *Reprod Biomed Online*. 2015;31(6):722–731.
2. Armstrong A et al. The role of fallopian tube anastomosis in training fellows: a survey of current reproductive endocrinology fellows and practitioners. *Fertil Steril*. 2004;82(2):495–497.
3. Hoffman BL et al. Evaluation of the infertile couple. In: *Williams Gynecology*, 4th edn. New York: McGraw-Hill Education; 2020.
4. Strandell A et al. Why does hydrosalpinx reduce fertility? The importance of hydrosalpinx fluid. *Hum Reprod*. 2002;17(5):1141–1145.
5. Role of tubal surgery in the era of assisted reproductive technology: a committee opinion. *Fertil Steril*. 2021;115(5):1143–1150.
6. Strandell A et al. Hydrosalpinx and IVF outcome: a prospective, randomized multicentre trial in Scandinavia on salpingectomy prior to IVF. *Hum Reprod*. 1999;14(11):2762–2769.
7. Hoffman BL et al. Endometriosis. In: *Williams Gynecology*, 4th edn. New York: McGraw-Hill Education; 2020.
8. Olive DL et al. Endometriosis. *N Engl J Med*. 1993;328(24):1759–1769.
9. Endometriosis and infertility: a committee opinion. *Fertil Steril*. 2012;98(3):591–598.
10. Miguet-Bensouda C et al. Clinical improvement after Essure® devices removal: a systematic review. *Eur J Contracept Reprod Health Care*. 2023;28(4):238–248.
11. Hillis SD et al. Poststerilization regret: findings from the United States collaborative review of sterilization. *Obstet Gynecol*. 1999;93(6):889–895.
12. Grigovich M et al. Evaluating fallopian tube patency: what the radiologist needs to know. *Radiographics*. 2021;41(6):1876–1896.
13. Dun EC et al. Tubal factor infertility: diagnosis and management in the era of assisted reproductive technology. *Obstet Gynecol Clin North Am*. 2012;39(4):551–566.
14. Gomel V. Reconstructive tubal surgery. In: *Te Linde's Operative Gynecology*, 11th edn. Wolters Kluwer; 2015:365–402.
15. Schaefer SD et al. Prevention of peritoneal adhesions after gynecological surgery: a systematic review. *Arch Gynecol Obstet*. 2024;310(2):655–672.
16. Nezhat C et al. Surgical treatment of endometriosis via laser laparoscopy. *Fertil Steril*. 1986;45(6):778–783.
17. Alkatout I et al. The development of laparoscopy - a historical overview. *Front Surg*. 2021;8:799442.
18. Keltz M et al. Fluoroscopically-guided hysteroscopic tubal cannulation: a procedure for proximal tubal obstruction. *JSLS*. 2022;26(4).
19. Su H et al. Restoring tubal patency with laparoscopic tubocornual anastomosis. *Taiwan J Obstet Gynecol*. 2022;61(5):858–862.
20. Chu J et al. Salpingostomy in the treatment of hydrosalpinx: a systematic review and meta-analysis. *Hum Reprod*. 2015;30(8):1882–1895.
21. Candiani M et al. Assessment of ovarian reserve after cystectomy versus 'one-step' laser vaporization in the treatment of ovarian endometrioma: a small randomized clinical trial. *Hum Reprod*. 2018;33(12):2205–2211.
22. Daniels K et al. Current contraceptive status among women aged 15–49: United States, 2017–2019. *NCHS Data Brief*. 2020;(388):1–8.
23. van Seeters JAH et al. Tubal anastomosis after previous sterilization: a systematic review. *Hum Reprod Update*. 2017;23(3):358–370.
24. Csöbönyeiová M et al. The overview of anatomical variations and congenital anomalies of the uterine tubes and their impact on fertility. *Physiol Res*. 2022;71(Suppl 1):S35–S49.
25. Rasheed SM et al. Hydatid of Morgagni: a possible underestimated cause of unexplained infertility. *Eur J Obstet Gynecol Reprod Biol*. 2011;158(1):62–66.

34 PEDIATRIC AND ADOLESCENT GYNECOLOGY

MIGS Considerations for Our Youngest Patients

Lissa Yu and Kate McCracken

As the subspecialty of pediatric and adolescent gynecology (PAG) grows, MIGS surgeons may be tasked to handle more complex gynecologic procedures in pediatric and adolescent patients. Gynecologists are uniquely trained in open, laparoscopic, and vaginal approaches to pelvic structures, but knowing key considerations for a pediatric or adolescent patient will help to ensure appropriate care and ease of surgical procedure and recovery.

34.1 Preoperative Assessment and Care

Initial evaluation may be limited compared to the preoperative evaluation performed on an adult patient. The role of in-office exam may be limited to pubertal staging, abdominal exam if the patient permits, and a visual examination of the external genitalia. A frog-legged position, the patient held by a caregiver, or positioning with knees tucked to the chest may be helpful to visualize the external genitalia. Ensuring appropriate communication with the patient and family and utilizing distractors such as toys, stickers, technological devices, and child life specialists, if available, are critical to maximizing the utility of the examination. Despite best efforts, if the examination is limited or not tolerable by the patient or family, examination under anesthesia may be a better way to evaluate anatomy. In both an office examination and as a sedated examination, the use of labial traction in a downward and outward direction permits direct evaluation of the introitus without use of instrumentation. In other circumstances such as examination of an obstructive anomaly, a rectal exam may be helpful and better tolerated by the patient (1).

Speculum exams and digital vaginal/bimanual exams are deferred in the pediatric patient (and in most teens). The use of vaginoscopy (performed in the office with a handheld camera or other office vaginoscopy equipment if the patient tolerates, or under anesthesia with typical endoscopic equipment) allows for visualization of the upper vagina. Vaginal instruments may not otherwise be sized appropriately or available. Consideration of equipment used by pediatric general surgery, urology, or other pediatric surgical specialties should be utilized to ensure appropriate sizing of equipment used. Some cystoscopes may differ in length and size and allow for fluid to be used as a distention medium. This can be carefully performed to evaluate the vagina using one hand to apply pressure to close the labia around the scope to minimize spilling of water. Care should be taken to place the scope within the hymenal opening to minimize the risk of tissue injury.

The patient may have already undergone imaging to demonstrate a need for surgical intervention prior to referral to a gynecologic surgeon, but if not, transabdominal pelvic ultrasound is the preferred modality for initial evaluation rather than transvaginal ultrasound (2). A bladder filled with at least 200–300 cc urine or backfilled with water or saline is sufficient to allow views of uterine and adnexal structures. Larger structures may be seen without a full bladder, and a full bladder may be difficult to facilitate in patients with developmental delay or young children. MRI is preferred over CT for second-line imaging to avoid radiation and can be done with or without contrast. This may be particularly necessary for a patient whose ultrasound findings are indeterminate and may require anesthesia if unable to otherwise be immobile during MRI.

Planning the appropriate surgical approach is critical to success but may depend on the availability of the equipment, the experience of the surgeon, and the pathology itself. Additionally, in patients with complex gynecologic anomalies, the presence of concomitant anomalies (particularly associated renal and colorectal anomalies) must be considered due to the prevalence of additional comorbidities (3). Collaboration may be needed with pediatric subspecialists for preoperative medical optimization, intraoperative surgical collaboration (i.e., urology, pediatric surgery), and postoperative considerations such as pain control and need for inpatient admission.

34.2 Laparoscopic Considerations

Patients and parents with a planned laparoscopic procedure should be counseled on the usual surgical risks including bleeding, infection, injury to surrounding structures, need to convert to laparotomy, poor wound healing and cosmesis, and anesthesia. The postoperative course will be dependent on the surgical incisions and extent of surgery but can often be limited to a same-day discharge for many laparoscopic procedures. Contraindications for the minimally invasive approach are few; however, patients with a history of congenital cardiac defect may have adverse effects from increased systemic vascular resistance with pneumoperitoneum (4). Risks may be minimized by limiting insufflation pressures to 8 mmHg in a small and/or prepubertal patient; however, in older adolescents this can often be increased to 12–15 mmHg, similar to an adult patient, with clear and regular communication with the anesthesia team and taking into consideration any additional comorbidities or patient factors such as habitus, abdominal wall distensibility, and muscle relaxation (5). Antibiotics should be selected in accordance with standard recommendations based on the proposed surgery; weight-based dosing may be more appropriate in some pediatric patient scenarios (6).

Insertion of a urinary catheter may be recommended at the start of the procedure for decompression of the bladder and adequate visualization of pelvic structures. This can be done in a frog-legged position by staff prior to placing the patient in a supine position for the surgical case or can be done in a sterile fashion after prepping and draping the patient if the entire case will be done in lithotomy position. An appropriately sized urinary catheter can be determined when the caliber approximates the urethral meatus to minimize urine leaking around but does not traumatize the tissue without resistance with placement (Figure 34.1) (7). Surgery is typically done in the supine or lithotomy position, as in most gynecologic procedures. A uterine manipulator or narrow sponge stick may be placed in the postpubertal patient but is rarely indicated in the prepubertal patient given concern for trauma to hymenal,

DOI: 10.1201/9781003312109-34

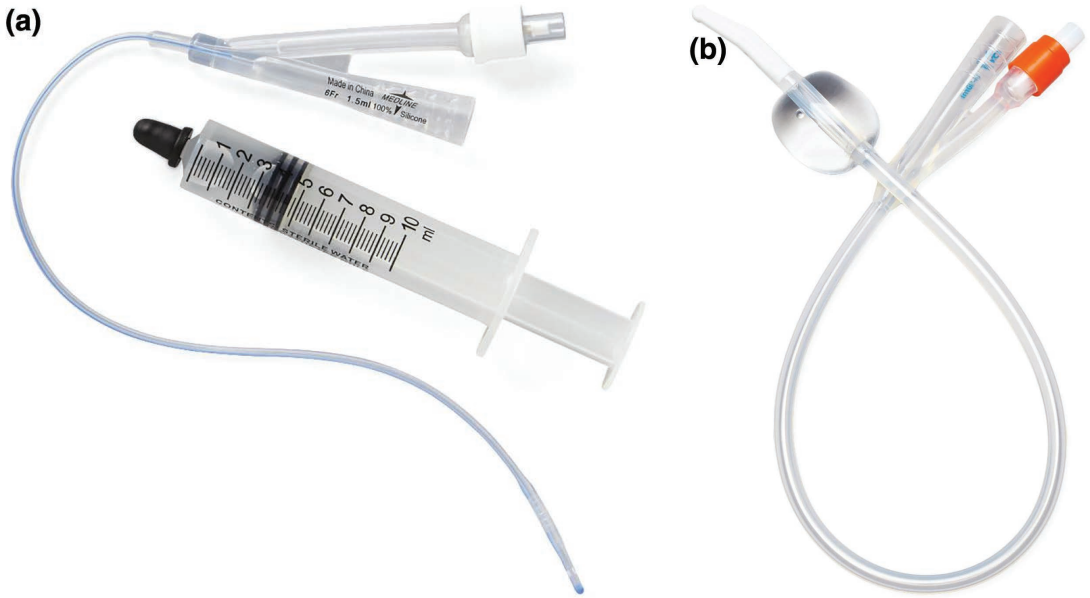


FIGURE 34.1 Appropriate catheter sizes for use in girls: (a) size 6 French Foley catheter with smaller 3 mL balloon; (b) size 16 French Foley catheter and 10 mL balloon. (From Medline.com, with permission.)

vaginal, cervical, or uterine tissue. Of note, if vaginal preparation is necessary for the case, for pediatric patients, iodine can be injected into the vagina using a syringe, rather than traditional preparation sponges (8).

The spacing of laparoscopic ports may be limited in a more petite patient and care should be taken to acknowledge surrounding anatomy such as an enlarged liver, position of the bladder, and location of inferior epigastric vessels to minimize injury, while optimizing appropriate space between ports to allow working space for the surgical procedure. Abdominal wall pliability is increased in young children as compared to the adult population, so it is important to ensure no injury to underlying structures with the introduction of cannulas. The short distance between the skin and the fascia in many young patients also highlights the importance of closely monitoring to avoid injury; the use of an 11 blade to make a laparoscopic port incision may reach the fascial or even peritoneal layer. Holcomb et al. highlight the movement of the Veress needle to direct transversely across the abdominal cavity rather than toward the underlying viscera to minimize injury; for gynecologic cases this can also be done towards the pelvis once initial entry through the peritoneum has been achieved (4). Gastric decompression with an orogastric tube is helpful particularly if upper abdominal ports will be placed, such as in the case of a Palmer's point entry.

While laparoscopy for gynecologic surgery often utilizes the umbilicus as an initial entrance, there are risks to this entry site in newborns due to theoretical risk of CO_2 insufflation into the umbilical vein, documented with both open Hasson approach and Veress needle technique and thus some propose use of a curvilinear approach at the inferior aspect of the umbilical ring in a newborn patient to avoid this risk (Holcomb). Regardless, a 5 mm incision is typically placed at the umbilicus in either a vertical or curvilinear fashion. A 2–3 mm pediatric laparoscopic camera may be used, but typically use is limited due to availability (8). Laparoscopic 3 mm ports may be used, though this is not normally used for the camera port due to inferior image quality and with minimal benefit to cosmesis for a 3 mm versus a 5 mm incision. There may be benefit for an angled 5 mm laparoscope (30°) as this allows for increased views over a 0° scope. Most vessel sealing devices come with a 5 mm option, and some additional sealer devices exist at a 3 mm size, which may be helpful in neonates and in times where the anticipated thermal spread of a 5 mm device is especially of concern. In particular, a 3 mm bipolar vessel sealer is available that may seal blood vessels up to 5 mm with minimal lateral thermal spread. To aid in removal of larger specimens, an incision may be extended to 10–12 mm without significant impairment of cosmesis, particularly if this remains hidden in the umbilical incision. There also exists a 5 mm endoscopic bag that can be used for removal of smaller specimens through the 5 mm ports. For some surgeons, a stab incision technique is used in place of side ports, under direct visualization. This utilizes a #11 blade (Bard-Parker) to incise the skin and directly through fascia and peritoneal layers, with passage of the instrument directly into this incision. This is ideal for instruments that do not need to be exteriorized and replaced and can be useful to minimize need for additional ports or larger incisions (5). An example of this technique in pediatric gynecologic surgery is in the case of oophorectomy for ovarian tissue cryopreservation in an infant, when one lateral port may be a stab incision used for placement of an instrument to elevate the adnexa, and then also to place the ovary into a bag that is placed through the contralateral 5 mm port (4). After completion of the case and removal of instruments and ports, closure of the fascia should be considered for a smaller incision than in an adult patient given the risk of herniation of a smaller lumen bowel (9–11); 10 mm fascial incisions should always be closed.

For surgeries that require laparotomy, consideration should be made of diagnostic laparoscopy initially to evaluate if the surgical plan is unclear. This may permit some laparoscopic dissection to minimize the need for a larger skin incision or vertical skin incision. With a thorough preoperative evaluation and assessment favoring a benign process, often large cystic

adnexal/pelvic masses can be safely dissected laparoscopically and then drained to reduce the size of the specimen and minimize the need for a larger skin incision. In some cases, the entire case can be performed laparoscopically with 5 mm ports (with the specimen excised through the port directly, using a 5 mm bag, or by enlarging one port to accommodate removal of the specimen). Alternatively, for masses that seem amenable to access from a low transverse skin incision 1–2 cm above the pubic symphysis, a minilaparotomy of 2–4 cm can often be used in conjunction with a retractor (such as a self-retaining Alexis retractor) to permit for drainage of large cystic structures. This may be particularly useful in patients for whom the mass extends significantly above the umbilicus of the patient, limiting the feasibility of laparoscopic approach. The skin incision itself may be made very small as it may stretch an addition 5–10 mm with use of the retractor, and for some patients the cosmetic outcome of this incision hidden under the pubic hair line may be preferred over smaller but more superiorly located laparoscopic incisions. Patients are typically able to be discharged home the same day with either a laparoscopic or minilaparotomy approach.

34.3 Obstructive Müllerian and Hymenal Anomalies

The differential diagnosis of pelvic pain with suspected adnexal mass should consider not only the ovarian and tubal pathology commonly seen in adult patients, but also obstructed Müllerian anomalies such as a rudimentary uterine horn, vaginal agenesis, or imperforate hymen. Preoperative MRI may be critical when the diagnosis is uncertain to facilitate appropriate surgical planning. In cases of an obstructed Müllerian or vaginal anomaly that may require a vaginal approach to repair, a vitamin E or fish oil capsule may be taped to the perineum, or lubricant gel placed in the vagina, to help measure the distance from an upper tract anomaly to the perineum and/or the thickness of the obstruction itself (12) (Figure 34.2). Based on this imaging, the surgical approach and plan can then be determined. Characterization of Müllerian anomalies can be found in the revised ASRM guidelines; we recommend using standardized terminology as able to minimize misunderstanding by patients or other medical providers (13). A thicker obstruction, such as a greater than 3 cm distal vaginal agenesis, may require an interposition graft (made from bowel, buccal tissue, or skin), while a thinner obstruction such as a 2 cm thick transverse vaginal septum may be repaired primarily using a flap technique to bridge a shorter distance.

Müllerian obstructions are very rarely a surgical emergency; these require detailed surgical planning and often may be temporized with pain control, menstrual suppression, or drainage of the hematometra or hematocolpos. It may be helpful to consult with interventional radiology to determine whether image-guided drainage may afford a temporizing measure with minimal risk or intraoperative imaging may assist with surgical repair itself (14). It is important to consider the age and maturity of the patient if dilation postoperatively will be required, as in the case of a thicker obstruction, particularly with a buccal graft vaginoplasty. If patients do not seem ready for this postoperative management, as typically true around the time of menarche when these anomalies are usually diagnosed, we recommend menstrual suppression with hormonal management including progesterone-only or combined hormonal contraceptives, or GnRH agonists, until they are older and more ready for dilation. Thin hymenal anomalies are typically repaired at the time of diagnosis, as these are unlikely to stenose. These rarely require additional management beyond incision, drainage of hematometrocolpos, and excision of excess hymenal tissue. Therefore, it is important to ensure that the appropriate diagnosis is made using physical exam and imaging to determine not only the surgical techniques used but also the timing of surgical intervention itself.

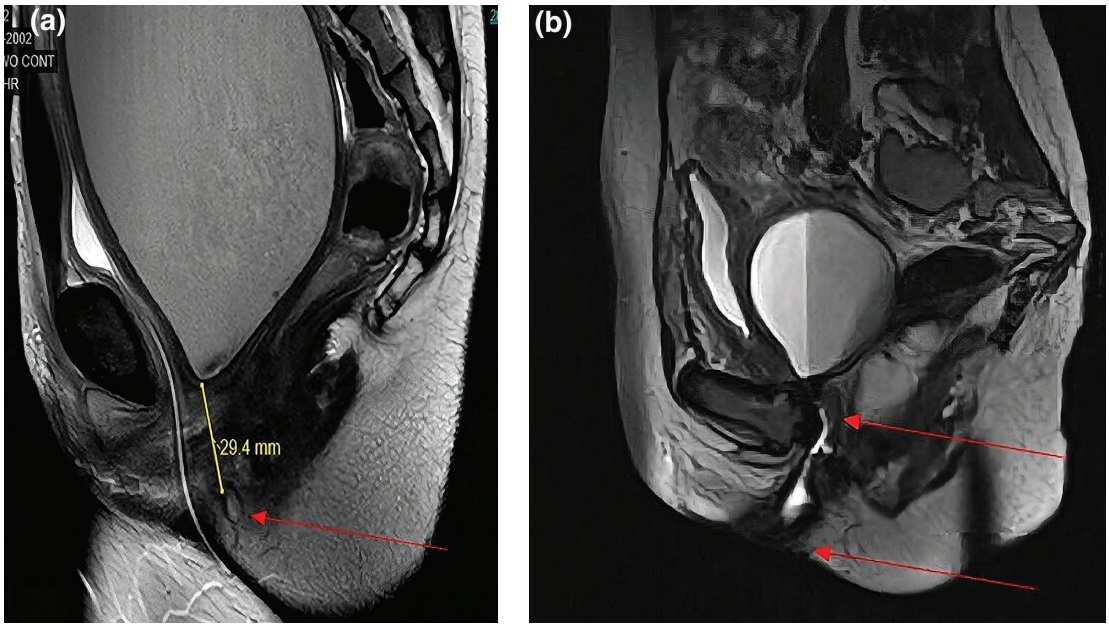


FIGURE 34.2 Use of preoperative MRI imaging to determine length and location of obstruction: (a) perineal vitamin E capsule (red arrow); (b) intravaginal lubricant gel placed by radiologist demonstrates distance of obstruction (red arrow).

34.4 Management of Nonobstructive Müllerian and Hymenal Anomalies

Nonobstructive anomalies may be diagnosed at birth, in early childhood, or later in adolescence and adulthood. The first presentation of nonobstructive hymenal anomalies may be when a menarchal patient desires to use tampons but experiences pain with attempted insertion. These do not require urgent management; timing may be delayed until the patient desires surgical treatment. Hymenal variants may include a septate, microperforate, or cribiform hymen or hymenal remnants that present as small tags that protrude beyond the remaining hymenal tissue.

Examination is valuable to ensure the suspected hymenal anomaly is isolated to the hymen, as opposed to a vaginal anomaly such as a longitudinal vaginal septum. A small cotton swab may be used to elevate the septal tissue and ensure no proximal anomaly is connected to this septum. If the anomaly is isolated to the septum, this may be removed using a small hemostat to crush the tissue at both ends of the septum, then cutting out the intervening tissue. Septate hymenal excision may be performed in the office with topical or local injected analgesia, as tolerated by the patient. If more significant hymenal tissue is to be excised or anatomy is unclear, sedation and electrocautery are helpful to ensure no significant bleeding and optimize patient tolerance of the procedure. When a vaginal anomaly is suspected, preoperative imaging is generally recommended to assess for additional Müllerian anomalies. If a longitudinal vaginal septum is suspected from preoperative imaging or identified on examination, this is commonly excised using electrocautery and the vaginal epithelium oversewn using interrupted or running delayed absorbable suture to minimize bleeding.

34.5 Müllerian Agenesis

Patients with Müllerian and vaginal agenesis may present with primary amenorrhea or be diagnosed incidentally during evaluation for other medical conditions. The most common cause of Müllerian and vaginal agenesis is Mayer–Rokitansky–Küster–Hauser (MRKH) syndrome due to failure of organogenesis. There is no standardized treatment, but it is widely accepted that vaginal dilation with increasing in size dilators should be recommended as first-line treatment. Vaginal lengthening may also be performed coitally or with sexual devices if patients prefer, and patients may benefit from teaching from clinicians including OB/GYNs and pelvic floor physical therapists to ensure the appropriate pressure and angle of

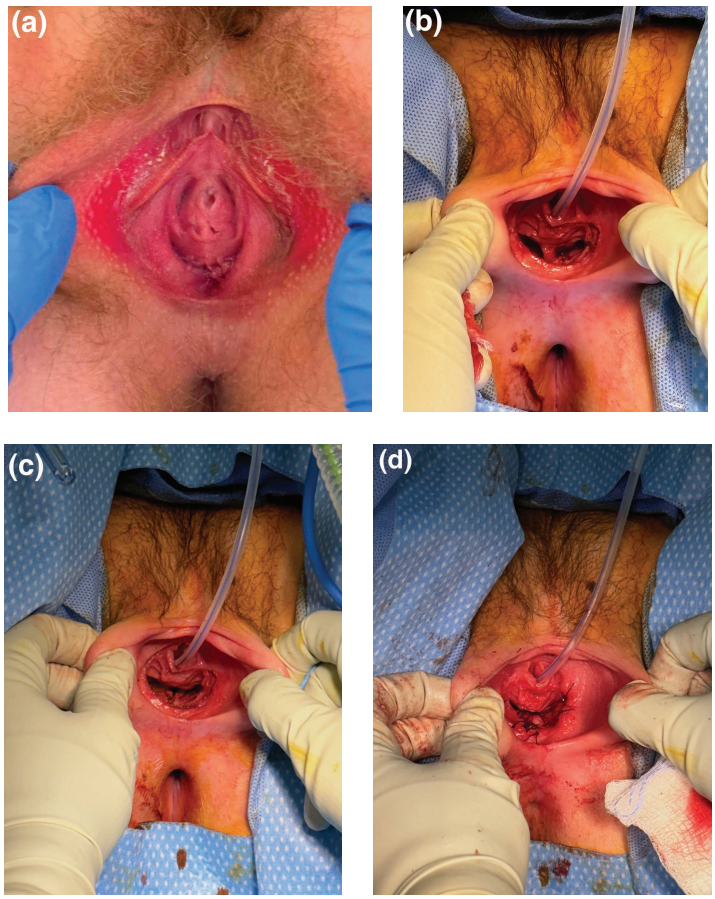


FIGURE 34.3 Patient with microperforate hymen and longitudinal vaginal septum who presented due to concerns with tampon use. Preoperatively suspected based on ultrasound imaging with didelphys uterus and vaginal septum. (a) Microperforate hymen, resected with electrocautery. (b) Visualization of longitudinal septum. Speculum examination confirmed two cervices. (c) After excision of septum. (d) Interrupted sutures to oversew vaginal epithelium.

application. While vaginal length may be longer after surgical treatment, studies assessing sexual function and quality of life have shown similar outcomes with vaginal dilation as compared to surgical treatment. Nonsurgical treatment with dilators should therefore remain the first-line treatment for patients with MRKH/Müllerian agenesis (15, 16).

In the event that dilation is inadequate, several surgical approaches have been well studied for neovaginal creation. Common surgical interventions may include use of bowel, buccal, or skin grafts, the Davydov method (peritoneal), and the Vecchietti method. While historically abdominal procedures were performed via laparotomy, current methods typically utilize laparoscopy as standard. The Davydov method requires a dissection of the rectovesical space and attachment of mobilized peritoneum to the introitus which has been dissected from the perineum. The Vecchietti method utilizes a small "olive"-shaped mold placed at the vaginal dimple that is connected to a device on the patient's abdomen via subperitoneal sutures and gradually tightened over the course of a week. A meta-analysis summarizing outcomes between Davydov and Vecchietti methods suggest similar outcomes in sexual function and vaginal length (17). Most surgeries for vaginal lengthening typically require patients to continue to dilate postoperatively to maintain vaginal length and patency; thus, preoperative dilation may be helpful to ensure patients are able to comply with postoperative care.

34.6 Adolescent Endometriosis

While endometriosis has historically been attributed to women 20–40 years of age, many report symptoms beginning in adolescence (18, 19). In adult patients, a pathologic diagnosis is the gold standard (20), and the classical pathologic diagnosis of endometriosis requires two of the three following criteria: presence of stroma, presence of glands, and evidence of prior bleeding and inflammation. Laparoscopic findings of lesions (clear, red, brown) and associated adhesive disease may also suggest a diagnosis of endometriosis in the adult patient (21–26). On the other hand, there is little agreement in the necessary criteria for a diagnosis of adolescent endometriosis, as surgical appearance may be atypical, including vesicular lesions, neovascularity, and adhesions, and the variable appearance may lead to an increased risk of false negative biopsy (27). The optimal management of adolescent endometriosis is also not yet understood. It is important to use the opportunities for surgical evaluation for endometriosis as a time to also discuss need for ongoing contraception in the adolescent and ensure an opportunity for confidential conversation with the patient without presence of parents or other caregivers. Hormonal suppression remains a mainstay of endometriosis treatment in this patient population. Additional study of adolescent endometriosis is ongoing to better clarify the optimal means for diagnosis and treatment in the adolescent with endometriosis.

34.7 Postoperative Care

For pediatric patients as with adult patients, it is important to be mindful of narcotic use. Use of adjunctive nerve blocks performed by anesthesiology pain teams can be deployed at the beginning of the surgery to minimize narcotic use. While laparoscopic procedures in adult patients often require a narcotic prescription, a pediatric patient may have minimal narcotic need after surgery, particularly if adjunctive pain management is used (28). The use of ERAS pathways has been shown to be helpful in recovery in adult gynecologic patients and pediatric surgery population; multiple studies evaluating utility in the pediatric gynecologic procedures are underway (29). The patient should be counseled on return to appropriate activities such as an adult patient would, with avoidance of heavy lifting as indicated and appropriate notes written to permit excuses from school or extracurricular activities. It is important to counsel both the patient and the parent on the reasons for these limitations to encourage compliance during the postoperative period.

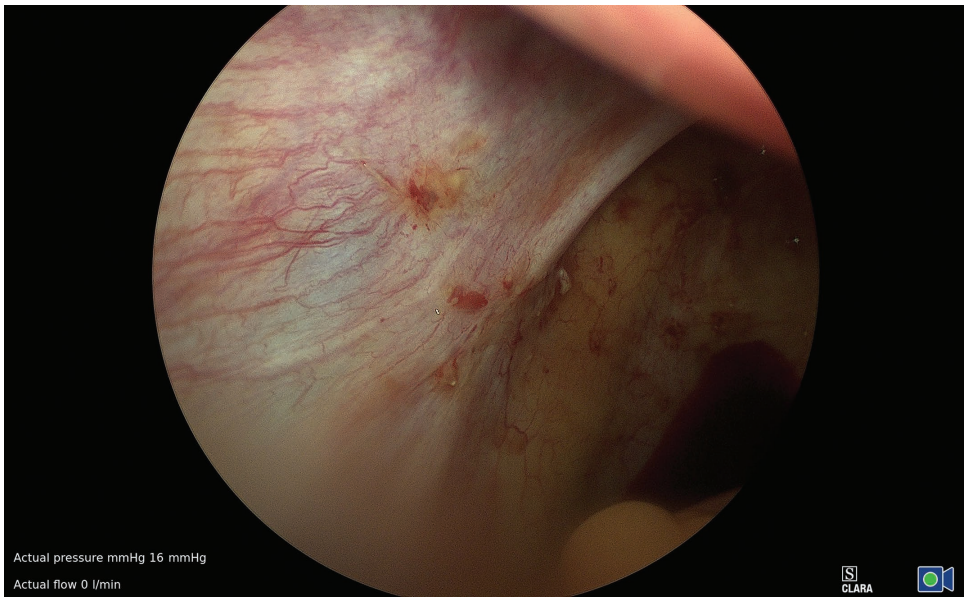


FIGURE 34.4 Adolescent endometriosis (clear and red vesicular lesions) in a 17-year-old patient, prior to excision and pathology confirmation.

Employing minimally invasive surgical techniques for pediatric and adolescent gynecologic patients is safe and effective when care is taken to follow surgical principles and necessary modifications for this unique population. In some cases, referral to gynecologic surgeons with expertise in our youngest patients may be appropriate and is crucial for patient safety and maximizing gynecologic and reproductive health outcomes.

References

1. Emans SJ et al., eds. *Pediatric and Adolescent Gynecology*, 4th edn. Philadelphia: Raven-Lippincott; 1998.
2. Adnexal torsion in adolescents: ACOG Committee opinion 783. *Obstet Gynecol*. 2019;134(2):e56–e63.
3. Kapczuk K et al. Obstructive Müllerian anomalies in menstruating adolescent girls: a report of 22 cases. *J Pediatr Adolesc Gynecol*. 2018;31(3):252–257.
4. Holcomb et al. Taskforce for abdominal entry: principles of safe laparoscopic entry. *Eur J Obstet Gynecol Reprod Biol*. 2016;201:179–188.
5. Broach AN et al. Pediatric and adolescent gynecologic laparoscopy. *Clin Obstet Gynecol*. 2009;52:380.
6. Prevention of infection after gynecologic procedures. ACOG practice bulletin number 195. *Obstet Gynecol*. 2018.
7. Manzano et al. Catheterization of the urethra in girls. *N Engl J Med*. 2014;371:e2.
8. Mansuria SM et al. Laparoscopy in the pediatric and adolescent population. *Obstet Gynecol Clin North Am*. 2004;31:469.
9. Peters CA. Complications in pediatric urological laparoscopy: results of a survey. *J Urol*. 1996;155:1070.
10. Cost NG et al. Hernia after pediatric urological laparoscopy. *J Urol*. 2010;183:1163.
11. Paya K et al. Trocar-site hernia as a typical postoperative complication of minimally invasive surgery among preschool children. *Surg Endosc*. 2008;22:2724.
12. Brown MA et al. MRI of the female pelvis using vaginal gel. *Am J Roentgenol*. 2005;185(5).
13. Pfeifer SM et al. ASRM Mullerian anomalies classification 2021. *Fertil Steril*. 2021;116(5).
14. Ahluwalia S et al. Use of interventional radiology and wire localization for septum resection in a 13-year-old patient with a high OHVIRA. *AAGL Newsscope*, 38(2). Available at: https://newsscope.aagl.org/volume-38-issue-2/spotlight-on-endometriosis-3/ (Accessed Sept 2024).
15. Kang J et al. Sexual function and quality of life after the creation of a neovagina in women with Mayer-Rokitansky-Küster-Hauser syndrome: comparison of vaginal dilation and surgical procedures. *Fertil Steril*. 2020;113(5):1024–1031.
16. Dabaghi S et al. Sexual satisfaction in patients with Mayer-Rokitansky-Küster-Hauser syndrome after surgical and non-surgical techniques: a systematic review. *Int Urogynecol J*. 2019;30(3):353–362.
17. Martens L et al. Laparoscopic Davydov vs. laparoscopic Vecchietti neovaginoplasty in women with Mayer-Rokitansky-Küster-Hauser syndrome; a systematic review and meta-analysis. *Fertil Steril*. 2024;121(4):679–692.
18. Tyson N et al. Surgical considerations in the management of adolescent endometriosis – an expert commentary. *J Minim Invasive Gynecol*. 2024;31(5):378–386.
19. Shim JY et al. Evaluation and management of endometriosis in the adolescent. *Obstet Gynecol*. 2024;143(1):44–51.
20. Clement PB. The pathology of endometriosis: a survey of the many faces of a common disease emphasizing diagnostic pitfalls and unusual and newly appreciated aspects. *Adv Anat Pathol*. 2007;14(4):241–260.
21. Ueki M et al. Visual findings and histologic diagnosis of pelvic endometriosis under laparoscopy and laparotomy. *Int J Fertil Menopausal Stud*. 1995;40:248–253.
22. Jansen RP et al. Nonpigmented endometriosis: clinical, laparoscopic, and pathologic definition. *Am J Obstet Gynecol*. 1986;155:1154–1159.
23. Martin DC et al. Laparoscopic appearances of peritoneal endometriosis. *Fertil Steril*. 1989;51:63–67.
24. Redwine DB et al. A serial section study of visually normal pelvic peritoneum in patients with endometriosis. *Fertil Steril*. 1990;54:648–651.
25. Martin DC. *Laparoscopic Appearance of Endometriosis: A Color Atlas*. Philadelphia: Resurge Press; 1991.
26. Walter AJ et al. Endometriosis: correlation between histologic and visual findings at laparoscopy. *Am J Obstet Gynecol*. 2001;184(7):1407–1411; discussion 1411–1413.
27. Dun EC et al. Endometriosis in adolescents. *JSLS*. 2015;19(2):e2015.00019.
28. Hafeman M et al. Caudal block vs transverse abdominis plane block for pediatric surgery: a systematic review and meta-analysis. *Front Pediatr*. 2023;11:1173700.
29. Smith AE et al. Enhanced recovery after surgery in pediatric and adolescent gynecology: a pilot study. *J Pediatr Adolesc Gynecol*. 2020;33(4):403–409.

35 SURGICAL MANAGEMENT OF FEMALE REPRODUCTIVE ANOMALIES

Leila V. Adamyan and Assia A. Stepanian

35.1 Introduction

Congenital malformations of the female genitalia comprise approximately 4% of all congenital anomalies and are seen in 5.5% of the population and 24.5% of women who experience miscarriage and infertility (1). These malformations are associated with extragenital anomalies in about 74% of cases, such as skin marks, skeletal defects, and breast, heart, renal, and gastrointestinal anomalies (2) (Figure 35.1). Diagnosis of these malformations requires awareness to prevent an incorrect or unwarranted aggressive radical surgery. Using noninvasive tools (ultrasonography, hysterosalpingography, magnetic resonance imaging and spiral computer tomography), a detailed study of each patient's anatomical defects and relationships, careful evaluation and management of associated pathology, and discussion of treatment goals and expectations are essential for optimal surgical strategy.

35.2 Classification Systems of Female Genital Tract Anomalies

Various classification systems have been proposed to characterize and guide care to women with reproductive anomalies. In 1988, the American Fertility Society (AFS) classification focused primarily on uterine anomalies and has been the most accepted classification system in the United States (3). Subsequent systems included the Acien classification (2011), which detailed the embryologic aspects of these malformations (4), and the ESHRE/ESGE classification of genital tract congenital anomalies (2016), which individually described uterine, cervical, and uterine anomalies to allow surgeons to communicate on specific individual defects (5). The AFS/ASRM Task Force updated the AFS system in 2021 to encompass all categories and broaden its application (6).

L.V. Adamyan introduced a clinic-morphological system in 1993, which provided guidelines for examination, surgical treatment, and reproductive and functional rehabilitation of patients for each class of anomalies (2, 7). Updated in 2014 and 2016, this taxonomy aligns closely with the AFS/ASRM classification system (8). This chapter will explore each class of anomalies in Adamyan's classification system and associated surgical techniques.

35.2.1 Class I: Complete Uterovaginal Aplasia

Mayer–Rokitansky–Küster–Hauser syndrome (MRKH) or Müllerian agenesis is a congenital malformation characterized by the absence of the uterus and vagina with normal ovarian function. Patients present with a female phenotype and 46, XX karyotype (Figure 35.2). This syndrome is often accompanied by other congenital anomalies (skeletal, urinary, digestive) (9–11). Variants include rudimentary uterine tissue, symmetric

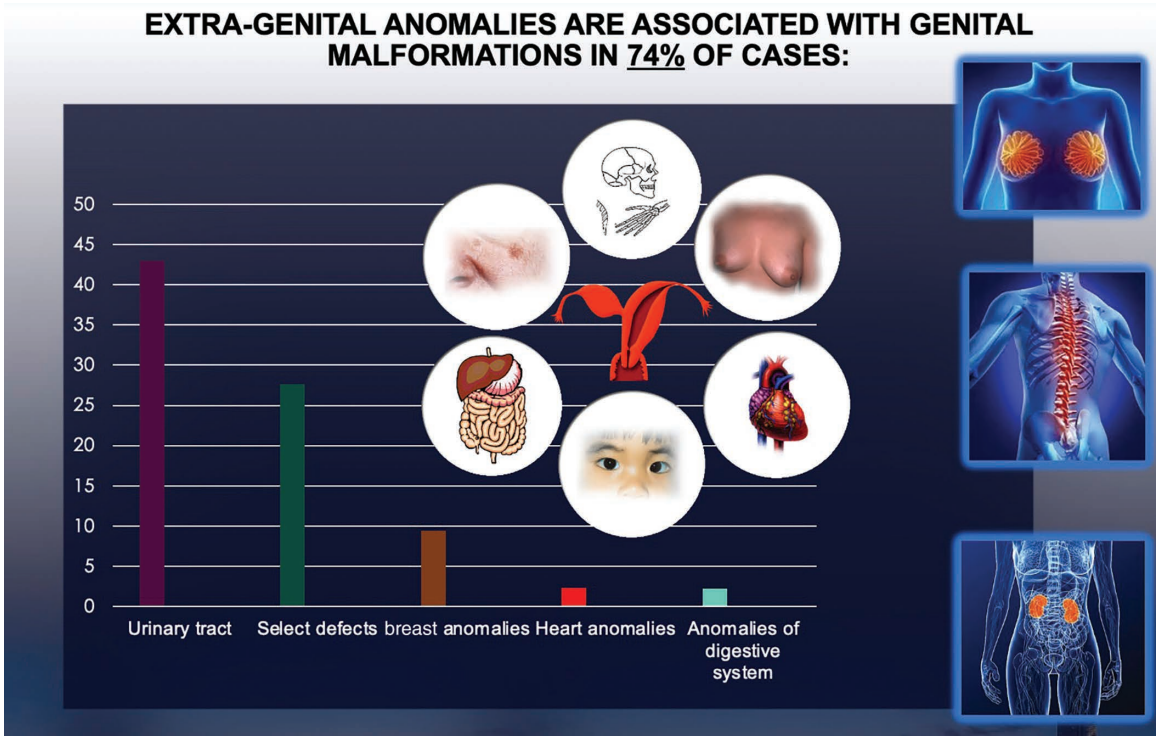


FIGURE 35.1 Anomalies associated with genital malformations (in 74% of cases).

DOI: 10.1201/9781003312109-35

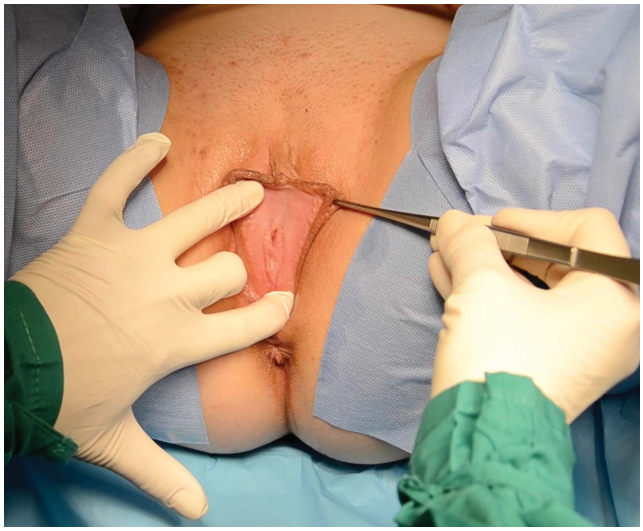


FIGURE 35.2 Normal external genitalia in a patient with MRKH syndrome.

or asymmetric muscular mounds, absent rudiments, and others. Key clinical features include primary amenorrhea, pelvic pain, and the inability to have vaginal intercourse as patients typically present with normal external genitalia and a vaginal dimple (Figure 35.2). The rudimentary uterine horns may be affected by adenomyosis or other gynecologic pathologies even without a functional endometrium (12, 13).

Treatment options for MRKH patients include nonsurgical and surgical approaches for a neovagina. Nonsurgical vaginal elongation can be relatively effective but requires time and commitment with inconsistent results and pelvic floor defects (14). Among surgical methods, surgical techniques to create a neovagina include the laparoscopic Vecchietti procedure, surgical formation of the vaginal canal using skin or bowel grafting, and peritoneal colpopoiesis.

L.V. Adamyan's laparoscopic peritoneal colpopoesis was introduced in 1992 (2, 7). Using the laparoscopic approach, this technique uses a highly positioned purse-string and peritoneal stitch to engage the fibromuscular tissue of the sidewall and provide long-lasting apical support, forming a well-supported neovagina of 11–12.5 cm in length. A 15-year follow-up study assessing the sexual experience of women after Adamyan's laparoscopic peritoneal colpoiesis compares well to that of women born with a normal vagina (Figure 35.3) (15). This approach is reproducible with sustainable results, has minimal blood loss and complication rates, and is applicable to various surgical scenarios such as a failed neovagina, iatrogenic shortened vagina, or complex genitourinary anomaly cases (12, 15–18).

35.2.1.1 Surgical Technique

Adamyan's laparoscopic peritoneal colpopoiesis technique is performed by a combination of a laparoscopic and vaginal approach. The method begins with a diagnostic laparoscopy to evaluate the Müllerian anomaly, mobility of peritoneum, and location of the ureters due to the association with genitourinary abnormalities. Next, the colpopoesis is performed by introducing a blunt laparoscopic instrument, such as a grasper or pusher, to identify the most mobile aspect of the pelvic peritoneum in the pouch of Douglas. Once identified, the grasper can then be manipulated through a transvestibular digital palpation. The distance between the peritoneum and vaginal dimple should be minimal and no more than 5 cm. A 3.0–3.5 cm transverse incision is made on the vaginal dimple, and the underlying tissue is then dissected to reach the pelvic peritoneum, creating the neovagina (Figure 35.4A). Using vaginal retractor, the pelvic peritoneum is then grasped through this neovagina and transected to enter the peritoneal cavity (Figure 35.4B and C). The peritoneal incision edges and vaginal dimple are approximated with interrupted 1–0 and 2–0 Vicryl stitches in a circumferential fashion, forming the vaginal walls.

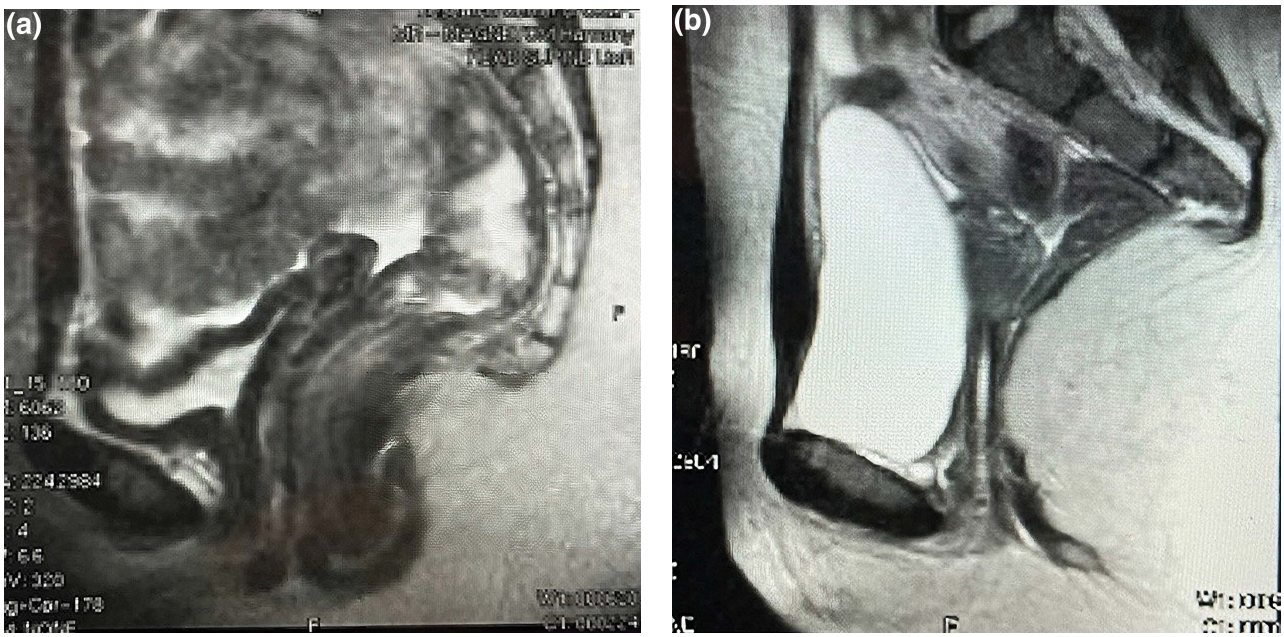


FIGURE 35.3 MRI images of the pelvis in a patient with MRKH syndrome before (a) and after (b) Adamyan's colpopoesis.

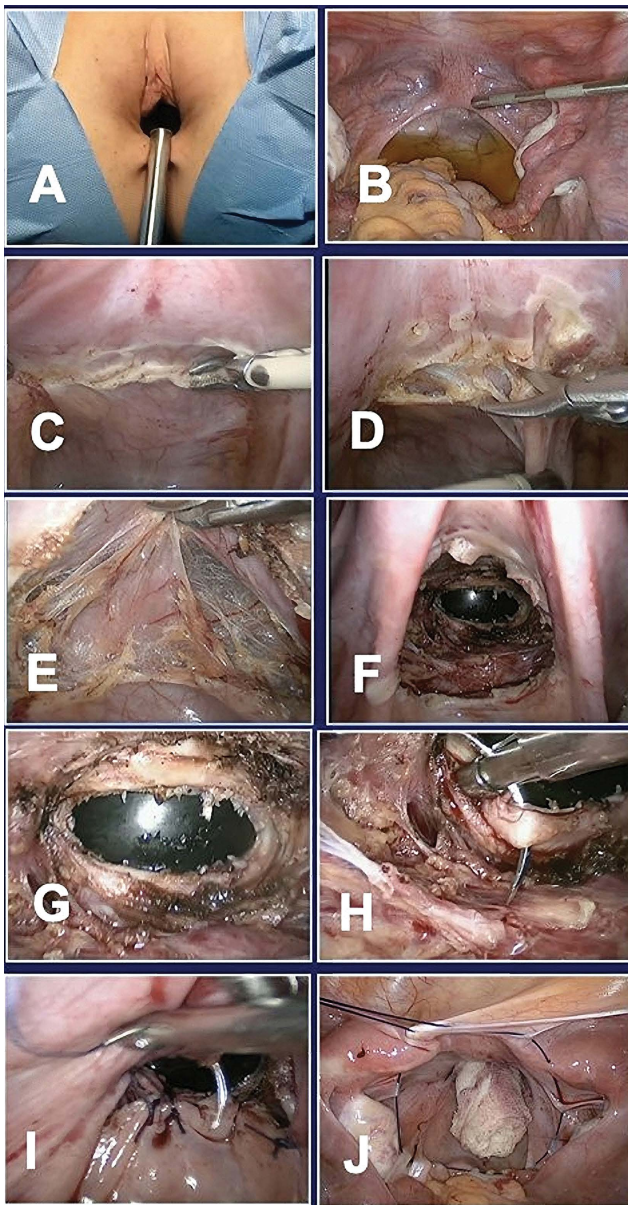


FIGURE 35.4 The steps of Adamyan's laparovaginal peritoneal colpopoesis: (A) Transverse perineal incision; (B) introduction of the most mobile aspect of the peritoneum of the pouch of Douglas into the perineal incision; (C) peritoneal incision; (D) the approximation of the peritoneum and the mucosa of the vaginal dimple; (E) two surgeon's fingers are placed to confirm patency; (F) placement of the 4-inch Cling over the retractor placed to protect the rectum, urethra, and the bladder; (G) laparoscopic purse-string peritoneal stitch placement; (H) laparoscopic view of the completed peritoneal colpopoesis.

The vaginal canal should be at least two finger breadths to confirm adequate width (Figure 35.4B–E).

Next, a 4-inch vaginal Cling or tampon moistened with Vaseline or vaginal estrogen cream is gently placed in the neovagina. The apex of the neovagina is created by laparoscopically placing an extracorporeal purse-string stitch with 0-PDS to incorporate the bladder and pelvic sidewall peritoneum, fibromuscular streaks of the rudimentary horn, and superficial aspect of the bowel serosa (Figure 35.4F–I).

Perioperative considerations for this procedure include preoperative broad-spectrum antibiotics, a Foley catheter for the bladder intra- and postoperatively, encouraging postoperative ambulation, and pelvic self-examinations. Resumption of sexual activity is allowed 4 weeks postoperatively. The neovaginal is assessed again 3–4 months after the operation to evaluate the suture line and vaginal length. The vaginal walls should be well lubricated as morphologic and electron-microscopic examination of the neovaginal walls at 3 months reveal completely formed stratified squamous epithelium. Other Adamyan colopoiesis techniques include using a vaginal probe to help create a neovagina and a peritoneal pull-down technique (Figure 35.5) for patients with a fragile peritoneum (17, 18).

35.2.2 Class II: Vaginal Aplasia with the Presence of Functioning Uterus

Partial or complete vaginal aplasia is often associated with a normal functional or rudimentary uterus (Figure 35.6a). The main clinical feature of this malformation is absence of menstruation, cyclic or chronic pelvic pain, and inability to have sexual intercourse (19). In these patients, it not uncommon for hematocolpos, hematometra, pyometra, pyosalpinx, chronic endometritis, adenomyosis, or endometriosis to develop (Figure 35.6b and c) (20). Uterine-preserving or definitive surgery (hysterectomy) while establishing effective uterovaginal outflow is essential in the management of these patients (21).

35.2.2.1 Surgical Technique

Patients with partial vaginal aplasia and a functional uterus require vaginoplasty only. However, patients with complete vaginal aplasia and a functional uterus will need colpopoeisis to establish an outflow tract. Anatomical knowledge and orientation of the endocervical canal is critical for successful reconstructive surgery. Adamyan introduced retrograde hysteroscopy through an abdominal approach in which hysteroscopy is performed from the uterine fundus to identify the endocervical canal and tract. The following describes the surgical technique to establish a neovagina and outflow tract:

- Diagnostic laparoscopy to assess and restore anatomy and treat presenting pathology.
- Create a transverse perineal incision between urethra and posterior aspect of labia minora. Dissect the space between urinary bladder and rectum to create vaginal canal.

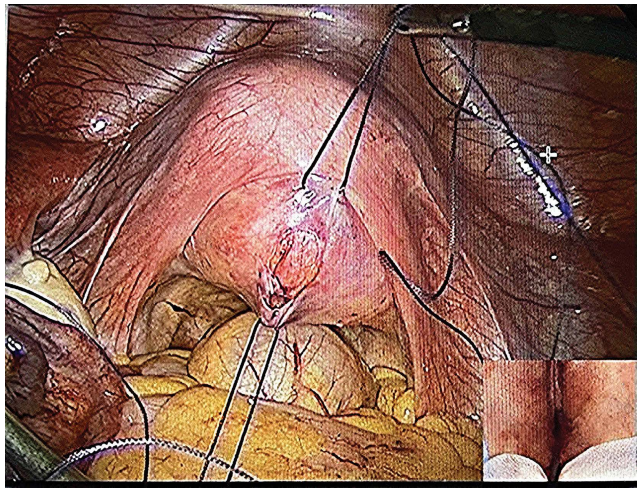


FIGURE 35.5 Laparoscopic pull-down technique.

- Perform a laparoscopic hysterotomy at the fundus and retrograde hysteroscopy to confirm presence of internal cervical os. Introduce a grasper/probe from endometrial cavity into neovagina.
- Perform Adamyan's modified colpopoeisis (as detailed in previous section).
- Place a 10F 5 cc balloon intrauterine catheter into the endometrial cavity through the neovagina and then place estrogen enriched vaginal tampon in the neovagina.
- Repair hysterotomy laparoscopically.

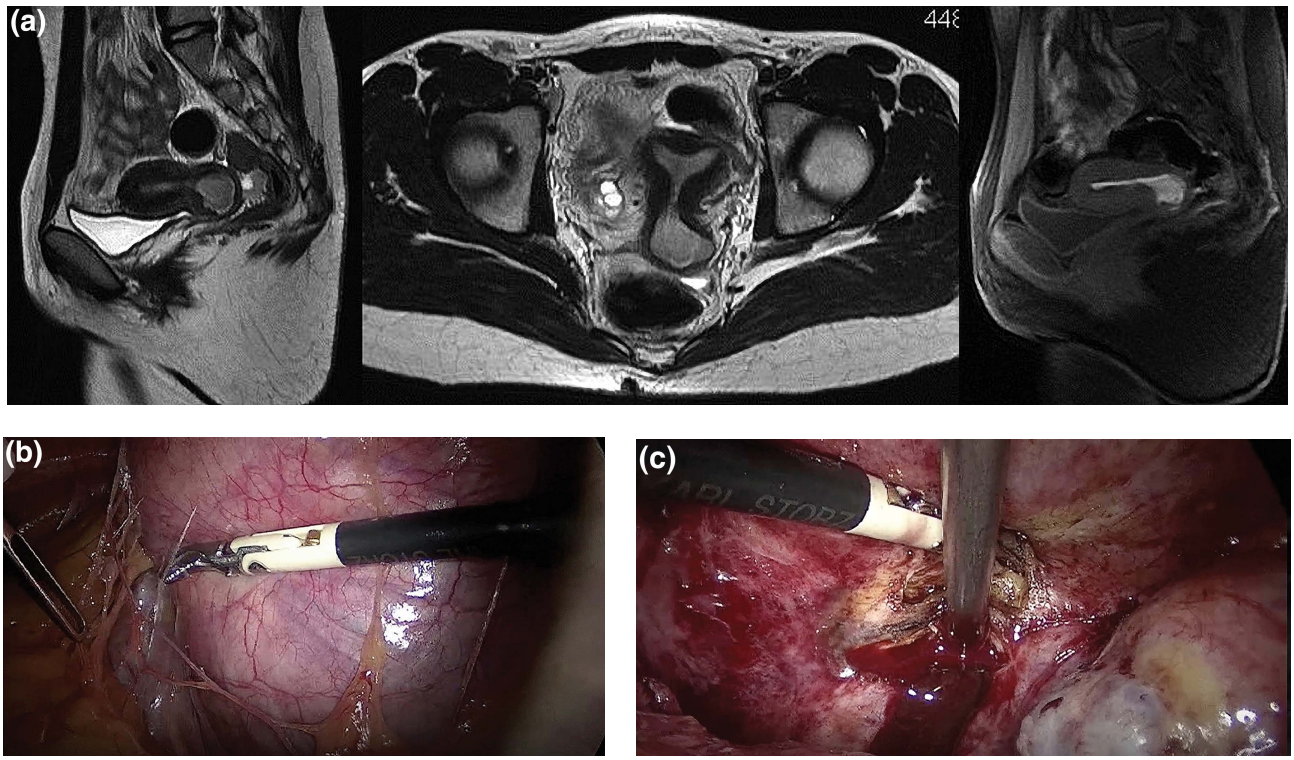


FIGURE 35.6 (a) MRI image of the patient with a functional uterus with the presence of vaginal aplasia. (b) Endometrioma in a patient with vaginal agenesis and functioning uterus. (c) Hematocolpos in a patient with vaginal agenesis and functioning uterus.

Postoperatively, the vaginal tampon can be removed 48–72 hours after surgery. The intrauterine catheter can be removed 5–7 days after surgery. The patient should be counseled on the need of cesarean section in subsequent pregnancy.

If a hysterectomy is desired due to extensive uterine pathology, recurrent closure of endocervix, or general clinical state, a total laparoscopic hysterectomy with Adamyan's laparoscopic peritoneal colpopoeisis is recommended (22, 23). Hysterectomy in patients with complete vaginal aplasia should be performed with maximal preservation of pelvic peritoneum to perform colpopoeisis. Considerable fibrosis can be encountered in patients with prior colpopoeisis attempts. Therefore, knowledge and attention to involved anatomy is imperative to successfully perform this procedure.

35.2.3 Class III: Vaginal and/or Cervical Aplasia with the Presence of a Single Functioning Uterus

Patient with this class of malformations may present with a multitude of gynecologic pathology including hematometra, pyometra, hematoperitoneum, hemato- or pyosalpinx, adenomyosis, endometriosis, and adhesive disease (24). The specifics of surgery are dependent on the formation of a uterine outflow tract in the absence of an endocervical canal (25) (Figure 35.7).

35.2.3.1 Surgical Technique

Surgical treatments of these malformations include laparoscopic evaluation and treatment of associated gynecologic pathology, creation of neovagina as specified previously, and retrograde hysteroscopy to form an outflow tract. The following outlines surgical technique:

- After laparoscopic evaluation and treatment of hematometra, a neovaginal canal is formed. Fundal laparoscopic hysterotomy and retrograde hysteroscopy confirm cervical aplasia and identify the uterine outflow site.
- Using retrograde-hysteroscopic guidance, the uterine outflow is created neovaginally, and a laparoscopic probe is introduced.
- Two 0-Vicryl sutures are placed circumferentially ~1.5 cm above the uterine incision to simulate a short cervix.
- A 14 Fr Foley catheter is inserted via the neovagina into the uterine cavity, inflated, and secured to the cervix.
- The most mobile aspect of the peritoneum of the Douglas pouch is brought down following Adamyan's colpopoesis technique; a peritoneal incision is made and the posterior-lateral aspect of the peritoneal incision is attached to the epithelial incision of the posterior-lateral aspect of the vaginal dimple.
- A tampon is placed in the neovagina, and the uterine hysterotomy is closed.
- The neovaginal apex is formed using bilateral 0-PDF purse-string sutures, incorporating peritoneum and pelvic tissue. Separation of peritoneum from adjacent structures is permitted if tension is excessive. A serosal sigmoid stitch is not required.

Patients should be counseled on the need for preconceptual cervical cerclage which can be performed at the time of surgery. However, we recommend a later placement due to risk of spontaneous closure of neo-endocervical canal. Patients should be advised to undergo cesarean section for future pregnancies (12, 26).

35.2.4 Class IV: Unicornuate Uterus

A unicornuate uterus is a Müllerian anomaly caused by formation of only one paramesonephric duct while the other remains underdeveloped (Figure 35.8) (27). A unicornuate horn without a supplementary horn usually does not cause any gynecologic problems. However, patients with a noncommunicating or obstructed rudimentary horn may experience painful menses or chronic pelvic pain due to hematometra or adenomyosis (28, 29). Patients may be at risk for ectopic pregnancy, endometrial pathology, or endometriosis (30). Thus, treatment of this noncommunicating rudimentary horn is essential. Surgical technique is dependent on location of rudimentary

FIGURE 35.7 Pelvic MRI image of a patient with a functional uterus and vaginal and cervical canal aplasia, incomplete uterine septum, and adenomyosis.

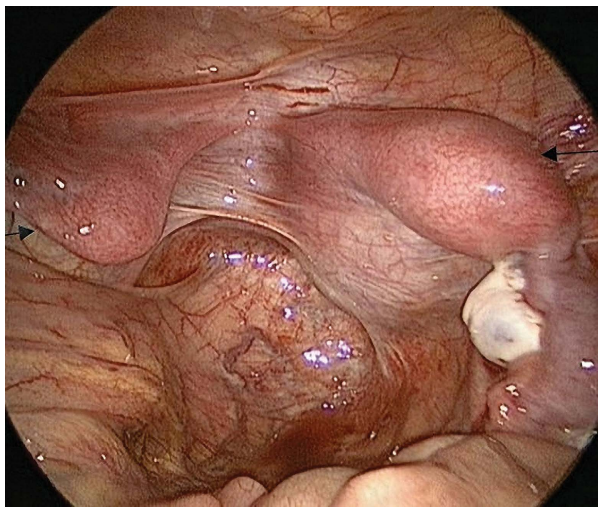


FIGURE 35.8 Laparoscopic view of the unicornuate uterus (right black arrow) and the rudimentary horn (left arrow).

horn. The following describes a brief overview of laparoscopic removal of a rudimentary horn (Figure 35.9):

- The uterine horn is grasped, and the ipsilateral round ligament, fallopian tube, and utero-ovarian ligament are coagulated and transected.
- The broad ligament and uterovesical fold are dissected to the junction uterus and rudimentary horn to expose its vasculature.
- These vessels are desiccated and rudimentary horn is then excised from the uterus.
- The myometrium is then reapproximated with 1–0 or 0-Vicryl suture.

For intramural or embedded rudimentary horns (Figure 35.10), an incision can be made in the uterine myometrium over the endometrial cavity of the rudimentary horn (2, 22). The nonfunctional lining can be ablated with energy and the uterine incision can then be reapproximated using Vicryl suture.

Postoperatively, patients can be discharged on the same day as these techniques are typically free of complications. Patients may attempt pregnancy 2–3 months following surgery and have a vaginal delivery.

35.2.5 Class V: Uterus Duplex/Didelphys

Uterine didelphys is characterized by the presence of two uteri and one or two vaginas. The clinical manifestation can vary. Uterine didelphys without an obstruction to menstrual outflow does not typically cause any issues; yet patients that present vagina aplasia or septum can have pelvic pain or dyspareunia (Figures 35.11 and 35.12) (31, 32). TVS, laparoscopy, and hysteroscopy provide a definitive diagnosis and differentiation between uterine didelphys, bicornuate uterus, and septate uterus (Figure 35.13) (33). Dynamic contrast-enhanced MRI can compare myometrial perfusion between the hemicavities to assist in identifying the cavity with higher reproductive potential (34).

35.2.5.1 Surgical Considerations

Uterine didelphys without outflow obstruction does not necessitate surgical correction. In patients that present with a vaginal septum, excision is often performed in those who desire pregnancy and vaginal delivery. In symptomatic patients, laparoscopy is performed to establish diagnosis and to guide the resection of hemivaginal septum or aplasia if necessary. Surgeons should be aware of the anatomic anomalies with this Müllerian malformation, especially the location of the ureters, endometrial and endocervical canals, and cervices. Hysteroscopy can aid in identifying and treating any

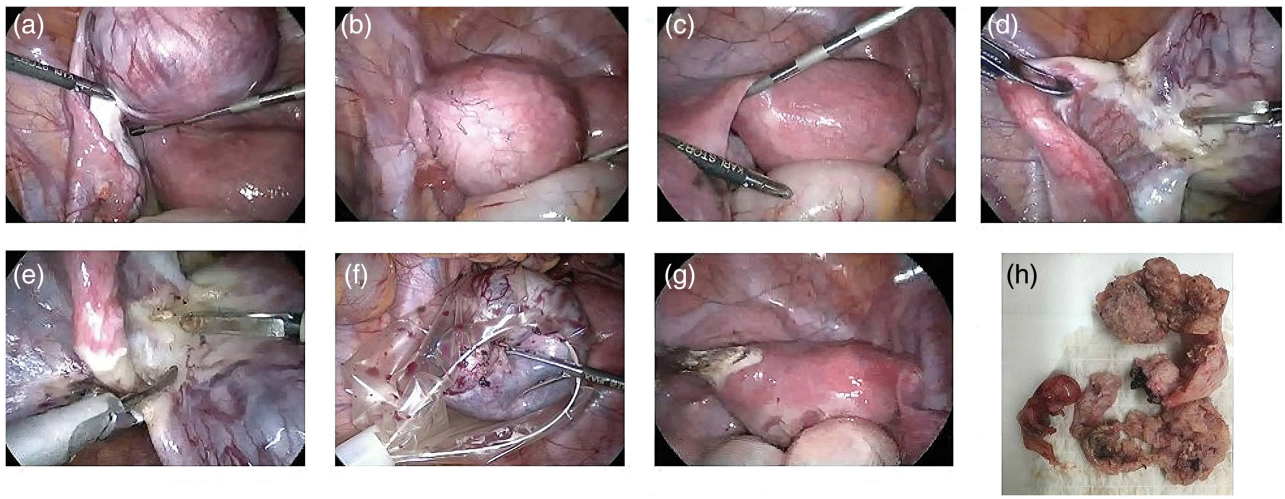


FIGURE 35.9 (a–h) Excision of the rudimentary horn with ectopic pregnancy in a patient with the unicornuate uterus.

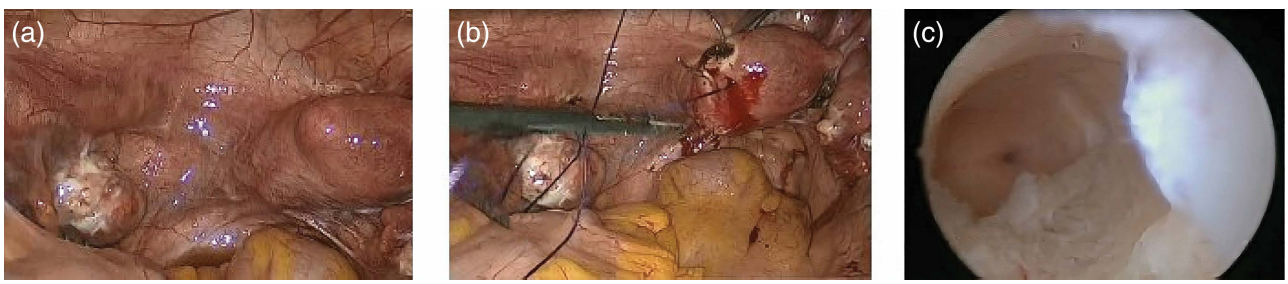


FIGURE 35.10 (a–c) Excision of the embedded uterine horn in a patient with a unicornuate uterus.

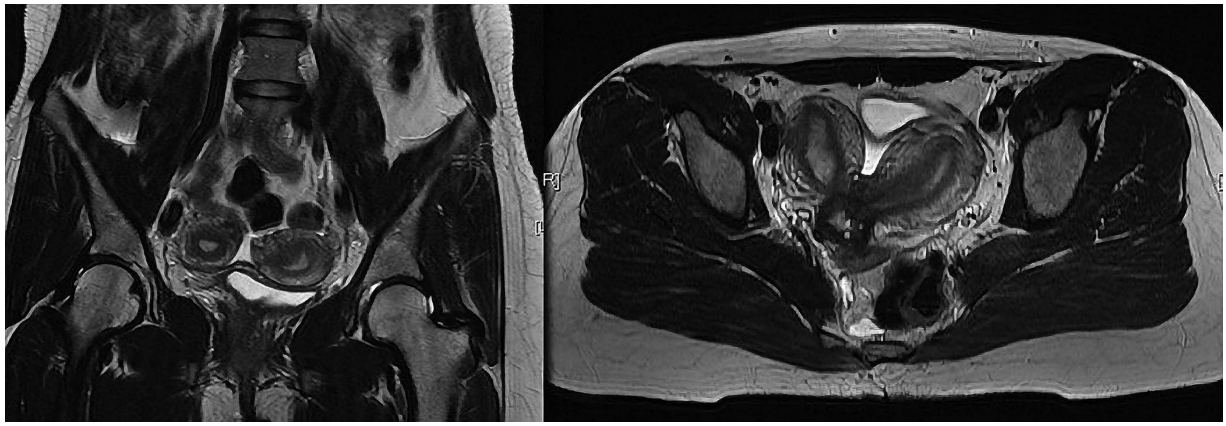


FIGURE 35.11 MRI images of a uterus and vaginal duplex, nonobstructed outflow.

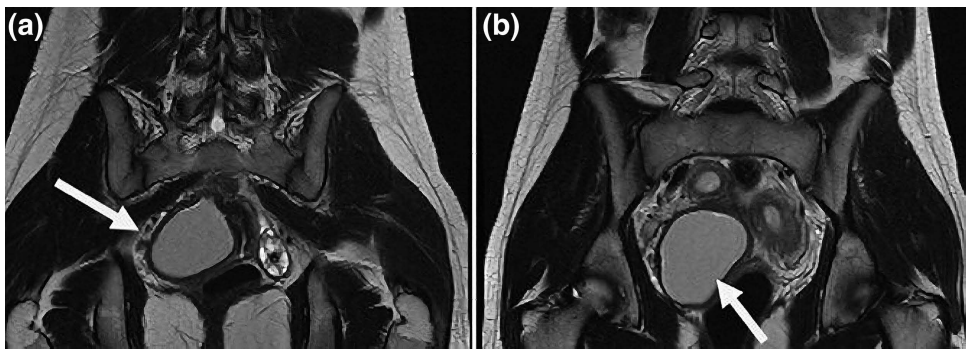


FIGURE 35.12 (a, b) MRI images of doubling of the uterus and the vagina with an obstructed right hemivagina (white arrows point to obliterated vagina).

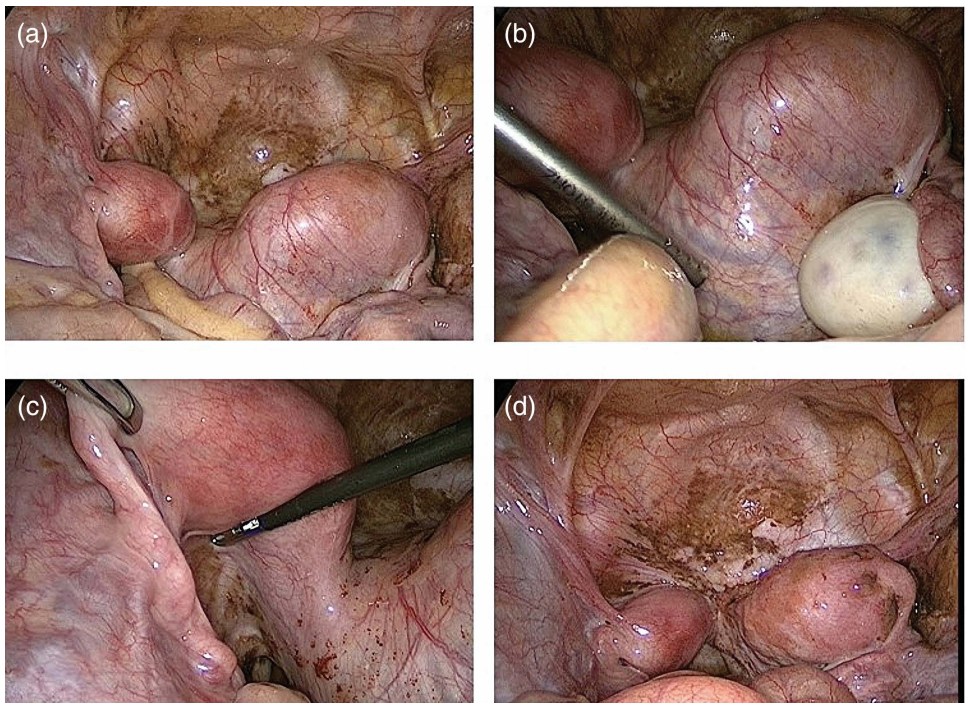


FIGURE 35.13 (a–d) Laparoscopic views of uterus duplex with aplasia of the lower 2/3 of the right hemivagina and formation of right hemihematocolpos and right hematometra.

intrauterine pathology. If clinically necessary, vaginal estrogen can be used.

Management of patients with a hemivaginal aplasia requires detailed knowledge of the ipsilateral ureter's position relative to the aplastic region. Using this anatomical guide, an incision is made over the aplastic hemivaginal area with a needlepoint monopolar electrode. For small aplastic regions near the hemicervix, the vaginal epithelial edges are sutured to the lateral side of the ipsilateral cervix using interrupted 3–0 Vicryl stitches. An intrauterine catheter ensures continuous uterine outflow.

In cases requiring hemihysterectomy or other pathologies, preoperative verification of cervical, ureteral, and renal anatomy is essential. Special attention should be given to aberrant vasculature between the hemiuteri. The cervices may be positioned laterally, and such lateral cervical positions may bring operative fields closer to the pelvic sidewalls and alter the location of the uterine vessels. All efforts should be made to preserve the blood supply for patients desiring future pregnancy and who require hemihysterectomy to retain the nondiseased uterus. The cervix of the diseased uterus should be spared if possible, and excision of the endocervix can be performed to minimize future pathology risks.

35.2.6 Class VI: Bicornuate Uterus

A bicornuate uterus is a malformation resulting from the incomplete fusion of the Müllerian ducts, dividing the cavity into two separate horns (Figure 35.14). Often diagnosed during routine gynecologic examination or evaluation of miscarriage, cervical insufficiency, or abnormal labor, recent advancements in 3D ultrasonography and MRI have enabled improved accuracy in distinguishing between bicornuate and septate uterus (35, 36).

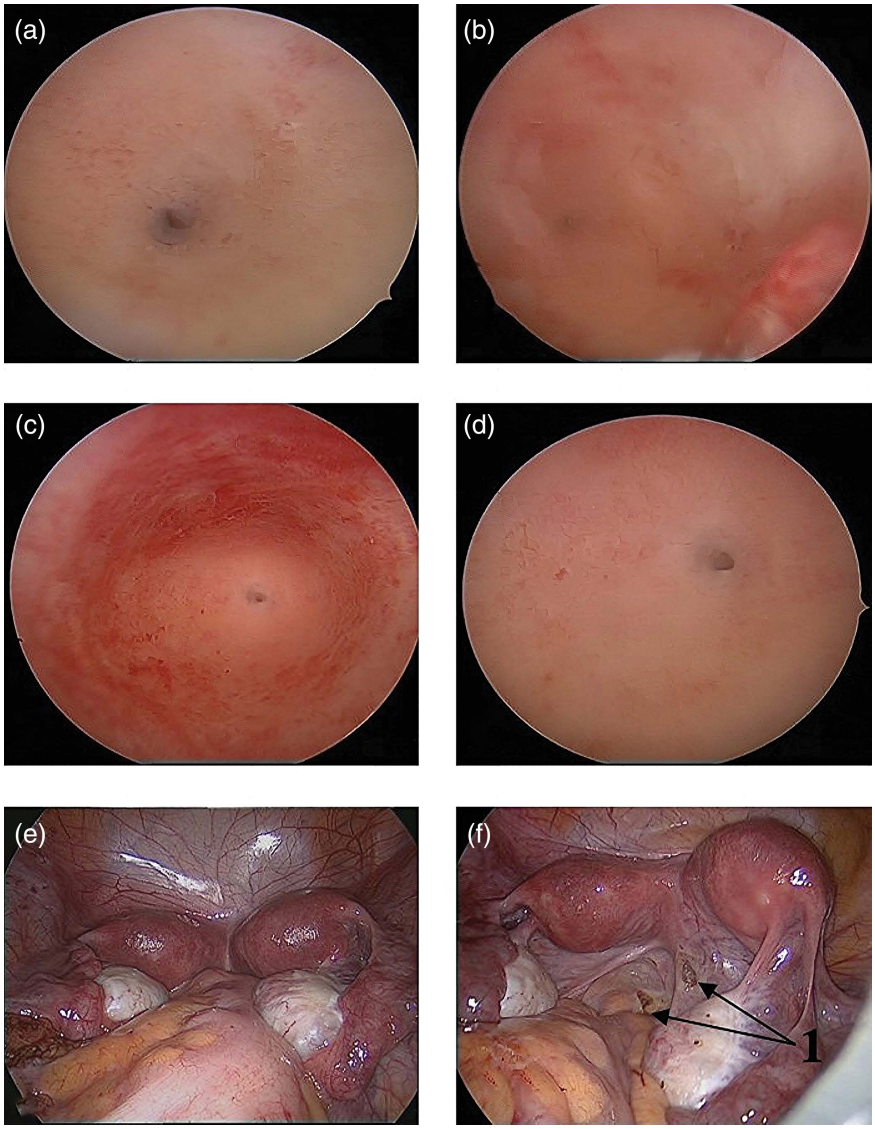


FIGURE 35.14 (a–f) Laparoscopic and hysteroscopic views of uterine and vaginal duplex (f: arrows indicate left and right uterine cervix).

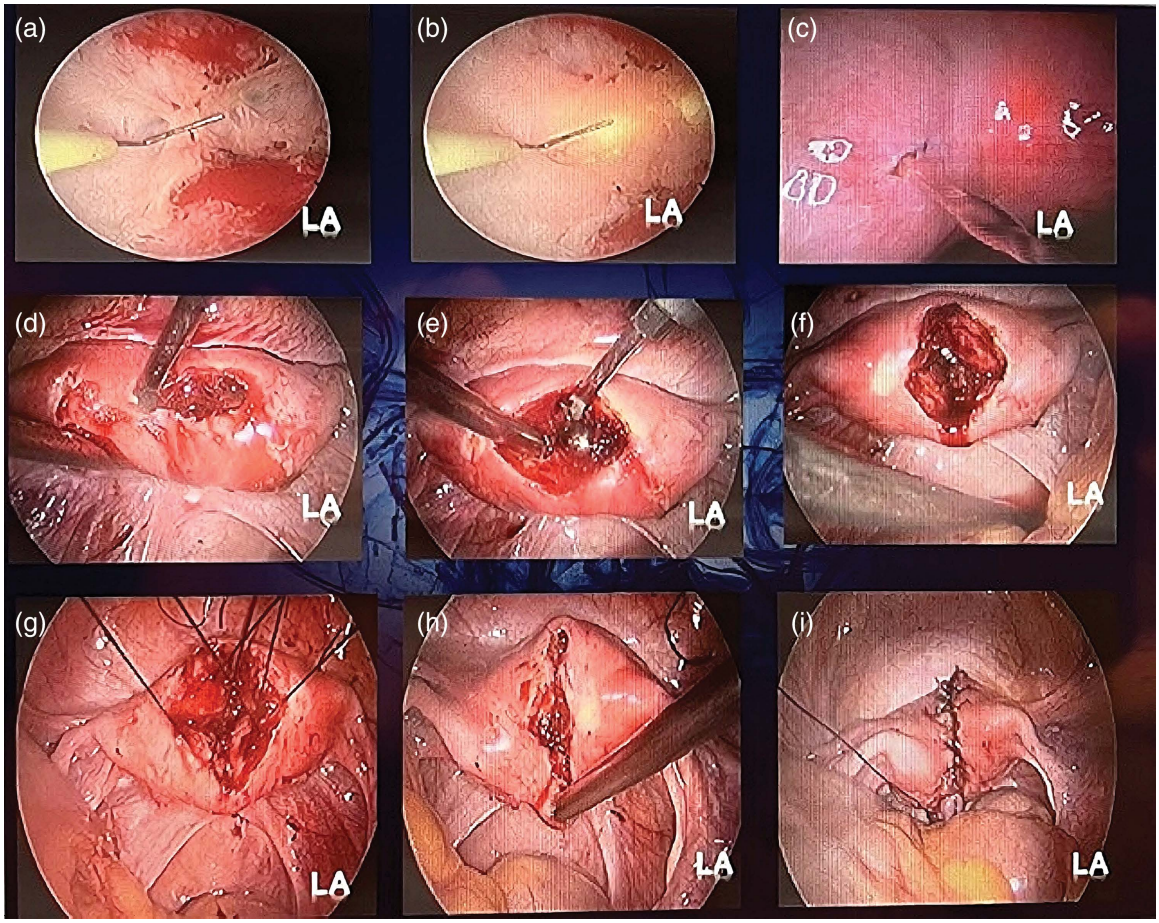


FIGURE 35.15 (a–i) Laparoscopic Strassman metroplasty.

35.2.6.1 Surgical Technique

Surgical correction is considered in patients who have had a miscarriage with this malformation. Laparo-hysteroscopic metroplasty, based on the Strassman technique, is performed to create a united cavity (Figure 35.15) (37). The principles of this procedure include (1) dissection of the uterine fundus in the frontal plane in a manner to open each uterine cavity, and (2) suturing uterine incision in a sagittal plane.

In patients with incomplete bicornuate uterus, hysteroscopy serves as the initial approach if both cavities can be distended. The mucosal-muscular layer of the uterine wall is dissected with a resectoscope up to the serosa, avoiding the tubal ostia. The depth of dissection is controlled visually and can be monitored laparoscopically, utilizing transillumination of the uterine wall to enhance safety and precision. Laparoscopically, the uterine serosa is transected in the frontal plane using a monopolar electrode or ultrasonic scalpel. Absorbable sutures are placed in the two layers of the uterine incision in the sagittal direction (serosa-myometrium and myometrium-endometrium).

The first layer's ends are withdrawn through a central puncture outside the trocar sleeve and left untied until all sutures are positioned. The sutures are then introduced into the trocar sleeve and tied extracorporeally. To minimize tissue tension during knot tying, the uterine halves are aligned to the midline with manipulators. The serosal-muscular layer can be sutured continuously. Second-look laparoscopy and hysteroscopy performed 3 months post-metroplasty have shown no adhesions in the pelvis or uterine cavity, confirming the effectiveness of the repair (2, 12, 22).

35.2.7 Class VII: Intrauterine Septum

A uterine septum is a malformation that results from incomplete resorption of the tissue connecting the Müllerian ducts and presents as a longitudinal septum of varying length. Three-dimensional imaging and MRI provide diagnostic capabilities in identifying this anomaly (Figures 35.16 and 35.17). Patients with an intrauterine septum may experience reproductive failures such as miscarriage or infertility.

Hysteroscopy is the mainstay of evaluation and treatment. First performed by DeCherney et al. in 1986, a uterine septum should be resected immediately after or in the early follicular phase of the menstrual cycle (38, 39). The procedure can also be performed after preparing the endometrium on continuous monophasic hormone therapy. Surgical considerations include dilating the cervix to allow a resectoscope, using cutting energy to transect the septum from the most caudal portion until the uterine cavity appears as a normal triangular shape, and using coagulation energy to control any bleeding

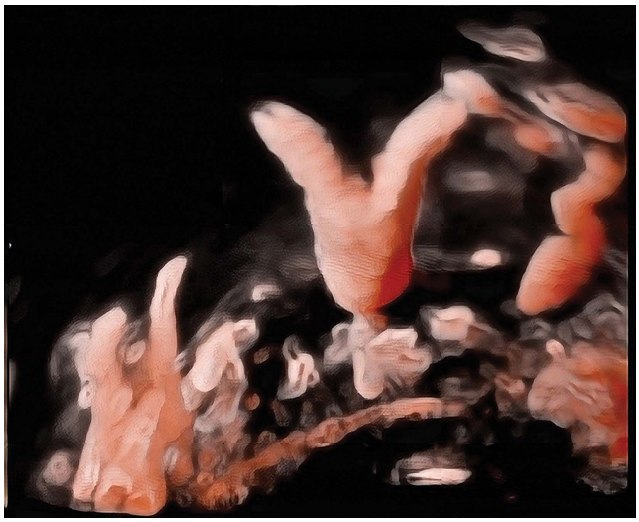


FIGURE 35.16 3D image of complete uterine septum.

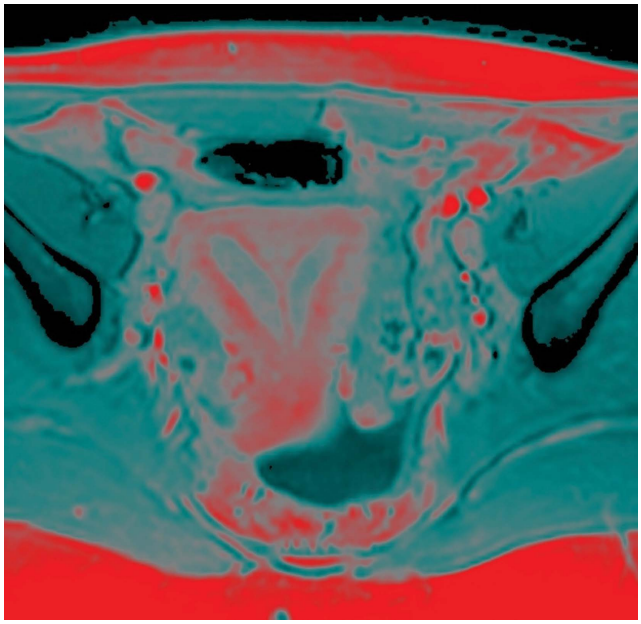


FIGURE 35.17 Dynamic contrast-enhanced MRI of an incomplete uterine septum demonstrates reduced myometrial perfusion at the septum site.

(Figure 35.18). Diagnostic laparoscopy can be performed to exclude other anomalies or if the septum resection is associated with a high risk of perforation, especially in those with a wide uterine septum. Contraception is recommended for 2–3 months after surgery and reproductive potential is restored in patients after surgical correction (12, 39–41).

Various protocols and agents have been proposed to prevent intrauterine synechiae following surgery. Optimal outcomes are achieved through meticulous surgical techniques combined with postoperative hormonal therapy and, in complex cases or prior surgical attempts, platelet-rich plasma (PRP) as an adjunctive or alternative strategy (42).

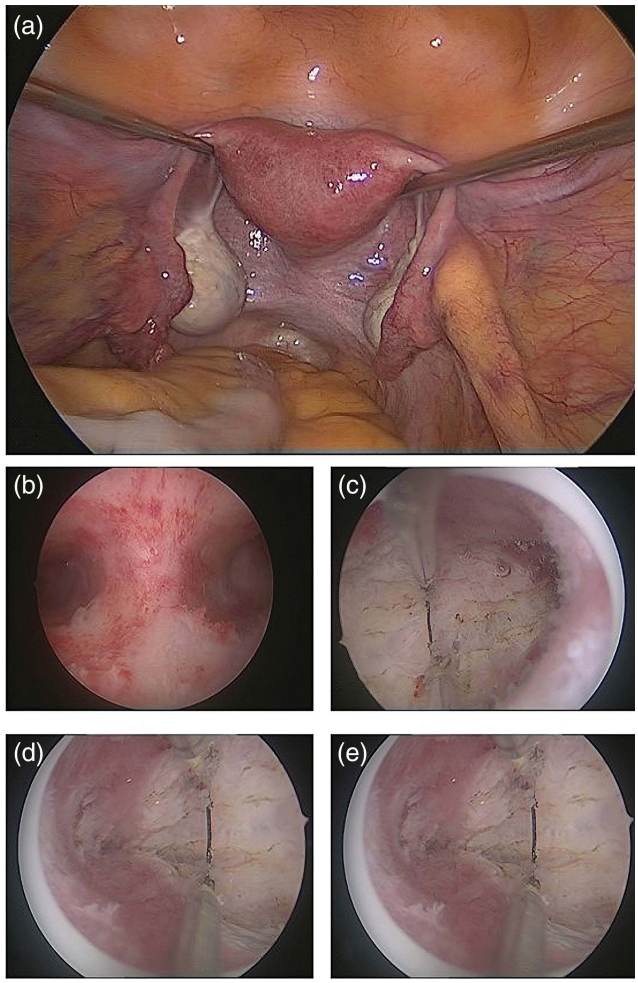


FIGURE 35.18 (a–e) Uterine septum resection.

35.3 Conclusion

Minimally invasive surgery can be used to surgically correct female reproductive anomalies. Reproductive anomalies vary widely in clinical, structural, and topographic presentations. Their management demands an individualized approach that balances innovation with adherence to established principles. Advancements in technology now provide detailed anatomical, immunohistochemical, and molecular data, enriching our understanding of gynecologic diseases and reproductive pathologies.

This chapter outlined our original surgical techniques for managing Müllerian anomalies, developed over 30 years of experience and research. These methods have consistently improved symptomatic, anatomical, reproductive, and quality-of-life outcomes and serve as a reliable guide to achieving excellent treatment results.

References

1. Chan YY et al. The prevalence of congenital uterine anomalies in unselected and high-risk populations: a systematic review. *Hum Reprod Update.* 2011;17(6):761–771.
2. Adamyan LV. Additional international perspectives: colpopoiesis in vaginal and uterine aplasias. In: Nichols D, ed. *Gynecologic and Obstetric Surgery.* Mosby; 1993:1167–1182.

3. American Fertility Society. Classification of adnexal adhesions, distal tubal occlusion, tubal occlusion secondary to tubal ligation, tubal pregnancies, Müllerian anomalies, and intrauterine adhesions. *Fertil Steril*. 1988;49:944–955.
4. Acien P et al. The history of female genital tract malformation classifications and proposal of an updated system. *Hum Reprod Update*. 2011;17:693–705.
5. Grinbizis GF et al. The ESHRE/ESGE consensus on the classification of female genital tract congenital anomalies. *Hum Reprod*. 2013;28:2032–2044.
6. Pfeifer SM et al. ASRM müllerian anomalies. *Fertil Steril*. 2021;116(5):1238–1252.
7. Adamyan LV. Therapeutic and endoscopic perspectives: colpopoiesis in vaginal and uterine aplasias. In: Nichols D, ed. *Gynecologic and Obstetric Surgery*. Mosby; 1999:187–219.
8. Adamyan LV et al. Reconstructive surgical treatment and classification of female genital anomalies. *Minim Invas Gynecol*. 2014;21(6):151.
9. Rokitansky K. Uber die sogenannten Verdoppelungen des. *Med JB Obstrics Staat*. 1838;26:39–77.
10. Kuster H et al. Uterus bipartitus solidus rudimentarius cum vagina solida. *Gynecology*. 1910;67:692–718.
11. Hauser GA. Das Mayer-Rokitansky-Küster-Syndrom. *Schweiz Med Wochenschr*. 1961;91:381–384.
12. Arakelyan AS. *Uterine and vaginal anomalies: modern methods of diagnostics, surgical treatment, and rehabilitation*. Dissertation. Moscow: National Medical Scientific Center for Perinatology, Obsterics, and Gyneology; 2022.
13. Adamyan LV et al. Uterovaginal aplasia (MRKH syndrome) in combination with endometriosis: unresolved aspects in the etiology and pathogenesis (literature review). *Problems Reprod*. 2016;22(3);8–14.
14. Frank R. The formation of an artificial vagina without operation. *Am J Obstet Gynecology*. 1938;35(6):1053–1055.
15. Adamyan LV et al. Sexual function of women after surgical correction of the vaginal and uterine aplasia. *Proceedings of the XXVII Congress of New Technologies for Diagnosis and Treatment of Gynecologic Disease*. Moscow: National Medical Research Center for Obstetrics, Gynecology and Perinatology; 2014.
16. Adamyan L. Total laparoscopic colpopoiesis. *RU2*,015,199,396.
17. Adamyan L. Total laparoscopic colpopoiesis with 2 provisionary sutures. *RU2*,585,739.
18. Adamyan L. Laparoscopic peritoneal colpopoiesis. *RU2*,015, 126,640.
19. Adamyan LV. Laparoscopic management of vaginal aplasia with or without functional noncommunicating uterus. In: Arreguia ME et al., eds. *Principles of Laparoscopic Surgery: Basic and Advanced Techniques*. Springer-Verlag; 1995:652–671.
20. Gadjiyeva ZA. *Reconstructive plastic surgeries in women with anomalies of the development of the pelvic organs associated with the disorders of menstrual outflow*. Dissertation. Moscow; 2014:113.
21. Jones HJ et al. Salvage of the reproductive potential of women with anomalous development of the Müllerian ducts: 1868–1968–2068. *A J Obstet Gynecol*. 1969;104:348–364.
22. Adamyan LV et al. Endoscopic diagnosis and correction of malformations of female genitalia. In: Pasic RP et al., eds. *A Practical Manual of Laparoscopy and Minimally Invasive Gynecology: A Clinical Cookbook*, 2nd edn. CRC Press; 2007:347–364.
23. Adamyan LV. Laparoscopy in surgical treatment of vaginal aplasia: laparoscopy assisted colpopoiesis and perineal hysterectomy with colpopoiesis. *Int J Fertil*. 1996; 41(1):40–45.
24. Miroshnikova NA et al. *Obstet Gynecol*. 2017(5):16–22.
25. Adamyan LV. The anomalies of development of the uterus and the vagina. In: Adamyan LV et al., eds. *Medicine*. 1998:320.
26. Adamayn LV et al. Cervico-vaginal aplasia: methods of surgical correction. *Obstet Gynecol*. 2013;(2):51–56.
27. Adamayn LV et al. Genetic aspects of gynecologic diseases. *Geotar Media*. 2008:182.
28. Maneschi M et al. Reproductive impairment of woman with unicornuate uterus. *Acta Obstetrics Gynecol Scand*. 1988;67(6):557–560.
29. Khati NJ et al. The unicornuate uterus and its variants: clinical presentation, imaging findings, and associated complications. *J Ultrasound Med*. 2012;31(2):319–331.
30. Adamyan LV et al. Complex approach to diagnosis, surgical correction, and rehabilitaton of patients with combined utero-vaginal anomalies and endometriosis. *Problems Reprod*. 2016;(3):84–90.
31. Findley P. Pregnancy in uterus dideIphys. *Am J Obstr Gynecol*. 1926;12:318.
32. Bogdanova EA et al. Clinical aspects, diagnostics, and treatment of the doubling of the uterus and vagina with partial aplasia of the hemi-vagina in adolescents. *Obstet Gynecol*. 1990;9:43–46.
33. Adamyan LV et al. Anomalies of the development of the female reproductive organs: the matters of identifications and classification (literature review). *Problems Reprod*. 2010;16(2):7–15.
34. Miroshnikova NA. *Optimization of the surgical treatment of patients with symmetric anomalies of the uterus with consideration of the myometrial perfusion*. Dissertation. Moscow; 2018:136.
35. Maneschi F et al. Reproductive performance in women with bicornuate uterus. *Acta Eur Fertility*. 1993:24(3);117–120.
36. Arakelyan AS et al. The role of 3-dimensional echographic diagnostics in chosing the tactic of reconstructive surgeries in patients with anomalies of development of the uterus and the vagina. *Problems Reprod*. 2021;27(4):32–42.
37. Strassmann P. Die operative Vereinigung eines doppelten Uterus. *Zentralbl Gynakol*. 1907;43:1322–1335.
38. DeCherney AH et al. Resectoscopic management of müllerian fusion defects. *Fertil Steril*. 1986;45(5):726–728.
39. Di Spiezio Sardo A et al. Long-term reproductive outcomes after hysteroscopic treatment of dysmorphic uteri in women with reproductive failure: an European multicenter study. *J Minim Invasive Gynecol*. 2020;27(3):755–762.
40. Makyan ZN et al. Functional MR tomography for the evaluation of the myometrial perfusion in patients with symmetric uterine anomalies. *Obstet Gynecol*. 2016;10:73–79.
41. Pabuçcu R et al. Reproductive outcome after hysteroscopic metroplasty in women with septate uterus and otherwise unexplained infertility. *Fertil Steril*. 2004;81(6):1675–1678.
42. Martinov SA et al. Possibilities of using platelet-rich autoplasm in the complex treatment of patients with intrauterine synechiae. *Gynecology*. 2021;23(3):250–254.

36 GENITOURINARY SYNDROME OF MENOPAUSE AND ENERGY-BASED THERAPIES

Johnathan Pai and Bobby Garcia

36.1 Introduction

Menopause is characterized by a decline of ovarian function – leading to a hypoestrogenic state within the body potentially resulting in vasomotor disturbances, impact on sleep, changes to sexual function, urinary tract infections, and vulvovaginal symptoms. It is defined by the absence of a menstrual period during a 12-month span with a median age of 51 in North America (1). In 2014, the North American Menopause Society (NAMS) and the International Society for Study of Women's Sexual Health proposed the term genitourinary syndrome of menopause (GSM), acknowledging the previous utilized terminology of vulvovaginal atrophy (VVA) to be inclusive of postmenopausal changes on the lower urinary tract while avoiding the negative terminology of atrophy (2, 3). The resulting symptoms include vaginal dryness, burning, and irritation; sexual symptoms of dyspareunia and impaired function; and urinary symptoms of urgency, dysuria, and recurrent urinary tract infection. As many as 84% of postmenopausal women will experience GSM symptoms from decreased estrogen levels during their menopause transition or after onset of menopause, highlighting the need for providers to be cognizant of the presenting symptoms and be knowledgeable of the various management options to improve the quality of life for these women (4). In this chapter we will briefly review the physiology pertinent to menopause, followed by a discussion of vasomotor symptoms, GSM, and then the emerging technology of energy-based therapy.

36.2 Anatomy and Physiology

The female genital and lower urinary tracts both arise from the primitive urogenital sinus and share a common estrogen receptor function. Vaginal physiology is primarily influenced by estrogen where estrogen receptors are most dense. However, these receptors can also be located in the vulva, urethra, and trigone of the bladder. Estradiol levels from a premenopausal to a postmenopausal state can decrease up to approximately 95%, resulting in specific changes in tissue composition leading to clinical manifestation of GSM.

The vaginal wall consists of a nonkeratinized stratified squamous vaginal epithelium, lamina propria with dense connective tissues rich in blood and lymphatic vessels; a muscular layer of smooth muscle and tunica adventitia with loose connective tissue collagen and elastic fiber. As estrogen levels decrease with menopause, the vaginal epithelium and lamina propria thin, smooth muscle atrophies, blood flow decreases, and tissue elasticity decreases. This results in loss of vaginal rugae which clinically may present in severe cases as a shortened and narrow vagina with loss of tissue distension and thinning of the epithelium.

Within the vaginal epithelium, the cellular composition of deep immature parabasal cells, intermediate cells, and mature superficial cells which store glycogen are present at different ratios throughout a woman's life depending on the level of estrogen stimulation. During reproductive years, vaginal cytology demonstrates an abundance of superficial cells while declining estrogen with menopause results in a return of parabasal cell predominance with fewer intermediate and superficial cells comparable to a premenarche state. The change of composition and thinning of vaginal epithelium increases susceptibility to inflammation and infection. Specifically, the reduction of mature superficial cells containing glycogen corresponds with a decrease in lactobacilli, leading to an increase in vaginal pH. The overall change in vaginal microbiota increases the potential for overgrowth and recurrence of pathogenic organisms responsible for vaginal and urinary tract infections.

Two known estrogen receptors have been identified as estrogen receptor alpha (ER-α) and estrogen receptor beta (ER-β) with variable expression and action of each receptor depending on specific tissue. Even though both ER-α and ER-β expression decrease with menopause, only ER-α appears to be responsive to estrogen supplementation. The increase of ER-α expression compared to the persistent decrease of ER-β expression despite estrogen supplementation indicates that the primary mechanism of exogenous estrogen is the beneficial response modulated through ER-α expression. Estrogen supplementation can influence the collagen content of the epithelium by increasing the thickness and elasticity of the vagina, keep the epithelial surface moist by maintaining intercellular acid mucopolysaccharides and hyaluronic acid, and promote optimal genital blood flow (5).

36.3 Vasomotor Symptoms and Systemic Treatments

Vasomotor symptoms are characterized by the sudden feeling of warmth or flushing in the upper body such as the chest and face, with a resultant rise in skin temperature due to peripheral vasodilation. The symptoms can also be associated with perspiration, chills, anxiety, and palpitations. While the exact pathophysiology of these "hot flashes" is unclear, the release of neurotransmitters such as norepinephrine and serotonin has an effect on hypothalamic temperature regulation with resultant loss of heat. First-line treatment for vasomotor symptoms includes behavioral modifications such as layering clothing, avoiding alcohol and caffeine, utilizing a portable fan, and drinking cold beverages (6). Many phytoestrogenic foods such as soy, alfalfa, and red clover have been studied; however, a Cochrane review has shown that there is no conclusive evidence these supplements reduce the severity or frequency of vasomotor symptoms (7). The gold standard for treatment of these symptoms is systemic hormone therapy. This includes either estrogen alone or estrogen with progestin to prevent endometrial hyperplasia in women with a uterus. Routes of administration are varied and include oral, transdermal, intranasal, and buccal. Risks of hormone therapy include breast cancer and thromboembolism. Patients should

DOI: 10.1201/9781003312109-36

be placed on the lowest effective dose for the shortest duration in treating vasomotor symptoms. Of note, discontinuation of therapy is associated with recurrent vasomotor symptoms in 50% of women (1). Testosterone utilized in combination with hormone replacement has a beneficial effect on sexual function but has not been shown to improve vasomotor symptoms, and it is also associated with hair growth, acne, and a reduction in HDL cholesterol (8). Selective serotonin reuptake inhibitors (paroxetine) and serotonin–norepinephrinereuptake inhibitors (venlafaxine) have been utilized off label, at subpsychiatric doses, to treat hot flashes. In patients who have failed a trial of antidepressants, gabapentin was shown to reduce vasomotor symptoms by 50% (9).

36.4 Clinical Manifestation of GSM

Common presenting symptoms of GSM as mentioned earlier include vaginal dryness, dyspareunia, vaginal itching, discharge, and pain; urinary symptoms include urinary frequency, dysuria, and increased risk for urinary tract infections. Of presenting symptoms, vaginal dryness is the most prevalent and found to be the most bothersome. The array of symptoms can lead to negative impact on emotional, physical, and functional aspects of life for women affected by GSM.

36.5 Evaluation

As GSM is a clinical diagnosis, obtaining a thorough medical history and pelvic examination is essential. Women of peri- or postmenopausal age should routinely be questioned regarding symptoms of urogenital atrophy during their visits with providers, as many women may feel hesitancy or fear of embarrassment from discussing their concerns and prevent the communication of bothersome symptoms that delay initiation of treatment. A complete obstetric and gynecologic history including menstrual history should also be obtained. Patients with significant medical history including breast cancer may be using medications such as selective estrogen modulators (SERMS) or aromatase inhibitors (AIs) that result in a low estrogen state and should be assessed. At each visit, patients should have their pertinent sexual history taken to address any distressing symptoms that may impact their sexual activity and whether previous interventions provided appropriate response. Lastly, a thorough review on history of pelvic radiation, exposure to irritants or allergens, and infectious or inflammatory conditions can help distinguish any other differential causes resulting in symptoms of GSM. Each patient may have unique quality-of-life concerns, and their therapeutic goals should be addressed with shared decision making together with the provider.

Pelvic examination in the office is paramount in identifying objective signs of tissue atrophy associated with symptoms of GSM. The pelvic examination can be facilitated with a mirror for the patient to aid in mutual evaluation of areas of concern. It is important to take into consideration the appropriate size of speculum with adequate lubrication utilized as atrophic tissue during pelvic examination is prone to pain and bleeding even with gentle contact. Common physical exam findings of menopausal women include a decrease in pubic hair, loss of labial adipose tissue, thinning and resorption of the labia minora, narrowing of the introitus, and increased vaginal pH. The urethral meatus may appear to be more prominent and erythematous due to atrophic changes to the mons pubis, labia majora, and labia minora. On speculum examination, hypoestrogenic changes are seen with decreased vaginal caliber, smooth, shiny, pale epithelium with loss of folds, loss of cervical length with cervix flush with the vaginal apex, and obliteration of the vaginal fornices (3). Dermatologic conditions such as lichen sclerosus or lichen planus should be ruled out as they may be mistaken for GSM.

36.6 Management of GSM

Despite the relatively high prevalence of women who are affected by GSM, the frequency in which they are treated is low. A possible combination of hesitancy to bring up symptoms to providers, the perceived normalcy of symptoms attributed to aging, provider's lack of familiarity with treatment options, or inadequate time during the visit to address symptoms largely leave women with bothersome concerns of GSM untreated. Simple lifestyle modifications have been shown to improve symptoms of GSM including smoking cessation, increased coital activity, and pelvic floor physiotherapy (Table 36.1).

TABLE 36.1 Therapeutic Management of Menopause/GSM

Therapeutic Categories	Options
Lifestyle modifications	• Smoking cessation • Increased coital activity • Pelvic floor physiotherapy
Nonhormonal therapy	• Vaginal lubricant • Vaginal moisturizer
Hormonal therapy	• Systemic estrogen* • Testosterone • Custom compound bioidentical formulations (not FDA approved) • Topical vaginal estrogen ** (see Table 36.2) • SERM (ospemifene) • Dehydroepiandrosterone (DHEA)
Antidepressants	• Selective serotonin reuptake inhibitor (SSRI): paroxetine • Serotonin norepinephrine reuptake inhibitor (SNRI): venlafaxine
Therapies that needs further investigation	• CO_2 laser • Er:YAG laser

* In menopausal women with intact uterus, consider adding combined hormonal therapy with addition of progestin to mitigate risk of endometrial hyperplasia from estrogen-only therapies.

** In patients with significant history of breast cancer, consider topical vaginal therapy with discussion with oncology.

36.7 Lubricants and Moisturizers

Vaginal dryness is often the primary or most bothersome symptom for patients with GSM. Currently the first-line therapies for women with mild to moderate vaginal dryness are lubricants and vaginal moisturizers. Various commercial products of both lubricants and vaginal moisturizers are available on the market. The primary mechanism of benefit for vaginal moisturizers is due to the insoluble hydrophilic cross-linked polymer bioadhesives that bind to the vaginal wall by retaining water. When used on a regular basis, moisturizers improve GSM symptoms with long-lasting effect by trapping moisture, improving vaginal pH balance, and reducing itching (1). In contrast, lubricants are used predominantly for short-term relief of vaginal dryness during intercourse to relieve dyspareunia and improve perceived sexual satisfaction. Recommendation to treat mild to moderate vaginal dryness with routine application of vaginal moisturizer two to three times weekly with the addition of vaginal lubricants during sexual intercourse has been shown to be effective. However, it should be noted that these interventions improve symptomatic relief but do not reverse atrophic vaginal changes associated with GSM.

36.8 Low-Dose Vaginal Estrogen

Vaginal estrogen is a common second-line treatment for patients not responding to first-line treatment for GSM, with available formulations on the market that can be administered through cream, ring, insert, or tablets (Table 36.2). Application of this localized therapy results in an increase in the vaginal maturation index (VHI), decreases the vaginal pH, improves tissue vascularity and epithelial integrity, and restores vaginal flora (10). Vaginal estrogen is superior to systemic estrogen for the treatment of GSM (11). Vaginal preparations have minimal systemic absorption, particularly at low-dose formulations, and have been found to be overall safe, without the need for commitment progesterone therapy for endometrial protection. Current recommendations do not require routine endometrial evaluation for patients on vaginal estrogen therapy; however, if a woman presents with abnormal uterine bleeding while on such therapy then endometrial evaluation should be performed (1). Similarly, data from the Women's Health Initiative have shown no increase in risk of invasive breast cancer, stroke, colorectal cancer, endometrial cancer, pulmonary embolism or deep vein thrombosis, coronary heart disease, or death with vaginal estrogen (12). Despite this data, the US Food and Drug Administration (FDA) still labels this medication with a black label warning against the elevated risk of these conditions, and patients should be counseled appropriately prior to initiation of therapy.

36.9 Selective Estrogen Receptor Modulators

Selective estrogen receptor modulators are synthetic nonsteroidal agents that exert estrogen agonist or antagonist effects based on target tissue. Two current SERMs have been shown to be beneficial for patients with GSM including ospemifene and lasofoxifene; however, ospemifene is the only FDA-approved agent for GSM in menopausal women regardless of their uterus-possessing status. An oral dose of 60 mg per day exerts estrogenic effects on the vulva vaginal tissues demonstrated through increased epithelial thickness, glycogen content, and collagen content with clinical improvement of vaginal dryness and dyspareunia (13–15).

36.10 Vaginal Energy-Based Devices (EBDs)

Recently, the application of an energy source to the vaginal canal has been trialed with the intent to either alleviate symptoms of vaginal dryness or increase the tightness of the canal. While these therapies have recently come into vogue and are often offered as a cash-based fee for service, the data concerning these therapies is limited. In the remainder of this chapter we will briefly survey these technologies and proposed indications.

Historically, EBDs have been employed across a broad range of specialties including gynecology, urology, plastic surgery, and dermatology. CO_2 laser was first used to treat erosions of the uterine cervix in 1973 (16). While various modalities of EBDs exist, they are broadly divided into two categories: laser and radiofrequency.

LASER is an acronym for "light amplification by stimulated emission of radiation." This technology consists of application of light or electricity to a laser medium which results in the generation and amplification of a unified wavelength which is then directed at the target tissue (17). There are many different types of laser each operating at a different frequency on the electromagnetic spectrum. Beyond a laser's particular wavelength, additional variables necessary for consideration are the absorption characteristics of the target tissue and the time and pattern of energy application. Of the various types, the most common studied for gynecologic application are CO_2 (10,600 nm), Er:YAG (2940 nm), and hybrid (2940 + 1470 nm) lasers.

Radiofrequency (RF) involves transmission of electric current from 3 kHz to 300 MHz from a probe to the target tissue with resultant generation of heat. When a target temperature of 40°C to 45°C is reached, collagen production is stimulated by

TABLE 36.2 Topical Vaginal Estrogen

Preparation Type	Brand	Recommended Clinical Dose
Vaginal cream	Premarin	0.625 mg per 1 g cream – use 0.5 to 1.0 g nightly for 2 weeks then titrate to 3× weekly
	Estrace	0.1 to 1 g cream – use 0.5 to 1.0 g nightly for 2 weeks then titrate to 3× weekly
Vaginal tablet	Imvexxy	4 to 10 μg insert daily for 2 weeks then titrate to 2× weekly
	Intrarosa	6.5 mg insert daily
Vaginal insert	Vagifem	10 μg tablet daily for 2 weeks then titrate to 2× weekly
Vaginal ring	Estring	2 mg ring that delivers 7.5 μg daily, to change every 90 days

fibroblasts (18). There are two main type of RF: monopolar that utilizes a grounding pad and may be coupled with crogyneic cooling, and unipolar RF where the probe is applied directly to the patient. Most data for RF are for the indication of vaginal laxity.

Each specific laser or RF device has a manufacturer suggested number of treatment passes or time of application and intervals for treatment. In general, this is two to three treatments spaced 4–6 weeks apart for laser, with interval maintenance yearly, while RF is completed in one session. It is very important to note that while the mechanism of action is similar and they may be applied for similar indications, the research data from each type should not be considered interchangeable (19).

EBDs have been investigated for the treatment of GSM, stress urinary incontinence, overactive bladder, and vaginal laxity. For GSM it should be noted that the NAMS recommends moisturizers and lubricants as first-line therapy, with vaginal estrogen for those with persistent symptoms (20). A clinical consensus statement by the American Urogynecologic Society reviewing the available literature concluded that EBDs have yet to show promise for the treatment of atrophy, dryness, or dyspareunia. They may, however, offer short-term efficacy lasting less than a year and have a beneficial effect on sexual function. While serious adverse events have been reported, they are rare, and this therapy is usually well tolerated with a favorable safety profile, though long-term data are still needed (21). Given the efficacy and data available, EBDs should be limited to a research setting.

Key Points

- Menopause is characterized by a decline in ovarian function.
- Symptoms include vasomotor symptoms, vaginal dryness, dyspareunia, and urinary complaints
- Hormone replacement is the gold standard for treatment of vasomotor symptoms.
- Treatments for GSM include moisturizers and vaginal estrogen.
- Energy-based device treatments for GSM are still experimental and should be limited to a research setting.

References

1. American College of Obstetricians and Gynecologists. Practice bulletin 141: management of menopausal symptoms. *Obs Gynecol*. 2014;123(5):1118–1132.
2. Faubion R et al. Genitourinary syndrome of menopause: management strategies for the clinician. *Mayo Clin Proc*. 2017;92(12):1842–1849.
3. Portman DJ et al. Genitourinary syndrome of menopause: new terminology for vulvovaginal atrophy from the international society for the study of women's sexual health and the North American Menopause Society. *Menopause*. 2014;21(10):1063–1068.
4. Faubion SS et al. The 2020 genitourinary syndrome of menopause position statement of The North American Menopause Society. *Menopause*. 2020;27(9):976–992.
5. Gebhart JB et al. Expression of estrogen receptor isoforms alpha and beta messenger RNA in vaginal tissue of premenopausal and postmenopausal women. *Am J Obstet Gynecol*. 2001;185(6):1325–1331.
6. Kaunitz AM et al. Management of menopausal symptoms. *Obstet Gynecol*. 2015;126(4):859–876.
7. Lethaby A et al. Phytoestrogens for menopausal vasomotor symptoms. *Cochrane Database Syst Rev*. 2013;2013(12).
8. Somboonporn W et al. Testosterone for peri and postmenopausal women. *Cochrane Database Syst Rev*. Published online 2005;(4):2.
9. Sideras K et al. Nonhormonal management of hot flashes for women on risk reduction therapy. *J Natl Compr Cancer Netw*. 2010;8(10):1171–1179.
10. Palacios C et al. Update on management of genitourinary syndrome of menopause: a practical guide. *Maturitas*. 2015;82(3):308–313.
11. Long CY et al. A randomized comparative study of the effects of oral and topical estrogen therapy on the vaginal vascularization and sexual function in hysterectomized postmenopausal women. *Menopause*. 2006;13(5):737–743.
12. Investigators WG for the WHI. Risks and benefits of estrogen plus progestin in health postmenopausal women principle results from the womens health initiative randomized controlled trial. *JAMA Express*. 2002;288(3):321–333.
13. Pinkerton JV et al. Clinical effects of selective estrogen receptor modulators on vulvar and vaginal atrophy. *Menopause*. 2014;21(3):309–319.
14. Alvisi S et al. Structure of epithelial and stromal compartments of vulvar and vaginal tissue from women with vulvo-vaginal atrophy taking ospemifene. *J Sex Med*. 2018;15(12):1776–1784.
15. Alvisi S et al. Effects of ospemifene on vaginal epithelium of postmenopausal women. *Gynecol Endocrinol*. 2017;33(12):946–950.
16. Kaplan I et al. The treatment of erosions of the uterine cervix by means of the CO2 laser. *Obstet Gynecol*. 1973;41(5):795–796.
17. Gambacciani SMP. Laser therapy for the restoration of vaginal function. *Maturitas*. 2017;99:10–15.
18. Dunbar SW et al. Radiofrequency in cosmetic dermatology: an update. *J Drugs Dermatol*. 2015;14(11):1229–1238.
19. Garcia B et al. Energy based device applications in female urology. *AUA Updat Ser*. 2021;40(Lesson 4).
20. North American Menopause Society. Management of symptomatic vulvovaginal atrophy: 2013 position statement of the North American Menopause Society. *Menopause*. 2013;20(9):888–902.
21. Alshiek J et al. Clinical consensus statement: vaginal energy-based devices. *Female Pelvic Med Reconstr Surg*. 2022;28:633–648.

37 HEREDITARY MALIGNANCIES, GENETIC TESTING, AND RISK-REDUCING SURGERIES

Yovanni Casablanca

37.1 Introduction

Since the advent of genetic testing over 20 years ago, multiple inherited mutations and associated cancer syndromes have been identified that confer an increased risk of certain gynecologic cancers. The most notable example is the hereditary breast and ovarian cancer (HBOC) syndrome, with recognized pathogenic mutations in the *BRCA1* and/or *BRCA2* genes, which increase the risk of breast, ovarian, tubal, and peritoneal cancers. Multigene panel testing has expanded availability to a customizable number of genes and pathogenic mutations with varying cancer risk and penetrance. The volume of the resultant data has yielded interest and demand for prophylactic surgery when abnormal results are identified. Gynecologists are often consulted to evaluate a patient's cancer risk with incorporation of genetic testing, personal history, and family history. The decision to recommend prophylactic, or risk-reducing, surgery is complex and is influenced by additional gynecologic symptoms or medical conditions. This chapter provides guidance about genetic testing and supplies data that supports risk-reducing surgery based on specific pathogenic germline mutations and inherited cancer syndromes. This is a rapidly evolving and nuanced field that also includes factors such as family history and other comorbidities that may modify individualized guidance.

37.2 Genetic Testing and Counseling

The general population's lifetime risk for development of epithelial ovarian cancer in the United States is estimated to be 1.1%, and the risk for endometrial cancer is estimated to be about 3.1% (1). Patients who are predicted to have an elevated risk for these cancers based on genetic testing results or family history could be considered potential candidates for prophylactic surgery. However, the magnitude of cancer risk and potential benefit must be weighed against patient-specific surgical risk and morbidity.

There are many different forms of genetic testing, but for detection of inherited cancer syndromes, testing of the individual's germline DNA is the most valuable. Germline DNA is DNA that exists in the chromosomes of every cell of the body and is present in an individual at birth. Germline testing can be performed with blood, buccal swabs, or saliva testing kits. Specimen collection kits are available for mail delivery to aid in patient convenience. Tumor or tissue specimens can also undergo genomic testing, which can reveal potentially actionable DNA mutations that may impact cancer-related treatment decisions. It is imperative to recognize that these somatic results do not reliably reflect the presence or absence of germline mutations. Since cancer cells frequently acquire multiple somatic mutations, the presence or absence of genomic alterations in the tumor cell may or may not reflect a patient's inherited mutation status. It is prudent to follow or pair tumor (genomic) testing with germline testing to confirm the origin of any identified mutations. Furthermore, genomic tumor testing may fail to detect about 10% of clinically actionable pathogenic germline variations such as deletions, duplications, and splicing variants and therefore should not be considered comprehensive testing of the germline (2).

Pretest counseling is imperative prior to any form of genetic testing. Patients should be informed of the basic purpose of the test and understand the relevance of the information that will be received and how the results may impact future care or medical management. Pedigree evaluation including the family history from three generations of relatives on each side of the family should be obtained, with particular emphasis on individuals with cancer, including age at diagnosis. This is critical to ascertain whether a patient meets disease-specific criteria for testing. A summary of testing criteria is provided in Table 37.1. Detailed medical and surgical history for the patient is also relevant to include environmental and occupational exposures and history of hormone or oral contraceptive use. A physical examination is also pertinent, as the urgency of testing is increased if cancer signs or symptoms are present. The cost of genetic testing is important to discuss, though coverage by insurance and healthcare payers is increasing for genetic testing. However, there may be additional costs or copays charged to the patient, and these should be disclosed in pretest financial counseling. Finally, it should be emphasized that although results are private and protected by HIPAA, the results may have implications for a patient's relatives, and patients should consider disclosing any resulting information to their relatives.

Many patients fear negative consequences, such as loss of health or life insurance, if results are abnormal. Current legislation is protective of patients' rights and prevents discrimination based on genetic testing. The Genetic Information Nondiscrimination Act (GINA) of 2008 prohibits insurance companies from determining the eligibility, cost, coverage, or benefits of an insurance policy based on genetic information and prohibits employment discrimination based on genetic information (3).

Due to time constraints, it may not be feasible to cover all these topics within a single visit. Patients with complicated family histories or personal cancer histories should undergo pretest and usually posttest counseling by a certified medical professional, genetic counselor, or geneticist who can perform these aspects of care. Some genetic testing companies provide this as a part of their service.

The decision whether to perform testing is often guided by personal and family history and is highly subjective. There is tremendous choice in testing platforms with increasingly rapid turnaround of results using next generation sequencing technology. Testing panels are often customizable and should be inclusive of all genes that may be relevant to a patient's personal or family history. As the number of tested genes increases, the likelihood of finding a variant of uncertain significance (VUS) increases. Also, some genes that are available for testing have little to no actionable impact. Additionally, when patients have a known inherited pathogenic mutation in their family, multigene testing may still be indicated due to the potential for other pathogenic germline variants within a family. The amount of

DOI: 10.1201/9781003312109-37

TABLE 37.1 Criteria for Genetic Testing

General Testing Criteria
Any blood relative with a known P/LP variant in a cancer susceptibility gene
P/LP variant seen on tumor genomic testing that is actionable if germline as well
Prior negative testing that was limited (e.g., single gene)
To aid in decision making (surgical or systemic therapy)
Consider for any patient with Ashkenazi Jewish ancestry or personal history of USC
OC Susceptibility Genes (*ATM*, *BRCA1*, *BRCA2*, *BRIP1*, *MLH1*, *MSH2*, *MSH6*, *EPCAM*, *PALB2*, *RAD51C*, *RAD51D*). Above general testing criteria plus:
Personal history of OC; FT; or peritoneal cancer; any age
FH of cancer: 1st or 2nd degree blood relative with OC, FT, or peritoneal cancer at any age
FH of cancer: Probability over 5% of a *BRCA1/2* variant based on a probability model
Uterine Cancer Susceptibility Genes (*MLH1*, *MSH2*, *MSH6*, *PMS2*, *EPCAM*)
FH of a LS pathogenic variant
Personal or FH of LS-related cancer
Personal history of mismatch repair deficient (dMMR) tumor
Personal history of a LS-related cancer (CRC, EC, gastric, ovarian, pancreatic, urothelial, brain, biliary tract, small intestine sebaceous carcinoma, keratoacanthoma) diagnosed at < 50 y; or a synchronous or metachronous LS-related cancer regardless of age; or ≥1 1st or 2nd degree relative with LS-related cancer < 50 y; or ≥2 1st degree or 2nd degree relatives with a LS-related cancer regardless of age
FH of ≥1 1st degree with CRC or EC < 50; ≥1 1st degree with CRC or EC and a synchronous or metachronous LS-related cancer regardless of age; ≥2 1st or 2nd degree relatives with LS-related cancers including ≥1 < 50 y; or ≥3 1st or 2nd degree relatives with LS-related cancers regardless of age
Increased model predicted risk for LS (> 5% threshold)

Source: Data from Ref. 20.
Abbreviations: *P*: pathogenic; *LP*: likely pathogenic; *USC*: uterine serous cancer; *OC*: epithelial, nonmucinous ovarian cancer; *FT*: fallopian tube; *FH*: family history; *LS*: Lynch syndrome; *CRC*: colorectal cancer.

financial assistance and coverage for cascade testing of relatives can also vary between testing providers. Sometimes payers have negotiated more economical pricing with specific testing companies and, as such, the decision of which testing provider to utilize is often made outside of the clinician's office and is determined by institutional or organizational agreements. Furthermore, patients may have already undergone commercially available or direct-to-consumer options for genetic testing and ancestry analysis. These findings are not always reliable, as the false positive and false negative rates are high. Any identified mutation and its actionability need to be certified by a laboratory that is College of American Pathologists (CAP) or Clinical Laboratory Improvement Amendments (CLIA) certified. Finally, patients who have obtained germline genomic analysis through a research clinical study should have these reports evaluated by genetics professionals to interpret the need for subsequent confirmatory testing before action is taken on these results.

Posttest counseling is also critical to understand and interpret testing results. The absence of a pathogenic mutation does not signify that the patient has the same risk as the general population, particularly in the case of a strong family history of cancer. It is possible that a pathogenic mutation responsible for cancer in a family has not yet been identified, and so it cannot be detected with germline testing. This is a so-called uninformative negative result. The impact of family history on cancer risk can be difficult to estimate based on the degree of proximity of the family member to the individual and the age of onset of the cancer in the affected family member. Other environmental and personal factors also impact individual risk, including current age, with older age likely indicative of decreased risk. While no perfect algorithm yet weighs each factor, having a first-degree relative with cancer seems to confer particular risk. A meta-analysis of 16 studies determined that the relative risk (RR) of a patient developing endometrial cancer was higher when a first-degree family member had endometrial or colorectal cancer (RR of 1.82 and 1.17, respectively) (4). Similarly, a consortium analysis of over 6000 ovarian cancer patients demonstrated that a first-degree family history of ovarian cancer conferred an increased odds ratio (OR) of developing high-grade serous ovarian carcinoma (OR of 2.32 [95% CI: 1.5–3.59] in black patients and 2.48 [95% 1.82–3.38] in white patients); an association was also present for second-degree family history, but these datapoints were limited (5).

Variants of uncertain significance (VUS) describe a change in DNA sequence whose association with disease risk is not yet known. Reports of VUS are particularly problematic as they may occur in genes without identifiable associations with cancer syndromes or in genes that are known to have other pathogenic variants. They are more likely to occur in racial and ethnic minorities (6). When discussing a VUS, it is relevant to share with the patient that the vast majority, once classified, are reclassified as benign (7). Follow-up with a genetic counselor and testing company is critical to get information about reclassification updates.

Finally, posttest counseling is essential to discuss any detected pathogenic mutations. Information should include an explanation of the exact mutation, associated medical risks, medical management options, potential screening or

TABLE 37.2 Genes with Pathogenic Mutations Associated with Increased Risk for Gynecologic Cancers

Pathogenic Germline Mutation	Estimated Endometrial Cancer Risk	Estimated Epithelial Ovarian Cancer Risk
ATM	No established association	2%–3%
BRCA1	*	39%–58%
BRCA2	*	13%–29%
BRIP1	No established association	5%–15%
EPCAM	40%–60% via MSH2 silencing	10%–20% via MSH2 silencing
MLH1	34%–54%	4%–20%
MSH2/EPCAM	21%–57%	8%–38%
MSH6	16%–49%	1%–13%
PMS2	13%–26%	1.3%–3%
PALB2	No established association	3%–5%
PTEN	17%–39%	No established association
RAD51C	No established association	10%–15%
RAD51D	No established association	10%–20%

* No established association with endometrioid carcinoma of the uterus. *BRCA1* and *BRCA2* may have an increased risk of uterine serous carcinoma.
Source: Data from Ref. 22.

prevention strategies, and referral to specialty clinics that can further counsel patients on options and guide management.

37.3 Pathogenic Mutations in Gynecologic Cancer

Certain identified pathogenic mutations are associated with an increased risk of epithelial ovarian, fallopian tube, and peritoneal cancer (Table 37.2). While these are often described as "ovarian cancer," all are included under the same umbrella of risk. Such pathogenic mutations include founder and other mutations in *BRCA1* and *BRCA2* genes, and certain mutations in the following genes: *ATM*, *BRIP1*, *PALB2*, *RAD51C*, and *RAD51D*. While Lynch syndrome is known for endometrial and colorectal risk, pathogenic mutations in those associated genes also increase the risk of ovarian, tubal, and peritoneal cancer, including *MLH1*, *MSH2*, *MSH6*, and *PMS2*. *EPCAM* does not itself lead to an increased risk of ovarian cancer, but deletions in *EPCAM* lead to epigenetic silencing of the *MSH2* promoter, leading to *MSH2* activation and a 10%–20% lifetime risk of ovarian cancer. When the estimated risk of epithelial ovarian cancer is greater than the population risk of 1%–2%, prophylactic surgery can be considered. Family history is also of consequence when the risk associated with the germline mutation is less pronounced.

The general population risk of endometrial cancer is 3.1%, but patients with Lynch syndrome (*MLH1*, *MSH2*, *MSH6*, *PMS2*, and *EPCAM*) and Cowden syndrome (*PTEN* mutations) are at increased risk of endometrial cancer, with the magnitude of risk dependent on the specific mutation (Table 37.2). There is also mixed data to suggest an increased risk of uterine serous carcinoma in patients with *BRCA1* germline mutations by up to 15-fold and *BRCA2* germline mutations by up to fivefold (8, 9). Cervical cancer susceptibility genomic variants are incompletely understood, and there exists no currently available recommended testing to evaluate this (10).

37.4 Screening for Gynecologic Cancers in High-Risk Patients

Screening for gynecologic cancer in asymptomatic and low-risk women with pelvic ultrasound and CA-125 has been evaluated in several prospective clinical trials, and overall results do not support a reduction in ovarian cancer mortality associated with these strategies. Therefore, routine screening is not supported by national guidelines and is currently acceptable but not recommended (11). While these screening strategies do not reduce ovarian cancer mortality in high-risk women with pathogenic variants, some data suggest a shift toward earlier-stage diagnosis (12). The lack of effective screening strategies supports consideration of risk-reducing surgery at an appropriate age in patients at increased risk for epithelial ovarian cancer. This is specific to the mutation, influenced by family history, and the benefit must be balanced with risks of surgical morbidity and premature menopause in the case of younger patients.

Screening for endometrial cancer in patients with increased risk based on inherited factors has been challenging due to inadequate sensitivity and specificity and can be problematic in premenopausal women due to the dynamic nature of the endometrium throughout the menstrual cycle (13). Endometrial biopsy has been proposed as a potential screening strategy due to its sensitivity and specificity, and national guidelines suggest consideration for endometrial biopsy every 1–2 years starting at age 30–35 for Lynch syndrome patients. Data do not support ovarian cancer screening in patients with Lynch syndrome–associated mutations. Ultrasound and CA-125 levels should be reserved for the preoperative setting (14).

Risk reduction does include suppression of ovulation, such as with contraceptives, and this should be emphasized during the reproductive years prior to any risk-reducing surgery. Oral contraceptive use confers up to a 50% reduction in risk for

ovarian cancer and is recommended by national guidelines for high risk patients (15). The duration of therapy increases the magnitude of benefit.

37.5 Timing of Risk-Reducing Surgery and Hormone Replacement Therapy

Timing of prophylactic surgery varies depending on the clinical situation and depends on the specific gene that carries the pathogenic mutation (Table 37.3). Prophylactic risk-reducing bilateral salpingo-oophorectomy (BSO), with or without hysterectomy, is generally recommended for patients with *BRCA1* mutations between the age of 35 and 40 and upon completion of childbearing. Since the usual onset of cancer in patients with *BRCA2* mutations averages 8 to 10 years later than in patients with *BRCA1* mutations, national guidelines recommend delay of risk-reducing BSO until 40–45 years of age. Family history may justify earlier intervention, as risk-reducing surgery is recommended 5 years prior to the onset of cancer in their family member.

Childbearing should be complete prior to risk-reducing gynecologic surgery. When pathogenic mutations are discovered at an age when risk-reducing surgery would be otherwise appropriate but prior to completion of fertility desires, patients may wish to consider oocyte or embryo cryopreservation and fertility preservation. This allows the cancer risk reduction of prophylactic surgery prior to onset of cancer and still allows childbearing. This can cause significant stress for patients who are struggling to reconcile the timing of surgery with continued desire for fertility.

The consequences of premature menopause are also affected by the timing of the prophylactic surgery, with greater side effects and risk for those who have not yet reached the perimenopausal transition period. Premenopausal patients considering ovarian removal must be counseled on the potential menopausal sequelae, including vasomotor symptoms, decrease in bone density, vaginal atrophy, increased risk of osteopenia and osteoporosis, mental health changes with increased risk of depression and anxiety, sexual dysfunction, and changes in skin, hair, and nails. The association of increased cardiovascular disease with premature menopause has been hotly debated, and the data are inconclusive at this time (16).

Patients who are not found to have an invasive malignancy at the time of prophylactic surgery and who also do not have a history of hormone receptor positive breast cancer can be candidates for hormone replacement therapy following risk-reducing surgery. This does not diminish the benefit of risk-reducing surgery and does not increase the risk of subsequent cancer. If a hysterectomy is simultaneously performed, the patient can receive estrogen only, but if the uterus is left in place and only a BSO is performed, progesterone or a progestin-containing IUD must be given with estrogen to prevent uterine cancer. Conversely, if a patient does have a history of hormone receptor–positive breast cancer, hormone replacement therapy is not usually considered, but hysterectomy may be useful to simplify the use of endocrine therapy, as tamoxifen increases the risk of uterine cancer. That risk can be eliminated with hysterectomy.

Patients with pathogenic mutations in *BRCA1* and *BRCA2* have an increased risk of uterine serous carcinoma, so hysterectomy may also be beneficial for that reason at the time of risk-reducing BSO (8, 9). However, a systematic review was insufficient to provide strong evidence in favor of performing routine hysterectomy at the time of risk-reducing BSO in the setting of germline *BRCA* mutation. Taken together, these data are useful to counsel patients about potential risks and to decide on surgical preferences (17). This is an individualized decision, is not automatic, and should be weighed with the low but present risk of surgical morbidity associated with adding a hysterectomy to a BSO.

While the etiology of ovarian cancer is not well understood, data suggest that the fallopian tube may be the site of origin for some ovarian cancers, particularly those of high-grade serous histology. Modeling data support the concept that the incidence of ovarian cancer may be decreased with salpingectomy, suggesting uptake of opportunistic salpingectomy at the time of hysterectomy, tubal sterilization, and other procedures to decrease the incidence of ovarian and fallopian tube cancer. This remains theoretical at present. Most sources suggest that salpingectomy at time of hysterectomy does not significantly increase surgical risk or complications and does not impact ovarian hormonal output or ovarian hormone reserve as measured by anti-Müllerian hormone levels when compared to hysterectomy alone (18, 19). However, a Swedish registry-based study found a 33% higher risk of menopausal symptoms 1 year after surgery in women who had hysterectomy with bilateral salpingectomy compared to hysterectomy alone (adjusted RR 1.33; 95% confidence interval 1.04–1.69) (19).

At the time of this publication, prophylactic bilateral salpingectomy prior to performing a risk-reducing oophorectomy is not considered an acceptable standard of care for patients with increased risk of ovarian cancer. However, the pathologic understanding that ovarian cancer precursors may develop

TABLE 37.3 Timing of Risk-Reducing Surgery

Affected Gene Mutation	Recommended Surgical Intervention
ATM	Insufficient evidence for RRSO, manage based on family history
BARD1, CDH1, CDKN2A, CHEK2, NF1, PTEN, STK11, TP53	No established association, no intervention
BRCA1	RRSO ± hysterectomy age 35–40 y
BRCA2	RRSO ± hysterectomy age 40–45 y
BRIP1, PALB2, RAD51C, RAD51D	RRSO ± hysterectomy age 45–50 y
MLH1, MSH2, EPCAM	Hysterectomy + BSO age 40 y
MSH6	Hysterectomy + BS age 40 y with delayed oophorectomy age 50 y
PMS2	Hysterectomy + BSO age 50 y

Abbreviations: *BSO*: bilateral salpingo-oophorectomy; *y*: years.

in the fallopian tube has led to early salpingectomy as a preventive strategy. This is currently under investigation in the multi-institution collaborative network SOROCK study, where patients with a *BRCA1* mutation undergo prophylactic salpingectomy and are then followed long-term with delayed oophorectomy. It remains under investigation and should not be used as an effective or safe preventive strategy outside of a clinical trial.

For patients with Lynch syndrome, cost-effectiveness models support the practice of concurrent total colectomy with hysterectomy with or without BSO (20).

37.6 Risk-Reducing Surgery

When offering a risk-reducing surgery, it is important to rule out incidental cancer prior to entering the operating room. This includes relevant physical examination, imaging, and diagnostic studies prior to surgery, focusing on any patient symptoms. Given the rate of occult carcinomas discovered at the time of prophylactic surgery in BRCA patients, preoperative ultrasound with or without Ca 125 is recommended (14, 15).

The surgeon should note that an incidental visible cancer may be discovered during the procedure, or an occult cancer could be reported on final pathology. Upon entering the abdomen, a full abdominal and pelvic survey should be performed to include evaluation of the abdominal and pelvic peritoneal surfaces and the texture and mobility of the omentum, liver, stomach, and diaphragms. Cytologic washings are performed with normal saline to be utilized in staging should an incidental cancer be found. It is unlikely to identify isolated positive washings in the absence of other malignancy.

When the adnexae are removed, the entire ovary must be removed. This is facilitated by entering the retroperitoneum by incising the pelvic peritoneum lateral to the adnexa, skeletonizing the infundibulopelvic ligament, and performing a full dissection of the vasculature to the pelvic brim. This allows complete visualization of the ureter as it traverses the pelvic brim and allows elongation of the ovarian vasculature. Two centimeters of the infundibulopelvic ligament are resected proximal to the ovaries to decrease the chance of ovarian remnant syndrome (21). Adhesive disease from prior surgery, endometriosis, or radiation may limit the extent of resection. The entire fallopian tube must be removed, taking care to fully clamp or seal the proximal tube and utero-ovarian ligament at the uterine origin to eliminate any source of bleeding if the uterus is left in situ.

When possible, minimally invasive surgery is advised for BSO with or without simple hysterectomy. The patient's anatomy, previous surgical history, and uterine size guide the surgical approach. Endometrial biopsy prior to prophylactic surgery for patients at high risk for endometrial cancer is advised to avoid removing an incidental endometrial cancer without appropriate surgical staging. Lymphatic mapping with sentinel lymph node biopsy is the standard approach for surgical staging of endometrial cancer and requires preoperative identification of uterine cancer to prevent the need for full pelvic and para-aortic lymphadenectomy. If endometrial sampling is not possible, intraoperative pathology can be requested, and an incidental finding of endometrial cancer may prompt a full staging procedure.

All specimens that are removed via port sites should be removed by contained extraction to minimize the chance of a port site recurrence should incidental cancer be found within the specimen and to keep the ovarian epithelium intact for pathology examination. Alternatively, specimens can be removed vaginally, but contained extraction should still be used.

Current national guidelines recommend performance of the Sectioning and Extensively Examining the FIMbriated End (SEE-FIM) protocol when evaluating the ovary and the fallopian tube (15). This involves longitudinal sectioning of the fallopian tube as well as complete evaluation and submission of the fallopian tube and ovary for pathologic assessment rather than limited sectional sampling. Performance of this thorough evaluation has increased the recognition and identification of serous tubal intraepithelial lesions (STIL) and serous tubal intraepithelial carcinoma (STIC), which are identified as cancer precursors in the fimbriated end of the fallopian tube. STIL are considered precancerous and are thought to precede the development of STIC. STIC lesions are often found concurrently at the time of diagnosis of invasive cancer or can be found on the ipsilateral fallopian tube adjacent to an ovarian cancer. There is no established standard of care for management of these lesions. Possible management options include a return to the operating room for complete staging surgery with possible hysterectomy if not already performed and consideration of adjuvant chemotherapy following surgery. In addition, aberrant P53 signatures in the fallopian tube are not yet actionable and are found in normal fallopian tubes in patients without disease.

Key Points

The reality is that we do not have complete information and ability to predict a patient's individualized risk of developing cancer regardless of germline genetic predisposition. Individual factors, environmental factors, and the penetrance of genetic mutations play a role. However, significant reduction in risk can be provided by education, genetic testing, cascade testing of family members, screening, and risk-reducing surgery. Consideration of these interventions should involve shared decision making between the patient and the medical team.

References

1. *NIH seer program, cancer stat facts* [Internet]. 2025. Available at: https://seer.cancer.gov/statfacts/html/ovary.html (Accessed May 2025).
2. Terraf P et al. Comprehensive assessment of germline pathogenic variant detection in tumor-only sequencing. *Ann Oncol*. 2022;33(4):426–433.
3. *U.S Department of Health and Human Services, genetic information* [Internet]. 2025. Available at: www.hhs.gov/hipaa/for-professionals/special-topics/genetic-information/index.html (Accessed May 2025).
4. Win AK et al. Family history and risk of endometrial cancer: a systematic review and meta-analysis. *Obstet Gynecol*. 2015;125(1):89–98.
5. Bethea TN et al. First- and second-degree family history of ovarian and breast cancer in relation to risk of invasive ovarian cancer in African American and white women. *Int J Cancer*. 2021;148(12):2964–2973.
6. Kurian AW et al. Time trends in receipt of germline genetic testing and results for women diagnosed with breast cancer or ovarian cancer, 2012–2019. *J Clin Oncol*. 2021;39(15):1631–1640.
7. Mersch J et al. Prevalence of variant reclassification following hereditary cancer genetic testing. *JAMA*. 2018;320(12):1266–1274. https://doi.org/10.1001/jama.2018.131528.

8. de Jonge MM et al. Linking uterine serous carcinoma to BRCA1/2-associated cancer syndrome: a meta-analysis and case report. *Eur J Cancer*. 2017;72:215–225.
9. de Jonge MM et al. Endometrial cancer risk in women with germline BRCA1 or BRCA2 mutations: multicenter cohort study. *J Natl Cancer Inst*. 2021;113(9):1203–1211.
10. Ramachandran D et al. Genomic risk factors for cervical cancer. *Cancers (Basel)*. 2021;13(20).
11. Henderson JT et al. Screening for ovarian cancer: updated evidence report and systematic review for the US preventive services task force. *JAMA*. 2018;319(6):595–606.
12. Rosenthal AN et al. Evidence of stage shift in women diagnosed with ovarian cancer during phase II of the United Kingdom familial ovarian cancer screening study. *J Clin Oncol*. 2017;35(13):1411–1420.
13. *ACR – ACOG – AIUM – SPR – SRU practice parameter for the performance of ultrasound of the female pelvis* [Internet]. 2024. Available at: https://gravitas.acr.org/PPTS/DownloadPreviewDocument?ReleaseId=2&DocId=63 (Accessed May 2025).
14. *National comprehensive cancer network genetic/familial high-risk assessment: colorectal, endometrial, and gastric* [Internet]. 2024. Available at: www.nccn.org/guidelines/guidelines-detail?category=2&id=1544 (Accessed May 2025).
15. *National Comprehensive Cancer Network genetic/familial high-risk assessment: breast, ovarian, pancreatic, and prostate* [Internet]. 2025. www.nccn.org/professionals/physician_gls/pdf/genetics_bopp.pdf (Accessed May 2025).
16. Uddenberg ER et al. Menopause transition and cardiovascular disease risk. *Maturitas*. 2024;185:107974.
17. Gasparri ML et al. Endometrial cancer and BRCA mutations: a systematic review. *J Clin Med*. 2022;11(11).
18. Collins E et al. Menopausal symptoms and surgical complications after opportunistic bilateral salpingectomy, a register-based cohort study. *Am J Obstet Gynecol*. 2019;220(1):85 e81–85 e10.
19. Findley AD et al. Short-term effects of salpingectomy during laparoscopic hysterectomy on ovarian reserve: a pilot randomized controlled trial. *Fertil Steril*. 2013;100(6):1704–1708.
20. Ofshteyn A et al. Prophylactic gynecologic surgery at time of colectomy benefits women with lynch syndrome and colon cancer: a Markov cost-effectiveness analysis. *Dis Colon Rectum*. 2020;63(10):1393–1402.
21. Mallen A et al. Surgical prevention strategies in ovarian cancer. *Gynecol Oncol*. 2018;151(1):166–175.
22. Tan MH et al. Lifetime cancer risks in individuals with germline PTEN mutations. *Clin Cancer Res*. 2012;18(2):400–407.

38 ADNEXAL MASSES

Tullia Rushton, Rebecca L. Stone, and Amanda N. Fader

38.1 Introduction

Adnexal masses arise in women of all ages and are among the most frequently encountered clinical scenarios by gynecologists. Approximately 10% of women will be diagnosed with a pelvic mass in their lifetimes (1, 2), though the prevalence is likely higher among asymptomatic pre- and postmenopausal women (3). The differential diagnosis for an adnexal mass diagnosed by pelvic exam, imaging, or a combination of the two is broad but can typically be narrowed after consideration of the patient's presenting history, past medical history, physical exam, morphologic features, and ancillary labs.

The incidence of ovarian cancer in the United States is estimated at 10.3 per 100,000 women per year (4). While most adnexal masses are either benign or spontaneously resolve, as observed on serial imaging (3), the challenge for the gynecologist lies in determining when to intervene surgically.

A definitive diagnosis is typically confirmed only after surgical management. However, the diagnostic workup can inform operative strategy, from port placement and specimen removal to consultation with minimally invasive or gynecologic oncology subspecialists. This chapter will describe surgical planning and techniques for a minimally invasive approach to adnexal masses. Relevant aspects of perioperative care will be reviewed as well.

TABLE 38.1 Differential Diagnosis for a Pelvic Mass

Gynecologic causes – benign	• Functional cyst • Corpus luteum cyst • Hemorrhagic ovarian cyst • Paratubal cyst • Endometriosis/endometrioma • Mature teratoma • Serous or mucinous cystadenoma • Borderline ovarian tumor • Hydrosalpinx/pyosalpinx • Fibroid/fibroma • Ectopic pregnancy • Ovarian torsion
Gynecologic causes – malignant	• Epithelial tumors • Sex-cord stromal tumors • Germ cell tumors
Non-gynecologic causes	• Pelvic inflammatory disease (PID) • Tubo-ovarian abscess (TOA) • Appendiceal abscess • Peritoneal inclusion cyst • Diverticulosis/diverticulitis • Ureteral diverticulum • Pelvic kidney • Nerve sheath tumor • Metastases from a non-gynecologic malignancy

38.2 Preoperative Assessment

When determining whether surgical management for a patient with an adnexal mass is indicated, the gynecologist must consider not only the size and morphologic features on imaging but also pertinent symptoms, past medical and family histories, physical exam findings, and blood work. Synthesis of these elements is critical to formulating the best approach for each patient.

38.2.1 Initial Patient Evaluation

Presenting symptoms that subsequently prompt a pelvic exam or imaging can vary widely and include abdominopelvic pain (cyclic, intermittent, or sustained), pelvic fullness or bloating, changes in urinary or gastrointestinal function, fever, and abnormal uterine bleeding (5). However, patients can also be asymptomatic with initial detection of an adnexal mass on routine pelvic examination (6, 7) or incidentally on imaging obtained for a separate indication (8–10). To complement a patient's initial presentation and physical exam findings, a thorough assessment of past medical history, such as diverticulosis/diverticulitis and sexually transmitted infections, as well as past surgical history potentially predisposing to a peritoneal inclusion cyst masquerading as a cystic adnexal mass, can help determine proper imaging modality and narrow the differential diagnosis (Table 38.1). Patients should also be asked about any personal or family history of ovarian or breast cancer.

38.2.2 Preoperative Imaging

While valuable information can be gleaned from the physical exam, the imaging features of an adnexal mass are crucial in determining its origin and appraising the risk of borderline or invasive disease. Features most consistent with a benign etiology include simple, fluid-filled cysts that are homogenous or have thin septations (11, 12).

Certain benign adnexal masses display classic features. Endometriomas, for example, often have homogenously dispersed echogenic cystic contents ("ground-glass") or the "kissing-ovaries" sign, which may indicate the presence of pelvic endometriotic implants and adhesive disease (12, 13). Mature teratomas are associated with Rokitansky nodules (indicating the presence of calcifications and teeth) and either thin, band-like, or dense echogenicity. The presence of fat inside an ovarian tumor appears to be specific to ovarian cystic teratoma. Transvaginal ultrasonography has a greater than 95% specificity in diagnosing mature teratomas (14).

When a pelvic mass noted on imaging is coupled with systemic signs of infection, providers should look closely for features consistent with a pyosalpinx or tubo-ovarian abscess (TOA). Ultrasound identifies a pyosalpinx as a dilated, fluid-filled, and folded tubular structure in the adnexa (15). In contrast, TOAs often manifest as multilocular cystic masses with thick, rim-enhancing irregular walls with possible associated gas and bowel wall thickening (16). A right-sided TOA may mimic or be associated with appendicitis, and a left-sided TOA should trigger suspicion for complicated diverticulitis involving the sigmoid colon.

An ectopic pregnancy should be suspected in patients with positive serum or urine pregnancy tests in the context of a new adnexal mass without evidence of an intrauterine pregnancy.

DOI: 10.1201/9781003312109-38

Common ultrasonographic findings that support an ectopic pregnancy include the presence of a gestational sac or fetal pole outside of the uterine cavity or a complex adnexal mass, often noted to move independently from the adjacent ovary. A "tubal-ring" sign can also be visualized and is characterized by a hyperechoic ring around the gestational sac (17).

Thick papillary excrescences or projections, increased vascularity, and presence of both solid and cystic components, as well as associated abdominopelvic ascites or peritoneal carcinomatosis, should raise suspicion for malignancy, triggering collection of tumor markers and referral to a gynecologic oncologist (18–20).

38.2.3 Ovarian Torsion

Ovarian torsion should be the differential diagnosis for patients with sudden onset abdominopelvic pain often accompanied by low-grade fever as well as nausea and vomiting. Though technically a clinical diagnosis, torsion can occasionally present as a new adnexal mass on imaging. Additional ultrasonographic features that may support a clinical diagnosis of torsion include ovarian edema, a "whirlpool" sign (twisting of the ovarian pedicle), and the absence of Doppler flow to the ovary (21). Patients with pelvic masses greater than 5 cm incur a greater risk for torsion (22, 23). Ovarian torsion is a surgical emergency, and prompt intraoperative assessment and detorsion of the ovary are crucial in preserving ovarian function.

38.2.4 Imaging Modality

Transvaginal ultrasound (or transabdominal ultrasound for patients who cannot tolerate transvaginal scans) is typically the modality for initial imaging of an adnexal mass. In addition to providing optimal images of the pelvic viscera, ultrasound is quick, cost-effective, and noninvasive and avoids the risks associated with contrast and radiation exposure (24, 25).

However, the main limitations of ultrasound are that quality is contingent upon operator experience and that interpretation without the addition of other clinical data can be challenging. Evidence of extraovarian disease can be better visualized on a CT scan. MRI can be beneficial if the origin of the lesion in question is uncertain on ultrasound (25).

38.2.5 Tumor Markers and Other Labs

For patients with adnexal masses demonstrating complex features on imaging, serum tumor markers can help stratify the risk of a malignant process and determine whether consultation with a gynecologic oncologist is indicated. In addition to the complexity of the mass, the presence of ascites or carcinomatosis, as well as a history of familial breast and ovarian cancer syndrome, should prompt providers to obtain a CA-125 level, which is classically associated with epithelial ovarian cancer. However, the CA-125 may be falsely elevated in patients with endometriosis, pelvic inflammatory disease, or diverticulitis. Select decision-making algorithms that incorporate multiple serum studies in addition to CA-125, such as the Risk of Ovarian Malignancy Algorithm (ROMA) and a multivariate index assay (OVA1), are commonly used to identify high-risk patients and to triage the need for gynecologic oncology referral. Importantly, these tools complement a clinician's diagnostic workup and are not intended for ovarian cancer screening (26–29). Depending on the overall clinical picture, other tumor markers can also be collected with a CA-125, as detailed in Table 38.2.

Other serum labs, such as a complete blood count, could be useful adjunctive studies when evaluating an adnexal mass.

TABLE 38.2 Tumor Markers That Could Aid in Diagnosing a Pelvic Mass

Tumor Markers	Classically Associated Malignancy
CA-125	Epithelial ovarian/fallopian tube cancer Primary peritoneal cancer
AFP	Yolk sac tumor Immature teratoma
LDH	Dysgerminoma Immature teratoma Yolk sac tumor
β-hCG	Dysgerminoma Choriocarcinoma
Inhibin A/B	Granulosa cell tumor
CEA	Gastrointestinal cancer
CA 19–9	Pancreatobiliary cancer

Abbreviations: *CA-125*: cancer antigen 125; *AFP*: alpha-fetoprotein; *LDH*: lactate dehydrogenase; *β-hCG*: beta human chorionic gonadotropin; *CEA*: carcinoembryonic antigen; *CA 19–9*: cancer antigen 19–9.

An elevated serum β-hCG is highly suspicious for an ectopic pregnancy until proven otherwise. Downtrends in hemoglobin could be representative of a ruptured hemorrhagic ovarian cyst or granulosa cell tumor. Additionally, elevations in white blood count and/or lactic acid in combination with clinical and radiographic data should prompt consideration of the diagnosis of ovarian torsion or obtaining testing for sexually transmitted infections and start broad-spectrum antibiotics to treat TOA/pelvic inflammatory disease or diverticulitis empirically.

38.2.6 Surveillance

Surveillance with serial imaging is reasonable for benign-appearing adnexal masses in the setting of relatively minimal symptoms. An asymptomatic patient of any age with a simple cyst up to 10 cm and with a normal CA-125 can be observed with serial imaging (5). While beyond the scope of this text, several algorithms can be used to assist in triaging patients toward either requesting referral to a subspecialist or proceeding with surgical management (18, 30, 31). Ultimately, proceeding to the operating room for management of an adnexal mass must occur with shared decision making with the patient after counseling about benefits, alternatives, and possible risks, which can include the necessity of oophorectomy.

38.2.7 Surgical Planning

After deciding to proceed with surgical exploration and removal of an adnexal mass, the gynecologist must decide on a surgical approach. Given shorter recovery times, decreased duration of hospital stay, improved postoperative pain control, and increased overall patient satisfaction, a minimally invasive approach should be prioritized if feasible (32, 33).

Most adnexal lesions can be removed via a minimally invasive approach, accomplished with traditional straight-stick laparoscopy or robotics (34). While most adnexal masses can be removed with traditional laparoscopy, there are no data to suggest any benefit of either ovarian cystectomy or oophorectomy using conventional laparoscopy compared to a robotic approach (35). However, surgeons may prefer robotic-assisted laparoscopy, given the 3D visualization and more comprehensive range of instrumental motion when a more meticulous surgical dissection is anticipated, as can be the case for patients at

increased risk for adhesions (36, 37). This subgroup of patients often includes those with extensive past surgical histories or histories of prior pelvic inflammation, as is the case for endometriosis, pelvic inflammatory disease, and diverticulitis.

Furthermore, ovarian cystectomy or oophorectomy in morbidly obese patients, for whom straight-stick laparoscopy can be ergonomically challenging, can often be safely accomplished robotically (38). Regardless, patients must be able to tolerate both abdominal insufflation and Trendelenburg position for the duration of the procedure to enable safe visualization of pelvic anatomy.

No definitive criteria dictate a minimally invasive versus open approach to surgical management of an adnexal mass, and the selected approach is often dependent on the surgeon's comfort level. Limited prospective data suggest that adnexal lesions measuring greater than 10 cm can be safely removed with a minimally invasive approach (39, 40). In addition to the size of the adnexal mass, factors that may drive conversion to laparotomy include abdominopelvic adhesive disease, patient intolerance of abdominal insufflation or steep Trendelenburg position, inability to control active bleeding, intraoperative injury to surrounding structures, inability to remove the mass intact, or presence of disseminated disease indicative of a malignant process (41–43).

In select cases when a patient is hemodynamically unstable, as can be the case with a ruptured ectopic pregnancy, hemorrhagic cyst, or pelvic abscess, rapid abdominal entry via laparotomy may be necessary, allowing for maximal visualization.

Coordinating surgical backup by or referral to a gynecologic subspecialist, such as a minimally invasive gynecologic surgeon or gynecologic oncologist, should be considered for patients whose preoperative workup raises suspicion for either significant abdominopelvic inflammation and adhesions (especially in the case of severe endometriosis) or an invasive process.

38.3 Intraoperative Technique

38.3.1 Abdominal Entry

While the core tenets for laparoscopic or robotic entry pertain to the evaluation and removal of an adnexal mass, there are several key considerations the surgeon should be mindful of during port placement. Using a periumbilical or left upper quadrant port site to gain intra-abdominal access and subsequent insufflation is reasonable. However, placing lateral ports more cranial than typical practice can help manipulate a sizeable adnexal mass. Further, the surgeon should anticipate which port site, if not using a small Gelport® system, would be ideal for specimen extraction and possible fascial extension. Additionally, an access point that allows for easy interchange between 0° and 30° scopes can aid in maximizing visualization of the adnexal mass and surrounding structures.

Excluding patients with diagnostic findings of an ectopic pregnancy or pelvic infection, gynecologists should obtain pelvic washings after the initial abdominopelvic survey, to include visualization of the upper abdomen, paracolic gutters, omentum, and the small and large bowel. Pelvic washings are a critical aspect of surgical staging when final pathology reveals a malignancy of the ovary or fallopian tube.

38.3.2 Ovarian Cystectomy

For cystic adnexal masses arising from the ovary, the surgeon must determine whether ovarian cystectomy is feasible, safe, and desired by the patient. This may be a priority for premenopausal women who desire fertility preservation. Cystectomy is also preferable for cystic ovarian masses demonstrating benign features and a good opportunity for preservation of normal ovarian stroma, particularly given mounting evidence of endocrine benefit from ovarian preservation up until age 65 (44, 45). Cystectomy alone is not appropriate for patients with invasive ovarian cancer and does not constitute a staging procedure.

An incision in the capsule of the ovarian stroma overlying the cyst should be made either sharply or with the use of electrocautery. The cyst wall is then bluntly separated and shelled out from the surrounding ovarian stroma, employing traction and countertraction with a surgical assistant and sequentially extending the incision in the capsule as required for the dissection. Techniques that avoid cyst rupture should be prioritized. Excising the cyst intact maintains a more precise delineation between the normal ovary and cyst wall and prevents surgical spill. Gynecologic surgeons should remain vigilant in assessing anatomic proximity to the infundibulopelvic ligament, housing the gonadal vessels, during cystectomy to avoid inadvertent bleeding and compromising the blood supply to the remaining ovary. Ideally, the entirety of the cyst wall should be excised with the specimen, as this can decrease the risk of cyst reformation in the future (Figure 38.1).

After excision of the cyst, hemostasis is typically achieved with delayed absorbable suture, electrocautery, or topical hemostatic agents. While no data suggest any benefit to using topical hemostatic agents compared to suture, the use of bipolar electrocautery has been shown to negatively impact postoperative AMH levels and ovarian reserve (46, 47). Thus, the use of bipolar electrocautery should be minimized.

38.3.3 Oophorectomy

If ovarian preservation is neither technically feasible nor desired per patient preference, the gynecologic surgeon can alternatively proceed with a unilateral oophorectomy to remove an ovarian mass. The infundibulopelvic and utero-ovarian ligaments must be divided, for which the authors typically use a vessel-sealing device. Definitive identification of the ipsilateral ureter, either via transperitoneal or retroperitoneal approaches, should be done before transection of the gonadal blood supply.

38.3.4 Specimen Removal

After complete excision of the adnexal lesion, attention is turned toward specimen removal. Smaller adnexal masses can typically be removed through one of the existing port sites with or without a laparoscopic specimen retrieval bag and with fascial extension as needed.

Removal of larger adnexal masses poses several challenges, including avoiding cyst rupture and surgical spill while maintaining as small an incision as possible. For patients whose final pathology confirms borderline or invasive histology, inadvertent cyst rupture within the abdominal cavity is an independent prognostic factor for disease-free survival (48) and automatically increases the oncologic stage.

Various strategies to minimize the likelihood of intraoperative cyst rupture have been described. Adnexal masses can be placed within laparoscopic specimen retrieval bags, after which they can be brought to the anterior abdominal wall. Fascial extension using an Alexis® retractor not only helps with intra-abdominal visualization but also functions as an added barrier to cyst contents at the time of removal (49). With the opening of the specimen retrieval bag exteriorized at the

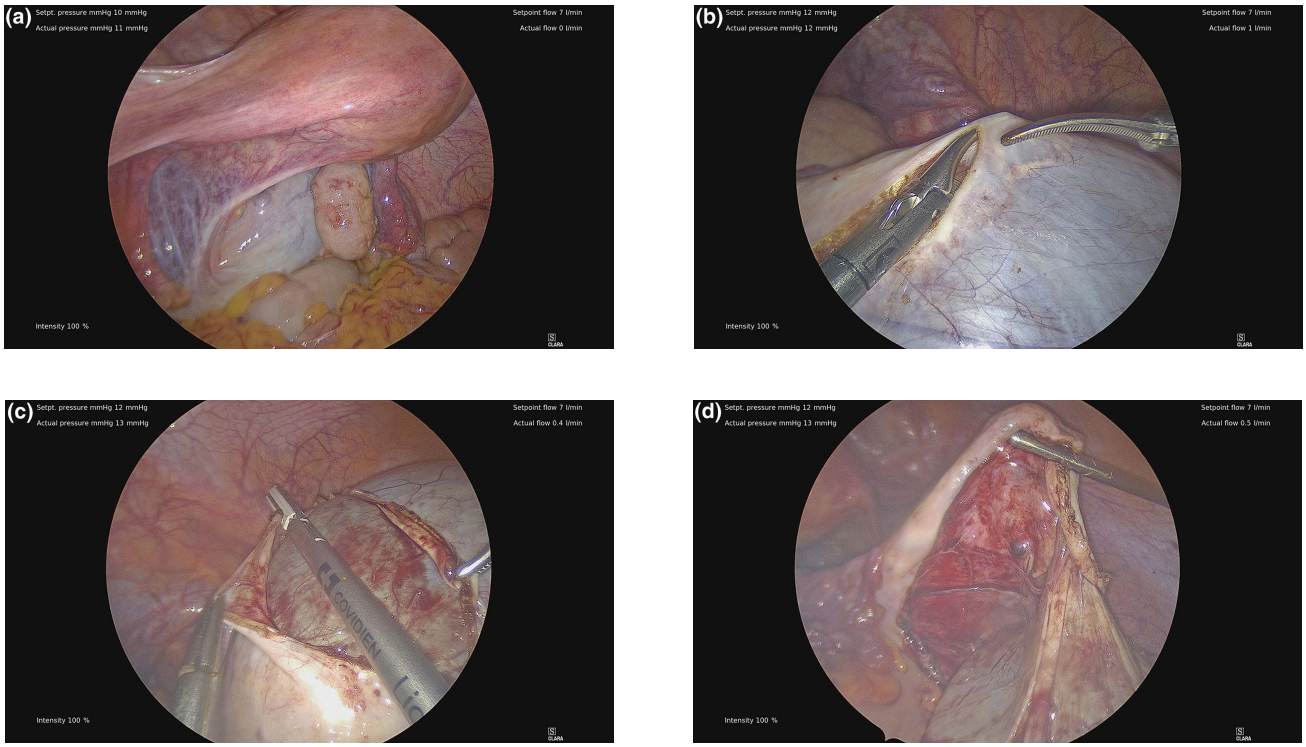


FIGURE 38.1 A broad overview of the steps of a laparoscopic ovarian cystectomy. (a) This patient has a large left ovarian mass positioned posterior to the uterus. A normal-appearing right ovary is also visible. (b) To begin the ovarian cystectomy, a small incision using either sharp scissors or electrocautery is made, after which the surgeon can begin to dissect the cyst wall free from normal ovary. (c) Traction and countertraction are used to separate the cyst and ovary, avoiding cyst rupture and inadvertent injury to the gonadal vessels. (d) This is done until the cyst wall is completely dissected from the remaining normal ovary. The remaining ovary is then reapproximated with a delayed-absorbable suture for hemostasis.

anterior abdominal wall and the intact cyst visualized, a small incision can be made in the cyst followed by quick placement of a suction-irrigator device, which ultimately decompresses the cyst and facilitates its contained removal. Using a purse-string maneuver around the intentional puncture site along the cyst wall has also been described to further minimize surgical spill (50–52). The suction irrigator used to evacuate the cyst should not be reintroduced into the abdominal cavity to avoid seeding the cavity if the mass represents an occult malignancy.

38.3.5 Utilization of Frozen Pathology Intraoperatively

Pathologists skilled in the preparation and interpretation of intraoperative frozen section can be a tremendous asset to gynecologic surgical practice. Several studies have documented high concordance rates between the preliminary frozen section and final pathology result, with specificity greater than 90%. Sensitivity appears to vary more widely, and concordance rates are lower for patients diagnosed with a borderline ovarian tumor on final pathology (53, 54). Naturally, reliable access to a pathologist adept at interpreting frozen sections for gynecologic pathology may be limited depending on practice location. Therefore, providers may rely on gross inspection of an adnexal mass to deduce whether surgical staging is warranted.

38.3.6 Tubo-Ovarian Abscess

Standard care management of tubo-ovarian abscesses for hemodynamically stable patients entails conservative measures with intravenous broad-spectrum antibiotics. However, recent data indicate better outcomes for patients who undergo early (less than 48 hours from diagnosis) surgical intervention, defined as drainage of the abscess surgically or under image guidance (55). For patients without evidence of abscess rupture, minimally invasive drainage should be prioritized, with image-guided drainage having slightly higher success rates (96%–100%) than laparoscopic drainage (89%–96%). Still, both are associated with improved outcomes compared to antibiotics alone (65%–83%) (56).

Endeavors to completely resect the abscess cavity is one mainstay of surgical management, acknowledging that tissue planes are likely to be distorted and friable due to associated inflammation and adhesions. Laparotomy is the recommended approach for cases of abscess rupture and/or hemodynamic instability (16, 57). Warm, sterile saline for irrigation should be liberally used before abdominal closure. For patients with severe intrapelvic infections or recurrent cases refractory to medical management, removal of one or both ovaries, with or without concurrent hysterectomy, may be necessary at the time of surgery. Importantly, there should be a lower threshold for oophorectomy and hysterectomy for postmenopausal patients presenting with a new TOA given an increased risk of associated malignancy (estimated at 47%) compared to premenopausal women (1%) (58).

Placement of either a Jackson–Pratt or Blake drain and an incisional wound vacuum (for larger incisions) can also be considered at the discretion of the primary surgeon.

Intra-abdominal bacterial and fungal cultures should be sent during surgery, which can help de-escalate from broad-spectrum antibiotics to a more tailored regimen postoperatively. Historically, a 14-day course of antibiotics has been the recommended treatment duration for TOA or pelvic inflammatory disease. Recent findings from the Study to Optimize Peritoneal Infection Therapy (STOP-IT) trial revealed no differences in outcomes for patients with a more limited 4-day course of antibiotics after intra-abdominal gastrointestinal source control (59). While interesting, the feasibility of a de-escalated approach to antibiotics in gynecologic patients with complex infections remains to be seen.

38.3.7 Ovarian Torsion

Surgery is the recommended treatment for patients clinically suspected to have ovarian torsion, with a relatively recent emphasis on the prioritization of ovarian preservation for premenopausal women (5, 60). This practice change is based on evidence that surgeons often incorrectly conclude during the index case that only necrotic ovarian tissue is present; both final pathology following oophorectomy (61) and subsequent reassessment of ovarian viability either on ultrasound or in follow-up laparoscopy among patients with conserved necrotic-appearing ovaries highlight the inconsistencies of intraoperative and postoperative assessment (62).

After identifying the affected adnexa upon abdominal entry, the surgeon should gently untwist the ovarian pedicle and then thoroughly inspect both the ovary and fallopian tube. Cystectomy can safely be completed at the time of ovarian detorsion. However, surgeons may opt for a staged procedure, deferring cystectomy until later, if ovarian parenchyma is particularly edematous and congested. There has been no evidence to support any increased risk of a postoperative thromboembolic event following detorsion of the ovarian pedicle, which is low at 0.2% (63, 64).

Oophoropexy following a patient's first ovarian detorsion is unlikely to be beneficial in preventing recurrent torsion (65, 66). However, there are some limited data to support oophoropexy for patients with recurrent ovarian torsion (67, 68). If oophoropexy is deemed necessary following detorsion, plication of the utero-ovarian ligament or fixation of the ovary to the round ligament, uterus, pelvic sidewall, or the uterosacral ligament can be done.

38.3.8 Adnexal Masses in Pregnancy

Adnexal masses in pregnancy are often incidentally discovered during routine obstetric imaging in the first trimester. Most adnexal masses diagnosed during pregnancy spontaneously resolve (68%–72% by 6 weeks postpartum) or are benign on final pathology, with dermoid cysts being the most common (32%), followed by endometriomas (15%) and functional cysts (12%). Provided the patient is asymptomatic and the mass has benign morphologic features on imaging, observation through delivery and postpartum can be feasible in collaboration with the patient's obstetrician and/or maternal–fetal medicine specialist (69–71).

Indications for surgical management of adnexal masses in pregnancy include intractable discomfort, which could indicate torsion or peritonitis from rupture and features on ultrasound or noncontrast MRI that raise suspicion for malignancy. However, the incidence of malignancy is low (1%–8%) in this patient population. Certain tumor markers commonly ordered in the workup of a new adnexal mass can be falsely elevated and thus unreliable during pregnancy. CA-125, often during the first trimester, and β-hCG, AFP, and LDH have documented elevations during routine antepartum courses (72, 73).

Nonemergent laparoscopy during the second trimester has classically been recommended given the completion of fetal organogenesis and a less encumbered view of the pelvic structures than occurs with a third-trimester gravid uterus. Beyond an increased risk of spontaneous miscarriage, several studies have not demonstrated any increase in adverse outcomes for patients undergoing laparoscopy in the first or third trimesters (74–77). Furthermore, laparoscopy in pregnancy has demonstrated decreases in postoperative pain, length of hospital stay, bleeding, and preterm contractions (78, 79).

While contingent on the size of the gravid uterus, placement of the initial port at Palmer's point is generally recommended. Thereafter, all remaining ports can be placed under direct visualization, thus minimizing risk of uterine injury while simultaneously optimizing port location with respect to anatomy (80). Placement of a uterine manipulator is contraindicated in pregnancy; in fact, manipulation of the gravid uterus is often unnecessary and discouraged. While the ideal insufflation pressure during a gravid laparoscopic procedure is undetermined, a goal intra-abdominal pressure of 10–12 mmHg is recommended to minimize difficulties with maternal ventilation intraoperatively. While some animal studies have reported uteroplacental perfusion with higher intra-abdominal pressures (81), a recent, small series demonstrated no change in uterine resistance index, umbilical artery pulsatility index, or fetal heart rate measured by transvaginal ultrasound intraoperatively (82). No adverse obstetric outcomes have been documented using monopolar or bipolar electrocautery (76, 78, 79).

Finally, patients in the second and third trimesters should be placed in the left lateral decubitus position to minimize IVC compression of the gravid uterus intraoperatively. Pre- and postoperative measurement of the fetal heart tones via Doppler ultrasound is recommended, though continuous fetal heart rate monitoring can be considered depending on gestational age (69, 83, 84).

38.3.9 Conclusion

The presentations, workups, and diagnoses for patients with adnexal masses are varied. A patient-centered approach to perioperative planning is key, though prioritization of a minimally invasive procedure is often feasible. Gynecologic surgeons must be both skilled in the core tenets of laparoscopy as well as adept in tailoring surgical technique to anatomy and clinical condition.

References

1. Bullock B et al. Management of the adnexal mass: considerations for the family medicine physician. *Front Med (Lausanne)*. 2022;9:913549.
2. Borgfeldt C et al. Transvaginal sonographic ovarian findings in a random sample of women 25–40 years old. *Ultrasound Obstet Gynecol*. 1999;13(5):345–350.
3. Pavlik EJ et al. Frequency and disposition of ovarian abnormalities followed with serial transvaginal ultrasonography. *Obstet Gynecol*. 2013;122(2 Pt 1):210–7.
4. Cronin KA et al. Annual report to the nation on the status of cancer, part 1: national cancer statistics. *Cancer*. 2022;128(24):4251–4284.
5. Eskander R et al. Practice bulletin no. 174: evaluation and management of adnexal masses. *Obstet Gynecol*. 2016;128(5):e210–e226.
6. Padilla LA et al. Limitations of the pelvic examination for evaluation of the female pelvic organs. *Int J Gynaecol Obstet*. 2005;88(1):84–88.

7. Padilla LA et al. Accuracy of the pelvic examination in detecting adnexal masses. *Obstet Gynecol*. 2000;96(4):593–598.
8. Patel MD et al. Managing incidental findings on abdominal and pelvic CT and MRI, part 1: white paper of the ACR Incidental Findings Committee II on adnexal findings. *J Am Coll Radiol*. 2013;10(9):675–681.
9. Wang PS et al. Benign-appearing incidental adnexal cysts at US, CT, and MRI: putting the ACR, O-RADS, and SRU guidelines all together. *Radiographics*. 2022;42(2):609–624.
10. Spencer JA et al. The adnexal incidentaloma: a practical approach to management. *Cancer Imaging*. 2011;11(1):48–51.
11. Valentini AL et al. Benign and suspicious ovarian masses-MR imaging criteria for characterization: pictorial review. *J Oncol*. 2012;2012:481806.
12. Timmerman D et al. Terms, definitions and measurements to describe the sonographic features of adnexal tumors: a consensus opinion from the International Ovarian Tumor Analysis (IOTA) Group. *Ultrasound Obstet Gynecol*. 2000;16(5):500–505.
13. Guerriero S et al. Systematic approach to sonographic evaluation of the pelvis in women with suspected endometriosis, including terms, definitions and measurements: a consensus opinion from the International Deep Endometriosis Analysis (IDEA) group. *Ultrasound Obstet Gynecol*. 2016;48(3):318–332.
14. Mais V et al. Transvaginal ultrasonography in the diagnosis of cystic teratoma. *Obstet Gynecol*. 1995;85(1):48–52.
15. Dupuis CS et al. Ultrasonography of adnexal causes of acute pelvic pain in pre-menopausal non-pregnant women. *Ultrasonography*. 2015;34(4):258–267.
16. Chappell CA et al. Pathogenesis, diagnosis, and management of severe pelvic inflammatory disease and tuboovarian abscess. *Clin Obstet Gynecol*. 2012;55(4):893–903.
17. Bhatt S et al. Sonographic evaluation of ectopic pregnancy. *Radiol Clin North Am*. 2007;45(3):549–560, ix.
18. Timmerman D et al. Predicting the risk of malignancy in adnexal masses based on the simple rules from the international ovarian tumor analysis group. *Am J Obstet Gynecol*. 2016;214(4):424–437.
19. Timmerman D et al. Simple ultrasound-based rules for the diagnosis of ovarian cancer. *Ultrasound Obstet Gynecol*. 2008;31(6):681–690.
20. Meys EMJ et al. Estimating risk of malignancy in adnexal masses: external validation of the ADNEX model and comparison with other frequently used ultrasound methods. *Ultrasound Obstet Gynecol*. 2017;49(6):784–792.
21. Garde I et al. Diagnostic accuracy of ultrasound signs for detecting adnexal torsion: systematic review and meta-analysis. *Ultrasound Obstet Gynecol*. 2023;61(3):310–324.
22. Houry D et al. Ovarian torsion: a fifteen-year review. *Ann Emerg Med*. 2001;38(2):156–159.
23. Oltmann SC et al. Cannot exclude torsion – a 15-year review. *J Pediatr Surg*. 2009;44(6):1212–1216; discussion 7.
24. Kaijser J et al. Imaging techniques for the pre-surgical diagnosis of adnexal tumours. *Best Pract Res Clin Obstet Gynaecol*. 2014;28(5):683–695.
25. Sadowski EA et al. Adnexal lesion imaging: past, present, and future. *Radiology*. 2023;307(5):e223281.
26. Bristow RE et al. Ovarian malignancy risk stratification of the adnexal mass using a multivariate index assay. *Gynecol Oncol*. 2013;128(2):252–259.
27. Dayyani F et al. Diagnostic performance of risk of ovarian malignancy algorithm against CA125 and HE4 in connection with ovarian cancer: a meta-analysis. *Int J Gynecol Cancer*. 2016;26(9):1586–1593.
28. Ueland FR et al. Effectiveness of a multivariate index assay in the preoperative assessment of ovarian tumors. *Obstet Gynecol*. 2011;117(6).
29. Coleman RL et al. Validation of a second-generation multivariate index assay for malignancy risk of adnexal masses. *Am J Obstet Gynecol*. 2016;215(1):82.e1–82.e11.
30. Kaijser J et al. Presurgical diagnosis of adnexal tumours using mathematical models and scoring systems: a systematic review and meta-analysis. *Hum Reprod Update*. 2014;20(3):449–462.
31. Aktürk E et al. Comparison of nine morphological scoring systems to detect ovarian malignancy. *Eur J Gynaecol Oncol*. 2015;36(3):304–308.
32. Peters A et al. Enhanced recovery after surgery outcomes in minimally invasive nonhysterectomy gynecologic procedures. *Am J Obstet Gynecol*. 2020;223(2):234.e1–234.e8.
33. Chapman JS et al. Enhanced recovery pathways for improving outcomes after minimally invasive gynecologic oncology surgery. *Obstet Gynecol*. 2016;128(1):138–144.
34. Dioun S et al. Trends in the use of minimally invasive adnexal surgery in the United States. *Obstet Gynecol*. 2021;138(5):738–746.
35. Magrina JF et al. Robotic adnexectomy compared with laparoscopy for adnexal mass. *Obstet Gynecol*. 2009;114(3):581–584.
36. Milone M et al. Conversions related to adhesions in abdominal surgery. Robotic versus laparoscopic approach: a multicentre experience. *Int J Med Robot*. 2021;17(2):e2186.
37. Milone M et al. The role of robotic visceral surgery in patients with adhesions: a systematic review and meta-analysis. *J Pers Med*. 2022;12(2).
38. Iavazzo C et al. Robotic assisted hysterectomy in obese patients: a systematic review. *Arch Gynecol Obstet*. 2016;293(6):1169–1183.
39. Kinay T et al. Feasibility and safety of laparoscopic surgery in large ovarian masses. *Gynecol Minim Invasive Ther*. 2022;11(4):215–220.
40. Ghezzi F et al. Should adnexal mass size influence surgical approach? A series of 186 laparoscopically managed large adnexal masses. *BJOG*. 2008;115(8):1020–1027.
41. Unger CA et al. Risk factors for robotic gynecologic procedures requiring conversion to other surgical procedures. *Int J Gynaecol Obstet*. 2016;135(3):299–303.
42. Richards L et al. Risk factors and outcomes of conversion to open surgery in benign gynecologic laparoscopies: a case-control study. *J Minim Invasive Gynecol*. 2021;28(10):1786–1794.
43. Jones N et al. Conversion from robotic surgery to laparotomy: a case-control study evaluating risk factors for conversion. *Gynecol Oncol*. 2014;134(2):238–242.
44. Adelman MR et al. Ovarian conservation vs removal at the time of benign hysterectomy. *Am J Obstet Gynecol*. 2018;218(3):269–279.
45. Erekson EA et al. Oophorectomy: the debate between ovarian conservation and elective oophorectomy. *Menopause*. 2013;20(1):110–114.
46. Ito TE et al. Systematic review of topical hemostatic agent use in minimally invasive gynecologic surgery. *JSLS*. 2018;22(4).
47. Stachowicz AM et al. Topical hemostatic agents in gynecologic surgery for benign indications. *Obstet Gynecol*. 2020;135(2):463–468.
48. Vergote I et al. Prognostic importance of degree of differentiation and cyst rupture in stage I invasive epithelial ovarian carcinoma. *Lancet*. 2001;357(9251):176–182.
49. Dubuisson J et al. Management of presumed benign giant ovarian cysts: a minimally invasive technique using the Alexis Laparoscopic System. *J Minim Invasive Gynecol*. 2015;22(4):540.
50. El Hajj H et al. Protected laparoscopic large ovarian cyst aspiration: a 5-step alternative to laparotomy. *J Minim Invasive Gynecol*. 2022;29(9):1038–1039.
51. Smorgick N et al. Laparoscopic removal of adnexal cysts: is it possible to decrease inadvertent intraoperative rupture rate? *Am J Obstet Gynecol*. 2009;200(3):237.e1–237.e3.
52. Atilgan R et al. Purse-string suture technique using a mini-Pfannenstiel incision to treat large dermoid cysts. *J Obstet Gynaecol*. 2020;40(8):1160–1163.
53. Geomini P et al. Diagnostic accuracy of frozen section diagnosis of the adnexal mass: a metaanalysis. *Gynecol Oncol*. 2005;96(1):1–9.
54. Taskiran C et al. The role of frozen section evaluation in the diagnosis of adnexal mass. *Int J Gynecol Cancer*. 2008;18(2):235–240.
55. Zhu S et al. Impact of early surgical management on tubo-ovarian abscesses. *J Obstet Gynaecol*. 2021;41(7):1097–1101.
56. Goje O et al. Outcomes of minimally invasive management of tubo-ovarian abscess: a systematic review. *J Minim Invasive Gynecol*. 2021;28(3):556–564.

57. Hattiangadi R et al. Minimally invasive approach to the management of tubo-ovarian abscesses. *Curr Opin Obstet Gynecol*. 2021;33(4):249–254.
58. Protopapas AG et al. Tubo-ovarian abscesses in postmenopausal women: gynecological malignancy until proven otherwise? *Eur J Obstet Gynecol Reprod Biol*. 2004;114(2):203–209.
59. Sawyer RG et al. Trial of short-course antimicrobial therapy for intraabdominal infection. *N Engl J Med*. 2015;372(21):1996–2005.
60. Ryles HT et al. Changing practices in the surgical management of adnexal torsion: an analysis of the national surgical quality improvement program database. *Obstet Gynecol*. 2023;141(5):888–896.
61. Chang-Patel EJ et al. Adnexal torsion: a review of diagnosis and management strategies. *Curr Opin Obstet Gynecol*. 2022;34(4):196–203.
62. Huchon C et al. Adnexal torsion: a literature review. *Eur J Obstet Gynecol Reprod Biol*. 2010;150(1):8–12.
63. McGovern PG et al. Adnexal torsion and pulmonary embolism: case report and review of the literature. *Obstet Gynecol Surv*. 1999;54(9):601–608.
64. Cohen SB et al. Laparoscopy versus laparotomy for detorsion and sparing of twisted ischemic adnexa. *JSLS*. 2003;7(4):295–299.
65. Dasgupta R et al. Ovarian torsion in pediatric and adolescent patients: a systematic review. *J Pediatr Surg*. 2018;53(7):1387–1391.
66. Smorgick N et al. Recurrent torsion of otherwise normal adnexa: oophoropexy does not prevent recurrence. *Arch Gynecol Obstet*. 2023;307(3):821–825.
67. Akdam A et al. Recurrent ovarian torsion: risk factors and predictors for outcome of oophoropexy. *J Minim Invasive Gynecol*. 2022;29(8):1011–1018.
68. Hartley J et al. Oophoropexy for recurrent ovarian torsion. *Case Rep Obstet Gynecol*. 2018;2018:8784958.
69. Cathcart AM et al. Adnexal masses during pregnancy: diagnosis, treatment, and prognosis. *Am J Obstet Gynecol*. 2023;228(6):601–612.
70. Hoover K et al. Evaluation and management of adnexal mass in pregnancy. *Am J Obstet Gynecol*. 2011;205(2):97–102.
71. Schmeler KM et al. Adnexal masses in pregnancy: surgery compared with observation. *Obstet Gynecol*. 2005;105(5 Pt 1):1098–1103.
72. Sarandakou A et al. Tumor markers in biological fluids associated with pregnancy. *Crit Rev Clin Lab Sci*. 2007;44(2):151–178.
73. Han SN et al. Physiologic variations of serum tumor markers in gynecological malignancies during pregnancy: a systematic review. *BMC Med*. 2012;10:86.
74. Weiner E et al. Laparoscopic surgery performed in advanced pregnancy compared to early pregnancy. *Arch Gynecol Obstet*. 2015;292(5):1063–1068.
75. Mathevet P et al. Laparoscopic management of adnexal masses in pregnancy: a case series. *Eur J Obstet Gynecol Reprod Biol*. 2003;108(2):217–222.
76. Minig L et al. Laparoscopic surgery for treating adnexal masses during the first trimester of pregnancy. *J Minim Access Surg*. 2016;12(1):22–25.
77. Upadhyay A et al. Laparoscopic management of a nonobstetric emergency in the third trimester of pregnancy. *Surg Endosc*. 2007;21(8):1344–1348.
78. Liu YX et al. Meta-analysis comparing the safety of laparoscopic and open surgical approaches for suspected adnexal mass during the second trimester. *Int J Gynaecol Obstet*. 2017;136(3):272–279.
79. Chen L et al. Comparative analysis of laparoscopy versus laparotomy in the management of ovarian cyst during pregnancy. *J Obstet Gynaecol Res*. 2014;40(3):763–769.
80. Stepp K et al. Laparoscopy in the second trimester of pregnancy. *Obstet Gynecol Clin North Am*. 2004;31(3):485–496, vii.
81. Hunter JG et al. Carbon dioxide pneumoperitoneum induces fetal acidosis in a pregnant ewe model. *Surg Endosc*. 1995;9(3):272–277; discussion 7–9.
82. Candiani M et al. Adnexal masses in pregnancy: fetomaternal blood flow indices during laparoscopic surgery. *J Minim Invasive Gynecol*. 2012;19(4):443–447.
83. ACOG committee opinion 775: nonobstetric surgery during pregnancy. *Obstet Gynecol*. 2019;133(4):e285–e286.
84. Pearl JP et al. SAGES guidelines for the use of laparoscopy during pregnancy. *Surg Endosc*. 2017;31(10):3767–3782.

39 MINIMALLY INVASIVE SURGERY APPLICATIONS FOR THE CARE OF WOMEN WITH EPITHELIAL OVARIAN CANCER

Roni Nitecki and J. Alejandro Rauh-Hain

Epithelial ovarian cancer (EOC), a term that encompasses ovarian, peritoneal, and fallopian tube cancers, is the second most common and the most lethal gynecologic cancer in developed countries, with an estimated 19,710 incident cases in the United States in 2023 and a 5-year relative survival of 50.8% (1). The role of surgery in the management of ovarian cancer has greatly developed since it was first described in a 1934 case series by Dr. Meigs (2). As technology evolves, the role of minimally invasive surgery (MIS) in particular continues to grow (3).

Based primarily on evidence from trials in patients with endometrial cancer (4, 5), the gynecologic cancer community accepted (6–8), and guidelines (9) reflected, the consensus that laparotomy and MIS were different approaches to the same operation. As the differences between the two approaches were thought to be only technical, the applications of MIS were broadly adopted in trials and oncologic training programs under the assumption that the mode of surgery had no impact on oncologic outcomes.

The widespread consensus about the oncologic safety of MIS was challenged when the Laparoscopic Approach to Cervical Cancer (LACC) trial, a randomized noninferiority trial published in 2018, unexpectedly showed that patients with cervical cancer who underwent minimally invasive radical hysterectomy had a higher risk of recurrence and death than those who underwent open surgery (10). A population-based study (11) and a meta-analysis of observational studies (12) comparing MIS and open surgery in cervical cancer also arrived at the same conclusion. In response, numerous international guidelines were revised to favor open surgery (13–16), and the use of MIS for early-stage cervical cancer substantially declined (17). This medical reversal (18) serves as a cautionary tale about the adoption of MIS in other disease sites in the absence of prospective data.

MIS currently has several applications in the treatment of patients with EOC. In this chapter, we cover surgical staging for apparent early-stage disease, diagnostic laparoscopy to determine resectability, MIS interval cytoreductive surgery for advanced-stage disease, and secondary cytoreductive surgery for recurrent disease. It is important to note that although there are many applications of MIS in the management of patients with ovarian cancer, most studies referenced in this chapter are observational studies and meta-analyses of observational studies, many of which did not adjust for potential confounding, are likely underpowered to assess primary outcomes, and are at high risk for bias.

39.1 Surgical Staging for Apparent Early-Stage Disease

Early-stage EOC is associated with excellent prognosis, with a 5-year relative survival of approximately 90%; however, only approximately a quarter of patients are diagnosed with localized disease (International Federation of Gynecology and Obstetrics [FIGO] stage I or II) (1). In early-stage ovarian cancer, comprehensive staging allows for proper triage to adjuvant therapy. Comprehensive surgical staging involves removal of the adnexa, hysterectomy, peritoneal washing and biopsies, omentectomy, and pelvic and para-aortic lymph node sampling (19). When comprehensive staging is performed, approximately a third of patients who are initially believed to have disease confined to the pelvis will be diagnosed with higher-staged disease (20). In the absence of a preoperative biopsy, malignancy may be suspected but is often unknown, and confirmation of malignancy requires a frozen section during surgery. This makes surgical handling of adnexal masses prognostically important because capsule rupture and spillage into the abdomen may result in tumor seeding of the abdominal cavity and technically upstage the disease from stage IA (confined to one ovary) or IB (confined to both ovaries) to IC. This stage shift carries a worse overall survival (OS) (approximately 80%) and a decrease in progression-free survival (PFS) of 10% to 15% (21–25). In a meta-analysis of observational studies comparing outcomes of women with early-stage EOC who experienced capsule rupture and those who did not, capsule rupture was associated with almost twice the hazard of recurrence or death (26).

Therefore, intact specimen extraction is paramount and has traditionally been completed via laparotomy. MIS can also be used for extraction, but the increased manipulation required in MIS presents three surgical challenges:

1. Removing the specimen from its native and adherent attachments without rupture
2. Containing and removing the specimen from the abdomen
3. Fully evaluating all peritoneal surfaces without palpation

While there are no prospective data comparing the oncologic outcomes of MIS and laparotomy for staging of clinical early-stage disease, initial observational studies found MIS to be safe (27, 28) and that the use of MIS for this indication is increasing (23). A systematic review found that minimally invasive surgical staging (both laparoscopic and robotic-assisted) was associated with better perioperative outcomes, such as lower complication rates, less blood loss, and shorter length of hospital stay compared to laparotomy (28). They also found no association between the quality of the staging procedure (as defined by the number of lymph nodes removed) and the mode of surgery.

In a meta-analysis of ten observational studies (totaling 1509 patients who underwent MIS and 1787 who underwent laparotomy), Knisely and colleagues (27) found that staging via MIS was not associated with PFS or all-cause mortality. The authors noted, however, that the quality of the data was poor, as eight of the ten included studies did not adjust for confounding variables. A Cochrane review compared the benefits and harms of MIS and laparotomy in the surgical treatment of FIGO stage I ovarian cancer and also noted the absence of high-quality evidence because of the lack of adjustment for confounders (age, final stage, tumor size, adjuvant treatment, etc.) and lack of consistent PFS and OS reports in the existing literature (29).

DOI: 10.1201/9781003312109-39

In general, many studies among patients with apparent early-stage ovarian cancer categorize laparoscopy and robotic-assisted laparoscopy as MIS. A population-based study that compared these two forms of MIS found that robotic-assisted laparoscopy was less likely to result in conversion to laparotomy compared with laparoscopy but did not find any difference in mortality between the two forms (30).

More recent data demonstrating the propensity of minimally invasive procedures to result in capsule rupture are concerning. A National Cancer Database study of 8850 women with stage I EOC revealed that MIS use increased from 19.8% in 2010 to 34.9% in 2015, with an accompanying relative increase in capsule rupture rate (i.e., upstaging) of 18.3% (23). Even though patients with capsule rupture were more likely than those without rupture to receive chemotherapy, the authors found a commensurate 5% decrease in 4-year OS from 2010 to 2015. In an adjusted model, MIS was independently associated with capsule rupture when compared with laparotomy, and among patients who underwent MIS, an increase in all-cause mortality was seen in patients with capsule rupture compared with those without rupture. The authors advised careful preoperative and perioperative patient selection, although how to select appropriate patients is unclear.

In the Laparoscopic Ovarian Cancer Spillage Score (LOChneSS) study, which included 151 patients with stage I ovarian cancer (22), Ghirardi and colleagues found that larger tumor diameter (median diameter 9 cm compared with 6 cm), higher BMI, multilocular and solid tumor characteristics on ultrasound examination, and adhesions to large bowel and other pelvic structures were associated with an increased rate of endoscopic rupture. However, on multivariable analysis, only larger tumor diameter and ovarian fossa adhesions remained significantly associated with an increased rate of endoscopic rupture. It is important to note that the effect size for larger tumors in this study was very small (odds ratio: 1.03, 95% confidence interval [CI]: 1.01–1.04) and that a specific tumor size cutoff for MIS has not been determined. Other studies found that histologic examination findings matter, with higher risk of capsule rupture for endometrioid and clear-cell histologic types than for serous ones, possibly because the former two types commonly arise from endometriosis (22, 31).

To quantify the risk of capsule rupture and the risk of malignancy, Dioun and colleagues (32) modeled a theoretical cohort of 10,000 women undergoing surgery for an adnexal mass, assuming a 5% risk of cancer and a higher risk of capsule rupture in women who underwent MIS (25.5%) compared with those who underwent laparotomy (21.3%); these values were derived from the literature. They found that, overall, MIS was more cost-effective than laparotomy, yielding lower costs and improved perioperative outcomes among women with a low baseline risk of ovarian cancer. However, laparotomy was favored in the model when the risk of cancer was greater than 15% and the risk of capsule rupture during MIS was 100%. Additionally, when a malignant diagnosis was known preoperatively (i.e., a 100% risk of cancer) laparotomy was favored when the risk of capsule rupture with MIS neared 40%.

In summary, there are no level I data supporting the use of MIS in staging early-stage EOC. Observational studies demonstrate improved perioperative outcomes with MIS compared to open surgery. Oncologic outcomes likely depend on intact removal of the specimen and thus capsule rupture should be avoided if possible.

39.2 Advanced-Stage Disease

39.2.1 Diagnostic Laparoscopy to Assess Surgical Resectability

Most patients with EOC are initially diagnosed with stage III or IV disease, with a 5-year relative survival of approximately 30% (1). Both surgery and chemotherapy are utilized in initial disease management. Most patients will respond to initial treatment; however, the majority will also experience recurrence. Historically, all patients with advanced ovarian cancer have undergone primary debulking surgery (PDS) followed by adjuvant chemotherapy, with the goal of surgery being to remove as much visible disease as possible, although the definition of optimal has shifted over time from less than 2 cm to less than 1 cm.

Over the past decade, studies have demonstrated a survival benefit to tumor-reductive surgery if it eradicates all visible disease (33, 34). With this goal in mind, neoadjuvant chemotherapy NACT followed by surgery evolved as a treatment strategy. Randomized controlled trials (35–38) demonstrated that neoadjuvant chemotherapy (NACT) followed by interval debulking surgery (IDS) had equivalent OS and PFS and decreased morbidity compared with PDS, yet debate regarding the optimal sequence of chemotherapy and surgery persists. Patients have historically been candidates for NACT if they have multiple medical comorbidities, poor performance status, or extensive disease on imaging that is not amenable to upfront surgery. The American Society of Clinical Oncology and the Society of Gynecologic Oncology now jointly recommend NACT for women who have a high perioperative risk profile or a low likelihood of achieving cytoreduction to less than 1 cm (ideally to no visible disease) (39). The guidelines further caution against PDS that results in greater than 1 cm of remaining tumor, which may result in high morbidity without a survival benefit. However, consensus has not been reached about how to select patients suitable for each treatment strategy. Studies evaluating the ability of standard diagnostic workup (clinical examination, CA-125 levels, imaging) to accurately predict who would benefit from primary surgery have produced poor estimates, as studies have found anywhere between 10% and 60% of patients undergo suboptimal debulking using clinical evaluation alone (40).

Diagnostic laparoscopy has emerged as a minimally invasive option to assess extent of disease and surgical resectability in patients with advanced EOC. In the research setting, this procedure is best understood as a valuable diagnostic test that can distinguish between those who, at laparotomy, will have disease too extensive to achieve an optimal cytoreduction with PDS (positive test result) and those for whom a laparotomy would achieve optimal cytoreduction (negative test result). Fagotti and colleagues developed the Fagotti score (41), a quantitative model using laparoscopy to predict the likelihood of an optimal cytoreductive surgery, by sequentially performing laparoscopy and standard vertical laparotomy among 64 patients with advanced EOC. The total score ultimately considers seven features evaluated by laparoscopy, and each feature is given a score of either 0 or 2. The scoring criteria for each feature are as follows.

1. Peritoneal carcinomatosis
   - 0: Involving limited area that could be resected by peritonectomy
   - 2: Unresectable massive peritoneal involvement and a miliary pattern of distribution

2. Diaphragmatic disease
   - 0: Isolated diaphragmatic disease
   - 2: Widespread infiltrating carcinomatosis or confluent nodules involving most of the diaphragmatic surface
3. Mesenteric disease
   - 0: Small nodules potentially treated by argon beam coagulation
   - 2: Large infiltrating nodules or assumed involvement of the root of the mesentery given limited movements of the various intestinal segments
4. Omental disease
   - 0: Isolated diaphragmatic disease
   - 2: Tumor diffusion along the omentum up to the large stomach curvature
5. Bowel infiltration
   - 0: Absence of below
   - 2: Bowel resection assumed to be required or miliary carcinomatosis on the mesenteric junction (excluding the rectosigmoid)
6. Stomach infiltration
   - 0: Absence of below
   - 2: Obvious neoplastic involvement of the gastric wall
7. Liver metastasis
   - 0: Absence of below
   - 2: Any surface lesion

The total score, also termed the predictive index value, is calculated by summing the scores for each feature. Fagotti and colleagues found that when the total score was greater than 8, the likelihood of a suboptimal cytoreduction was 100% (when optimal was defined as no more than 1 cm of remaining tumor). This model was later validated by the same group in a larger cohort of patients (42). In the validation study the accuracy of laparoscopy was greater than 85% for most of the features considered in the score. Notably, the features with the poorest negative predictive value were bowel infiltration, which was likely due to the difficulty in assessing the entire length of the bowel (especially when retracted by tumor), and stomach infiltration, which could not be assessed if a massive omental cake masked stomach involvement. The validation study demonstrated that a predictive index value greater than 8 had a specificity of 100%, positive predictive value of 100%, and negative predictive value of 70% for predicting a suboptimal PDS.

The Fagotti score has been widely adopted (43, 44). For example, its implementation as part of a quality improvement project at a comprehensive cancer center resulted in complete gross resection rates of 74% to 88% in both primary and interval cytoreductive surgical cases (43). It is important to note that in the Fagotti score, no other clinical or radiologic parameters are considered when assessing the likelihood of optimal cytoreductive surgery (41). Real-world applications include these other parameters when deciding if PDS is the appropriate treatment strategy for an individual patient (43). More recently, Fagotti's group updated the model, now stipulating that 10 is the lowest predictive value at which the likelihood of an optimal (≤ 1 cm of remaining tumor) PDS is 0% (45).

The Laparoscopy to Predict the Result of Primary Cytoreductive Surgery in Advanced Ovarian Cancer Patients (LapOvCa) trial is the only randomized trial examining the utility of a diagnostic laparoscopy in assessing resectability. Patients with suspected advanced EOC who were considered for PDS based on conventional workup were randomized to two groups: one group underwent PDS without prior diagnostic laparoscopy, and the other group underwent a diagnostic laparoscopy to assess whether PDS was feasible (defined as residual tumor ≤ 1 cm) (46, 47) and, based on those findings, underwent PDS or received NACT before undergoing IDS. In this study, surgeons were guided to determine if the tumor was resectable based on findings from the diagnostic laparoscopy, but a validated model was not utilized. Of patients randomized to the diagnostic laparoscopy group, 62% underwent PDS; this group experienced futile laparotomies less often (10%) than those randomized to the PDS-only group (39%), demonstrating the potential benefit of a diagnostic laparoscopy. The negative predictive value for diagnostic laparoscopy was 84%, meaning that 84% of those who underwent a diagnostic laparoscopy and proceeded to surgery had less than 1 cm of gross disease at the conclusion of surgery. Moreover, of the patients in the diagnostic laparoscopy group who underwent PDS, 57% had no gross residual disease.

A Cochrane review (and an update to the original review) summarizing the evidence supporting use of diagnostic laparoscopy in this setting, however, was not able to conclude whether laparoscopy is more accurate than clinical and radiological diagnostic workup (40, 48). In total, the review included 18 studies (14 cohorts of patients, 1563 participants), but only two studies could produce estimates of sensitivity and specificity, as all patients in these studies underwent both a diagnostic laparoscopy (the "test") and a laparotomy (the "gold standard") (42, 49). The sensitivities of laparoscopy in the two studies were 0.71 (95% CI: 0.44–0.89) and 0.95 (95% CI: 0.84–0.99), meaning that among patients who underwent a suboptimal PDS, 71% and 95% were thought to have unresectable disease at laparoscopy, respectively (42, 49). Conversely, of those thought to have resectable disease at laparoscopy, 5% and 29% had a suboptimal PDS. The Cochrane reviews did not include a meta-analysis or calculation of a pooled estimate of the negative predictive value because the studies had significant heterogeneity in the reasons for performing a laparoscopy, the inclusion and exclusion criteria, and the definition of optimal PDS.

In summary, there is level I evidence to support that a diagnostic laparoscopy to help determine resectability can decrease the rate of futile laparotomies. There is no consensus as to how to evaluate resectability at the time of a diagnostic laparoscopy, though the Fagotti score has been widely implemented.

39.2.2 Minimally Invasive Interval Cytoreductive Surgery

Although advanced EOC has traditionally been treated with primary cytoreductive surgery, NACT use has increased substantially in the United States (50). It has been proposed that, in women who respond to NACT and therefore have less remaining tumor, interval cytoreduction can be achieved using MIS (51, 52), with improved perioperative outcomes compared with laparotomy (3). Studies also suggest that MIS has a shorter recovery time that may allow patients to resume chemotherapy sooner (53). While these studies suggest that an MIS approach may be reasonable and effective in well-selected patients, no randomized data support this approach. Nevertheless, the use of MIS for interval cytoreductive surgeries is increasing, accounting for 29% of them in 2018 (3), and is endorsed by current National Comprehensive Cancer Network guidelines among select patients (54). Minimally invasive interval cytoreductive surgery has unique challenges compared to traditional open surgery: thorough evaluation of all areas in the abdomen

and pelvis may be more difficult (42) and disease may be missed, leading to occult residual disease (55). Port-site metastases have also been reported (56).

The feasibility and safety of minimally invasive interval debulking surgery have been documented in small retrospective case series and in a database analysis (51, 52, 57–60). These studies revealed high complete cytoreduction rates, ranging from 82% to 96%. However, these studies do not have identical inclusion or exclusion criteria. For example, the Feasibility of Interval Debulking Surgery by Laparoscopy for Peritoneal Carcinosis in Chemosensitive Patients (CILOVE) study was a prospective nonrandomized phase II study conducted in specialty centers in France to determine the feasibility of minimally invasive interval cytoreductive surgery, which they defined as a frequency of conversion below 15% (61). In this study, a surgeon completed surgery in a minimally invasive manner if complete removal of macroscopic disease could be achieved or continued with cytoreduction via laparotomy if not. Among the 32 patients, the conversion rate was 9% and there were no grade 3 or grade 4 complications. In the Minimally Invasive Interval Debulking Surgery in Ovarian Neoplasm (MISSION) trial, another feasibility study, no minimally invasive interval debulking surgeries were converted to laparotomy; however, there were strict inclusion criteria: BMI less than 40, Eastern Cooperative Oncology Group (ECOG) performance status less than or equal to 2, and a complete response to platinum-based chemotherapy (51).

These strict criteria underscore the importance of patient selection in these studies. Fagotti's group developed and validated a nomogram to help select patients who would most benefit from a minimally invasive interval cytoreductive surgery (62). They identified both patient and treating-center factors that suggest this approach would be able to identify cases suitable for MIS: absence of an omental cake, fewer than two involved peritoneal sites, normalization of CA-125 levels, and treatment by a high-volume surgeon.

The data regarding oncologic outcomes are sparse. In a single-institution study of 21 patients, Favero and colleagues (63) found a nonsignificant decrease in cancer-specific survival and a nonsignificant reduction in the chemotherapy-free interval among women who underwent minimally invasive cytoreductive surgery. In contrast, in the international MISSION study (52), patients who underwent minimally invasive cytoreductive surgery had a significantly longer median PFS (18 months) than those who underwent open surgery (12 months). This difference, however, did not remain significant in an adjusted model. In a meta-analysis of six observational studies, including 643 patients who underwent MIS and 2885 who underwent a laparotomy, residual disease and complications were not significantly associated with surgery type (64), and PFS appeared to be longer in the group who underwent minimally invasive interval cytoreductive surgery. However, this effect was mitigated by removing one of the six studies (65). In another recent systematic review, four studies met the inclusion criteria, but a meta-analysis was not conducted because only two studies performed any adjustment for covariables, and three of the four studies did not include enough patients to estimate clinically relevant effect sizes (27). The most recent study, an update to prior work by Melamed and colleagues (58), included patients reported in the National Cancer Database, of whom 5876 underwent a laparotomy and 2021 had minimally invasive interval surgery (1157 laparoscopic and 864 robotic-assisted procedures) (3). While the groups were significantly different regarding type of treatment facility, age, geographic location, comorbidity index, annual median household income, and type of insurance, the authors used propensity score matching to balance the observed covariates. The median OS was significantly shorter in the MIS group (41.0 months) than in the laparotomy group (46.7 months). Patients in the MIS group had a 14% lower hazard of all-cause mortality compared with patients in the laparotomy group (hazard ratio: 0.86; 95% CI: 0.79–0.94), with lower 30- and 90-day postoperative mortality. Although presence of residual disease was unknown for a third of the cohort, the MIS group appeared to have a higher rate of complete gross resection (43% vs 39%) and lower rate of additional cytoreductive procedures than the laparotomy group. These findings suggest that despite propensity score matching, there was important unmeasured confounding.

While the data are promising, prospective randomized trials are necessary to confirm the results of these retrospective studies. The Laparoscopic Cytoreduction after Neoadjuvant Chemotherapy (LANCE NCT04575935) trial (66) is an ongoing international, prospective randomized multicenter noninferiority phase III trial comparing disease-free survival after MIS or laparotomy in women with advanced high-grade EOC that responded (completely or partially) to three or four cycles of NACT. The study has strict inclusion criteria; it requires normalization of CA-125 levels and evidence on preoperative imaging that the disease is amenable to minimally invasive resection. Thus, patients are excluded if they have ascites that do not improve during NACT (trace ascites is allowed); small bowel, gastric, colon, rectal, significant diaphragmatic, splenic, hepatic-surface, parenchymal, or mesenteric tumor involvement; or tumor infiltration of the lesser peritoneal sac.

39.3 Secondary Cytoreductive Surgery for Recurrent Disease

Guidelines from the National Comprehensive Cancer Network recommend secondary cytoreductive surgery be considered for patients with platinum-sensitive disease, who have isolated or limited disease amenable to complete resection, and who do not have ascites (54). Three recent randomized trials, Gynecologic Oncology Group (GOG)-0213, Descriptive Evaluation of Preoperative Selection Criteria for Operability in Recurrent Ovarian Cancer (DESKTOP III), and Surgery or Chemotherapy in Recurrent Ovarian Cancer (SOC-1), were differentially designed with different patient populations and different endpoints, but all produced high rates of complete gross resection (67% to 77%) (67–69). While GOG-0213 did not demonstrate a survival advantage for surgical cytoreduction compared with chemotherapy alone (67), the other two randomized trials found that secondary cytoreductive surgery resulted in improved PFS (68, 69) and OS (68) compared with chemotherapy alone.

It has been suggested that if recurrent disease is low volume and localized, it may be approached via MIS (70–72). Conte and colleagues (72) retrospectively identified 276 patients with recurrent platinum-sensitive EOC; of these patients, 62 had MIS and 214 had open surgery, with an overall complete gross resection rate of 95%. All patients had preoperative imaging and a diagnostic laparoscopy prior to secondary cytoreductive surgery. In a smaller propensity-matched subset of patients, the investigators found no differences between the groups

regarding post-recurrence survival. It is important to note, however, that the groups differed regarding surgical complexity and recurrence patterns. In a study of 79 patients, Paik et al. (73) found that patients who underwent MIS had shorter operative times, shorter lengths of stay, and less blood loss than those who underwent open surgery, but both groups of patients had similar survival outcomes. Finally, Magrina and colleagues (74) found no statistically significant differences in operating time, complications, complete debulking, and survival between women who underwent minimally invasive versus open secondary cytoreductive surgery. Neither study accounted for confounding variables such as treatment-free interval or the extent of recurrent disease.

Although these data are thought-provoking, in the absence of prospective data, we can conclude only that at this point minimally invasive secondary cytoreductive surgery may be feasible for select patients at select centers preferably on a trial protocol.

References

1. *National Cancer Institute: surveillance, epidemiology, and end results program. Cancer stat facts: ovarian cancer.* Available at: https://seer.cancer.gov/statfacts/html/ovary.html (Accessed Jun 2023).
2. Schorge JO et al. Meigs to modern times: the evolution of debulking surgery in advanced ovarian cancer. *Gynecol Oncol*. 2018;149(3):447–454.
3. Jorgensen K et al. Minimally invasive interval debulking surgery for advanced ovarian cancer after neoadjuvant chemotherapy. *Gynecol Oncol*. 2023;172:130–137.
4. Walker JL et al. Recurrence and survival after random assignment to laparoscopy versus laparotomy for comprehensive surgical staging of uterine cancer: Gynecologic Oncology Group LAP2 study. *J Clin Oncol*. 2012;30(7):695–700.
5. Janda M et al. Effect of total laparoscopic hysterectomy vs total abdominal hysterectomy on disease-free survival among women with stage I endometrial cancer: a randomized clinical trial. *JAMA*. 2017;317(12):1224–1233.
6. Nezhat FR et al. Role of minimally invasive surgery in ovarian cancer. *J Minim Invasive Gynecol*. 2013;20(6):754–765.
7. Uppal S et al. Trends and comparative effectiveness of inpatient radical hysterectomy for cervical cancer in the United States (2012–2015). *Gynecol Oncol*. 2019;152(1):133–138.
8. Wright JD et al. Comparative effectiveness of minimally invasive and abdominal radical hysterectomy for cervical cancer. *Gynecol Oncol*. 2012;127(1):11–17.
9. Koh WJ et al. Cervical cancer, version 2.2015. *J Natl Compr Canc Netw*. 2015;13(4):395–404.
10. Ramirez PT et al. Minimally invasive versus abdominal radical hysterectomy for cervical cancer. *N Engl J Med*. 2018;379(20):1895–1904.
11. Melamed A et al. Survival after minimally invasive radical hysterectomy for early-stage cervical cancer. *N Engl J Med*. 2018;379(20):1905–1914.
12. Nitecki R et al. Survival after minimally invasive vs open radical hysterectomy for early-stage cervical cancer. *JAMA Oncol*. 2020;6(7):1019.
13. Querleu D et al. Laparoscopic radical hysterectomy: a European Society of Gynaecological Oncology (ESGO) statement. *IJGC*. 2020;30(1):15.
14. Koh WJ et al. Cervical cancer, version 3.2019. *J Natl Compr Cancer Netw*. 2019;17(1):64–84.
15. Society of Gynecologic Oncology. *Notice to SGO members: emerging data on the surgical approach for radical hysterectomy in the treatment of women with cervical cancer*. www.sgo.org/clinical-practice/guidelines/sgo-member-update-emerging-data-on-the-surgical-approach-for-radical-hysterectomy-in-the-treatment-of-women-with-cervical-cancer/le (Accessed Apr 2020).
16. FIGO statement on minimally invasive surgery in cervical cancer. *Int J Gynecol Obstet*. 2020;149(3):264–264.
17. Lewicki PJ et al. Effect of a randomized, controlled trial on surgery for cervical cancer. *N Engl J Med*. 2021;384(17):1669–1671.
18. Melamed A, Rauh-Hain JA, Ramirez PT. Minimally Invasive Radical Hysterectomy for Cervical Cancer: When Adoption of a Novel Treatment Precedes Prospective, Randomized Evidence. *J Clin Oncol*. 2019;37(33):3069–3074.
19. Weber S et al. Laparoscopic surgical staging of early ovarian cancer. *Rev Obstet Gynecol*. 2011;4(3–4):117–122.
20. Hengeveld EM et al. The value of surgical staging in patients with apparent early stage epithelial ovarian carcinoma. *Gynecol Oncol*. 2019;154(2):308–313.
21. Mutch DG et al. 2014 FIGO staging for ovarian, fallopian tube and peritoneal cancer. *Gynecol Oncol*. 2014;133(3):401–404.
22. Ghirardi V et al. A laparoscopic adjusted model able to predict the risk of intraoperative capsule rupture in early-stage ovarian cancer: laparoscopic ovarian cancer spillage score (LOChneSS Study). *J Minim Invasive Gynecol*. 2022;29(8):961–967.
23. Matsuo K et al. Minimally invasive surgery and risk of capsule rupture for women with early-stage ovarian cancer. *JAMA Oncol*. 2020;6(7):1110.
24. Higashi M et al. Survival impact of capsule rupture in stage I clear cell carcinoma of the ovary in comparison with other histological types. *Gynecol Oncol*. 2011;123(3):474–478.
25. Vergote I et al. Prognostic importance of degree of differentiation and cyst rupture in stage I invasive epithelial ovarian carcinoma. *Lancet*. 2001;357(9251):176–182.
26. Dioun S et al. Intraoperative rupture of the ovarian capsule in early-stage ovarian cancer. *Obstet Gynecol*. 2021;138(2):261–271.
27. Knisely A et al. The role of minimally invasive surgery in the care of women with ovarian cancer: a systematic review and meta-analysis. *J Minim Invasive Gynecol*. 2021;28(3):537–543.
28. Bouter ELM et al. Robot-assisted laparoscopic staging compared to conventional laparoscopic staging and laparotomic staging in clinical early stage ovarian carcinoma. *Curr Opin Oncol*. 2022;34(5):490–496.
29. Falcetta FS et al. Laparoscopy versus laparotomy for FIGO stage I ovarian cancer. *Cochrane Database Syst Rev*. 2016;2022(1).
30. Facer B et al. Survival outcomes for robotic-assisted laparoscopy versus traditional laparoscopy in clinical stage I epithelial ovarian cancer. *Am J Obstet Gynecol*. 2020;222(5):474.e1–474.e12.
31. Matsuo K et al. Intraoperative capsule rupture, postoperative chemotherapy, and survival of women with stage I epithelial ovarian cancer. *Obstet Gynecol*. 2019;134(5):1017–1026.
32. Dioun S et al. Minimally invasive surgery for suspected early-stage ovarian cancer; a cost-effectiveness study. *BJOG*. 2022;129(5):777–784.
33. Horowitz NS et al. Does aggressive surgery improve outcomes? Interaction between preoperative disease burden and complex surgery in patients with advanced-stage ovarian cancer: an analysis of GOG 182. *J Clin Oncol*. 2015;33(8):937–943.
34. Chi DS et al. What is the optimal goal of primary cytoreductive surgery for bulky stage IIIC epithelial ovarian carcinoma (EOC)? *Gynecol Oncol*. 2006;103(2):559–564.
35. Vergote I et al. Neoadjuvant chemotherapy or primary surgery in stage IIIC or IV ovarian cancer. *N Engl J Med*. 2010;363(10):943–953.
36. Fagotti A et al. Randomized trial of primary debulking surgery versus neoadjuvant chemotherapy for advanced epithelial ovarian cancer (SCORPION-NCT01461850). *Int J Gynecol Cancer*. 2020;30(11):1657–1664.
37. Kehoe S et al. Primary chemotherapy versus primary surgery for newly diagnosed advanced ovarian cancer (CHORUS): an open-label, randomised, controlled, non-inferiority trial. *Lancet*. 2015;386(9990):249–257.

38. Onda T et al. Comparison of survival between primary debulking surgery and neoadjuvant chemotherapy for stage III/IV ovarian, tubal and peritoneal cancers in phase III randomised trial. *Eur J Cancer*. 2020;130:114–125.
39. Wright AA et al. Neoadjuvant chemotherapy for newly diagnosed, ovarian cancer: society of gynecologic oncology and american society of clinical oncology clinical practice guideline. *J Clin Oncol*. 2016;34(28):3460–3473.
40. van de Vrie R et al. Laparoscopy for diagnosing resectability of disease in women with advanced ovarian cancer. *Cochrane Database Syst Rev*. 2019;2019(3).
41. Fagotti A et al. A laparoscopy-based score to predict surgical outcome in patients with advanced ovarian carcinoma: a pilot study. *Ann Surg Oncol*. 2006;13(8):1156–1161.
42. Fagotti A et al. Prospective validation of a laparoscopic predictive model for optimal cytoreduction in advanced ovarian carcinoma. *Am J Obstet Gynecol*. 2008;199(6):642.e1–642.e6.
43. Fleming ND et al. Laparoscopic surgical algorithm to triage the timing of tumor reductive surgery in advanced ovarian cancer. *Obstet Gynecol*. 2018;132(3):545–554.
44. Fagotti A et al. A multicentric trial (Olympia – MITO 13) on the accuracy of laparoscopy to assess peritoneal spread in ovarian cancer. *Am J Obstet Gynecol*. 2013;209(5):462.e1–462.e11.
45. Petrillo M et al. Definition of a dynamic laparoscopic model for the prediction of incomplete cytoreduction in advanced epithelial ovarian cancer: proof of a concept. *Gynecol Oncol*. 2015;139(1):5–9.
46. Rutten MJ et al. Laparoscopy to predict the result of primary cytoreductive surgery in advanced ovarian cancer patients (LapOvCa-trial): a multicentre randomized controlled study. *BMC Cancer*. 2012;12:31.
47. Rutten MJ et al. Laparoscopy to predict the result of primary cytoreductive surgery in patients with advanced ovarian cancer: a randomized controlled trial. *J Clin Oncol*. 2017;35(6):613–621.
48. Rutten MJ, Leeflang MMG, Kenter GG, Mol BWJ, Buist M. Laparoscopy for diagnosing resectability of disease in patients with advanced ovarian cancer. *Cochrane Database Syst Rev*. 2014;2014(2):CD009786. doi:10.1002/14651858.CD009786.pub2.
49. Fagotti A et al. Role of laparoscopy to assess the chance of optimal cytoreductive surgery in advanced ovarian cancer: a pilot study. *Gynecol Oncol*. 2005;96(3):729–735.
50. Patel A et al. Emerging trends in neoadjuvant chemotherapy for ovarian cancer. *Cancers (Basel)*. 2021;13(4):626.
51. Gueli Alletti S et al. Minimally invasive interval debulking surgery in ovarian neoplasm (MISSION trial – NCT02324595): a feasibility study. *Am J Obstet Gynecol*. 2016;214(4):503.e1–503.e6.
52. Fagotti A et al. The international mission study: minimally invasive surgery in ovarian neoplasms after neoadjuvant chemotherapy. *Int J Gynecol Cancer*. 2019;29(1):5–9.
53. Menderes G et al. The role of minimally invasive interval debulking surgery in advanced epithelial ovarian cancer. *Expert Rev Anticancer Ther*. 2016;7140:1–3.
54. *NCCN clinical practice guidelines in oncology: ovarian cancer including fallopian tube and primary peritoneal cancer, version 3*, 2020. www.nccn.org/professionals/physician_gls/pdf/ovarian_blocks.pdf.
55. Kremer KM et al. Practice patterns using minimally invasive surgery for the treatment of ovarian cancer: a survey of physician members of the Society of Gynecologic Oncologists. *Gynecol Oncol Rep*. 2020;33:100617.
56. Vergote I et al. Port-site metastases after open laparoscopy: a study in 173 patients with advanced ovarian carcinoma. *Int J Gynecol Cancer*. 2005;15(5):776–779.
57. Corrado G et al. Laparoscopic debulking surgery in the management of advanced ovarian cancer after neoadjuvant chemotherapy. *Int J Gynecol Cancer*. 2015;25(7):1253–1257.
58. Melamed A et al. Laparoscopy compared with laparotomy for debulking ovarian cancer after neoadjuvant chemotherapy. *Obstet Gynecol*. 2017;129(5):861–869.
59. Psomiadou V et al. Robotic interval debulking surgery for advanced epithelial ovarian cancer: current challenge or future direction? A systematic review. *J Robot Surg*. 2021;15(2):155–163.
60. Brown J et al. When less is more: minimally invasive surgery compared with laparotomy for interval debulking after neoadjuvant chemotherapy in women with advanced ovarian cancer. *J Minim Invasive Gynecol*. 2019;26(5):902–909.
61. Pomel C et al. Laparoscopic management of advanced epithelial ovarian cancer after neoadjuvant chemotherapy: a phase II prospective multicenter non-randomized trial (the CILOVE study). *Int J Gynecol Cancer*. 2021;31(12):1572–1578.
62. Conte C et al. Nomogram to predict feasibility of minimally invasive interval debulking surgery in advanced ovarian cancer. *Int J Gynecol Cancer*. 2022;32(4):532–539.
63. Favero G et al. Oncologic concerns regarding laparoscopic cytoreductive surgery in patients with advanced ovarian cancer submitted to neoadjuvant chemotherapy. *Oncology*. 2015;89(3):159–166.
64. Zeng S et al. Efficacy and safety of minimally invasive surgery versus open laparotomy for interval debulking surgery of advanced ovarian cancer after neoadjuvant chemotherapy: a systematic review and a meta-analysis. *Front Oncol*. 2022;12.
65. Abitbol J et al. Incorporating robotic surgery into the management of ovarian cancer after neoadjuvant chemotherapy. *Int J Gynecol Cancer*. 2019;29(9):1341–1347.
66. Nitecki R et al. Laparoscopic cytoreduction After Neoadjuvant ChEmotherapy (LANCE). *Int J Gynecol Cancer*. 2020;30(9):1450–1454.
67. Coleman RL et al. Secondary surgical cytoreduction for recurrent ovarian cancer. *N Engl J Med*. 2019;381(20):1929–1939.
68. Harter P et al. Randomized trial of cytoreductive surgery for relapsed ovarian cancer. *N Engl J Med*. 2021;385(23):2123–2131.
69. Shi T et al. Secondary cytoreduction followed by chemotherapy versus chemotherapy alone in platinum-sensitive relapsed ovarian cancer (SOC-1): a multicentre, open-label, randomised, phase 3 trial. *Lancet Oncol*. 2021;22(4):439–449.
70. Ramirez PT et al. Laparoscopic secondary cytoreductive surgery: let's not make the same assumptions. *Int J Gynecol Cancer*. 2023;33(2):145–146.
71. St. Laurent JD et al. Robotic resection of isolated ovarian cancer recurrence in the lesser sac. *Gynecol Oncol Rep*. 2022;41:100991.
72. Conte C et al. Role of minimally invasive secondary cytoreduction in patients with recurrent ovarian cancer. *Int J Gynecol Cancer*. 2023;33(2):137–144.
73. Paik ES et al. Feasibility of laparoscopic cytoreduction in patients with localized recurrent epithelial ovarian cancer. *J Gynecol Oncol*. 2016;27(3).
74. Magrina JF et al. Analysis of secondary cytoreduction for recurrent ovarian cancer by robotics, laparoscopy and laparotomy. *Gynecol Oncol*. 2013;129(2):336–340.

40 ENDOMETRIAL CANCER SURGERY

Emma Rossi

Endometrial cancer is the most common gynecologic cancer in the developed world. It is increasing in both incidence and lethality. Women with endometrial cancer typically present with postmenopausal bleeding and diagnosis is made through sampling of the endometrium in the office or surgical suites. Women with Lynch syndrome or Cowden syndrome carry higher risk for developing endometrial cancer and may receive preventative surgery or screening studies. For most women with endometrial cancer who are diagnosed with the more common endometrioid subtype, prognosis is typically favorable, and efforts are focused on strategies to minimize the morbidity of treatment through minimally invasive surgical techniques and selective lymphadenectomy or sentinel lymph node biopsy. For women with the more aggressive subtypes such as serous carcinomas or carcinosarcoma, prognosis is poorer and aggressive therapies including chemotherapy and radiation therapy are often necessary. Much more is being learned regarding the genomics characterizations and classification of this cancer, resulting in progressions towards targeted therapeutics.

Epidemiology of Endometrial Cancer

Endometrial cancer is the most common gynecologic cancer in the US with more than 67,880 cases diagnosed in 2024.[1] In contrast to most other cancers, the incidence of endometrial cancer continues to increase as does the mortality.[2] This may be attributable in part to an increasing incidence of aggressive subtypes of the malignancy and limited efficacy of therapeutic options for metastatic disease. Fortunately for most women with endometrial cancer, it is diagnosed at an early, potentially curable stage, and much focus in recent times has been on reducing the morbidity of diagnostics and intervention for these women to optimize quality of life. Surgery remains the cornerstone of therapy for most patients with the diagnosis of endometrial cancer.

Definition/Classification

Endometrial cancers include epithelial malignancies of the endometrium, the mucosal layer of the uterine cavity. Endometrioid cell types are the most common histologic subtype. Endometrial cancers are considered distinct from mesenchymal tumors of the subendometrial tissues, including endometrial stromal tumors and uterine sarcomas. These mesenchymal tumors are not considered in this chapter.

Traditionally, endometrial cancers have been classified into two groups: those that arise in response to excessive estrogen exposure ("type I" cancers) and those that develop as a result of DNA mutations in p53 ("type II" cancers).[3] Type I cancers are predominantly the endometrioid cell type tumors, arising in a background of endometrial hyperplasia, and most usually have low grade histologic features. They are most commonly diagnosed at an early stage and for these reasons are generally associated with favorable prognosis. Type II cancers, such as serous, clear cell, and carcinosarcoma, do not require the same pro-estrogenic environment or risk factors, and develop within carcinoma in situ of the endometrium. These type II tumors are aggressive and more commonly present with metastatic disease when compared to the type I malignancies.[4, 5]

In addition to these tumor subtypes having a different prognosis, the molecular profile of these tumors also differ with PIK3CA pathway mutations, particularly in PTEN and KRAS mutations more commonly associated with type I endometrioid cancers.[6] The mutational profile of the aggressive, type II serous carcinomas is similar to that seen in triple-negative breast cancer and serous ovarian cancers. Clear cell carcinomas of the endometrium more frequently possess mutations in $ARID_1A$ and are less likely to carry mutations in P53 compared with serous carcinomas, which brings into question how well they belong in the classic grouping of type II cancers.[7, 8]

In reality, theses histologic subcategorizations do not tell the whole story of tumor behavior. The Cancer Genome Atlas (TCGA) project was completed in an attempt to describe the genomic characterization of multiple cancers.[6] Four distinct genomic patterns emerged: those with a POLE ultra-mutated state, microsatellite instability (MSI) high tumors, and the remainder include copy number high or low patterns. Copy number high tumors were associated with TP53 mutations, the "serous-like tumors". The study noted significant overlap in the genetic alterations found in endometrioid and non-endometrioid endometrial cancers, suggestive of greater genetic heterogeneity in endometrial cancer than previously recognized by the traditional subcategorization of type I and type II or based on histology alone. Once separated into TCGA subgroups as defined by the specified genomic mutational patters, the investigators demonstrated that clinical behavior (such as recurrence and survival) closely could be predicted. Molecular classification of endometrial cancer has become integrated into staging definitions, treatment algorithms, and clinical trials. Figure 40.1 outlines how immunohistochemistry (IHC) staining for mismatch repair (MMR) proteins and p53 can be used as a simplified algorithm to categorize cancers in accordance with the Proactive Molecular Risk Classifier for Endometrial Cancer (ProMisE) algorithm.[9]

Pathophysiology/Risk Factors/Genetics/Prevention

The risk factors for endometrial cancer include conditions of increased estrogen exposure including obesity, early menarche, late menopause, anovulatory cycles, nulliparity, exposure to exogenous estrogens unopposed by progesterone, age over 55, and metabolic conditions such as diabetes.[10, 11] Smoking, low-fat diets, and physical exercise may be protective. Black race is a risk factor for the particularly aggressive serous subtype of endometrial cancer which, in part, accounts for some of the increased endometrial cancer mortality experienced by black women.[12]

Certain hereditary genetic conditions are associated with an increased risk for endometrial cancer and make up approximately 5% of endometrial cancers.[13] The first is Lynch syndrome (hereditary non-polyposis colorectal cancer syndrome), for which carriers have impaired functioning of tumor suppressor genes responsible for DNA mismatch repair.[14] As a result, these women accumulate microsatellite instability which can lead to malignancy. Lynch syndrome is associated with a 40% to 60%

DOI: 10.1201/9781003312109-40

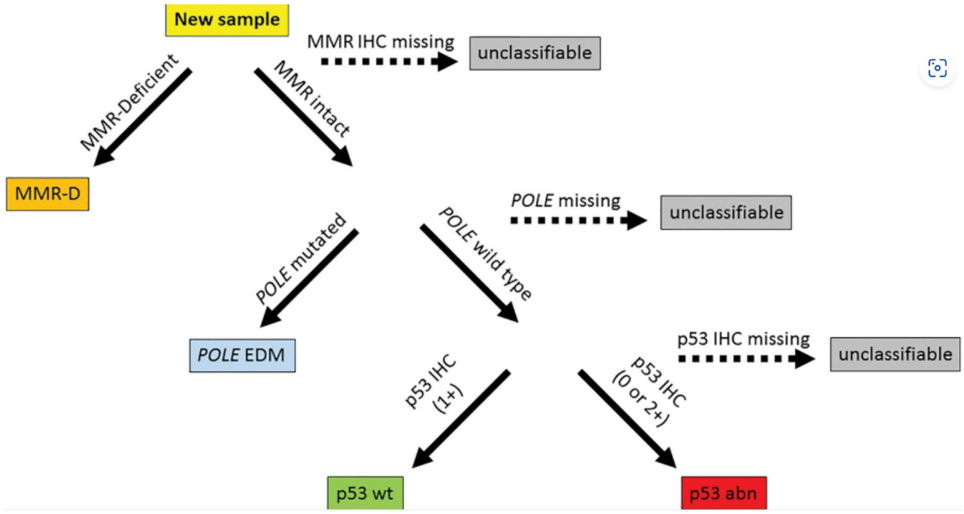


FIGURE 40.1 Use of IHC and p53 in a simplified algorithm to categorize cancers in accordance with the ProMisE algorithm (from ref 9 with permission).

chance of developing endometrial cancer, which is equivalent to their risk of colon cancer. For women carriers, their endometrial cancer may be the first to present, and therefore, young age at diagnosis should prompt clinicians to consider a work-up of Lynch syndrome.[15]

While the risk of endometrial cancer is not increased in women who carry BRCA 1 and 2 gene mutations, there may be an increased risk for serous endometrial cancer in BRCA 1 mutation carriers.[16]

Genetics

Tumor assessment for defects in DNA mismatch repair (of MLH1, MSH2, MSH6) is recommended for all endometrial cancers.[17] This testing identifies abnormalities in mismatch repair and microsatellite instability which serves to prognosticate and guide adjuvant therapies, in addition to triaging patients towards testing for Lynch syndrome.

Genetic mutations in PTEN are a feature of Cowden syndrome, which is associated with a high (20%–30%) lifetime risk for endometrial cancer.[18]

Surgical Staging of Endometrial Cancer

Endometrial cancer staging was originally made through clinical assessments. During this era, the role of surgery for the staging of endometrial cancer typically included fractionated dilation and curettage, or hysterectomy and bilateral salpingo-oophorectomy, with biopsies of clinically apparent metastases. As surgical technique matured among gynecologic oncologists, and surgical lymph node assessments became more routinely performed, it became appreciated that lymphatic spread was an important pattern of disease progression.

In 1987 the landmark clinical trial, GOG 33, was published.[19] Six hundred and twenty-one patients with clinical stage I disease underwent surgical staging with total abdominal hysterectomy and selective pelvic and para-aortic lymphadenectomy. Para-aortic lymph node assessment was felt to be important due to the hypothesized drainage pathways from the uterine fundus via the ovarian vessels to the infrarenal aortic basins.

The purpose of GOG 33 was to define the incidence and distribution of metastases. Occult extrauterine metastases were found in 22% of patients. This included 11% of patients with lymph node metastases. Table 40.1 includes these patients from the GOG 33 trial. Six percent of lymph node metastases were located in the pelvic basins only, and 3% were located in pelvic and para-aortic basins. Only 2% of patients had isolated para-aortic basin metastases.

The results of this clinical trial led to a change in FIGO staging to utilize the pathology results of surgical biopsies as opposed to clinical assessment. In 2017 the results of a confirmatory study, GOG 210, were released.[20] In this more

TABLE 40.1 Distribution of Pelvic and Para-Aortic Lymph Node Metastases in Clinical Stage I Endometrial Cancer

	Aortic		
Pelvic	**Negative**	**Positive**	**Total**
Negative	551 (89%)	12 (2%)	563 (91%)
Positive	36 (6%)	22 (3%)	58 (9%)
Total	587 (95%)	34 (5%)	621 (100%)

Source: From Creasman et al., Surgical pathologic spread patterns of endometrial cancer. A Gynecologic Oncology Group Study. *Cancer*. 1987:60, 2035–2041; Distribution of Pelvic and Para-aortic Lymph Node Metastases (from ref 19 with permission).

contemporaneous trial, patients with clinical stage I endometrial cancer underwent comprehensive surgical staging. This study validated the results of earlier trials with respect to the incidence of occult extrauterine disease when surgical staging is performed for clinical stage I disease.

FIGO Staging of Endometrial Cancer

Several iterations of FIGO staging for endometrial cancer have replaced those that followed the findings of GOG 33. These adjustments factor changes in knowledge regarding prognosis and incorporation of molecular subtyping. Their most recent (2023) staging classifies stage I as confined to the uterine corpus and ovary; stage II as invasion of cervical stroma without extrauterine extension or with substantial lymphovascular space involvement or aggressive histological types with myometrial invasion; stage III as local and/or regional spread of the tumor of any histological subtype; and stage IV as spread to the bladder mucosa and/or intestinal mucosa and/or distant metastasis; each stage has further subclassifications.[21]

Elements of Surgical Staging

The components of surgical staging are designed to provide information both for prognosis and to aid in adjuvant therapy decision making. They include the collection of peritoneal washings and the assessment of the intraperitoneal and retroperitoneal spaces for gross extrauterine disease, which, if found, should be biopsied or removed. While peritoneal washings are no longer included as part of the staging for endometrial cancer, they have been associated with prognosis and serve as a valuable data point in the assessment of risk factors for metastases.[22, 23] In the case of high grade serous endometrial cancer, the status of peritoneal washings is a discriminating factor for the prescription of adjuvant systemic therapy according to NCCN treatment algorithms for stage I disease.[24]

Following peritoneal assessment, retroperitoneal assessment and peritoneal washing collection, a total extrafascial hysterectomy, with removal of both the uterine fundus and cervix, follows. Bilateral salpingo-oophorectomy is preferred but oophorectomy can be omitted in premenopausal women with clinically normal ovarian tissue and the absence of inherited genetic mutations, such as some Lynch syndrome cohorts, which might confer an elevated risk for ovarian cancer. The risk of synchronous ovarian cancer and endometrial cancer is approximately 5% among women with endometrial cancer.[25]

Pelvic lymphadenectomy is performed, which includes removal of all lymphatic tissue overlying major vasculature between the boundaries of the mid-portion of the common iliac artery proximally, the circumflex iliac vein distally, the psoas muscle and genitofemoral nerve laterally, and the ureter medially. The obturator nerve serves as the deep margin for the dissection (Figure 40.2a). Evidence suggests that extending the pelvic nerve dissection distal beyond the circumflex iliac vein towards the inguinal ligament significantly increases the risk for lymphedema and is generally discouraged in the presence of clinically normal lymph nodes.

The para-aortic lymph node dissection involves removal of all fatty and lymphatic tissue from the great vessels, including the vena cava and aorta, between the boundaries of the mid-portion of the common iliac to the renal veins (Figure 40.2b). The inferior mesenteric artery has historically been used as the upper limit of dissection; however, this anatomic landmark constitutes an arbitrary boundary of dissection, and the probability of lymph node metastases remains high above this level.

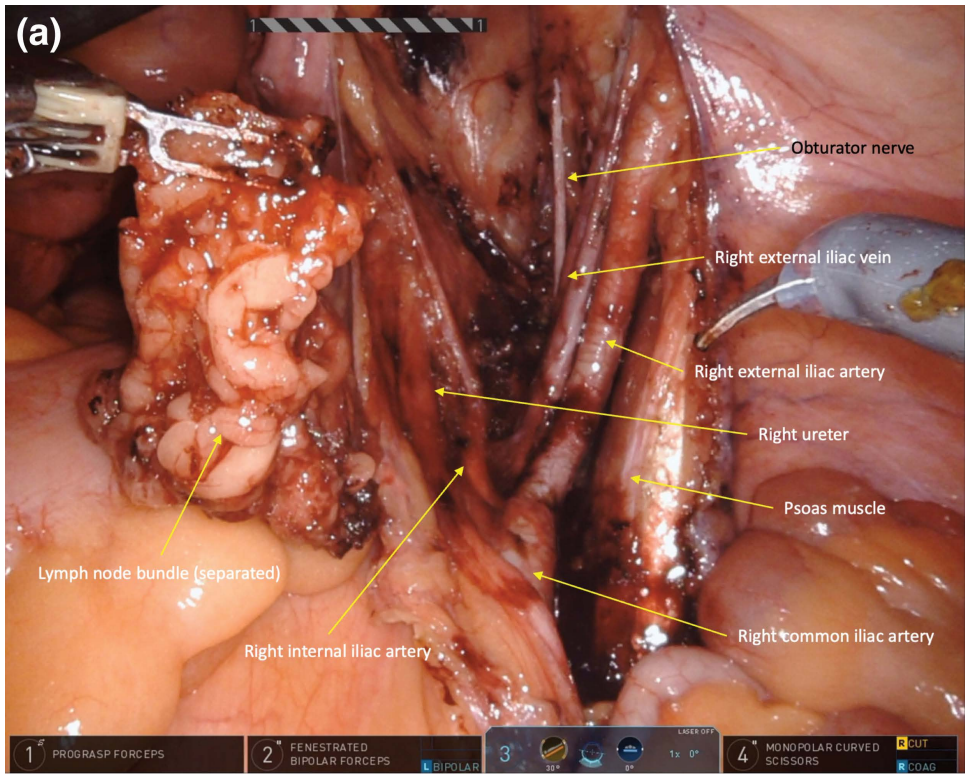


FIGURE 40.2A Anatomy of right pelvic lymphadenectomy.

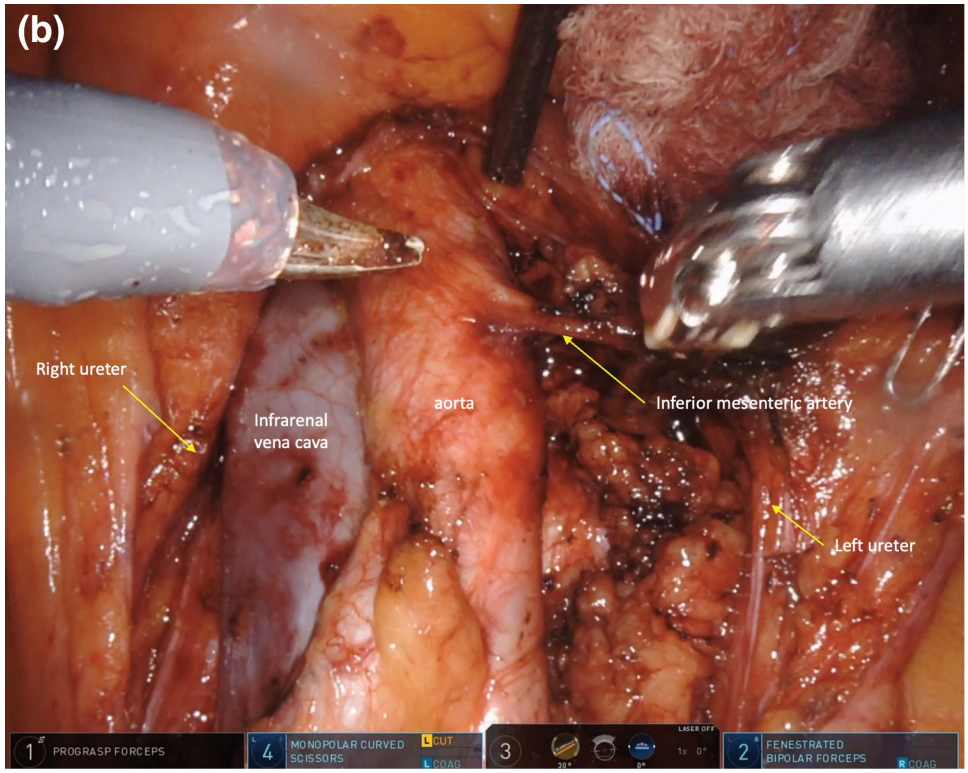


FIGURE 40.2B Anatomy of para-aortic lymphadenectomy.

Omental biopsy can be included in this surgical staging of endometrial cancer but is typically reserved for high grade and non-endometrioid histologies for whom the risk is highest. Retrospective series suggest that microscopic omental metastases are rare in cases when there are no metastases at other extrauterine sites, making the role of routine omental biopsy less clear.[26]

The Importance of Surgical Staging in Treatment Algorithms

The identification of occult microscopic extrauterine disease allows for identification of patients for whom systemic therapy is most appropriate. Systemic therapy is associated with improved cure for metastatic disease.[27] However, clinical trials are yet to identify a benefit for the addition of systemic therapy for stage I disease.[28] Therefore, the identification of patients for whom systemic therapy is of most benefit is a valuable consequence of surgical staging.

In contrast, surgical staging confirming true stage I disease through negative pathologic staging biopsies can provide de-escalation of therapy. Patients who do not undergo surgical staging with lymphadenectomy are more likely to receive whole pelvic radiation therapy for uterine pathologic features that confer high risk for recurrence than those who have similar features and negative lymph node assessments.[29]

Lymphadenectomy for Endometrial Cancer Staging

Routine lymphadenectomy, including pelvic and para-aortic sampling, became standard of care following the results of prospective cohort studies that identified approximately 11%–12% of patient harbored occult metastatic lymphatic disease.[20] However, questions remained regarding the therapeutic virtue of routinely performing lymph node dissections for patients with clinically normal lymph nodes. Retrospective series observed improved survival rates with an increasing number of lymph nodes removed at the time of staging.[30] This finding is likely indicative of comprehensiveness of nodal assessments, rather than debulking of disease, given that most of these nodal specimens contain no metastases.

The question of the therapeutic virtue of lymphadenectomy has been addressed in randomized control trials. The largest of these trials was the international ASTEC trial.[31] This study randomized 1408 patients with clinical stage I disease to routine pelvic (with or without para-aortic) lymphadenectomy or hysterectomy alone. The study found no survival benefit among patients undergoing lymphadenectomy. Criticisms of the study included the high rate of crossover between the study arms, the low yield in lymph nodes removed, and the lack of standardized adjuvant therapy prescription for node positive patients (in this trial adjuvant therapy was determined by a separate randomization process which did not take into consideration the presence of lymph node metastases). Additionally, the trial population was not enriched with high risk and high grade cancers, thus included a population at low risk for positive nodal disease.

Despite these criticisms, a second international randomized clinical trial validated the results of ASTEC, finding no survival benefit to routine lymphadenectomy at the time of endometrial cancer staging for 514 patients.[32] In this second study, average lymph node counts were higher, suggesting a more comprehensive lymphadenectomy was performed, and adjuvant therapy was prescribed according to clinician choice. To date, no level 1 evidence supports a benefit in survival for patients undergoing lymphadenectomy at the time of endometrial cancer staging.

Complications of Lymphadenectomy

Intraoperative Complications

Lymphadenectomy is associated with risk of hemorrhage and vascular injury as surgeons are required to strip the major vessels of the abdomen and pelvis of their fatty and lymphatic investments. Occult perforator vessels can be avulsed during the dissection, and due to the high pressure dynamics of these vessels, rapid exsanguination can occur. Patients undergoing lymphadenectomy should have preoperative lab assessments for type and antibody screen in case urgent transfusion is necessary.

Ureteral injuries can occur during pelvic dissection, particularly if the para-rectal space is not opened adequately. Similarly, during the para-aortic nodal dissection the ureter, which runs parallel and immediately lateral to the vena cava and aorta in close approximation to the gonadal vessels, can be injured. Care must be taken during aortic node dissection to visualize and mobilize the ureter to free it from surgical instrumentation and electrosurgical devices.

Bowel injury can result during maneuvers to create exposure because the pelvic and aortic nodal basins lie beneath the mesentery of the small intestine. The duodenum passes ventral to the aortic nodes in the infrarenal aortic basin and must be mobilized from the underlying nodes in order to safely access the most cephalic border of the dissection. Patients with increased abdominal and retroperitoneal adiposity present challenges to safe exposure of the nodal basins, particularly in this region, due to crowding of small intestinal structures overlying the planes of dissection. Strategies to create better visualization, and avoidance of intestinal injury, include placement of the patient in steep Trendelenburg (greater than 25 degrees) to displace the bowel into the upper abdomen, use of retractor blades to deflect and hold the intestines cephalad, and suturing of adjacent peritoneum to the anterior abdominal wall to create shelves beyond which the intestinal structures can remain while retroperitoneal dissection follows.

Several important neural structures are at risk for injury during pelvic and aortic node dissections including the genitofemoral nerve, which runs parallel to the external iliac artery and can be injured or transected during pelvic lymphadenectomy. This can result in sensory defects in the medial thigh and lateral labia. The obturator nerve travels in the floor of the obturator space after emerging under the bifurcation of the internal and external iliac vein. This nerve is encapsulated by nodal tissue, and care must be shown by the surgeon in identifying this structure. Transection or coagulation by electrosurgical devices are the most common mechanisms of obturator nerve injury. It can also be damaged by development of hematoma in the obturator space. The obturator nerve is a motor nerve without sensory component and supplies the obturator muscles of the medial thigh. Its injury results in inability or weakness in abduction of the hip which typically manifests as an inability or difficulty in crossing the affected leg over the contralateral knee, and difficulty getting in and out of a car or bed. The femoral nerve is less commonly injured during lymph node dissections; however, if dissection is inadvertently carried deep within the psoas muscle, particularly at the level of the pelvic brim, the femoral nerve can be injured. Injury to this nerve can present as weakness in flexion of the hip (difficult walking) and sensory loss to the anterior thigh.

Postoperative Complications

While intraoperative complications can be catastrophic, it is the postoperative complications of lymphadenectomy that are most common and can lead to significant quality of life impairment. Lymphedema of the lower extremity has been reported in up to 38% in retrospective series of patients undergoing lymphadenectomy for endometrial cancer.[33] However, there is substantial variability in the data with similar retrospective series reporting rates as low as 6%.[34] Retrospective assessments of lower extremity lymphedema are problematic as they typically rely upon clinician reporting of events. Prospective studies, such as the LEG study, have evaluated the incidence of lower extremity lymphedema after pelvic lymphadenectomy using limb measurements and reported up to 34% of patients have objective findings of the condition.[35] The development of lymphedema can be confounded by risk factors of age, weight, stage, and the receipt of adjuvant radiation therapy.[36] There is also a correlation between the incidence of lymphedema and the number of lymph nodes removed at the time of lymphadenectomy.[34] Lower extremity lymphedema has been associated

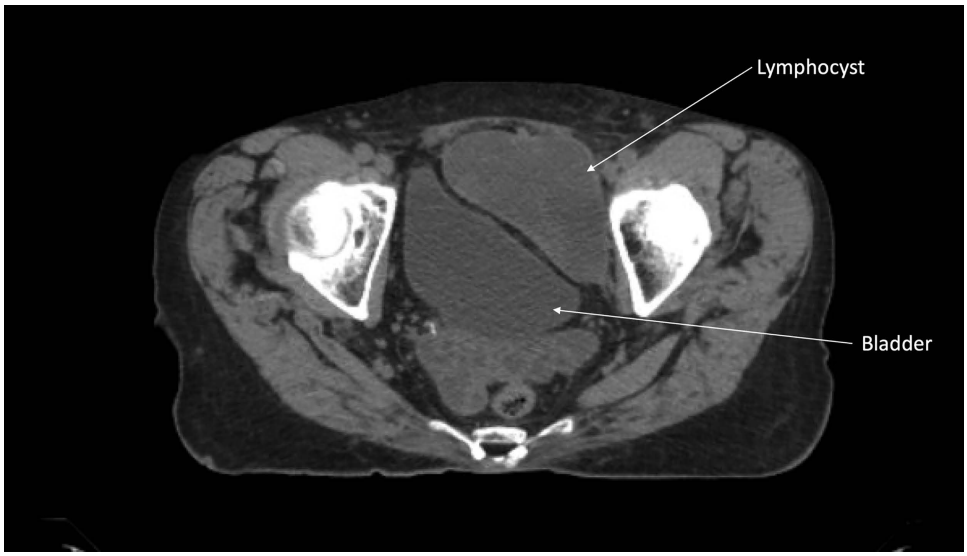


FIGURE 40.3 Right external iliac lymphocyst displacing bladder.

with impairments in quality of life and may require lifelong therapies such as massage, physical therapy, and compression garments.

Other late sequelae of lymphadenectomy include the formation of lymphocysts, which are encapsulated collections of lymph fluid adjacent to the iliac, vena cava, or aortic vessels (see Figure 40.3). These may cause compression on the great vessels, and subsequent VTE or edema, in addition to symptoms of pelvic pressure. If asymptomatic, they can be observed. However, symptomatic lymphocysts should be drained. In refractory cases, surgical marsupialization may be necessary.

Chylous ascites is a rare complication of lymphadenectomy that results from inadequate sealing of the lymphatic trunks, particularly at the cephalic boundary of the aortic dissection. This includes the formation of large volume milky ascites, abdominal pain, fevers and night sweats, and nausea. Treatment may involve surgery, but can also include dietary modification and administration of somatostatin or octreotide.

Selective Staging Algorithms

Abandonment of lymphadenectomy has the potential to result in lack of clinically valuable information for adjuvant treatment decision making.[29] Thus, clinicians have sought to identify subgroups of patients at higher risk for lymph node metastases in whom lymphadenectomy may be justified.

Patients in whom risk for lymph node metastases are higher include those with deep myometrial tumor infiltration, tumor size greater than 2 cm, and high grade histology.[37–39] Surgeons from the Mayo Clinic derived an algorithm in which:

1. Frozen section was performed on the hysterectomy for patients undergoing endometrial cancer staging surgery.[40, 41] Pathologists reviewed the above three high risk features, and
2. If all three were absent, lymphadenectomy was omitted, and hysterectomy alone was performed.
3. The remaining patients (73% of the cohort) underwent a complete pelvic and infrarenal para-aortic lymph node dissection.

Results from their cohort revealed disease-specific survival of 96% among those in whom lymphadenectomy was omitted due to the absence of high risk features. Among patients with at least one high risk feature, 22% were identified as having node positive disease, and 16% with isolated para-aortic lymph node metastases. These results suggest that a selective algorithm for lymphadenectomy utilizing intraoperative frozen section assessment of high risk features to triage the completion of staging is a safe alternative to routine lymphadenectomy in all and can reduce futile lymph node dissections in nearly a quarter of patients with an endometrial cancer diagnosis, without compromising disease-specific survival.

This algorithm is commonly referred to as the "Mayo Clinic Criteria" and has been widely adopted by surgeons. However, others criticize its reliance on frozen section, which can add cost and time to the operative procedure, in addition to the potential for inaccuracy of this modality among non-specialized pathology centers. Furthermore, the majority of patients who meet high risk criteria by Mayo Clinic Criteria will ultimately have negative nodal assessments, and therefore futile lymph node dissections remain common.

Sentinel Lymph Node Biopsy

Sentinel lymph node biopsy for the staging of endometrial cancer has emerged as a strategy that balances the harms of inadequate staging assessment following selective algorithms and the futile, potentially morbid, intervention of complete lymphadenectomy on all patients.

Sentinel lymph node mapping and biopsy, as a principle, serves to identify the specific first-in-chain lymph node to receive drainage from the uterine pathways. Thus, this nerve serves as the specimen most likely to harbor occult metastatic disease, eliminating the need for stripping non-clinically relevant nodal tissues, and yet obtaining the diagnostic information of interest to aid in adjuvant therapy decision making.

The origins of sentinel lymph node (SLN) biopsy are in the staging of cancers of the head and neck and penis, where lymphatic drainage can be complex and unpredictable. It was subsequently established as standard of care surgical technique for the dermal malignancies – breast cancer, melanoma, and vulvar cancer – by demonstrating satisfactory sensitivity in detecting metastatic disease and low false negative rates.

SLN biopsy for endometrial cancer has been explored as a response to the dilemma of data demonstrating a lack of therapeutic benefit for lymphadenectomy, yet knowledge that the information gleaned from lymph node evaluation can de-escalate toxic adjuvant therapy. This technique promised an alternative to the "all or none" phenomena of traditional staging procedures or selective staging algorithms. Early studies evaluating this technology focused on the use of injection of blue dyes with or without radiolabeled colloid as tracers for detection.[42, 43] Initial series were predominantly retrospective and demonstrated excellent disease-specific survival for those undergoing SLN biopsy alone for endometrial cancer provided attention to certain steps were followed. These steps have been described as the SLN algorithm (Figure 40.4) and include assessment of intraperitoneal regions for evidence of metastatic disease, followed by retroperitoneal assessment for any suspicious nodes (which should be removed), removal of identified SLNs with subsequent ultrastaging by pathology, and side-specific pelvic, with or without para-aortic, lymphadenectomy if no SLN is identified within a hemipelvis.[44]

Choice of Tracer

Early studies of SLN biopsy for endometrial cancer focused on use of traditional tracer dyes, such as calorimetric detection of blue dyes, or measurement of radiolabeled colloids via gamma counters. When used in combination these tracers appear to have higher rates of detection than when either is used in isolation.[43]

However, use of radiolabeled colloids such as Tc99 can be problematic. The safe handling of nuclear medical tracers requires specialized training and appropriate perioperative handling. Furthermore, due to the close proximity of the site of injection with respect to the nodal basins, it can be difficult to accurately capture SLN signal from background injection-site "noise."

Calorimetric detection with blue dyes such as indigo carmine and methylene blue present challenges for obese patients. There are significantly lower rates of detection of SLNs as BMI increases, likely due to the obscuring of the visible dye by fatty retroperitoneal tissues.[45]

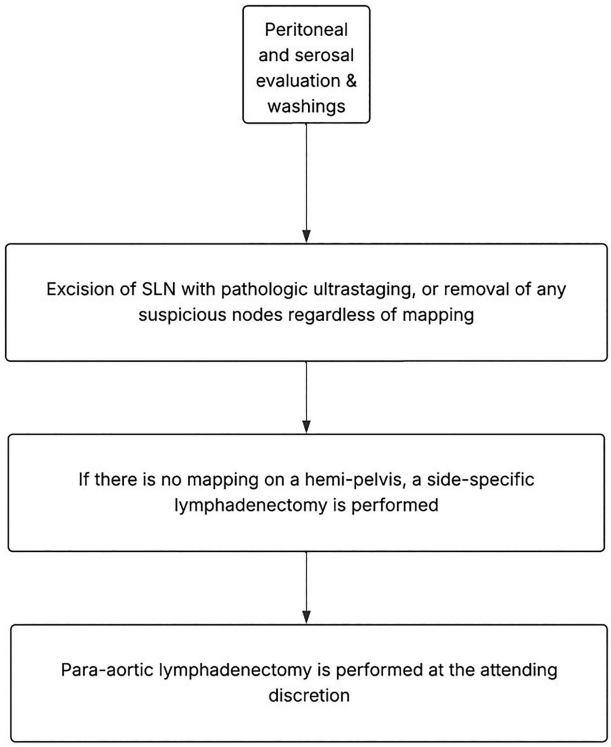


FIGURE 40.4 The sentinel lymph node algorithm for endometrial cancer (from ref 44 with permission).

Indocyanine green (ICG; Acorn Industries) is a water-soluble tracer that has a long history in use for perfusion imaging. When injected at low concentrations it is not visible to the human eye. However, its signal can penetrate through tissue and be detected within the near-infrared range (NIR) by NIR imaging cameras.[45] The ability of ICG to penetrate through fatty tissue is likely a contributory factor to its increased detection in patients with higher BMI. In a randomized control trial comparing the use of blue dye with ICG, detection rates of SLNs were significantly higher with the ICG and NIR imaging scopes, thus making it the tracer of choice for this disease.[46]

Choice of Injection Site

The highest rate of successful detection of SLN comes from injection of tracer dye into the cervix.[47] In addition to being associated with superior detection rates, this is a feasible site of injection which can be easily accessed within the operating room with minimal equipment. Injection of tracer into the uterine cervix (Figure 40.5) has been associated with detection rates in excess of 90%.[48] Dual site injections, typically at 3 o'clock and 9 o'clock on the face of the cervix at two depths, 1 mm and 1 cm, have been associated with optimal detection rates.

However, cervical injections have been criticized for their lack of continuity with the endometrium itself and the concern that surgeons are failing to map the true drainage from the fundal endometrium, hypothesized to be via the ovarian vessels and lymphatics to the infrarenal aortic basins. Concerns exist that if cervical injection is employed, surgeons may "miss" isolated aortic metastases which are not assessed. This concern has been challenged in a series that evaluated mapping rates following cervical versus endometrial (hysteroscopic) or fundal injections.[47] While uterine site injections are associated with higher rates of aortic SLN detection, these studies failed to identify isolated para-aortic nodal metastases within these SLNs.[49] This suggests that the true drainage of the endometrium is, in fact, predominantly via the parametrial channels to the sidewall and presacral spaces, rather than directly to the aortic basins via the ovarian vessels.

Patterns of Lymphatic Drainage

Two dominant pathways have emerged as the classic drainage pathways from the uterus when cervical injection has been employed.[42] The first travels laterally from the parametrium, lying anterior to the course of the uterine artery and vein through the cardinal ligament complex until it reaches the internal iliac artery where it continues to traverse the paravesical and pararectal spaces and deposits into a proximal obturator SLN and/or an external iliac SLN on the medial surface of the vein. It is the obturator SLN that carries the highest probability of harboring metastatic disease. This anterior and lateral pathway is the dominant pathway and makes up approximately 85% of cases of mapping (see Figure 40.6a).

The less common pathway carries the tracer deep or dorsal to and parallel with the ureter, depositing into an SLN on the medial surface of the internal iliac artery or on the presacral space overlying the common iliac vein (Figure 40.6b). This can be an overlooked pathway and requires meticulous and deep pararectal space development to identify.

Given that the virtue of SLN biopsy lies in its diagnostic accuracy, it is important that surgeons carefully assess for both of these pathways in both hemi-pelvises of all patients. Dual pathways (via both the anterior/lateral and posterior/medial lymphatic trunks), as demonstrated in Figure 40.6c, can occur and should always both be assessed.

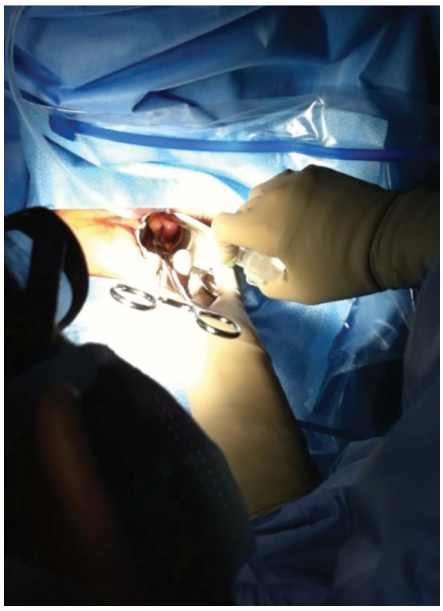


FIGURE 40.5 Cervical injection of tracer dye for SLN mapping of endometrial cancer.

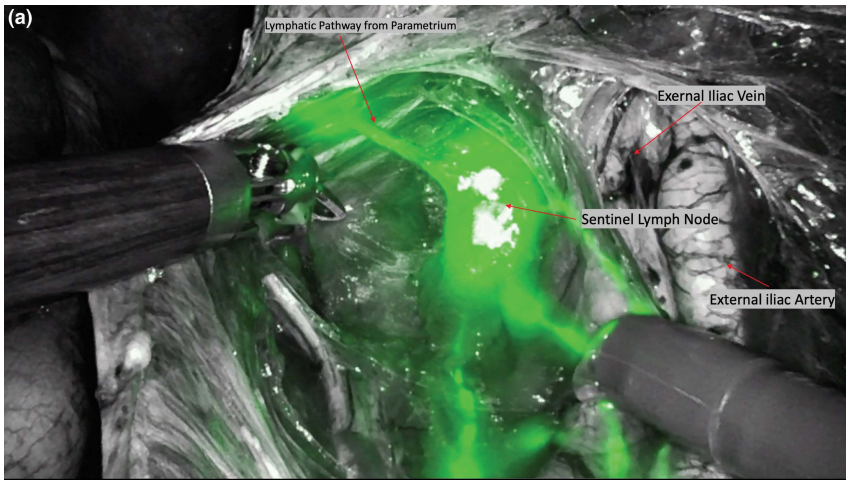


FIGURE 40.6A Right pelvic anterior lateral lymphatic pathway during SLN mapping.

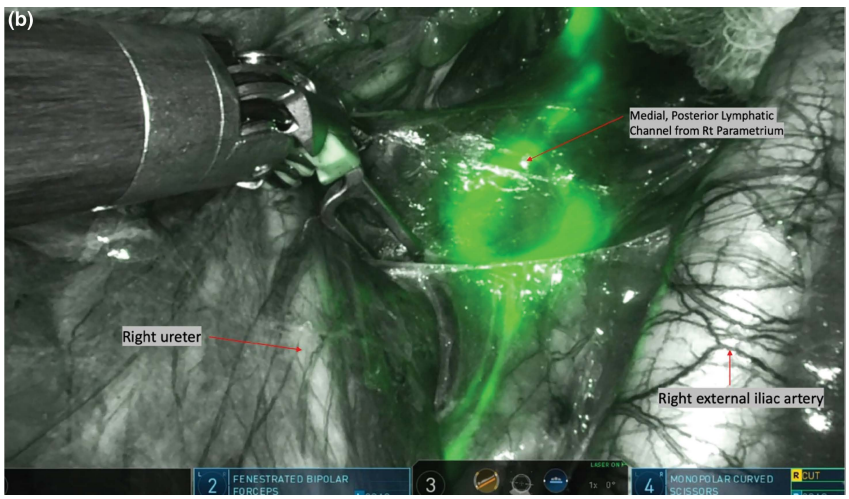


FIGURE 40.6B Right posterior medial SLN mapping pathway for endometrial cancer.

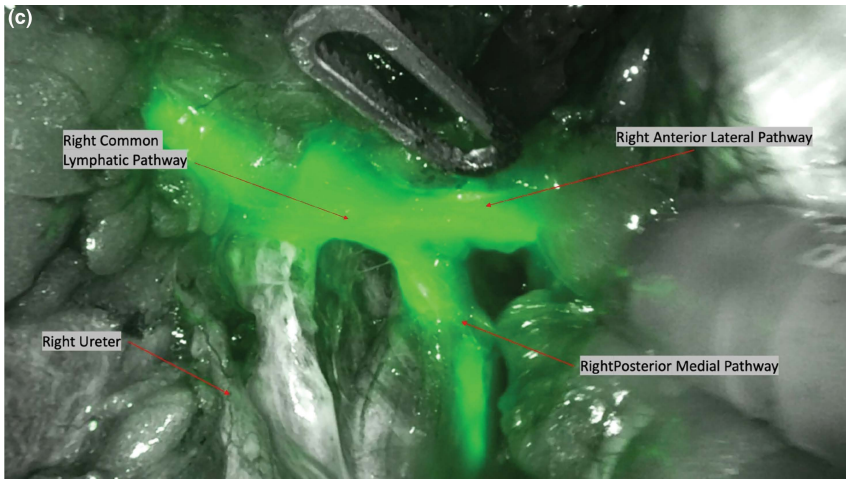


FIGURE 40.6C Dual anterior and posterior right pelvic lymphatic channels during SLN mapping for endometrial cancer.

Establishing the Accuracy of SLN Biopsy

Multiple prospective clinical trials have been performed in which patients have received both SLN mapping and biopsy in addition to completion lymphadenectomy, all of which have confirmed as a clinically acceptable accuracy of SLN biopsy in diagnosing metastatic disease (Table 40.2). The first of these studies, SENTI-ENDO, evaluated 133 patients undergoing SLN biopsy with blue dyes and radiolabeled colloid followed by pelvic lymphadenectomy.[43] The sensitivity for detecting metastatic disease within the lymph node was estimated to be 84%.

SENTI-ENDO was followed by the FIRES trial.[50] This trial enrolled patients with clinical stage I disease in whom 340 mapped at least one SLN and were evaluable for the sensitivity (and false negative rate) analysis. This trial was unique in its use of the robotic surgical platform and the novel tracer, indocyanine green. This study enrolled patients of all histologies and grades, although 43% of the study population had low grade disease, which is known to be associated with low risk for metastatic disease. The lack of enrichment of the study population for the outcome of interest (node positive disease) was overcome by the statistical design which specified the number of node positive patients, rather than a pre-specified total number of patients enrolled. All patients underwent pelvic lymphadenectomy, and para-aortic lymphadenectomy was assessed in 58% of the cohort (though 75% among those with high grade histology). After identifying 36 patients with lymph node positive, one of whom had a false negative SLN biopsy, the study determined that the sensitivity for SLN biopsy in detecting metastatic disease was 97.2% (95% CI 85–100) with a false negative rate of 2.8%. This met the predetermined boundaries of clinically acceptable accuracy.

A criticism of the FIRES trial was its enrolment of an "all-comer," heavily low risk population. Concerns remained regarding the lack of confidence in the technique in the high grade and high risk populations. The SENTOR trial evaluated the accuracy of SLN biopsy in exclusively grade 2 and 3 tumors.[51] This study followed a similar design to the FIRES trial, enrolling 156 patients. Patients all underwent pelvic lymphadenectomy, and aortic lymph node biopsy was performed in all grade 3 cancers. The SENTOR trial validated the results of the FIRES trial with false negative rates of 4% observed in this high risk population.

The SHREC trial provided further validation of the technique in cancers at high risk for metastatic disease.[52] Pelvic with para-aortic lymphadenectomy in addition to SLN biopsy was performed in 257 patients with high/intermediate risk disease. False negative rates were observed to be 2% in this population.

In the wake of these consistent findings that consistently supported a clinically meaningful accuracy for detection of metastases, SLN biopsy has been increasingly adopted as a strategy for surgical staging. It mitigates the harms of routine complete lymphadenectomy, while still yielding histologic staging information that can be crucial in the escalation (to systemic therapy) or de-escalation (from whole pelvic radiation) of patients with endometrial cancer. While no randomized control trials have established the survival or oncologic benefits of the SLN technique relative to routine lymphadenectomy or hysterectomy alone, it is unlikely that such a benefit would be observed given the historical data which have demonstrated a lack of survival benefit for the performance of complete lymphadenectomy.[31, 32] Any survival benefit derived, or maintained,

TABLE 40.2 Accuracy of SLN Biopsy in Endometrial Cancer Staging

Author	Number of Patients	Number of Patients with High-Grade Histology	Proportion of Lymph Node-Positive Patients(%)	Sensitivity	Negative Predictive Value	False-Negative Rate	Para-Aortic Nodes Assessed (%)
Ballester (2011)[43]	111	54 (49%)	17%	84%	97%	16%	0%
Rossi (2017)[50]	340	100 (29%)	11%	97.2%	99%	2.8%	58%
Cusimano (2020)[51]	156	126 (83%)	17%	96%	99%	4%	80%
Persson (2019)[52]	257	220 (85%)	21%	98%	99.5%	2%	84%

from SLN biopsy would be secondary to its diagnostic ability to triage patients appropriately to systemic adjuvant therapy. Therefore, any clinical trial evaluating SLN biopsy in a randomized fashion would need to include adjuvant therapy prescription algorithms as part of its study design.

Surgical Modalities for Endometrial Cancer

The traditional modality for endometrial cancer staging was through laparotomy, most commonly through a vertical midline incision in order to access the pelvic and high aortic lymph node basins. Laparotomy, in contrast to vaginal approach surgery, affords the surgeon the ability to assess the peritoneal cavity to rule out disseminated disease and to access pelvic and aortic nodal basins for lymphadenectomy. However, the coexistence of obesity and endometrial cancer makes laparotomy particularly morbid for this patient population. The patient population is at high risk for the sequelae of obesity-related complications such as wound healing impairment, hyperglycemia, and poor operative visualization associated with visceral injury.

In recent decades the development of minimally invasive surgery has matured in the specialty of gynecologic surgery. The question of whether laparoscopic approaches could safely be applied to endometrial cancer staging surgeries has been investigated in phase 3 studies with consistent findings supporting its efficacy, and both perioperative and oncologic safety.

In the 2616 patient study, LAP2 led by the GOG cooperative group, patients with clinical stage I endometrial cancer were randomly assigned 2:1 to laparoscopic approach (including laparoscopic assisted vaginal hysterectomy and total laparoscopic hysterectomy) or open approach via laparotomy.[53] Primary end point was noninferiority of recurrence-free survival with secondary endpoints of perioperative complications and quality of life. Final results did not meet the statistical endpoint for noninferiority of the experimental approach (laparoscopy) compared to laparotomy; however, this was explained by the lower than anticipated rate of observed events of interest (recurrence and death). There was, however, no significant difference in the recurrence-free survival or overall survival between the two cohorts (11% recurrence rate for the laparoscopy arm and 10% for the laparotomy cohort). While oncological outcomes were not appreciably different between the two surgical modalities, there were significantly fewer perioperative and postoperative complications and superior quality of life in the laparoscopic cohort.[54] Quality of life scores were most notably different within the first six weeks postoperatively. The conclusions of the LAP2 trial were that laparoscopic surgical approaches could safely replace laparotomy for the staging of endometrial cancer due to superior perioperative morbidity outcomes following laparoscopy, without a significant difference in oncologic outcomes.

Validation of these study results came soon thereafter by an international study called the Laparoscopic Assisted surgery for Cancer of the Endometrium (LACE) study.[55] This study enrolled 760 patients with clinical stage I endometrial cancer and randomized patients 1:1 between total laparoscopic hysterectomy and bilateral salpingo-oophorectomy, with or without lymphadenectomy. This trial addressed disease-specific survival as a primary endpoint with a study designed to address the noninferiority of the laparoscopic approach. LACE confirmed the results of the earlier LAP2 trial, but met the predetermined boundaries of noninferiority of disease-specific survival, supporting the noninferior oncologic outcomes observed following laparoscopic staging. Once again, perioperative morbidity was significantly worse in the laparotomy cohort.[56]

Challenges of the Minimally Invasive Approach for Endometrial Cancer Surgery

Patient Access

The results of these two prospective trials formed the basis for subsequent society guidelines to recommend that minimally invasive surgery be the standard of care approach for staging of apparent early stage disease. The Commission on Cancer and the Society of Gynecologic Oncology have set benchmarks for the optimal rates of minimally invasive surgery for endometrial cancer staging at 80% in order for institutions to meet standards of high quality oncologic surgical practice.[57] This benchmark does not reside at 100% due to technical limitations in the ability to execute a minimally invasive approach for all patients, particularly those with particularly bulky uteri (e.g., secondary to fibroid distortion) or patients with complex intraperitoneal pathology (such as adhesive disease which precludes safe minimally invasive surgery).

Unfortunately, evidence suggest that these standards are not met equally across all patient populations.[58, 59] Women of black race are less likely to receive surgery via a minimally invasive surgical approach. These inferior rates of minimally invasive approach surgery do not appear to be completely explained by a higher incidence of fibroid uteri among patients of black race. Similarly, patients in rural communities without access to gynecologic oncology within or near their counties are more likely to receive endometrial cancer staging through laparotomy. Efforts are in place to improve access to the superior outcomes afforded by minimally invasive endometrial cancer surgery to most women in all populations.

Completeness of Lymphadenectomy

The ability to complete lymphadenectomy via a minimally invasive approach appears inferior relative to laparotomy. This may be due to the confounder of obesity resulting in "crowding" of the retroperitoneal spaces by bulky adjacent viscera and the inability of patients to tolerate the patient positioning in steep Trendelenburg necessary to achieve exposure to aortic basins.

These limitations in lymphadenectomy via laparoscopic approach were observed in both the LAP2 and LACE trials.[53, 55] The LAP2 trial required lymphadenectomy to be performed as part of surgical staging in order to avoid protocol deviations. As a result, there was a relatively high conversion rate to laparotomy observed (26%). A closer look at these conversions identified that the most commonly cited reason for conversion was lack of exposure to the nodal basins, and these conversions were correlated directly with patient BMI. Patients in the highest BMI cohort experienced conversions to laparotomy in as many as one third of patients.

In contrast, in the LACE trial, lymphadenectomy was not mandated. However, despite a randomized trial design in which both experimental and control arms had similar rates of risk factors for lymph node metastases, lymphadenectomy was performed significantly more frequently in the laparotomy cohort (58% compared to 40% in the laparoscopic cohort, $p = < 0.001$).

Some of these limitations to the performance of lymphadenectomy, including in high BMI patient cohorts, may have been overcome with the development of novel minimally invasive surgical modalities such as robotic-assisted laparoscopy.

Use of Uterine Manipulation

Placement of a transcervical uterine manipulator is common in the performance of minimally invasive hysterectomy, including for the indication of endometrial cancer. Their virtue is that they provide the countertension necessary against which the surgeon, limited by their minimally invasive toolset, can apply tension. The cervical cup or ring provides definition of the vaginal fornices and can help prevent ureteral injury during cardinal ligament transection or colpotomy. However, there remains debate regarding the safety of such devices in malignant hysterectomy with a hypothesis that transcervical manipulators may encourage transit of malignant material into the peritoneal space via iatrogenic "massage" of the endometrium. Retrospective series have suggested inferior outcomes for patients undergoing endometrial cancer staging with use of transcervical manipulation compared with no such manipulators.[60] However, such retrospective data are limited by confounders, particularly confounders for surgical technique. There are no prospective data which suggest inferior oncologic outcomes when transcervical uterine manipulation is used, and meta-analyses do not suggest this confers worse outcomes.[61]

Minimally Invasive Approaches for Endometrial Cancer Surgery: Laparoscopic vs Robotic-Assisted

Conventional laparoscopic staging for endometrial cancer involves use of rigid instrumentation through a variety of three to five ports. Figure 40.7a illustrates a typical configuration for port placement in a laparoscopic staging procedure. Consideration for port placement includes the ability of the surgeon to reach to the pelvis, including the vaginal cuff for closure, optimization of angles for access to both pelvic and abdominal (aortic) anatomy, and concerns for pain and herniation with respect to choice of port size and location.

Conventional laparoscopy formed the cornerstone of traditional surgical approaches for endometrial cancer and was the modality exclusively studied in the seminal prospective trials which established minimally invasive surgery as the modality of choice. However, limitations and challenges exist with this approach, particularly with respect to successful completion of procedures in very obese patients.

In 2005 the robotic-assisted surgical platform (da Vinci, Intuitive Surgical) became commercially available for use in gynecologic surgery. The robotic surgical platform affords surgeons added capabilities beyond conventional laparoscopy included wristed instrumentation, 3-D vision, tremor-free movement, and surgeon autonomy of all instruments. Figure 40.7b illustrates a common port site configuration for robotic-assisted laparoscopic endometrial cancer staging procedures.

Meta-analyses and retrospective database evaluations have evaluated these two minimally invasive modalities for the purpose of completing endometrial cancer staging. The robotic-assisted surgical platform is consistently a more expensive surgical modality with respect to operating room costs.[62] Additionally, access to the technology is more limited relative to conventional laparoscopy. However, there appear to be benefits of the robotic approach with respect to completion of minimally invasive surgery (without conversion) in high BMI patient cohorts, decreased rates of conversion to laparotomy, and an increased ability to comprehensively complete staging procedures with lymphadenectomy.[63] No benefits have been observed for either modality with respect to oncologic outcomes such as overall survival.

In practice, surgeons will choose a minimally invasive surgical approach to endometrial cancer that weighs factors such as access to technology, patient factors, and disease factors (predicting a need for comprehensive lymphadenectomy) when deciding upon preferred route of minimally invasive surgery.

Patient Positioning for Endometrial Cancer Staging

Both minimally invasive surgical modalities are limited by the patient's ability to tolerate the positioning in steep Trendelenburg that is typically required for exposure to the deep retroperitoneal spaces, including in the infrarenal aorta. In order to achieve this positioning, care must be taken to cushion the bony prominences. Patients with high BMI are at higher risk for positioning-related nerve injury. In order to gain access to the pelvis, arms are served best if tucked by the patient's side in military position and carefully padded. The importance of tucking arms by the patient's side lies in the ability for the

FIGURE 40.7A Surgical robot during endometrial cancer staging procedure.

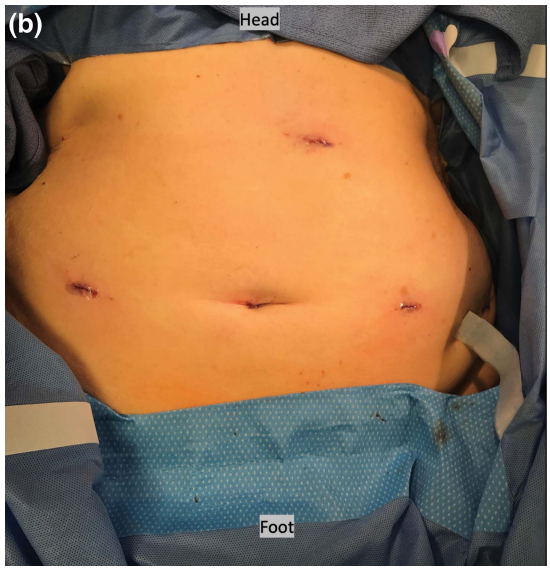


FIGURE 40.7B Typical configuration for port site configuration for robotic-assisted laparoscopic endometrial cancer staging procedures.

surgeon to gain better access to the pelvis by positioning themselves at the level of the patient's shoulder level, an otherwise impossible request if the arm is positioned abducted on an arm board. The lower extremities are placed in low lithotomy position with knees gently flexed to approximately 100–110 degrees to clear the limbs from the surgeon's or robotic platform's access to the abdominal ports. The patient should be positioned on an anti-slide technology such as an anti-slip pad, a bean bag, or a specialized positioning device to prevent sliding. Bolsters placed at the shoulder, "shoulder blocks," can be used to augment anti-slip mattresses; however, great care must be given to their positioning on the acromion of the shoulder, as incorrect positioning of such devices can be associated with devastating nerve injuries to the neck and upper extremity. Figure 40.8 demonstrates a typical positioning for minimally invasive surgical staging of endometrial cancer.

Surgery for Advanced Endometrial Cancer

Surgery remains an important adjunct for advanced stage disease, both for the cytoreduction of extrauterine metastases and to define and characterize the distribution of disease so that clinicians may better tailor adjuvant therapies. There are three dominant distributions of advanced endometrial cancer: bulky nodal dissemination, peritoneal carcinomatosis, and locally advanced direct extension into the cervix and parametria. The latter of these patterns of disease is typically inoperable until regression has been induced with other therapies such as pelvic radiation or systemic therapy. Bulky retroperitoneal nodal disease may also be considered inoperable, particularly if a patient's body habitus prevents safe visualization and access to the affected nodal basins, or if the nodal metastases are infiltrating into the great vessels. Peritoneal carcinomatosis most closely

FIGURE 40.8 Optimal patient positioning for minimally invasive surgery.

mimics the disease distribution of advanced ovarian cancer, a disease in which paradigms have long existed that favor primary cytoreductive surgeries to minimal or no gross residual disease.

The value of cytoreductive surgery for advanced endometrial cancer has not been established in prospective trials. Early retrospective institutional or database studies which addressed this question observed that patients who underwent primary cytoreduction of their metastatic endometrial cancer and achieved no gross residual disease at surgery's completion were more likely to survive or have longer disease-free intervals.[64, 65] However, these series, being retrospective, were heavily biased towards patients receiving primary surgery having confounders for favorable clinical risk factors and disease distribution relative to those who received primary chemotherapy.

Despite the fact that early series report improved survival following primary debulking surgeries, there is an increasing trend towards the use of neoadjuvant chemotherapy for patients with clinical stage IV and bulky stage IIIC disease.[65] This clinical adoption of an unproven treatment strategy may be tied to the increasing acceptability of neoadjuvant chemotherapy among ovarian cancer populations and the observed improved perioperative complications and recovery observed after neoadjuvant chemotherapy.[66]

It is highly probable that there is no one-size-fits-all approach to the surgical management of advanced endometrial cancer, but rather a nuanced approach that takes into consideration the molecular subtype of cancer, its disease distribution, and the patient's risk factors for major surgery. More work should be done in this space to define the optimal timing and value of debulking procedures with a biomarker-driven approach.

Fertility Sparing Surgery for Endometrial Cancer

While endometrial cancer predominantly effects women in their postmenopausal years, it can arise in younger women who have not yet met their reproductive goals. This is particularly true among women who carry germline mutations, such as Lynch syndrome, which carry high risks for developing the disease. For such women it remains important to consider fertility-preserving strategies in their surgical management. Prior to embarking upon a fertility-sparing option, all patients should undergo comprehensive evaluation for both metastatic disease and a deeply invasive local disease. MRI is typically employed for the latter due to its fairly high sensitivity in detecting deep myometrial invasion.

Progestin-Releasing IUDs and Hysteroscopic Resection

A highly effective surgical strategy in managing endometrial intra-epithelial neoplasia or invasive carcinoma is performance of repeat dilation and curettage (D&C) with placement of a progestin-releasing IUD. Rates of regression as high as 72% have been reported in prospective series.[67] The highest rates of regression have been observed when repeated D&C procedures have been performed while leuprolide has been administered for ovarian suppression. In the FeMMe trial, 165 patients received a progestin-releasing intrauterine device after the diagnosis of endometrial malignancy. The use of progestin-releasing IUDs has been associated with a 60% probability of reversal of the underlying malignancy.

If preoperative MRI is suggesting a degree of myometrial invasion, it is reasonable to attempt hysteroscopic resection of the tumor.[68] This approach remains highly experimental, and patients pursuing this conservative approach to treatment should be followed closely by a gynecologic oncologist and have surveillance biopsies performed until definitive hysterectomy is performed after childbearing goals are complete.

Ovarian Preservation

Finally, if uterine preservation is not desired and cannot be recommended due to other risk factors, it is reasonable to retain ovaries. This can offer the possibility for pregnancy via gestational carries, but also the ability to maintain ovarian hormone reserve until natural menopause. However, prior to embarking upon ovarian-preserving surgery, patients should undergo imaging, such as pelvic ultrasound, of the pelvic organs to establish no synchronous metastases or primary cancers are present. It is particularly important that patients diagnosed with endometrial cancer under the age of 50 receive genetic testing. Patients identified as having Lynch syndrome, particularly if there are germline mutations in MLH1, MSH2, or MSH6, should be counseled that they should consider oophorectomy at the time of hysterectomy.

References

1. Siegel RL et al. Cancer statistics, 2024. *CA Cancer J Clin*. 2024;74(1):12–49.
2. NCI. *Cancer Stat Facts: Uterine Cancer*. NCI; 2019. Available at: http://seer.cancer.gov.
3. Suarez AA et al. Bokhman Redux: endometrial cancer "types" in the 21st century. *Gynecol Oncol*. 2017;144(2):243–249.
4. Bokhman JV. Two pathogenetic types of endometrial carcinoma. *Gynecol Oncol*. 1983;15(1):10–17.
5. Hendrickson M et al. Uterine papillary serous carcinoma: a highly malignant form of endometrial adenocarcinoma. *Am J Surg Pathol*. 1982;6(2):93–108.
6. Cancer Genome Atlas Research et al. Integrated genomic characterization of endometrial carcinoma. *Nature*. 2013;497(7447):67–73.
7. DeLair DF et al. The genetic landscape of endometrial clear cell carcinomas. *J Pathol*. 2017;243(2):230–241.
8. Bae HS et al. Should endometrial clear cell carcinoma be classified as Type II endometrial carcinoma? *Int J Gynecol Pathol*. 2015;34(1):74–84.
9. Kaaks R et al. Obesity, endogenous hormones, and endometrial cancer risk: a synthetic review. *Cancer Epidemiol Biomarkers Prev*. 2002;11(12):1531–1543.
10. Purdie DM, Green AC. Epidemiology of endometrial cancer. *Best Pract Res Clin Obstet Gynaecol*. 2001;15(3):341–354.
11. Long B et al. Disparities in uterine cancer epidemiology, treatment, and survival among African Americans in the United States. *Gynecol Oncol*. 2013;130(3):652–659.
12. Resnick KE et al. Current and emerging trends in Lynch syndrome identification in women with endometrial cancer. *Gynecol Oncol*. 2009;114(1):128–134.
13. Meyer LA et al. Endometrial cancer and Lynch syndrome: clinical and pathologic considerations. *Cancer Control*. 2009;16(1):14–22.
14. Lancaster JM et al. Society of gynecologic oncologists education committee statement on risk assessment for inherited gynecologic cancer predispositions. *Gynecol Oncol*. 2007;107(2):159–162.
15. Shu CA et al. Uterine cancer after risk-reducing salpingo-oophorectomy without hysterectomy in women with BRCA mutations. *JAMA Oncol*. 2016;2(11):1434–1440.
16. Goodfellow PJ et al. Combined microsatellite instability, MLH1 methylation analysis, and immunohistochemistry for Lynch syndrome screening in endometrial cancers from GOG210: an NRG oncology and gynecologic oncology group study. *J Clin Oncol*. 2015;33(36):4301–4308.

17. Gammon A et al. Genetic basis of Cowden syndrome and its implications for clinical practice and risk management. *Appl Clin Genet*. 2016;9:83–92.
18. Creasman WT et al. Surgical pathologic spread patterns of endometrial cancer. A gynecologic oncology group study. *Cancer*. 1987;60(8 Suppl):2035–2041.
19. Creasman WT et al. Surgical-pathological findings in type 1 and 2 endometrial cancer: an NRG oncology/gynecologic oncology group study on GOG-210 protocol. *Gynecol Oncol*. 2017;145(3):519–525.
20. Berek JS et al. FIGO staging of endometrial cancer: 2023. *Int J Gynaecol Obstet*. 2023;162(2):383–394.
21. Scott SA et al. Prognostic significance of peritoneal cytology in low-intermediate risk endometrial cancer. *Gynecol Oncol*. 2017;145(2):262–268.
22. Seagle BL et al. Prognosis and treatment of positive peritoneal cytology in early endometrial cancer: matched cohort analyses from the national cancer database. *Am J Obstet Gynecol*. 2018;218(3):329–e1–e15.
23. Abu-Rustum N et al. Uterine neoplasms, 1.2023, NCCN clinical practice guidelines in oncology. *J Natl Compr Canc Netw*. 2023;21(2):181–209.
24. Tong SY et al. Clinical analysis of synchronous primary neoplasms of the female reproductive tract. *Eur J Obstet Gynecol Reprod Biol*. 2008;136(1):78–82.
25. Joo WD et al. Microscopic omental metastasis in clinical stage I endometrial cancer: a meta-analysis. *Ann Surg Oncol*. 2015;22(11):3695–3700.
26. Randall ME et al. Randomized phase III trial of whole-abdominal irradiation versus doxorubicin and cisplatin chemotherapy in advanced endometrial carcinoma: a gynecologic oncology group study. *J Clin Oncol*. 2006;24(1):36–44.
27. Randall ME et al. Phase III trial: adjuvant pelvic radiation therapy versus vaginal brachytherapy plus paclitaxel/carboplatin in high-intermediate and high-risk early stage endometrial cancer. *J Clin Oncol*. 2019;37(21):1810–1818.
28. Sharma C et al. Lymphadenectomy influences the utilization of adjuvant radiation treatment for endometrial cancer. *Am J Obstet Gynecol*. 2011;205(6):562–e1–e9.
29. Chan JK et al. The impact of the absolute number and ratio of positive lymph nodes on survival of endometrioid uterine cancer patients. *Br J Cancer*. 2007;97(5):605–611.
30. Kitchener H et al. Efficacy of systematic pelvic lymphadenectomy in endometrial cancer (MRC ASTEC trial): a randomised study. *Lancet*. 2009;373(9658):125–136.
31. Benedetti Panici P et al. Systematic pelvic lymphadenectomy vs. no lymphadenectomy in early-stage endometrial carcinoma: randomized clinical trial. *J Natl Cancer Inst*. 2008;100(23):1707–1716.
32. Todo Y et al. Risk factors for postoperative lower-extremity lymphedema in endometrial cancer survivors who had treatment including lymphadenectomy. *Gynecol Oncol*. 2010;119(1):60–64.
33. Abu-Rustum NR et al. The incidence of symptomatic lower-extremity lymphedema following treatment of uterine corpus malignancies: a 12-year experience at memorial Sloan-Kettering cancer center. *Gynecol Oncol*. 2006;103(2):714–718.
34. Carlson JW et al. GOG 244-the lymphedema and gynecologic cancer (LEG) study: incidence and risk factors in newly diagnosed patients. *Gynecol Oncol*. 2020;156(2):467–474.
35. Tada H et al. Risk factors for lower limb lymphedema after lymph node dissection in patients with ovarian and uterine carcinoma. *BMC Cancer*. 2009;9:47.
36. Lampe B et al. Prognostic factors that predict pelvic lymph node metastasis from endometrial carcinoma. *Cancer*. 1994;74(9):2502–2508.
37. Schink JC et al. Tumor size in endometrial cancer: a prognostic factor for lymph node metastasis. *Obstet Gynecol*. 1987;70(2):216–219.
38. Larson DM, et al. Prognostic significance of gross myometrial invasion with endometrial cancer. *Obstet Gynecol*. 1996;88(3):394–398.
39. Mariani A et al. Low-risk corpus cancer: is lymphadenectomy or radiotherapy necessary? *Am J Obstet Gynecol*. 2000;182(6):1506–1519.
40. Mariani A et al. Prospective assessment of lymphatic dissemination in endometrial cancer: a paradigm shift in surgical staging. *Gynecol Oncol*. 2008;109(1):11–18.
41. Abu-Rustum NR. Sentinel lymph node mapping for endometrial cancer: a modern approach to surgical staging. *J Nat Comprehensive Cancer Network*. 2014;12(2):288–297.
42. Ballester M et al. Detection rate and diagnostic accuracy of sentinel-node biopsy in early stage endometrial cancer: a prospective multicentre study (SENTI-ENDO). *Lancet Oncol*. 2011;12(5):469–476.
43. Barlin JN et al. The importance of applying a sentinel lymph node mapping algorithm in endometrial cancer staging: beyond removal of blue nodes. *Gynecol Oncol*. 2012;125(3):531–535.
44. Tanner EJ et al. Factors associated with successful bilateral sentinel lymph node mapping in endometrial cancer. *Gynecol Oncol*. 2015;138(3):542–547.
45. Frumovitz M et al. Near-infrared fluorescence for detection of sentinel lymph nodes in women with cervical and uterine cancers (FILM): a randomised, phase 3, multicentre, non-inferiority trial. *Lancet Oncol*. 2018;19(10):1394–1403.
46. Rossi EC et al. Detection of sentinel nodes for endometrial cancer with robotic assisted fluorescence imaging: cervical versus hysteroscopic injection. *Int J Gynecol Cancer*. 2013;23(9):1704–1711.
47. Jewell EL et al. Detection of sentinel lymph nodes in minimally invasive surgery using indocyanine green and near-infrared fluorescence imaging for uterine and cervical malignancies. *Gynecol Oncol*. 2014;133(2):274–277.
48. Perrone AM, et al. Cervical and hysteroscopic injection for identification of sentinel lymph node in endometrial cancer. *Gynecol Oncol*. 2008;111(1):62–67.
49. Rossi EC et al. A comparison of sentinel lymph node biopsy to lymphadenectomy for endometrial cancer staging (FIRES trial): a multicentre, prospective, cohort study. *Lancet Oncol*. 2017;18(3):384–392.
50. Cusimano MC et al. Assessment of sentinel lymph node biopsy vs lymphadenectomy for intermediate- and high-grade endometrial cancer staging. *JAMA Surg*. 2021;156(2):157–164.
51. Persson J et al. Pelvic sentinel lymph node detection in high-risk endometrial cancer (SHREC-trial)-the final step towards a paradigm shift in surgical staging. *Eur J Cancer*. 2019;116:77–85.
52. Walker JL et al. Recurrence and survival after random assignment to laparoscopy versus laparotomy for comprehensive surgical staging of uterine cancer: gynecologic oncology group LAP2 study. *J Clin Oncol*. 2012;30(7):695–700.
53. Kornblith AB et al. Quality of life of patients with endometrial cancer undergoing laparoscopic international federation of gynecology and obstetrics staging compared with laparotomy: a gynecologic oncology group study. *J Cin Oncol*. 2009;27(32):5337–5342.
54. Janda M et al. Effect of total laparoscopic hysterectomy vs total abdominal hysterectomy on disease-free survival among women with stage I endometrial cancer: a randomized clinical trial. *JAMA*. 2017;317(12):1224–1233.
55. Janda M et al. Quality of life after total laparoscopic hysterectomy versus total abdominal hysterectomy for stage I endometrial cancer (LACE): a randomised trial. *Lancet Oncol*. 2010;11(8):772–780.
56. Polan RM et al. Minimally invasive surgery rate as a quality metric for endometrial cancer. *J Minim Invasive Gynecol*. 2020;27(6):1389–1394.

57. Anastasio MK et al. Geographic and racial disparities in the quality of surgical care among patients with nonmetastatic uterine cancer. *Am J Obstet Gynecol*. 2025;232(3):308–e1–e8, e15.
58. Fleury AC et al. Racial disparities in surgical care for uterine cancer. *Gynecol Oncol*. 2011;121(3):571–576.
59. Padilla-Iserte P et al. Impact of uterine manipulator on oncological outcome in endometrial cancer surgery. *Am J Obstet Gynecol*. 2021;224(1):65-e1–e65, e11.
60. Scutiero G et al. Influence of uterine manipulator on oncological outcome in minimally invasive surgery of endometrial cancer: a systematic review and meta-analysis. *Eur J Surg Oncol*. 2022;48(10):2112–2118.
61. Wright JD et al. Comparative effectiveness of robotic versus laparoscopic hysterectomy for endometrial cancer. *J Clin Oncol*. 2012;30(8):783–791.
62. Park DA et al. Comparative safety and effectiveness of robot-assisted laparoscopic hysterectomy versus conventional laparoscopy and laparotomy for endometrial cancer: a systematic review and meta-analysis. *Eur J Surg Oncol*. 2016;42(9):1303–1314.
63. Bristow RE et al. Stage IVB endometrial carcinoma: the role of cytoreductive surgery and determinants of survival. *Gynecol Oncol*. 2000;78(2):85–91.
64. Tobias CJ et al. Association of neoadjuvant chemotherapy with overall survival in women with metastatic endometrial cancer. *JAMA Netw Open*. 2020;3(12):e2028612.
65. Wilkinson-Ryan I et al. Neoadjuvant chemotherapy versus primary cytoreductive surgery for stage IV uterine serous carcinoma. Int *J Gynecol Cancer*. 2015;25(1):63–68.
66. Pronin SM et al. Fertility-sparing treatment of early endometrial cancer and complex atypical hyperplasia in young women of childbearing potential. *Int J Gynecol Cancer*. 2015;25(6):1010–1014.
67. De Marzi P et al. Hysteroscopic resection in fertility-sparing surgery for atypical hyperplasia and endometrial cancer: safety and efficacy. *J Minim Invasive Gynecol*. 2015;22(7): 1178–1182.

41 CERVICAL CANCER

R. Wendel Naumann

41.1 Gynecologic Aspects

41.1.1 Epidemiology

In 2025, there will be an estimated 13,360 new cases and 4320 deaths from cervical cancer in the United States (1). The incidence of cervical cancer has decreased by more than half in the United States since the mid-1970s due to widespread uptake of screening, treatment of precancerous lesions, and vaccination. Despite being preventable, cervical cancer remains the second leading cause of cancer-related death in women ages 20–39.

The burden of cervical cancer is more pronounced in developing countries. Cervical cancer is the fourth most frequently diagnosed cancer and the fourth leading cause of cancer death in women worldwide and is the leading cause of death from gynecologic cancer, causing more deaths than ovarian and uterine cancer combined (2, 3). According to GLOBOCAN 2020 there were an estimated 604,127 cases and 341,831 annual deaths from cervical cancer, with 85% of those deaths occurring in low- and middle-income countries (2).

41.1.2 Etiology and Natural History

Human papilloma virus (HPV) is a circular, non-enveloped, double-stranded DNA virus of approximately 8000 base pairs. The genome consists of seven early transcribed genes designated E1–E7. There are two late genes (L1, L2) which code for the viral capsid protein. HPV infects the basal layer of stratified cutaneous and mucosal epithelia through microabrasions and skin-to-skin contact. The virus then localizes to the nucleus and can integrate into the host cell genome (4, 5). Primary HPV oncogenes E6 and E7 cause oncogenic transformation by binding and disabling the tumor suppressor proteins p53 and retinoblastoma (Rb), respectively.

Of the 488 known HPV types, 12 are carcinogenic: 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, and 59 (6, 7). HPV 68 has been designated as probably carcinogenic. These 13 HPV types cause 96% of all HPV-related cervical cancers. Infection by oncogenic HPV is common, but 80% are cleared by the immune system within 3 years, and only 3% progress to cervical dysplasia or cancer within 7 years, if untreated (6). The greatest risk of high-grade dysplasia and cancer is from HPV 16 and HPV 18, responsible for 50% and 10%–15% of cervical cancers, respectively. Infection with HPV 16 or 18 has a 14%–17% 10-year risk of progression to high-grade cervical dysplasia compared with 3% with other high-risk types. The risk of progression is higher with non-16/18 oncogenic types in women under 30 years old compared to older women (8).

Persistent high-risk HPV infection is the strongest risk factor for the development of high-grade cervical dysplasia and is essential for progression from precancer to cancer (9). Additional risk factors for progression from high-grade cervical dysplasia to invasive cancer among HPV-infected women include history of smoking, multiparity, long-term oral contraceptive use, chronic inflammation, and human immunodeficiency virus (HIV) (5). Squamous cell cancers account for 70%–80% of cervical cancers and are most often caused by HPV 16 (10). Adenocarcinoma or adenosquamous cancers account for 15%–20% of cervical cancers and are more commonly associated with HPV 18. Only 5%–10% of cervical cancers are not caused by HPV; these include gastric type, clear cell, mesonephric, and endometrioid types, and they have a worse prognosis (11, 12).

41.1.3 Screening

Cervical cytology has been the primary mode of cervical cancer screening based on identification of abnormal cells in cancer and precancerous lesions (13). Despite a false negative rate, annual screening effectively reduces cervical cancer incidence and mortality. One large study demonstrated that the 5-year incidence of cervical intraepithelial neoplasia (CIN) 3 or worse after a negative pap smear was 3.6 per 1000 women (14).

Since HPV causes nearly all cervical cancer, HPV detection has increasing importance in screening (15). While HPV testing was initially FDA approved to triage cytology with atypical squamous cells of undetermined significance to colposcopy, co-testing for high-risk HPV at the time of cytology reduced the 5-year progression to CIN-3 or worse by half, from 3.6 to 1.7 per 1000 women. HPV testing is more sensitive than cytology, and a negative test predicts a longer duration of normal cytology since persistent HPV infection precedes dysplasia by several years. HPV testing is more reproducible than cervical cytology, as subjective interpretation is eliminated. However, HPV testing is less specific than cytology, especially in young patients with a higher rate of transient HPV infections that clear without consequence.

Five HPV tests are FDA approved for cervical cancer screening (16). All include the 13 primary HPV types (16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, and 68), and HPV 66 is included in all the tests except the Hybrid Capture II (Table 41.1). Testing involves different methods including the detection of DNA or mRNA by in situ hybridization or by PCR, and false negative results can be caused by vaginal medication cream, lubricating jelly, acetic acid, or mucin. Changes in HPV infection rates will influence sensitivity and specificity of these tests. When the BD Onclarity test was specifically evaluated in HPV vaccinated individuals and compared to historical controls, sensitivity for detection of CIN 2+ decreased from 100% to 80%, and the specificity increased from 46% to 100% (16).

Current guidelines do not support screening of women less than 21 years of age (Table 41.2). Recommendations of the US Preventative Service Task Force (USPSTF) and the American College of Obstetrics and Gynecology (ACOG) are identical (17, 18). For women between the ages of 21 and 30, a liquid-based cytology test should be performed every 3 years. After age 30, patients should receive either high-risk HPV testing alone every 5 years, cytologic testing alone every 3 years, or co-testing every 5 years. The American Cancer Society recommends primary high-risk HPV screening and co-testing starting at age 21 with eventual elimination of cervical cytology (19).

Screening may be discontinued after 65 years of age only if patients have had either two consecutive negative primary HPV tests or three negative cytology tests in the last 10 years with one being within the last 3 years. Screening after hysterectomy for benign conditions is not indicated if

DOI: 10.1201/9781003312109-41

the cervix has been removed and there is no history of high-grade cervical dysplasia. The role of HPV testing in women after hysterectomy has not been established. Current screening guidelines are not altered in patients who have had HPV vaccination (20).

41.1.4 Vaccination

HPV vaccination was introduced in 2006 and is highly effective against HPV infection. It is 100% effective in preventing high-grade cervical dysplasia that results from the types of HPV in the vaccine (21). However, the vaccine must be given prior to HPV exposure. The immune response to the vaccine is much stronger than the response to natural infection (20). There are multiple vaccines available around the world, including bivalent, quadrivalent, and nonavalent types (Table 41.3). Bivalent vaccines protect against HPV 16 and HPV 18. Quadrivalent vaccines protect against HPV 6 and HPV 11, which cause approximately 90% of genital warts. Nonavalent vaccines add coverage for HPV 31, 33, 45, 52, and 58, and protect against 90% of the HPV types that cause cervical cancer. Currently available vaccines contain only the highly variable L1 capsid protein. Ongoing efforts seek to create a universal vaccine against the L2 capsid protein which is highly conserved between HPV types (22).

The World Health Organization (WHO) recommends HPV vaccination as part of routine vaccination. The WHO's goal for vaccination is to provide coverage to at least 90% of women vaccinated by age 15 years as part of the 90/70/90 cervical cancer elimination program (20, 23).

With vaccination and screening cervical cancer could virtually be eliminated. Modeling studies estimate that vaccination with the nonavalent vaccine will decrease the overall incidence of cervical cancer to less than 1 per 100,000 with screening and less than 3 per 100,000 even without screening (24).

41.2 Surgical Aspects

41.2.1 Evaluation of Abnormal Cervical Cytology

Any patient with abnormal cervical cytology or high-risk HPV should have colposcopic evaluation with cervical biopsy and endocervical curettage; this should be performed prior to any planned surgery. A study of 18,537 patients with abnormal cytology showed a 0.6% rate of occult cervical cancer. Of these patients, 55% did not have a diagnosis of cancer prior to

TABLE 41.1 FDA-Approved HPV Tests for Cervical Cancer Screening

Test	Year FDA Approved	# HPV Tested	Type Test	Approved for 1° Screening	Internal Control
Hybrid Capture II	2001	13	DNA hybridization – whole genome	No	No
Cervista	2009	14	DNA hybridization – E6, E7, and L1	No	Yes
Roche	2011	14	DNA by PCR of L1	Yes	Yes
Aptima	2011	14	mRNA – E6, E7	No	Yes
BD Onclarity	2018	14	DNA by PCR of E6, E7	Yes	Yes

Note: See further Ref. 16.

TABLE 41.2 Recommended Screening for Cervical Cancer

Age	US Preventative Service Task Force (8)	American College of Obstetricians and Gynecologists (8)	American Cancer Society (8)
< 21	Screening not recommended	Screening not recommended	Screening not recommended
21–25	Cytology only q 3 yr	Cytology only q 3 yr	Screening not recommended
25–29	Cytology only q 3 yr	Cytology only q 3 yr	– HPV testing q 5 yr (preferred) – Cytology + HPV testing q 5 yr – Cytology alone q 3 yr
30–64	– Cytology only q 3 yr – Cytology with HPV testing q 5 yr – HPV testing q 5 yr	– Cytology only q 3 yr – Cytology with HPV testing q 5 yr – HPV testing q 5 yr	– Cytology only q 3 yr – Cytology with HPV testing q 5 yr – HPV testing q 5 yr
Prior Total Hysterectomy (no history of CIN 2/3)	Screening not recommended if prior testing preformed*	Screening not recommended if prior testing performed*	Screening not required if no history of CIN 2+
Prior Total Hysterectomy (History of CIN 2+)		Screening with cytology alone q 3 yr x 20 yr	

* Adequate prior testing defined as two consecutive negative primary HPV tests, two negative co-tests, or three negative cytology tests within the last 10 years, and the most recent in the past 3–5 years

TABLE 41.3 Currently Available Cervical Cancer Vaccines

Vaccine	Type	HPV Types Covered	Recommendations
Cervarix	Bivalent	16/18	Girls and boys aged 9–14 years as a 2-dose schedule (0, 5–13 months) If ≥ 15 years as a 3-dose schedule (0, 1–2.5 months, and 5–12 months)
Cecolin	Bivalent	16/18	Girls aged 9–14 years as a 2-dose schedule (0, 6 months) If > 15 years as a 3-dose schedule (0, 1–2 months, and 5–8 months)
Walrinvax	Bivalent	16/18	Girls aged 9–14 years as a 2-dose schedule (0, 6 months) If > 15 as a 3-dose schedule (0, 2–3 months, and 6–7 months)
Gardasil	Quadrivalent	6/11/16/18	Girls and boys aged 9–13 years as a 2-dose schedule (0, 6 months) If > 14 years as a 3-dose schedule (0, 1–2 months, and 4–6 months)
Cervavax	Quadrivalent	6/11/16/18	Girls and boys aged 9–14 years as a 2-dose schedule (0, 6 months) If > age 15 years as a 3-dose schedule (0, 2 months, and 6 months)
Gardasil-9	Nonavalent	6/11/16/18/31/33/45/52/58	Girls and boys aged 9–14 years as a 2-dose schedule (0 and 5–13 months apart) If > age 15 years as a 3-dose schedule (0, 1–2 months, and 4–6 months)

Note: See further Ref. 20.

an excisional procedure. Since the occult cancer risk is higher when CIN 2/3 is noted in the endocervical curettage (5.0%) or when CIN 3 is present in a cervical biopsy (3.9%), an excision procedure (cone biopsy or loop electrosurgical excision procedure) is recommended in these situations (25).

Historically, accepted practice was for surgery following an excision procedure to be performed within 48 hours or after 6 weeks. The rationale was to reduce morbidity and infection from post-excision inflammation (26). While some studies have shown a marginal increased risk in infectious morbidity after hysterectomy in this inflammatory period, others have not shown a difference (26, 27). Therefore, a firm recommendation with respect to a waiting period after an excision procedure cannot be made.

41.2.2 Staging

The International Federation of Gynecology and Obstetrics (FIGO) updated cervical cancer staging in 2018 from the previous version in 2014 (28). Critical changes included:

1. Stage IA was limited to microscopic lesions; lateral dimensions were removed
2. Stage IA1 was limited to tumors < 3 mm deep
3. Stage IA2 included tumors ≥ 3 mm and < 5 mm deep
4. Stage I was subdivided based on size
5. Stage IB2 included only tumors 2–4 cm (compared to > 4 cm)
6. Stage IB3 was added to include tumors over 4 cm
7. Stage IIA tumors were subdivided based on size > 4 cm
8. Stage IIIC tumors were subdivided into positive pelvic nodes (stage IIIC1) and positive para-aortic nodes (stage IIIC2), and staging indicated that the classification was made radiologically (r) or pathologically (p)

The American Joint Committee on Cancer (AJCC) updated the TNM staging system for cervical cancer to version 9 in 2019 to align with the 2018 FIGO staging system (29) (Table 41.4). The TNM system subdivided positive nodes based on nodal size and defined N0(i+) as isolated tumor cells in nodes ≤ 0.2 mm or clusters ≤ 200 cells in a single node. In the TNM system, isolated tumor cells were reported but do not change stage and are considered N0. Nodes that are > 0.2 mm and ≤ 2 mm are designated N1mi (pelvic) or N2mi (para-aortic). Nodes larger than 2 mm are designated N1a or N2a. Nodal involvement diagnosed with fine-needle aspiration is designated with the suffix "f." Nodal involvement diagnosed by sentinel lymph node biopsy is designated with the suffix "sn."

41.2.3 Preoperative Evaluation

Candidates for surgical treatment of cervical cancer should undergo a thorough history and physical examination with biopsy confirmation of pathology. Complete blood count and metabolic panel should be performed to assess renal and liver function (30). If surgery is considered, pelvic magnetic resonance imaging (MRI) can accurately determine the tumor size and depth of invasion. Imaging with computerized tomography (CT) or positron emission tomography (PET)-CT scan is recommended for stage IB1 and higher. HIV testing should be considered. Tobacco cessation should be addressed for any tobacco user. Fertility preservation should be discussed with patients of reproductive age with tumors < 2 cm. Patients with more advanced cancers may warrant consideration of ovarian transposition to preserve ovarian function (31). Examination under anesthesia and cystoscopy can be performed if there is concern for bladder involvement.

41.2.4 Lymph Node Evaluation

Lymph node involvement is a poor prognostic factor. The stage-specific increased risk of recurrence is 2.4-fold for pelvic nodal involvement and 5.88-fold for para-aortic nodal involvement (32). One prospective trial evaluated outcomes of patients with negative PET scans who underwent para-aortic lymphadenectomy. The 3-year progression-free survival (PFS) was 74% with negative para-aortic nodes, 69% with ≤ 5 mm para-aortic metastasis, and 17% with > 5 mm para-aortic metastases (33). Imaging has limited sensitivity to detect positive nodes. In patients with FIGO 2014 stage IB-IV disease, PET scan missed 22% of positive nodes when compared to surgical staging (34). Twelve percent of patients with PET-negative pelvic and para-aortic nodes have surgically positive para-aortic nodes. Additionally, 22% of patients with PET-positive pelvic nodes have positive para-aortic nodes. PET scans also have up to a

TABLE 41.4 2018 FIGO and Version 9 (2019) AJCC TNM Staging of Cervical Cancer

FIGO	TNM	
I		Confined to the cervix or uterine corpus
IA		Microscopy only, with maximum depth of invasion ≤ 5 mm
IA1	T1a1 N0 M0	Measured stromal invasion ≤ 3 mm in depth
IA2	T1a2 N0 M0	Measured stromal invasion > 3 and ≤ 5 mm in depth
IB		Visible without microscopy or with the deepest invasion > 5 mm
IB1	T1b1 N0 M0	Invasive carcinoma ≥ 5 mm depth of stromal invasion and < 2 cm in size
IB2	T1b2 N0 M0	Invasive carcinoma ≥ 2 and < 4 cm in size
IB3	T1b3 N0 M0	Invasive carcinoma ≥ 4 cm in size
II		Spread to the upper 2/3 of the vagina or parametrium without pelvic sidewall involvement or hydronephrosis
IIA		Involvement limited to the upper 2/3 of the vagina
IIA1	T2a1 N0 M0	Invasive carcinoma < 4 cm in greatest dimension
IIA2	T2a2 N0 M0	Invasive carcinoma ≥ 4 cm in greatest dimension
IIB	T2b N0 M0	With parametrial involvement but not to the sidewall
III		Involves the lower third of the vagina or extends to the pelvic wall and/or hydronephrosis or a nonfunctioning kidney or nodal involvement of the pelvic or para-aortic lymph nodes
IIIA	T3a N0 M0	The carcinoma involves the lower third of the vagina
IIIB	T3b N0 M0	Extension to the pelvic wall and/or hydronephrosis or nonfunctioning kidney
IIIC		Positive pelvic or para-aortic nodes. Should be denoted "r" if radiologic diagnosis or "p" with confirmed pathologic diagnosis
IIIC1	TX N1 M0	Pelvic lymph node metastasis
IIIC2	TX N2 M0	Para-aortic lymph node metastasis
IV		The carcinoma involves the mucosa of the bladder or rectum or extended beyond the pelvis
IVA	T4 NX M0	Spread to adjacent pelvic organs
IVB	TX NX M1	Spread to distant organs

Note: See further Refs. 28 and 29.

29% false positive rate for para-aortic lymph nodes. Surgical staging of para-aortic nodes is therefore reasonable, especially when pelvic nodes are PET-positive, as results may alter radiation planning (30).

Nodal metastases are usually controlled with radiation. In a group of patients that received curative radiation, the overall control of positive nodes (median 2.5 cm; range 1.1–5.6) was 98% (35). Nodal disease less than 2.4 cm was controlled with a total dose of 50.4 Gray but larger nodes required higher doses. Neoadjuvant chemotherapy with cisplatin and gemcitabine showed disappointing results with inferior PFS and overall survival (OS) (36).

Nodal evaluation is vitally important to appropriately plan radiation. Surgical resection may also have a therapeutic benefit. In a review of GOG-85, GOG-120, and GOG-165, patients with FIGO 2008 stage III/IV cancer had a higher 4-year PFS (49% vs 36%) and OS (54% vs 40%) if nodes were sampled. Additionally, recurrence in para-aortic nodes was 32% in patients with imaging compared to 15% with surgical evaluation of nodes (37).

Surgical technique for pelvic and para-aortic lymphadenectomy requires (1) opening the retroperitoneal space, (2) developing the pararectal space to isolate the ureter, external and internal iliac vessels, superior vesical artery, and obturator nerve, and (3) removing the nodal tissue inferiorly from the circumflex iliac vein superior to at least the bifurcation of the aorta into the common iliac arteries, and ideally superior to the inferior mesenteric artery, and from the border of the external iliac artery deep to the obturator nerve (Figure 41.1).

41.2.5 Surgery for Cervical Cancer

The radical hysterectomy for cervical cancer was first described by John Clark with the goal of achieving negative margins around larger tumors by removing the parametrium (38). While radical surgery can technically be performed on women with stage IIA cancers or even IIB cancers, morbidity increases with surgical radicality, and radiation techniques with concurrent chemotherapy and immunotherapy have improved. In addition, adjuvant radiation is indicated for most patients with larger tumors even after surgery. Therefore, the

use of radical hysterectomy is limited to patients with stage I tumors less than 4 cm who are at low risk of needing adjuvant radiation after surgery. It has been estimated that only 9% of women with cervical cancer in the United States are candidates for surgical treatment (39).

Surgery for cervical cancer has been described based on the radicality of the procedure needed to remove the tumor, classically described by Piver (40). Type II–V procedures were combined with a full systematic lymphadenectomy including obturator, iliac, and presacral nodes to the level of the low para-aortic lymph nodes. Several other classifications that describe a more modern approach to radical hysterectomy have been proposed and are described in Table 41.5 (40, 41).

Patients with stage IA1 cancers without lymph-vascular space invasion (LVSI) are eligible for a cold knife conization or a simple hysterectomy. Cold knife conization is preferred for conservative therapy, but a LEEP, or Loop Electrical Excision Procedure, may be sufficient if margins are evaluable and negative. Nodal metastasis occurs in 1%–2% of patients with tumor invasion < 3 mm. Patients with stage IA1 disease with LVSI should undergo surgical nodal assessment, as LVSI is an independent risk factor for nodal involvement (30).

Patients with stage IA2 to stage IIA1 tumors should either undergo radical hysterectomy with nodal assessment or undergo radiation. Patients with stage IA2 tumors (depth of invasion 3–5 mm) have a 7% of nodal metastasis, so nodal evaluation is essential (42). Comparison of radical hysterectomy with nodal assessment or radiation in a randomized trial showed no difference in the outcomes between the two modalities (43). Recurrence risks between surgery and radiation are no different, and surgery is preferred for younger women due to long-term morbidity associated with radiation, such as vaginal scarring, decreased sexual function, ovarian failure, and fistula formation.

For smaller tumors, a modified radical hysterectomy may be preferred due to decreased morbidity with no significant difference in recurrence risk (44).

Differences in the extent of surgical resection between simple and radical hysterectomy are depicted in Figure 41.2.

Radical hysterectomy, whether open, laparoscopic, or robotic, is performed with the following steps: (1) the retroperitoneum is opened and the pararectal and paravesical spaces are opened to exclude extracervical involvement, (2) the bladder flap is created and is mobilized to 2 cm below the cervicovaginal junction, (3) the ureter is dissected away from the peritoneum through the tunnel inferior to the uterine vessels, (4) the uterine vessels are isolated and ligated at their origin from the internal iliac vessels, (5) the infundibulopelvic ligament or utero-ovarian ligaments are divided depending on ovarian conservation, (6) the parametria are divided and reflected over the ureter, (7) the rectovaginal space is created and the uterosacral ligaments are divided, and (8) the vagina is divided inferior to the cervicovaginal junction and the specimen is removed. Table 41.6 depicts steps in the procedure.

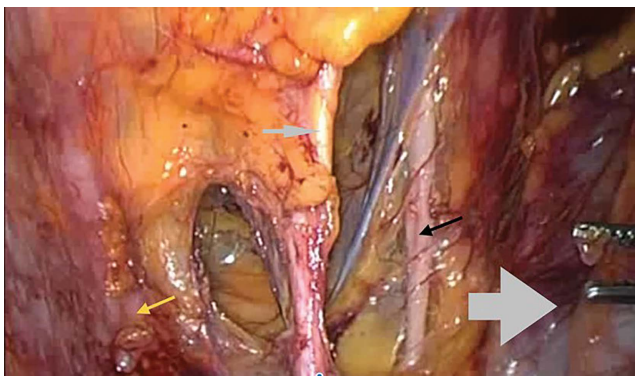


FIGURE 41.1 View of the right pelvic sidewall anatomy with structures labeled: yellow arrow, ureter; small gray arrow, superior vesical artery; small black arrow, obturator nerve; thick gray arrow, external iliac vessels.

41.2.6 Lymphadenectomy

A full pelvic lymphadenectomy has been the standard of care for lymphatic evaluation in patients with cervical cancer. Most lymphatic channels from the cervix drain to the obturator and internal iliac or external iliac pelvic nodes. A posterior drainage pathway also exists along the uterosacral ligament into the common iliac lymph node chain (46). Among patients with stage I–IIA cervical cancer with positive nodes, the site of involvement includes 50% obturator and internal iliac; 30% external iliac; 15% common iliac; and 8% para-aortic (47). Isolated para-aortic nodal metastasis has been rarely reported even above the inferior mesenteric artery (46). The extent of para-aortic dissection is controversial since para-aortic lymph nodes are unlikely to be positive unless the pelvic nodes are involved. However, the direct drainage of the presacral nodal chain into the common iliac chain mandates that the extent of dissection should extend to at least the top of the common iliac chains. While a more extensive lymphadenectomy has not been associated with an improved survival in patients with positive nodes, higher nodal counts have been associated with improved outcomes in node-negative patients (48). This is due to improved detection of patients with occult nodal disease.

41.2.7 The Role of Minimally Invasive Surgery for Cervical Cancer

As minimally invasive and robotic-assisted surgery became more popular, these techniques were adopted for the treatment of cervical cancer. Compared to laparotomy, minimally invasive techniques have been associated with lower blood loss, lower transfusion rate, decreased length of hospitalization, and no change in the operative time or complication rate (49). Retrospective comparisons showed similar results with respect to oncologic outcomes (50, 51). The Laparoscopic Approach to Cervical Cancer (LACC) trial was an international, randomized, noninferiority trial comparing open surgery to either laparoscopic or robotic surgery for patients with stage I cervical cancer (52). Patients were eligible if they had cervical cancer that was FIGO 2009 stage IA1 with LVSI, stage IA2 with ≥ 3 mm stromal invasion and < 7 mm in greatest dimension, and stage IB1 ≤ 4 cm without nodal involvement. The noninferiority boundary of the trial was a disease-free survival (DFS) rate of 7.2% at 4.5 years. This trial was conducted from June 2008 to June 2017 when the Data Safety Monitoring committee closed the trial due to a prespecified imbalance in the number of recurrences in the laparoscopic arm. At that time, the trial had enrolled 85% of the planned 740 patients.

The LACC trial was inconclusive to the primary endpoint of the trial, as the confidence interval for the difference in the DFS crossed the 7.2% noninferiority boundary (52). However, an increase in the local recurrence rate was noted from 1.28% to 8.46% (HR: 4.26; 95% CI: 1.44–12.60). The 3-year DFS rate

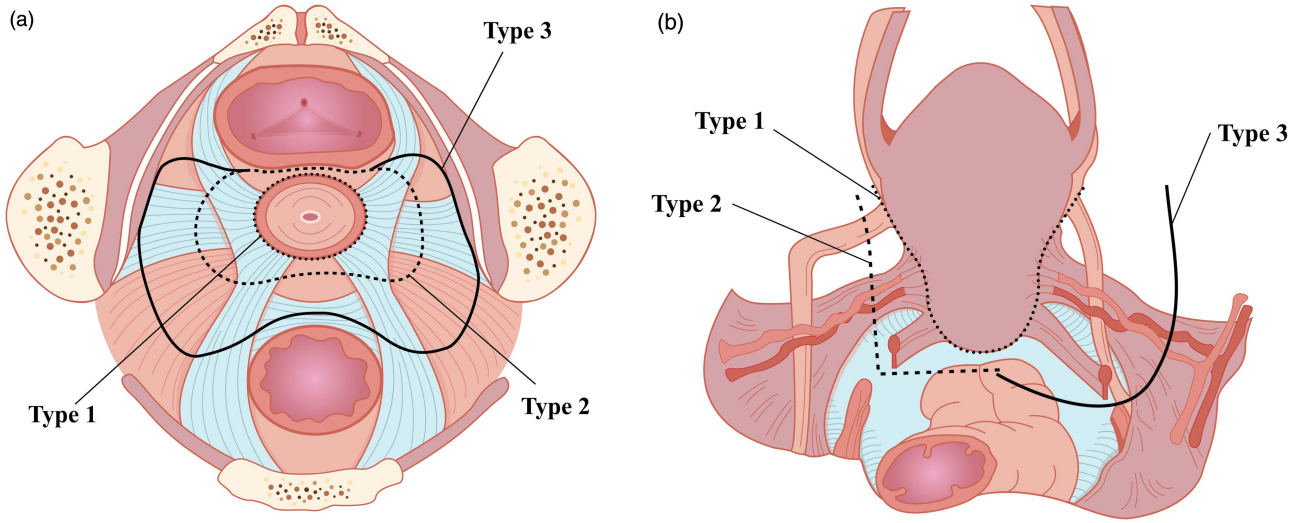


FIGURE 41.2 (A, B) View of the uterus and surrounding structures with depiction of simple or extrafascial hysterectomy (dotted line), Type 2 or modified radical hysterectomy (dashed line), and Type 3 radical hysterectomy (solid line). (Artist: Elizabeth Robinson.)

decreased from 97% to 91% (HR: 3.74, 95% CI: 1.63–8.58), and the 3-year OS decreased from 99% to 94% with the minimally invasive approach (HR: 6.00; 95% CI: 1.77–20.30).

Because of the differences noted in the LACC trial, the minimally invasive approach to surgery decreased significantly. However, several weaknesses in the LACC trial suggest that the results might not be generalizable to high-volume centers that have experience with minimally invasive radical hysterectomy. The LACC trial started when most surgeons had little experience with minimally invasive radical hysterectomy. Since surgical experience impacts surgical outcomes in open procedures for cervical cancer, and since recurrence rates are significantly higher in a surgeon's first 10 minimally invasive radical hysterectomies, this may confound application of the LACC trial findings to large centers with experienced surgeons (53). The LACC trial was conducted by approximately 100 surgeons at 33 sites over a 9-year period, suggesting that each surgeon would contribute an average of less than one minimally invasive radical hysterectomy to the protocol every 2 years (52).

Additionally, conduct of an international trial has unique challenges due to differences in the level of care and patient follow-up. The 3-year DFS and OS in the open group of the LACC trial are higher than would be expected in a group of patients with stage IA to IB cancers (39). The 3-year DFS in the open arm was 99.6% in a population in which almost one-half of patients had tumors > 2 cm or > 50% cervical invasion and 13% had positive nodes. The DFS and OS in the open arm were abnormally high compared with other series of abdominal radical hysterectomy (54). Other concerns around the LACC trial are that preoperative imaging was not required, postoperative adjuvant therapy was not standardized, and basic pathology variables such as tumor size were missing in approximately 15% of cases. In a review of the cause of deaths in the trial, there were five unexplained deaths in the minimally invasive group versus none in the open group. Because of these factors, a large multicenter study reviewed the experience with minimally invasive surgery and open surgery in high-volume centers in the United States (55). In this retrospective series of 1058 cases, the 3-year PFS was similar between minimally invasive and open cases (88% vs 89%, $p = 0.6$). No difference was seen between 3-year OS between the two groups (96% vs 97%; $p = 0.8$).

Other concerns include technical aspects of surgery, regarding use of a uterine manipulator, leading to potential contamination of the peritoneal cavity or vaginal cuff (52). Conversely, the vaginal cuff is closed with a surgical clamp during open surgery. The SUCCOR study evaluated this issue in a retrospective analysis of 1272 patients who had open or minimally invasive surgery for cervical cancer with entrance criteria similar to the LACC trial. DFS at 4.5 years and OS were compared in a propensity-matched cohort of 693 patients, and subgroups were compared between patients with a uterine manipulator versus patients with tumor containment. A twofold increase in recurrence risk was detected in the minimally invasive surgery group (HR: 2.07; 95% CI: 1.35–3.15; $p = 0.001$). This was associated with a similar increased risk of death (HR: 2.35; 95% CI: 1.30–4.60). However, the use of a uterine manipulator was associated with a 2.76-fold increase in recurrence (HR: 2.76; 95% CI: 1.75–4.33; $p < 0.001$). Patients treated without a uterine manipulator had a non-statistically significant difference in outcomes (HR 1.58;95% CI: 0.79–3.15; $p = 0.20$). For those patients treated with tumor containment there was no increase in the risk of recurrence (HR: 0.63; 95% CI: 0.15–2.59; $p < 0.52$) (56). A meta-analysis of more recent trials conducted with robotic-assisted surgery also found no difference in oncologic outcomes with robotic versus open surgery (57).

The Robotic versus Open Hysterectomy in Cervical Cancer (ROCC) trial is an ongoing noninferiority trial sponsored by the Gynecologic Oncology Partners (GOG-3043) that compares robotic versus open surgery in patients with cervical cancer. Preoperative imaging is mandated. The trial design is similar to the LACC trial and is planned for 840 patients to exclude a noninferiority boundary of 7% difference in DFS at 4.5 years. Use of a uterine manipulator is prohibited, and tumor containment is mandated. The RACC trial is another noninferiority

TABLE 41.5 Classification System for Radical Hysterectomies

Piver Class	Term	Piver (40)	Gynecologic Cancer Group (41)	Querleu and Morrow (45)
I	Simple Hysterectomy	– Removal of all cervical tissue (extrafascial)	– Removal of all cervical tissue (extrafascial)	Type A – Removal of all cervical tissues – Minimal parametrial, vaginal, or cardinal ligament resection
II	Modified Radical Hysterectomy	– Removal of some paracervical tissue but preserving the blood supply of the distal ureter (not dissected out of the pubovesical ligament) – Ligation of the uterine artery medial to the ureters – Uterosacral and cardinal ligaments are resected 1/2 way to the sidewall	– Removal of the uterus, paracervical tissues, upper 1–2 cm of vagina – Uterine artery ligated lateral to ureter and removal of the medial half of the parametria – Resection of the proximal uterosacral ligaments	Type B1 – Partial resection of uterosacral and vesicouterine ligaments – The ureter is unroofed and retracted laterally with the paracervix transected at the level of the ureteral tunnel – Neural elements of the paracervix are preserved – At least 10 mm of the vagina is resected Type B2 – Includes removal of lateral paracervical nodes
III	Radical Hysterectomy	– Removal of all parametrial and paravaginal tissues – Uterine artery is ligated at the origin – Uterosacral and cardinal ligaments are resected at the sidewall – 1/2 of the vagina is removed	– Removal of the uterus, upper 1/3 of the vagina, and paravaginal and paracervical tissues – Ureters ligated at their origin and the entire parametria is resected – Resection of the as much of the uterosacral ligament as possible	Type C1 – Transection of the uterosacral ligament at the rectum and vesicouterine ligament at the bladder – The ureter is mobilized completely – 15–20 mm of vagina is resected – The neural complex to the bladder is preserved Type C2 – Same as Type C1 without nerve preservation
IV	Extended Radical Hysterectomy	Same as class III except: – Complete dissection of the ureters – Resection of the superior vesical artery – 3/4 of the vagina is removed	– Same as the class III but removal of 3/4 of the vagina	Type D1 – Resection of the parametrium at the pelvic sidewall including the hypogastric vessels and exposing the sciatic nerve roots – Resection of the branches of the internal iliac artery Type D2 – Type D1 plus resection of the entire parametrium with the hypogastric vessels and adjacent fascial or muscular structures. This resection corresponds to a laterally extended endopelvic resection (LEER) procedure
V	Partial Exenteration	– Partial exenteration with removal of part of the ureter, bladder, or rectum	– Partial exenteration with removal of part of the ureter, bladder, or rectum	

trial comparing robotic radical hysterectomy to open radical hysterectomy. This trial also mandates vaginal cuff closure for tumor containment. The RACC trial also utilizes sentinel lymph node dissection with ICG-10 prior to a full lymphadenectomy so the accuracy and sensitivity of this technique can be assessed. The endpoint of the trial is a noninferiority margin of 1.57 for PFS at 5 years (41).

41.2.8 Neoadjuvant Chemotherapy Prior to Surgery

Neoadjuvant chemotherapy has been investigated to decrease the size of tumors prior to surgery (Table 41.7). In one study, 70% of 43 patients with stage I or II tumors > 4 cm decreased the size of tumor by > 50%, thereby potentially converting patients from borderline to acceptable surgical candidates. Six

TABLE 41.6 Steps to Performing a Radical Hysterectomy

1.	Obtain access, either through a Maylard or Cherney incision or via laparoscopic or robotic approach
2.	Place into Trendelenburg position and obtain visualization of pelvic structures
3.	Open retroperitoneum
4.	Dissect pararectal and paravesical spaces
5.	Isolate the ureter from the medial peritoneum
6.	Skeletonize the uterine vessels and separate the ureter from the uterine vessels, developing the "tunnel"
7.	Dissect the urinary bladder away from the lower uterine segment, cervix, and upper vagina
8.	Divide the parametrial tissue over the tunnel
9.	Reflect the parametria and uterine vessels over the ureter and dissect the ureter out to its entry into the bladder
10.	Open the rectovaginal space
11.	Ligate the infundibulopelvic ligament or utero-ovarian ligament and divide the peritoneum to the level of the cervix
12.	Divide the uterosacral ligament
13.	Clamp across the vagina below the cervix, and remove the specimen
14.	Repair the vaginal apex
Lymph node mapping, dissection, or lymphadenectomy is described separately.	

randomized trials of neoadjuvant chemotherapy showed an inconsistent improvement in the surgical resectability with an improved PFS (HR: 0.75; 95% CI: 0.61–0.93; $p = 0.008$) and OS (HR: 0.77; 95% CI: 0.62–0.96; $p = 0.02$). Potential disadvantages include chemotherapy-related toxicity and potential improved outcomes from modern chemoradiation.

41.2.9 Adjuvant Therapy Following Surgery

Patients who meet Sedlis criteria are at high risk of recurrence after radical hysterectomy and warrant adjuvant radiation therapy. These factors include (1) tumors ≥ 4 cm with deep or middle 1/3 stromal invasion, (2) tumors with LVSI invading the deep 1/3 of the cervix, (3) tumors ≥ 2 cm with middle 1/3 invasion, or (4) tumors ≥ 5 cm with superficial invasion. GOG-92 randomized patients with these risk factors at the time of a radical hysterectomy to 5040 cGy of whole pelvic radiation without brachytherapy or observation. Radiation decreased the recurrence risk from 28% to 15% (HR: 0.56; $p = 0.02$) with the greatest impact in patients with adenocarcinomas (64).

Patients with positive margins or positive nodes are also at high risk of recurrence. GOG-109 demonstrated that the addition of cisplatin to adjuvant radiation improved the disease-free survival from 69% to 86% and the OS from 77% to 88%. Ninety-five percent of the patients enrolled in this trial had positive nodes (65).

RTOG 117 (NRG 0274) found no benefit to the addition of systemic chemotherapy to cisplatin and radiation in patients with stage IA2 through IIA disease with positive pelvic nodes, positive parametrial margins, or positive para-aortic nodes (66).

41.2.10 Decreasing Radicality of Surgery for Cervical Cancer

Lymphadenectomy is important in cervical cancer as lymphatic spread occurs in approximately 10% of apparent stage I cancers without LVSI and is as high as 40% in patients with LVSI (67). However, this procedure can be associated with significant morbidity, with a 10%–15% risk of lymphedema after surgery. Adjuvant radiation increases this more than threefold (68). Therefore, sentinel node dissection as a replacement for full pelvic and low para-aortic lymphadenectomy has been described for patients with early cervical cancer undergoing surgery and has been found to decrease lymphatic complications.

Lymphatic mapping originally used isosulfan blue dye injected into the cervix superficially at two or four sites. Technetium-99 (99Tc) was added to improve the sensitivity of the procedure (69). In all trials and in practice, ultrastaging of sentinel nodes is used with sentinel node biopsy to improve detection rate (70). In addition, all suspicious nodes should be removed at the time of surgery. Evaluation of lymphatic mapping success is side-specific; if only one side maps, a unilateral pelvic lymphadenectomy should be performed only on the side that did not map. Early reports were in patients with up to stage IB2 tumors (< 4 cm), but accuracy may be higher for tumors < 2 cm. Negative predictive value for patients with stage IB2 tumors (2–4 cm) was 94%, but this increased to 99% in patients with stage IB1 tumors (< 2 cm) (71). The sensitivity of the combined blue dye and 99Tc for sentinel nodes was 92%, and lymphedema was significantly decreased. Indocyanine green (ICG) dye has since become the preferred method for lymphatic mapping, as a randomized trial found a detection rate of 97% for ICG compared to 50% for isosulfan blue (72) (Figure 41.3). Currently the RACC trial and the Phenix trials are prospectively evaluating sentinel lymph node biopsy in cervical cancer (73).

Parametrial involvement is rare in patients with small cervical cancers; this challenges the need for radical resection of the cervix in patients with early stage, small tumors, and several trials have examined this (74).

The ConCerv trial is a single arm trial of conservative surgery in 100 women with early-stage low-risk cervical cancer (75). The trial included women with tumors < 2 cm, no LVSI, and < 10 mm of stromal involvement on conization. This trial included patients with squamous cancers and adenocarcinomas, but patients with grade 3 adenocarcinoma and LVSI

TABLE 41.7 Trials of Neoadjuvant Chemotherapy Prior to Surgery for Cervical Cancer

Author	Year	Surgery Alone	Neoadjuvant Chemotherapy and Surgery	Regimen	Cycles
Sardi (58)	1997	106	104	• Cisplatin 50 mg/m^2 d1 • Vincristine 1 mg/m^2 d1 • Bleomycin 25 mg/m^2 (continuous d1–3)	3 cycles at 10 d
Napolitano (59)	2003	70	86	• Cisplatin 50 mg/m^2 d1 • Vincristine 1 mg/m^2 d1 • Bleomycin 25 mg/m^2 d1–3	3 cyst cycles q 21 d
Cai (60)	2006	54	52	• Cisplatin 75 mg/m^2 d1 • 5-FU 24 mg/kg/d d1–5	2 cycles q 21 d
Katsumata (61)	2006	67	67	• Bleomycin 7 mg d1–5 • Vincristine 0.7 mg/m^2 d5 • Mitomycin 7 mg/m^2 d5 • Cisplatin 14 mg/m^2 d1–5	2–4 cycles q 21 d
Eddy (62)	2007	143	145	• Cisplatin 50 mg/m^2 • Vincristine 1 mg/m^2	3 cycles q 21 d
Chen (63)	2008	68	68	• Cisplatin 50 mg/m^2 d1 • Mitomycin 4 mg/m d1–5 d • 5-FU 24 mg/kg/day d1–5	2–3 cycles q 10 d

were excluded. Patients underwent a conization and surgical nodal evaluation and were enrolled if they had negative nodes and negative margins. Patients desiring fertility had no further treatment if the conization had negative margins. Forty patients underwent conization alone and the fertility rate was 28% with 93% term delivery. Simple hysterectomy was performed on patients who did not desire fertility. Overall, the rate of node positivity was 5%, and the cumulative incidence of recurrence was 3.5% (95% CI: 0.9% to 9.0%) with a median follow-up of 3.5 years.

The SHAPE trial was designed to determine if simple hysterectomy was noninferior to a radical hysterectomy in patients with tumors < 2 cm with < 10 mm of invasion on excisional biopsy or < 50% on MRI (76). The trial did include patients with LVSI. The original statistical plan was to compare the PFS in the pelvis, but the recurrence rate was lower than expected, and the trial endpoint was changed to the pelvic recurrence rate at 3 years with a noninferiority margin of 4%. The rate of pelvic recurrence in the radical hysterectomy group was 2.2%, and the rate of pelvic recurrence in the simple hysterectomy group was 2.5%. The absolute difference in pelvic failure was 0.35% (90% CI: –1.62%–2.32%). Since the confidence interval excluded the 4% noninferiority boundary, simple hysterectomy was declared noninferior to radical hysterectomy for this group of patients, and the per-protocol relative risk of local recurrence was 1.01. Postoperatively, patients undergoing a simple hysterectomy were much less likely to experience long-term urinary retention (0.6% vs 11.0%, $p < 0.001$) or incontinence (4.7% vs 11%, $p = 0.003$).

Overall, the groups were well balanced with respect to the use of sentinel lymph node biopsies in the simple versus radical hysterectomy groups (37.0% vs 38.2%). Similarly, the use adjuvant radiation was similar between the two arms (9.2 vs 8.4%). Positive margins were more common in the radical hysterectomy group although this difference was not statistically significant (2.7% vs 2.4%). Most patients in the SHAPE trial were treated with minimally invasive surgery, but rates were different between the two arms. The rate of minimally invasive surgery in the simple arm was 83.1% as compared to 71.2% in the radical arm but this did not appear to influence the pelvic recurrence risk. The pelvic recurrence rates were similar between patients that had simple laparoscopic and simple open hysterectomies (3.2% vs 3.5%). This was also true with the pelvic recurrence rates of those that underwent minimally invasive versus open radical hysterectomies (2.9% vs 3.0%).

GOG-278 was a prospective trial that evaluated cold knife cone biopsy with or without a simple hysterectomy in patients with squamous cell, adenocarcinoma, or adenosquamous carcinomas with stage IA1 tumors with LVSI or stage IA2–IB1 tumors $\leq$ 2 cm; depth of invasion could be no more than 10 mm. Recurrence rate at 3 years was 1.5%; three of 68 patients with cone only recurred, compared with none of the 135 patients

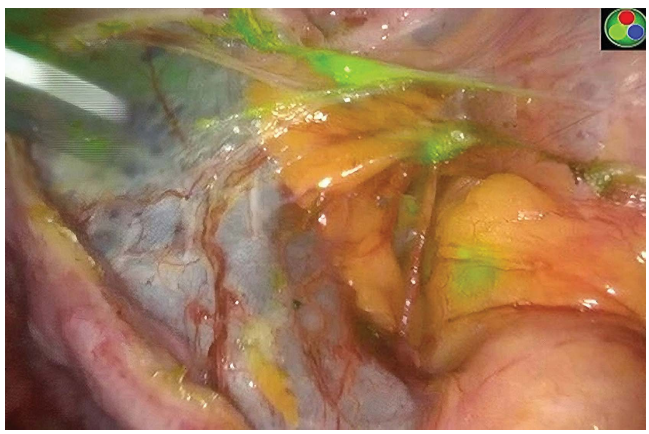


FIGURE 41.3 Lymphatic mapping with sentinel lymph node biopsy using ICG-10.

who underwent simple hysterectomy (77). These trials are summarized in Table 41.8.

41.2.11 Radical Parametrectomy

Radical parametrectomy is the removal of the parametrial tissues and vaginal cuff when a simple hysterectomy has been performed and cervical cancer is found to be present in the final specimen. This can be combined with a lymphadenectomy to complete surgical staging in patients with stage IA2 to IB2 cervical cancers. This procedure has been used for low-risk patients with negative margins on the hysterectomy specimen in lieu of adjuvant radiation. In a small study, the 5-year OS for 33 patients after radical parametrectomy was 96% (79). This procedure has been described both robotically and laparoscopically (71, 80, 81). However, the SHAPE trial brings into question the need for radical parametrectomy for patients who meet the SHAPE criteria.

41.2.12 Radical Trachelectomy

Radical trachelectomy removes the cervix, parametrium, and upper vagina in same manner as a radical hysterectomy, but the vagina is reanastomosed with the lower uterine segment. A permanent cerclage is placed so that fertility can be maintained. This procedure may be considered for patients with tumors < 2 cm who do not meet the criteria for more conservative management (82). This procedure has been reported abdominally, vaginally, laparoscopically, and robotically. The uterine margin must be negative for tumor at the time of the surgery. Approximately 9% are converted to hysterectomy. The overall recurrence risk after radical trachelectomy is 3.3%. One report demonstrated a pregnancy rate of 24% with a live birth rate of 75% and a premature birth rate at < 32 weeks of 10% (83).

There is interest in trying to treat larger tumors with chemotherapy prior to undergoing fertility-sparing surgery. The CNteSSa trial (NCT04016389) is currently enrolling patients to three cycles of neoadjuvant chemotherapy with cisplatin and paclitaxel for patients with tumors that are 2–4 cm who desire fertility-sparing treatment. If the tumor is reduced to < 2 cm, a radical trachelectomy is planned. This study has enrolled approximately 90 patients and continues to enroll (76).

41.2.13 Ovarian Transposition

Patients treated with whole pelvic radiation will experience ovarian failure. Ovarian transposition can be performed to locate the ovaries out of the radiated field. This procedure is performed by dividing the utero-ovarian vessels and mobilizing the ovarian pedicle. An oophoropexy is then performed locating the ovaries superiorly and laterally out of the radiation field. A meta-analysis of over 1000 patients undergoing ovarian transposition showed that 61% of women treated with external beam radiation for cervical cancer maintained ovarian function, and the risk ovarian metastatic spread was 1% (31).

41.2.14 Adjuvant Hysterectomy after Radiation

Patients with tumors > 4 cm have a higher risk of local failure after radiation. Simple hysterectomy after primary radiation could theoretically decrease the risk of local failure. This concept was tested in GOG-71 (RTOG #84–12), where 256 patients with tumors between 4 and 7 cm were randomized to either radiation alone or radiation followed by a simple hysterectomy (84). This trial was performed prior to sensitizing cisplatin chemotherapy during radiation. Both groups received 40–45 Gy, but radiation dosing differed between groups, with a higher dose in the radiation-only group. While local recurrence was decreased in the hysterectomy group from 27% to 14%, there was no difference in OS. Based on this lack of survival difference, improvement of radiation techniques, and current use of sensitizing cisplatin with improved outcomes, post-radiation extrafascial hysterectomy is now rarely utilized.

41.2.15 Carcinoma of the Cervical Stump

Supracervical hysterectomies are sometimes performed for benign conditions, and cancer can develop in the residual cervix. When the uterus is removed, radiation planning becomes more difficult with respect to intracavitary radiation. A series of 200 cases of cervical cancer after supracervical hysterectomy has been reported with primarily squamous histology (85). OS in patients with stage I cancer was only 82% and is worse compared to matched controls with an intact uterus. Brachytherapy increased local control from 39% to 82%, but grade 3–4 complications occurred in 16% of patients. Of note, this was prior to modern radiation techniques.

41.2.16 Follow-Up after Treatment

Over 90% of recurrences from cervical cancer occur within 5 years of diagnosis (86). Follow-up after treatment consists of education regarding symptoms of recurrent cancer and examinations every 3–6 months for the first 2 years following diagnosis and then every 6–12 months until 5 years from diagnosis (30). Patients who underwent fertility-sparing surgery should have a pelvic MRI 6 months after surgery and annually

TABLE 41.8 Recent Trials to Limit Surgical Radicality

Trial Name Author	Year	Trial Design	Inclusion Criteria	Surgical Intervention	Primary Outcome	Results
ConCerv Schmeler (75)	2021	Prospective $n = 100$	IA2–IB1 ≤2cm ≤10mm depth	Cone ± Simple Hysterectomy	Residual Cancer in Hysterectomy Specimen	2.5% had residual disease on hysterectomy; 3.5% 2y recurrence rate
GOG 278 Covens (77)	2024	Prospective $n = 224$	IA1 LVSI+, IA2–IB2 ≤2 cm ≤10 mm depth	Cone ± Simple Hysterectomy	Postoperative morbidity	1.5% 3y recurrence rate; 3/68 cone, 0/135 hysterectomy recurred
SHAPE Plante (78)	2024	Randomized noninferiority $n = 700$	IA2–IB1 ≤ 2 cm ≤ 10 mm depth or < 50% invasion on MRI	Simple vs Radical Hysterectomy	Pelvic recurrence at 3 years	2.52% simple vs 2.17% radical hysterectomy, HR: 0.35 (90% CI: −1.62–2.32)

for 2–3 years. Patients with stage IB3 disease or those treated with chemoradiation should have a PET-CT scan at 6 months and then when prompted by symptoms or physical examination. Patients with stage II–IV should have a PET-CT scan 3–6 months after treatment and then as indicated by history or physical findings. Cytology from the vagina and cervix can be performed annually (30). While this screens for recurrent lower genital tract neoplasia, the utility to detect recurrent cancer is questionable (86). Workup of low-grade changes on cytology smears of the cervix after radiation are not recommended (30).

41.2.17 Surgical Treatment of Recurrent Disease

Patients with central pelvic recurrence after radiation are potential candidates for curative pelvic exenteration in the absence of metastatic disease. This is a complex surgical procedure that should be performed at centers with high expertise. The surgery is often combined with reconstructive procedures including vaginal reconstruction, continent or noncontinent urinary diversions, and colostomy. Patients must be physically and psychologically able to survive such a surgery. The mortality of this type of surgery has been reported between 2% and 6% (87).

Preoperative assessment should include a PET scan to rule out distant metastasis. A pelvic MRI may be helpful to determine resectability. If there is no metastatic disease noted on preoperative imaging, an intraoperative assessment of nodal status and the ability to achieve clear margins is performed. Symptoms such as lymphedema in the leg, hydronephrosis, and sciatic pain indicate possible sidewall involvement and are risk factors for stopping the procedure (87–89). Overall, the long-term disease-free survival depends on risk factors but approximates 50%. Patients with central recurrences < 3 cm and more than 1 year from treatment are excellent candidates for this surgery with a long-term disease-free rate of approximately 86% (88). Overall, the need for exenteration has decreased as primary radiation has improved and central pelvic recurrence has decreased.

Key Points

- Cervical cancer is preventable with vaccination and screening.
- Any abnormality on cytology or HPV testing should be evaluated prior to surgery.
- Staging was updated in 2018 with multiple critical changes.
- Nodal involvement must be evaluated for all but stage IA1 tumors without LVSI.
- Lymphatic mapping with sentinel node biopsy has advantages when compared to full lymphadenectomy.
- Radicality of hysterectomy is decreasing based on specific criteria.
- Fertility-sparing surgery is acceptable in limited circumstances.
- Minimally invasive surgery has been compared to open surgery for radical hysterectomy and is a subject of debate and current study.
- Ovarian transposition may be considered in patients undergoing radiation therapy.
- Appropriate follow-up is essential after surgery for cervical cancer.

References

1. Siegel RL et al. Cancer statistics, 2025. *CA Cancer J Clin*. 2025;75(1):10–45.
2. Sung H et al. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin*. 2021;71(3):209–249.
3. Bray F et al. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin*. 2018;68(6):394–424.
4. Nikmanesh N et al. Knowledge on human papillomavirus infections, cancer biology, immune interactions, vaccination coverage and common treatments: a comprehensive review. *Viral Immunol*. 2024;37(5):221–239.
5. Schiffman M et al. Human papillomavirus testing in the prevention of cervical cancer. *J Natl Cancer Inst*. 2011;103(5):368–383.
6. Nelson CW et al. Human papillomavirus genomics: understanding carcinogenicity. *Tumour Virus Res*. 2023;15:200258.
7. Arbyn M et al. Are 20 human papillomavirus types causing cervical cancer? *J Pathol*. 2014;234(4):431–435.
8. Khan MJ et al. The elevated 10-year risk of cervical precancer and cancer in women with human papillomavirus (HPV) type 16 or 18 and the possible utility of type-specific HPV testing in clinical practice. *J Natl Cancer Inst*. 2005;97(14):1072–1079.
9. Rositch AF et al. Patterns of persistent genital human papillomavirus infection among women worldwide: a literature review and meta-analysis. *Int J Cancer*. 2013;133(6):1271–1285.
10. Wang M et al. Global cervical cancer incidence by histological subtype and implications for screening methods. *J Epidemiol Glob Health*. 2024;14(1):94–101.
11. Rodriguez-Carunchio L et al. HPV-negative carcinoma of the uterine cervix: a distinct type of cervical cancer with poor prognosis. *BJOG*. 2015;122(1):119–127.
12. Nicolas I et al. HPV-negative tumors of the uterine cervix. *Mod Pathol*. 2019;32(8):1189–1196.
13. Papanicolaou GN et al. The diagnostic value of vaginal smears in carcinoma of the uterus. 1941. *Arch Pathol Lab Med*. 1997;121(3):211–224.
14. Katki HA et al. Cervical cancer risk for women undergoing concurrent testing for human papillomavirus and cervical cytology: a population-based study in routine clinical practice. *Lancet Oncol*. 2011;12(7):663–672.
15. Durst M et al. A papillomavirus DNA from a cervical carcinoma and its prevalence in cancer biopsy samples from different geographic regions. *Proc Natl Acad Sci USA*. 1983;80(12):3812–3815.
16. Salazar KL et al. A review of the FDA-approved molecular testing platforms for human papillomavirus. *J Am Soc Cytopathol*. 2019;8(5):284–292.
17. ACOG. *Clinical guidance practice advisory* [Internet], 2021. Available at: www.acog.org/clinical-guidance/practice-advisory/articles/2021/04/updated-cervical-cancer-screening-guidelines.
18. US Preventive Services Task Force et al. Screening for cervical cancer. *JAMA*. 2018;320(7):674–686.
19. Forman D et al. Global burden of human papillomavirus and related diseases. *Vaccine*. 2012;30(Suppl 5):F12–F23.
20. World Health Organization. Human papillomavirus vaccines: WHO position paper 2017, recommendations. *Vaccine*. 2017;35(43):5753–5755.
21. Harper DM et al. Sustained efficacy up to 4.5 years of a bivalent L1 virus-like particle vaccine against human papillomavirus types 16 and 18: follow-up from a randomised control trial. *Lancet*. 2006;367(9518):1247–1255.
22. Schellenbacher C et al. Developments in L2-based human papillomavirus (HPV) vaccines. *Virus Res*. 2017;231:166–175.
23. Canfell K et al. Mortality impact of achieving WHO cervical cancer elimination targets: a comparative modelling analysis in 78 low-income and lower-middle-income countries. *Lancet*. 2020;395(10224):591–603.

24. Hall MT et al. The projected timeframe until cervical cancer elimination in Australia: a modelling study. *Lancet Public Health*. 2019;4(1):e19–e27.
25. Pretorius RG et al. Loop electrosurgical excision procedure or cervical conization to exclude cervical cancer before simple hysterectomy. *J Low Genit Tract Dis*. 2020;24(2):202–205.
26. Tae Kim Y et al. The influence of time intervals between loop electrosurgical excision and subsequent hysterectomy on the morbidity of patients with cervical neoplasia. *Gynecol Oncol*. 2005;96(2):500–503.
27. Ni T et al. Effect of time interval between LEEP and subsequent hysterectomy on postoperative infectious morbidity. *Ther Clin Risk Manag*. 2020;16:839–847.
28. Bhatla N et al. Revised FIGO staging for carcinoma of the cervix uteri. *Int J Gynaecol Obstet*. 2019;145(1):129–135.
29. Olawaiye AB et al. The new (Version 9) American Joint Committee on Cancer tumor, node, metastasis staging for cervical cancer. *CA Cancer J Clin*. 2021;71(4):287–298.
30. Abu-Rustum NR et al. NCCN guidelines(R) insights: cervical cancer, version 1.2024. *J Natl Compr Canc Netw*. 2023;21(12):1224–1233.
31. Laios A et al. Outcomes of ovarian transposition in cervical cancer; an updated meta-analysis. *BMC Womens Health*. 2022;22(1):305.
32. Kidd EA et al. Lymph node staging by positron emission tomography in cervical cancer: relationship to prognosis. *J Clin Oncol*. 2010;28(12):2108–2113.
33. Gouy S et al. Prospective multicenter study evaluating the survival of patients with locally advanced cervical cancer undergoing laparoscopic para-aortic lymphadenectomy before chemoradiotherapy in the era of positron emission tomography imaging. *J Clin Oncol*. 2013;31(24):3026–3033.
34. Ramirez PT et al. Laparoscopic extraperitoneal para-aortic lymphadenectomy in locally advanced cervical cancer: a prospective correlation of surgical findings with positron emission tomography/computed tomography findings. *Cancer*. 2011;117(9):1928–1934.
35. Hata M et al. Radiation therapy for pelvic lymph node metastasis from uterine cervical cancer. *Gynecol Oncol*. 2013;131(1):99–102.
36. da Costa SCS et al. Neoadjuvant chemotherapy with cisplatin and gemcitabine followed by chemoradiation versus chemoradiation for locally advanced cervical cancer: a randomized phase II trial. *J Clin Oncol*. 2019;37(33):3124–3131.
37. Gold MA et al. Surgical versus radiographic determination of para-aortic lymph node metastases before chemoradiation for locally advanced cervical carcinoma: a Gynecologic Oncology Group study. *Cancer*. 2008;112(9):1954–1963.
38. Clark J. A more radical method of performing hysterectomy for cancer of the uterus. *Johns Hopkins Hosp Bull*. 1895;6:120.
39. Naumann RW. Minimally invasive radical hysterectomy has many benefits compared with open radical hysterectomy: will the LACC trial cause the premature demise of this procedure? *J Minim Invasive Gynecol*. 2019;26(3):379–380.
40. Piver MS et al. Five classes of extended hysterectomy for women with cervical cancer. *Obstet Gynecol*. 1974;44(2):265–272.
41. Falconer H et al. Robot-assisted approach to cervical cancer (RACC): an international multi-center, open-label randomized controlled trial. *Int J Gynecol Cancer*. 2019;29(6):1072–1076.
42. Takeshima N et al. Assessment of the revised International Federation of Gynecology and obstetrics staging for early invasive squamous cervical cancer. *Gynecol Oncol*. 1999;74(2):165–169.
43. Landoni F et al. Randomised study of radical surgery versus radiotherapy for stage Ib-IIa cervical cancer. *Lancet*. 1997;350(9077):535–540.
44. Landoni F et al. Class II versus class III radical hysterectomy in stage IB-IIA cervical cancer: a prospective randomized study. *Gynecol Oncol*. 2001;80(1):3–12.
45. Querleu D et al. Classification of radical hysterectomy. *Lancet Oncol*. 2008;9(3):297–303.
46. Ouldamer L et al. Upper margin of para-aortic lymphadenectomy in cervical cancer. *Acta Obstet Gynecol Scand*. 2012;91(8):893–900.
47. Chen Y et al. Distribution patterns of lymph node metastasis in early stage invasive cervical cancer. *Medicine (Baltimore)*. 2020;99(42):e22285.
48. Shah M et al. Therapeutic role of lymphadenectomy for cervical cancer. *Cancer*. 2011;117(2):310–317.
49. Zhang SS et al. Efficacy of robotic radical hysterectomy for cervical cancer compared with that of open and laparoscopic surgery: a separate meta-analysis of high-quality studies. *Medicine* (Baltimore). 2019;98(4):e14171.
50. Nam JH et al. Laparoscopic versus open radical hysterectomy in early-stage cervical cancer: long-term survival outcomes in a matched cohort study. *Ann Oncol*. 2012;23(4):903–911.
51. Levine MD et al. Outcomes of minimally invasive versus open radical hysterectomy for early stage cervical cancer incorporating 2018 FIGO staging. *J Minim Invasive Gynecol*. 2021;28(4):824–828.
52. Ramirez PT et al. Laparoscopic and robotic techniques for radical hysterectomy in patients with early-stage cervical cancer. *Gynecol Oncol*. 2008;110(3 Suppl 2):S21–S24.
53. Matsuo K et al. Association of radical hysterectomy surgical volume and survival for early-stage cervical cancer. *Obstet Gynecol*. 2019;133(6):1086–1098.
54. Wang YZ et al. Laparoscopy versus laparotomy for the management of early stage cervical cancer. *BMC Cancer*. 2015;15:928.
55. Leitao MM et al. The MEMORY study: MulticentEr study of minimally invasive surgery versus open radical hYsterectomy in the management of early-stage cervical cancer: survival outcomes. *Gynecol Oncol*. 2022;166(3):417–424.
56. Chiva L et al. SUCCOR study: an international European cohort observational study comparing minimally invasive surgery versus open abdominal radical hysterectomy in patients with stage IB1 cervical cancer. *Int J Gynecol Cancer*. 2020;30(9):1269–1277.
57. Marchand G et al. Meta-analysis of laparoscopic radical hysterectomy, excluding robotic assisted versus open radical hysterectomy for early stage cervical cancer. *Sci Rep*. 2023;13(1):273.
58. Sardi JE et al. Long-term follow-up of the first randomized trial using neoadjuvant chemotherapy in stage Ib squamous carcinoma of the cervix: the final results. *Gynecol Oncol*. 1997;67(1):61–69.
59. Napolitano U et al. The role of neoadjuvant chemotherapy for squamous cell cervical cancer (Ib-IIIb): a long-term randomized trial. *Eur J Gynaecol Oncol*. 2003;24(1):51–59.
60. Cai HB et al. Randomized study of preoperative chemotherapy versus primary surgery for stage IB cervical cancer. *J Obstet Gynaecol Res*. 2006;32(3):315–323.
61. Katsumata N et al. Phase III randomised controlled trial of neoadjuvant chemotherapy plus radical surgery vs radical surgery alone for stages IB2, IIA2, and IIB cervical cancer: a Japan Clinical Oncology Group trial (JCOG 0102). *Br J Cancer*. 2013;108(10):1957–1963.
62. Eddy GL et al. Treatment of ("bulky") stage IB cervical cancer with or without neoadjuvant vincristine and cisplatin prior to radical hysterectomy and pelvic/para-aortic lymphadenectomy: a phase III trial of the gynecologic oncology group. *Gynecol Oncol*. 2007;106(2):362–369.
63. Chen H et al. Clinical efficacy of modified preoperative neoadjuvant chemotherapy in the treatment of locally advanced (stage IB2 to IIB) cervical cancer: randomized study. *Gynecol Oncol*. 2008;110(3):308–315.
64. Sedlis A et al. A randomized trial of pelvic radiation therapy versus no further therapy in selected patients with stage IB carcinoma of the cervix after radical hysterectomy and pelvic lymphadenectomy: A Gynecologic Oncology Group study. *Gynecol Oncol*. 1999;73(2):177–183.
65. Peters WA et al. Concurrent chemotherapy and pelvic radiation therapy compared with pelvic radiation therapy alone as adjuvant therapy after radical surgery in high-risk early-stage cancer of the cervix. *J Clin Oncol*. 2000;18(8):1606–1613.

66. Mileshkin LR et al. Adjuvant chemotherapy following chemoradiotherapy as primary treatment for locally advanced cervical cancer versus chemoradiotherapy alone (OUTBACK): an international, open-label, randomised, phase 3 trial. *Lancet Oncol*. 2023;24(5):468–482.
67. Sakuragi N et al. Incidence and distribution pattern of pelvic and paraaortic lymph node metastasis in patients with Stages IB, IIA, and IIB cervical carcinoma treated with radical hysterectomy. *Cancer*. 1999;85(7):1547–1554.
68. Kim SI et al. Comparison of survival outcomes between minimally invasive surgery and conventional open surgery for radical hysterectomy as primary treatment in patients with stage IB1-IIA2 cervical cancer. *Gynecol Oncol*. 2019;153(1):3–12.
69. Rob L et al. Study of lymphatic mapping and sentinel node identification in early stage cervical cancer. *Gynecol Oncol*. 2005;98(2):281–288.
70. Cibula D et al. Bilateral ultrastaging of sentinel lymph node in cervical cancer: lowering the false-negative rate and improving the detection of micrometastasis. *Gynecol Oncol*. 2012;127(3):462–466.
71. Altgassen C et al. Multicenter validation study of the sentinel lymph node concept in cervical cancer: AGO Study Group. *J Clin Oncol*. 2008;26(18):2943–2951.
72. Frumovitz M et al. Near-infrared fluorescence for detection of sentinel lymph nodes in women with cervical and uterine cancers (FILM): a randomised, phase 3, multicentre, non-inferiority trial. *Lancet Oncol*. 2018;19(10):1394–1403.
73. Tu H et al. Sentinel lymph node biopsy versus pelvic lymphadenectomy in early-stage cervical cancer: a multi-center randomized trial (PHENIX/CSEM 010). *Int J Gynecol Cancer*. 2020;30(11):1829–1833.
74. Schmeler KM et al. Conservative management of early stage cervical cancer: is there a role for less radical surgery? *Gynecol Oncol*. 2011;120(3):321–325.
75. Schmeler KM et al. ConCerv: a prospective trial of conservative surgery for low-risk early-stage cervical cancer. *Int J Gynecol Cancer*. 2021;31(10):1317–1325.
76. Plante M et al. FIGO 2018 stage IB2 (2–4 cm) Cervical cancer treated with Neo-adjuvant chemotherapy followed by fertility Sparing Surgery (CONTESSA); Neo-Adjuvant Chemotherapy and Conservative Surgery in Cervical Cancer to Preserve Fertility (NEOCON-F). A PMHC, DGOG, GCIG/CCRN and multicenter study. *Int J Gynecol Cancer*. 2019;29(5):969–975.
77. Benseler A et al. Simple hysterectomy SHAPE-ing up to be the treatment of choice for early cervical cancer under 2 cm. *J Gynecol Oncol*. 2024;35(2):e49.
78. Plante M et al. Simple versus radical hysterectomy in women with low-risk cervical cancer. *N Engl J Med*. 2024;390(9):819–829.
79. Leath CA et al. The role of radical parametrectomy in the treatment of occult cervical carcinoma after extrafascial hysterectomy. *Gynecol Oncol*. 2004;92(1):215–219.
80. Lee CL et al. Total laparoscopic radical parametrectomy. *J Minim Invasive Gynecol*. 2005;12(2):168–170.
81. Vitobello D et al. Robotic radical parametrectomy with pelvic lymphadenectomy: our experience and review of the literature. *Eur J Surg Oncol*. 2012;38(6):548–554.
82. Smith ES et al. Radical trachelectomy for the treatment of early-stage cervical cancer: a systematic review. *Obstet Gynecol*. 2020;136(3):533–542.
83. Milliken DA et al. Fertility preserving surgery for carcinoma of the cervix. *Curr Opin Oncol*. 2008;20(5):575–580.
84. Keys HM et al. Radiation therapy with and without extrafascial hysterectomy for bulky stage IB cervical carcinoma: a randomized trial of the Gynecologic Oncology Group. *Gynecol Oncol*. 2003;89(3):343–353.
85. Barillot I et al. Carcinoma of the cervical stump: a review of 213 cases. *Eur J Cancer*. 1993;29A(9):1231–1236.
86. Elit L et al. Gynecology Cancer Disease Site G. Follow-up for women after treatment for cervical cancer: a systematic review. *Gynecol Oncol*. 2009;114(3):528–535.
87. Stanca M et al. Long-term survival, prognostic factors, and quality of life of patients undergoing pelvic exenteration for cervical cancer. *Cancers* (Basel). 2022;14(9).
88. Shingleton HM et al. Clinical and histopathologic factors predicting recurrence and survival after pelvic exenteration for cancer of the cervix. *Obstet Gynecol*. 1989;73(6):1027–1034.
89. Shepherd JH et al. Multivariate analysis of factors affecting survival in pelvic exenteration. *Int J Gynecol Cancer*. 1994;4(6):361–370.

42 THE ROLE OF MINIMALLY INVASIVE SURGERY IN THE MANAGEMENT OF GESTATIONAL TROPHOBLASTIC DISEASE

Neil Horowitz

42.1 Introduction

Gestational trophoblastic disease (GTD) is group of diseases encompassing both benign and malignant conditions that arise out of abnormal pregnancy events. By far, the most common entity is hydatidiform mole, a benign condition, with an incidence of approximately one to two per 1000 pregnancies in the United States and Western Europe. The incidence is two to three times higher in Asia and Brazil. Hydatidiform moles are either complete (CHM) or partial (PHM). These two types have distinctly different histology, biology, presentation, risk of malignancy, and long-term outcomes (1, 2). Gestational trophoblastic neoplasia (GTN), the malignant variant of GTD, can occur after any pregnancy event. GTN is most common after molar pregnancies (50%) but can follow term pregnancies or miscarriages (25%) or ectopic pregnancies (25%) (1). Different forms of GTN include invasive mole, choriocarcinoma, placental site trophoblastic disease (PSTT), and epithelioid trophoblastic disease (ETT).

Apart from PSTT and ETT, GTD/GTN arise from syncytiotrophoblast and cytotrophoblast and make abundant levels of human chorionic gonadotropin (hCG). Quantitative hCG levels are useful for diagnosis, for monitoring response to repeat treatment, and for surveillance. Unlike any other malignancy which requires a tissue diagnosis, the diagnosis of GTN is based solely on strict criterion of plateauing or rising hCG (2, 3). First-line management of CHM and PHM is primarily surgical, either by uterine evacuation or hysterectomy. Since GTN, except for PSTT and ETT, is exquisitely sensitive to chemotherapy, uterine evacuation followed in certain cases by chemotherapy is the first line of management, resulting in extremely high cure rates while maintaining fertility. Hysterectomy plays a critical role in (1) chemotherapy-resistant GTN, (2) patients who no longer desire to preserve fertility, and (3) patients with PSTT or ETT.

42.2 Evacuation of Hydatidiform Mole

Most CHM and PHM are diagnosed upon presentation to their obstetrician/gynecologist with a missed period, positive home pregnancy test, and signs or symptoms of pregnancy, such as bleeding, pelvic pressure, nausea, or vomiting. CHM and PHM are often suspected based on ultrasound findings and a markedly elevated hCG. Since home pregnancy tests and ultrasounds are routine, CHM and PHM are commonly diagnosed in the first trimester, so the historical symptoms of CHM such as anemia, pre-eclampsia, hyperthyroidism, and uterine size greater than dates are rarely seen (4, 5). Risk factors for molar pregnancy include extremes of maternal age (teens and > 40 years of age) and prior molar pregnancy (6–10). Despite earlier diagnosis, there has not been a subsequent decrease in the incidence of GTN, thus suggesting that molar pregnancies are biologically predestined to develop into GTN.

The ideal initial management of suspected CHM or PHM for women wishing to preserve fertility is uterine evacuation. This is most commonly performed with suction curettage, though some data suggest that manual evacuation is equally effective and yields comparable rates of complete evacuation, blood loss, and risk of post-molar GTN (11). Ultrasound guidance is often used to help ensure complete evacuation (Figure 42.1). A cannula size equal to the gestational age is ideally used. Surgeons must be prepared for bleeding as dilation begins and the hydatidiform mole is initially disrupted. Rapid evacuation of the tissue usually ensues with contraction of the uterus and decrease in bleeding. Oxytocin (10 units in 1-liter lactated ringers) is infused to increase uterine tone and decrease blood loss. Once the evacuation is considered complete, a gentle sharp curettage confirms no residual tissue.

Pre-eclampsia or hyperthyroidism should be managed prior to evacuation with antihypertensives and beta-blockers, respectively. While controversial in patients who have non-molar first trimester losses or evacuations, women with partial hydatidiform mole who are Rh-D negative should receive anti-D immune globulin.

42.3 Hysterectomy for Hydatidiform Mole

Hysterectomy is the preferred primary management technique in women who have an exceedingly high risk of developing GTN, who have completed their family planning, or who present with uterine hemorrhage or perforation (Figure 42.2). Management with hysterectomy does not alleviate the need for hCG surveillance or the need for chemotherapy. A recent meta-analysis comparing hysterectomy to evacuation in the management of molar pregnancy showed that the odds ratio of developing GTN or needing chemotherapy is significantly decreased after hysterectomy compared with evacuation (OR: 0.19; 95% CI: 0.08–0.48, $p = 0.0004$) (12).

42.4 Postsurgical Surveillance and Diagnosis of GTN

After evacuation or hysterectomy for a molar pregnancy, women should have weekly measurements of serum hCG until normalization. The vast majority will have spontaneous normalization of hCG. Thereafter, monthly serum hCG measurements should be obtained for 3 months after a CHM or for 1 month after a PHM (13). These recommendations are based on the fact that development of GTN after hCG normalization is < 1% (14).

Unlike any other malignancy, the diagnosis of GTN is made based on International Federation of Gynecologists and Obstetricians (FIGO) guidelines for hCG levels. Post-molar GTN is defined as a rise in hCG (≥ 10% for three or more values over at least 2 weeks) or a plateau in hCG (± 10% on four tests over 3 weeks). GTN is also diagnosed based on histology of PSTT, ETT, or choriocarcinoma (1). Post-molar GTN is diagnosed if the hCG plateaus or rises per FIGO criteria. The rate of post-molar GTN varies but is approximately 20% after CHM and 1%–4% after PHM. Risk of GTN reaches 40%–60% in women > 40 years of age or with hCG > 100,000 mIU/mL at the time of diagnosis (10, 15).

DOI: 10.1201/9781003312109-42

FIGURE 42.1 Sonogram demonstrating hydatidiform mole with visible endometrial stripe.

FIGURE 42.2 Uterus removed at time of hysterectomy, distended with gestational trophoblastic neoplasia.

42.5 Role of Second Curettage

Once criteria for GTN are met, women undergo a workup and evaluation including physical exam, blood work, and imaging to appropriately stage their cancer and assign a WHO risk score. Initial imaging consists of a plain chest X-ray with computed tomography scans being used if there is evidence of metastases on exam or on plain chest X-ray. If a computerized tomography is obtained only metastases ≥1 cm should be used in the calculation risk score. Based on the WHO score, GTN is considered either low risk (stage I or stage II/III with WHO < 7), high risk (stage IV or stage II/III and WHO ≥ 7), or ultra-high risk (WHO ≥ 12). Cure rates approaching 100% are achieved in patients with low-risk disease by using single-agent or sequential single-agent chemotherapy, usually with methotrexate or actinomycin D. Many different protocols are employed. Patients with high-risk disease require multi-agent chemotherapy with EMA-CO (etoposide, methotrexate actinomycin D, cyclophosphamide, and vincristine). This regimen achieves remission rates of 75%–80%. Patients with ultra-high-risk disease are treated with low-dose induction chemotherapy (etoposide and cisplatin, or EP) before undergoing multi-agent chemotherapy (13).

The role of second curettage in the management of hydatidiform mole is controversial. Although counterintuitive, its routine use in close proximity to the first evacuation or prior to commencement of chemotherapy has not been shown to decrease the incidence of GTN or number of cycles of chemotherapy required to achieve remission if GTN is diagnosed (16). Less controversy exists for use of second curettage as a fertility-sparing alternative to chemotherapy for treatment of low-risk GTN (17, 18). Several studies have shown that 40%–60% of women with low-risk GTN treated with second curettage are cured with this procedure and do not need subsequent chemotherapy.

42.6 Hysterectomy for GTN

As with hydatidiform mole, the use of hysterectomy for primary management of nonmetastatic GTN or chemotherapy-resistant disease is mostly driven by patient age and preference. Hysterectomy is quite effective as primary treatment of GTN, yielding a cure rate of 50%–80%. Hysterectomy can also salvage 85%–90% of patients with chemotherapy-resistant disease (19, 20). Hysterectomy does not eliminate the need for hCG surveillance or the need for subsequent chemotherapy. Some centers administer a single dose of chemotherapy (usually actinomycin D) at the time of hysterectomy. This is based on concern for occult metastasis or tumor embolization resulting from uterine manipulation during surgery. Importantly, a cost-effectiveness analysis comparing chemotherapy to primary hysterectomy for nonmetastatic low-risk GTN favored chemotherapy based on cost for each quality-adjusted life year gained (21).

Whether performed for hydatidiform mole or GTN, the best surgical route for hysterectomy is not well established. There are indisputable benefits to a minimally invasive (robotic or laparoscopic) approach to hysterectomy. Historically, oncologic outcomes were considered equivalent for open and minimally invasive surgery (MIS). However, this has been questioned based on recent data suggesting worse survival in patients undergoing MIS for cervical cancer (22). Few data exist in patients with GTD or GTN that compare outcomes of minimally invasive versus open hysterectomy. A small retrospective review showed no difference in long-term survival among 39 women who underwent surgery for GTD or GTN (22 minimally invasive vs 17 open surgery) (23). While these data are reassuring, more information is needed. Minimally invasive hysterectomy can be recommended for women with GTD or GTN, but this should be done with thorough discussion and shared decision making.

The typical soft nature of the pregnant uterus, large volume of intracavitary disease, and propensity for embolization precludes the use of a uterine manipulator during minimally invasive hysterectomy. Early ligation or sealing of the uterine vessels limits blood loss and trophoblastic embolization.

Hysterectomy is also the primary mode of treatment for patients with PSTT and ETT based on their relative chemotherapy resistance (3). PSTT has a small risk of lymph node metastasis, but the role of routine lymphadenectomy is controversial and typically reserved for those with large tumors and deep invasion. Nonmetastatic disease treated by hysterectomy has a 90% 10-year survival rate (24). The addition of

chemotherapy does not improve outcomes. However, adjuvant chemotherapy with EMA/EP and consolidation with pembrolizumab is recommended for patients diagnosed with ETT or PSTT more than 4 years from the antecedent pregnancy due to the markedly poorer outcomes for this subgroup (25, 26).

42.7 Metastatectomy of Chemotherapy-Resistant GTN

While GTN is highly sensitive to chemotherapy and often is still cured after several lines of multi-agent chemotherapy, surgery remains an important treatment modality. Surgery is best used in the setting of persistent low levels of hCG, early relapse, or for isolated, chemotherapy-resistant disease (27). CT scan or FDG-PET imaging are used preoperatively to determine the extent of disease. Pulmonary, liver, and brain metastases are particularly amenable to surgical resection.

Pulmonary metastases are common in patients with GTN. While they increase disease stage at diagnosis, patients can still have low-risk disease with lung metastases and undergo treatment with single-agent chemotherapy. In approximately 40% of such cases, hCG normalizes after chemotherapy, but imaging shows persistent lung lesions. In this scenario, the normal hCG trumps the radiographic findings, and these "persistent" lesions do not need to be resected. For chemotherapy-resistant disease with persistent hCG elevation or for relapsed disease, surgical resection using video-assisted thoracoscopic surgery (VATS) or thoracotomy has been shown to be quite effective. Prior to surgical resection, extensive imaging should exclude other areas of metastatic disease. Ideal candidates for thoracotomy have isolated, unilateral lesions and low hCG values (28, 29). Rapid normalization of hCG after resection is predictive of prolonged remission. Several studies have noted that complete resection yields complete remission in greater than 90% of patients (30).

The brain is also a common site of metastatic GTN, accounting for up to 20% of non-molar choriocarcinoma amenable to surgical resection. Brain metastases are rarely isolated, but craniotomy may be the approach of choice especially if they are associated with increased intracranial pressure or bleeding. Salvage rates as high as 80% have been noted with combined resection, high-dose chemotherapy, and intrathecal methotrexate (31–33).

Key Points

1. Gestational trophoblastic disease (GTD) is distinct from its malignant counterpart, gestational trophoblastic neoplasia (GTN).
2. Surgery plays a critical role in the initial management of complete or partial hydatidiform mole.
3. Uterine evacuation is the primary method of treating hydatidiform mole, though hysterectomy may be preferred based on age and reproductive plans.
4. Second curettage can be used to treat low-risk GTN.
5. Hysterectomy is paramount in the setting of uterine hemorrhage or chemotherapy-resistant GTN.
6. Metastatectomy improves survival of patients with chemotherapy-resistant GTN.
7. Hysterectomy is first-line treatment for epithelioid trophoblastic tumor (ETT) and placental site trophoblastic tumor (PSTT).
8. The preferred approach to hysterectomy, i.e., laparotomy versus minimally invasive surgery (MIS), is not well established for patients with GTD.

References

1. Horowitz NS et al. Epidemiology, diagnosis, and treatment of gestational trophoblastic disease: A Society of Gynecologic Oncology evidenced-based review and recommendation. *Gynecol Oncol*. 2021;163(3):605–613.
2. Ngan S et al. Gestational trophoblastic neoplasia management: an update. *Curr Opin Oncol*. 2007;19(5):486–491.
3. Horowitz NS et al. Placental site trophoblastic tumors and epithelioid trophoblastic tumors: biology, natural history, and treatment modalities. *Gynecol Oncol*. 2017;144(1): 208–214.
4. Sun SY et al. Clinical presentation of complete hydatidiform mole and partial hydatidiform mole at a regional trophoblastic disease center in the United States over the past 2 decades. *Int J Gynecol Cancer*. 2016;26(2):367–370.
5. Lurain JR. Gestational trophoblastic disease I: epidemiology, pathology, clinical presentation and diagnosis of gestational trophoblastic disease, and management of hydatidiform mole. *Am J Obstet Gynecol*. 2010;203(6):531–539.
6. Sebire NJ et al. Risk of partial and complete hydatidiform molar pregnancy in relation to maternal age. *BJOG*. 2002;109(1):99–102.
7. Sebire NJ et al. Risk of recurrent hydatidiform mole and subsequent pregnancy outcome following complete or partial hydatidiform molar pregnancy. *BJOG*. 2003;110(1):22–26.
8. Gockley AA et al. The effect of adolescence and advanced maternal age on the incidence of complete and partial molar pregnancy. *Gynecol Oncol*. 2016;140(3):470–473.
9. Elias KM et al. Complete hydatidiform mole in women older than age 50. *J Reprod Med*. 2010;55(5–6):208–212.
10. Elias KM et al. Complete hydatidiform mole in women aged 40 to 49 years. *J Reprod Med*. 2012;57(5–6):254–258.
11. Padron L et al. Manual compared with electric vacuum aspiration for treatment of molar pregnancy. *Obstet Gynecol*. 2018;131(4):652–659.
12. Zhao P et al. Total hysterectomy versus uterine evacuation for preventing post-molar gestational trophoblastic neoplasia in patients who are at least 40 years old: a systematic review and meta-analysis. *BMC Cancer*. 2019;19(1):13.
13. Lok C et al. Practical guidelines for the treatment of gestational trophoblastic disease: collaboration of the European Organisation for the Treatment of Trophoblastic Disease (EOTTD)-European Society of Gynaecologic Oncology (ESGO)-Gynecologic Cancer InterGroup (GCIG)-International Society for the Study of Trophoblastic Diseases (ISSTD). *J Clin Oncol*. 2025:JCO2402326.
14. Albright BB et al. Gestational trophoblastic neoplasia after human chorionic gonadotropin normalization following molar pregnancy: a systematic review and meta-analysis. *Obstet Gynecol*. 2020;135(1):12–23.
15. Gockley AA et al. Impact of clinical characteristics on human chorionic gonadotropin regression after molar pregnancy. *Clinics* (Sao Paulo). 2021;76:e2830.
16. Hemida R et al. Second uterine curettage and the number of chemotherapy courses in postmolar gestational trophoblastic neoplasia: a randomized controlled trial. *Obstet Gynecol*. 2019;133(5):1024–1031.

17. Osborne RJ et al. Second curettage for low-risk nonmetastatic gestational trophoblastic neoplasia. *Obstet Gynecol*. 2016;128(3):535–542.
18. Vandewal A et al. Curative effect of second curettage for treatment of gestational trophoblastic disease – results of the Belgian registry for gestational trophoblastic disease. *Eur J Obstet Gynecol Reprod Biol*. 2021;257:95–99.
19. Bolze PA et al. First-line hysterectomy for women with low-risk non-metastatic gestational trophoblastic neoplasia no longer wishing to conceive. *Gynecol Oncol*. 2018;150(2):282–287.
20. Eysbouts YK et al. The added value of hysterectomy in the management of gestational trophoblastic neoplasia. *Gynecol Oncol*. 2017;145(3):536–542.
21. Mitric C et al. Hysterectomy versus chemotherapy for low-risk non-metastatic gestational trophoblastic neoplasia (GTN): a cost-effectiveness analysis. *Gynecol Oncol*. 2024;187:30–36.
22. Ramirez PT et al. Minimally invasive versus abdominal radical hysterectomy for cervical cancer. *N Engl J Med*. 2018;379(20):1895–1904.
23. Sugrue R et al. Outcomes of minimally invasive versus open abdominal hysterectomy in patients with gestational trophoblastic disease. *Gynecol Oncol*. 2021;160(2):445–449.
24. Schmid P et al. Prognostic markers and long-term outcome of placental-site trophoblastic tumours: a retrospective observational study. *Lancet*. 2009;374(9683):48–55.
25. Baas IO et al. Immunotherapy for gestational trophoblastic neoplasia: a new paradigm. *Gynecol Obstet Invest*. 2024;89(3):230–238.
26. Froeling FEM et al. Intensified therapies improve survival and identification of novel prognostic factors for placental-site and epithelioid trophoblastic tumours. *Br J Cancer*. 2019;120(6):587–594.
27. Essel KG et al. Complete resection is essential in the surgical treatment of gestational trophoblastic neoplasia. *Int J Gynecol Cancer*. 2018;28(8):1453–1460.
28. Kong Y et al. Management and predictors of treatment failure in patients with chemo-resistant/relapsed gestational trophoblastic neoplasia with lung metastasis. *J Clin Med*. 2022;11(24).
29. Fleming EL et al. The changing role of thoracotomy in gestational trophoblastic neoplasia at the New England Trophoblastic Disease Center. *J Reprod Med*. 2008;53(7):493–498.
30. Kanis MJ et al. Pulmonary resection in the management of high-risk gestational trophoblastic neoplasia. *Int J Gynecol Cancer*. 2016;26(4):796–800.
31. Savage P et al. Brain metastases in gestational trophoblast neoplasia: an update on incidence, management and outcome. *Gynecol Oncol*. 2015;137(1):73–76.
32. Ghorani E et al. Pembrolizumab is effective for drug-resistant gestational trophoblastic neoplasia. *Lancet*. 2017;390(10110):2343–2345.
33. Li Y et al. Effectiveness of craniotomy and long-term survival in 35 patients with gestational trophoblastic neoplasia with brain metastases: a clinical retrospective analysis. *J Gynecol Oncol*. 2022;33(3):e33.

43 LAPAROSCOPIC COLOSTOMY

Vance Broach

43.1 Introduction

For the gynecologic surgeon, laparoscopic colostomy is an effective tool to divert stool from the pelvis (1). The laparoscopic approach is feasible, minimizes the surgical morbidity of a laparotomy, and allows for successful formation of this bowel diversion (2). The indications for laparoscopic colostomy in gynecologic patients most commonly include large bowel obstruction, fistula, and bowel injury (1). In this chapter, the surgical indications and preoperative considerations will be reviewed focusing on the gynecologic patient. The operative approach and technique will be described, and postsurgical considerations and potential complications will be discussed. These can be applied to laparoscopic and single-port techniques (1–9).

43.2 Indications

The need for bowel diversion in gynecologic patients is relatively uncommon but can pose an urgent or emergent surgical need. Patients with gynecologic oncology conditions, including cervical cancer, ovarian cancer, and uterine cancer, can warrant laparoscopic colostomy in either a planned or emergent situation (1).

43.2.1 Large Bowel Obstruction

An enlarging pelvic tumor or radiation fibrosis can result in a large bowel obstruction that necessitates emergency surgical intervention. The degree of colon dilation determines the feasibility of a laparoscopic approach, as massively dilated bowel can limit visualization and require laparotomy.

43.2.2 Rectovaginal Fistula

Another common indication for laparoscopic colostomy in the gynecologic patient is a rectovaginal fistula which is not amenable to primary repair. Patient characteristics such as prior pelvic radiation, presence of pelvic tumor, extensive nature of the fistula, and poor tissue integrity may prevent primary repair and require diversion. In many cases, a laparoscopic approach to colostomy can be used.

43.2.3 Extraperitoneal Rectal Injury

An iatrogenic extraperitoneal rectal injury can occur at the time of minimally invasive surgery. Many iatrogenic injuries can be repaired primarily, but certain extensive rectal injuries may require temporary or permanent diversion. In this situation, continuation of the minimally invasive surgical approach may be utilized, and laparoscopic colostomy can be performed at the time of the initial procedure.

43.3 Preoperative Considerations

Patient success in colostomy management is largely dependent on the preoperative education, expectation setting, and clinical evaluation which precedes the procedure. The concept of diversion is foreign to many patients, so a detailed and clear discussion of bowel diversion in the context of the indication is of utmost importance. Particularly when diversion is being done electively, as in the case of a fistula, preoperative evaluation with a wound ostomy nursing specialist should be performed. During this visit, patients become familiar with the ostomy appliance and are educated about expectations regarding stoma management. Preoperative stoma site marking should occur, taking care to avoid the waistline and areas of natural folds. The surgeon may similarly counsel the patient on these aspects and perform stoma site marking. Site marking is of particular importance as it allows for the selection of the preferred location for a stoma to minimize complications related to pouching (6–9).

It is also important to set the expectation for bowel function following colostomy formation. Ideally, the ostomy is created as distally as can be safely performed given the clinical scenario so that the stool output is more formed and less frequent. Patients with a sigmoid colostomy can reasonably expect one to two formed bowel movements per day with passage of gas intermittently. Patients who require a more proximal transverse colostomy may find stools to be less formed and more frequent.

43.4 Procedure

In the operating room, patients anticipating laparoscopic colostomy are positioned in the supine or lithotomy position. Lithotomy allows access to the rectum should pelvic examination or colonoscopy be needed. Trocar placement depends on the anticipated location of the stoma. For a left-sided stoma, an umbilical trocar for the laparoscope with one to two right lateral trocars allows for adequate visualization and triangulation of instruments to the left colon (4). When possible, a trocar can be placed at the site of the anticipated colostomy, thereby minimizing total laparoscopic incisions (Figure 43.1). A single port technique can also be utilized (3, 5).

Once the trocars are placed, it is often helpful to position the patient in some right lateral tilt to expose the left colon. Some degree of Trendelenburg positioning may also help move the small bowel out of the pelvis. If visualization of the splenic flexure is needed, reverse Trendelenburg position may help, and this can be adjusted as needed during the case.

The colon is then evaluated for a suitable site for diversion. Bowel graspers are gently used to inspect the surfaces of the bowel. The ideal position is (1) tension free when reaching the abdominal wall (once pneumoperitoneum is deflated), (2) without any signs of obvious disease (as in the case of malignancy), and (3) outside of a previously radiated field. In some cases, the lateral physiologic attachments of the colon or omentum must be freed to achieve the desired length. Mobilizing the colon along the lateral peritoneal reflection, the white line of Toldt, so that it is sufficiently tension free allows for a technically more feasible diversion and reduces the risk of stomal retraction following the procedure.

Once the colon is sufficiently mobilized, a disk of skin at the site of the planned ostomy is grasped with a Kocher clamp and excised with a scalpel or cautery (2). This may be at the site of one of the ports, in which case it is removed. The caliber of

DOI: 10.1201/9781003312109-43

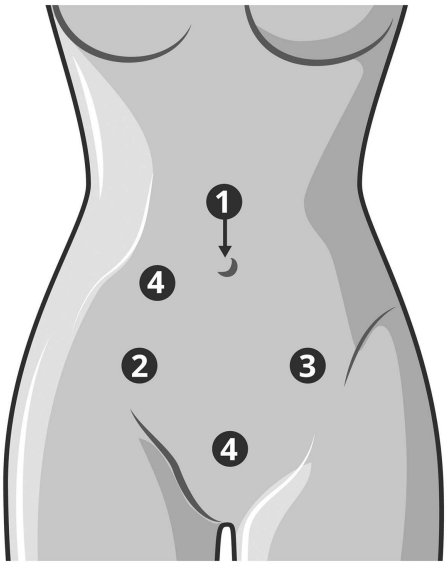


FIGURE 43.1 Port setup for left-sided colostomy. (1) Umbilicus, site of trocar for camera; (2) 12 mm trocar for instrumentation and stapling device; (3) trocar for manipulation, to be converted to colostomy site; (4) optional 5 mm trocar sites. (Artwork: Elisabeth Robinson.)

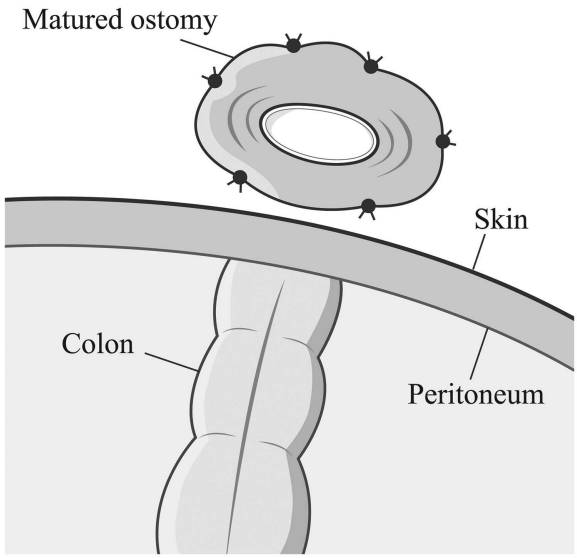


FIGURE 43.2 Axial view of matured end colostomy. The colon, whether end or loop, is brought through the opening in the peritoneum, fascia, rectus, and skin in a tension-free manner. The ostomy is matured after port closure using 2–0 or 3–0 absorbable suture. (Artwork: Elisabeth Robinson.)

the skin removed must be proportional to the planned stoma, considering the type of diversion planned (end, loop, or "end-loop"). The subcutaneous tissues and fat are dissected down to the anterior rectus sheath. A cruciate incision in the anterior fascia is made with the cautery, and the rectus muscle is separated. The posterior sheath and peritoneum are similarly incised to a width sufficient to allow two fingers to pass, and an atraumatic grasper such as a Babcock is inserted to pull the bowel at the desired site of the stoma through the skin (2).

At this point, prior to maturing the stoma, the pneumoperitoneum is reestablished, and the bowel is checked to ensure there is no malrotation and to verify that the proximal and distal limbs are aligned appropriately (6–9).

43.5 Choice of Stoma

The type of stoma created will depend on the clinical scenario and indication for the stoma. In general, the proximal and distal colonic limbs must each be diverted to allow stool to pass and to prevent mucous build up in the nonfunctional limb, a "mucocele." This is particularly important in cases of large bowel obstruction, where the distal segment of the bowel, no longer connected to the fecal stream, continues to produce mucus. The distal obstruction may prevent drainage of mucus from the anus, and a mucocele of the rectal stump, or Hartmann's pouch, can occur if not brought to the surface. This distal diversion can be performed as a mucous fistula or may prompt the choice of a loop rather than an end colostomy. In cases of fistula, diversion of the distal limb is less necessary but may still be considered; end colostomy without a mucus fistula is reasonable (1, 6–9).

When performing an end colostomy, the bowel is brought through the stoma, stapled using a linear stapler, and the distal limb is dropped back into the abdomen. This can be done intracorporeally using a laparoscopic stapler through a 12 mm port. The full laparoscopic technique may be more challenging but requires less colon mobility. The end colostomy is matured at the end of the procedure after pneumoperitoneum is deflated and ports are removed, typically in a "Brooked" or rosebud fashion to aid in pouching (Figure 43.2).

Alternatively, a loop colostomy can also be performed by mobilizing the bowel and bringing the most mobile and distant loop of the bowel up through the stoma opening with the Babcock. A temporary bridge may be used by making a small incision in the mesentery just adjacent to the bowel and inserting a plastic bridge or red Robinson catheter and suturing that to the skin to support the extraperitoneal location of the ostomy as it heals. Pneumoperitoneum is deflated, the ostomy is matured, and the bridge is removed in 7–10 days.

A third type of diversion, the so-called end-loop colostomy, may also be considered. In this diversion, an end colostomy is brought to the skin, and a corner of the distal limb is also sewn into the same site of diversion, functioning as a mucous fistula. This allows distal mucus and stool to drain into the same pouching system but may allow for a smaller stoma and more successful pouching than a loop colostomy.

Finally, an end colostomy with a separate mucous fistula can be considered. This is technically most feasible when performing a transverse colostomy, with the end colostomy to the right of the midline and the mucous fistula to the left (6–9).

The possibility of reversal at a later date should also be considered. When the stoma is planned to be permanent, the bowel should be affixed to the abdominal wall at the level of the fascia. This can be done laparoscopically with delayed absorbable or permanent suture. This may help prevent stomal prolapse, parastomal hernia formation, and stomal retraction.

43.6 Complications

Many complications associated with laparoscopic colostomy can be prevented and mitigated by careful preoperative planning. These include long-term complications associated with pouching due to poor site selection. As bodies change with time, however, it is not always possible to predict and prevent issues with pouching. This underscores the importance of long-term follow-up for these patients. Intraoperative attention to a tension-free stoma will similarly minimize the risk of stomal retraction and mucocutaneous separation. Other complications such as parastomal hernia and stomal prolapse may be minimized by intraoperative maneuvers, but these may be harder to predict and prevent (1, 6–9).

When bowel diversion is created laparoscopically, care must be taken not to rotate the bowel. Malrotation of the stoma is a complication that requires surgical correction.

References

1. Jandial DD et al. Laparoscopic colostomy in gynecologic cancer. *J Minim Invasive Gynecol*. 2008;15(6):723–728.
2. Khoo RE et al. Laparoscopic ileostomy and colostomy. *Ann Surg*. 1995;221(2):207–208.
3. Nguyen HM et al. Single-port laparoscopic diverting sigmoid colostomy. *Dis Colon Rectum*. 2011;54(12):1585–1588.
4. Palladino E et al. Laparoscopic colostomy for acute left colon obstruction caused by diverticular disease in high risk patient: a case report. *Int J Surg Case Rep*. 2015;12:78–80.
5. Shah A et al. Standardized technique for single port laparoscopic ileostomy and colostomy. *Colorectal Dis*. 2014;16(7):O248–O252.
6. Sidhu A et al. How to do laparoscopic loop ileostomy or colostomy. *ANZ J Surg*. 2020;90(9):1760–1761.
7. Singh N et al. Laparoscopic versus open sigmoid loop colostomy: a comparative study from a cohort of 62 patients requiring temporary faecal diversion at a tertiary care center in North India. *Niger J Surg*. 2019;25(2):139–145.
8. Varghese G et al. Laparoscopic versus open pre-treatment loop colostomy for fecal diversion in rectal cancer patients: is laparoscopic colostomy better? *Indian J Surg Oncol*. 2023;14(2):387–391.
9. Zarour A et al. Laparoscopic rapid totally diverting loop colostomy: a new twist on an old technique. *Am Surg*. 2009;75(7):608–609.

44 PELVIC ORGAN PROLAPSE AND STRESS URINARY INCONTINENCE

Kate V. Meriwether

44.1 Pelvic Organ Prolapse

44.1.1 Evaluation of Pelvic Organ Prolapse

Pelvic organ prolapse (POP) affects up to half the female population on exam, but fortunately only about 3%–6% are affected by symptoms of feeling a bulge (1). Nevertheless, 12.6% of women get surgery for POP in their lifetime (2), and this is increasing given the aging population (3). Prolapse is defined by descent of organs at the top of the vagina (level I), anterior and posterior walls of the vagina (level II), or perineal body or genital hiatus (level III) (4).

The most straightforward way to screen for prolapse bother is to ask women if they see or feel a vaginal bulge, a symptom that has 96% sensitivity and 79% specificity for prolapse beyond the hymen (5). When performing examination, the standard measure is the Pelvic Organ Prolapse Quantification (POP-Q) examination, which evaluates nine measurements in centimeters and gives the prolapse a severity, or "stage," based on the most prolapsed portion of the vagina (6) (Figure 44.1).

Validated patient-centered outcomes commonly used to assess POP symptoms include the pelvic floor distress inventory (PFDI), the pelvic floor impact questionnaire (PFIQ) (7, 8), and the prolapse and incontinence sexual function questionnaire, IUGA revised (PISQ-IR) (9). These questionnaires assess level of bother and impact on quality-of-life measures and can be used to track success after interventions (Table 44.1). Any questionnaires utilized to evaluate POP should be validated for the language and format in which they are being given.

44.1.2 Nonsurgical Treatment of Pelvic Organ Prolapse

Primary prevention of POP includes risk factor modification. Age, parity, vaginal delivery, levator muscle injury, and body mass index (BMI) are established risk factors for POP (10, 11). A BMI of > 30 kg/m^2 has an odds ratio (OR) of 1.44 for POP, and BMI reduction to < 25 kg/m^2 is protective at OR 0.71 (12). Other modifiable risk factors are waist circumference ≥ 88 cm (OR 1.80), hormone therapy (OR 1.18), constipation (OR 1.7), occupation (OR 1.86), persistent cough (OR 1.52), and varicose veins (OR 2.01) (12). As BMI is the most readily modifiable of these by the time women present for evaluation or treatment, weight control and interventions are a feasible and low-risk way to intervene.

Pelvic floor physical therapy (PFPT) is a safe and well-established treatment for POP. Particularly in POP stage ≤ II, symptoms can be significantly improved with 3–6 months of physical therapy (13). Although goal achievement is less than with pessary (30% of women) (14), women who undergo PFPT can lift the prolapse 3–5 mm and improve symptoms substantially (15).

Pessaries are a mainstay of nonsurgical treatment for POP, and historically predate any other POP treatment (16). About 58%–74% of women can be successfully fitted with a pessary (17, 18), and factors associated with failure to find a fitting pessary are older age (> 65 years old), a genital hiatus/total vaginal length ratio greater than 0.8, a lower beginning stage of POP, and a vaginal length of < 8 cm (17, 19). Providers must find a pessary that stays in place, is comfortable to the patient, and can be removed by the patient themselves or by the provider in accordance with the anticipated care regimen (20, 21). Pessary types are varied and each type comes in many sizes, and common types for POP include a ring with or without support and Gellhorn, Shaatz, and space-occupying pessaries like cube and doughnuts. Following pessary fitting, the majority of women (70%) totally obtain their treatment goals (14). Unfortunately, 25%–44% of women discontinue pessary use by 1 year or longer (22, 23), and 25% of patients need another fitting within the first 3 months (24). Mainstays of care are appropriate follow-up at 6–24 month intervals, vaginal estrogen use for postmenopausal patients, and prompt evaluation of symptoms such as vaginal bleeding or pain (20, 21). Common side effects of pessary use include increased discharge (40%), erosion or irritation of vaginal walls (28.5%), and increased or new urinary incontinence (14%) (25). Minor complications that are common with pessaries in the first year include vaginitis (14%), urinary tract infection (44%), and dyspareunia (17%), but fistulae are fortunately rare (3% incidence at 9 years) (24).

44.1.3 Surgical Treatment of Pelvic Organ Prolapse

Surgeries for prolapse are selected based on the portions of the vagina, or compartments, including the apical, posterior, anterior, and distal/perineal compartments, that are being repaired (26). Although repairs of the apical (level I) compartment are the most impactful and durable, women without anterior or apical prolapse can consider surgery to address the other compartments individually. Common surgeries that repair the apical compartment are divided into transabdominal surgeries with graft (such as sacrocolpopexy or sacrohysteropexy), either with laparoscopic/robotic or open abdominal routes, surgeries through the vagina that suspend to natural ligaments (such as uterosacral ligament suspension or sacrospinous ligament fixation), and surgeries that close the inside of the vagina (colpocleisis). Examples of surgeries that repair the anterior compartment include anterior vaginal repair with or without graft and paravaginal repair, and surgeries that address the posterior compartment include posterior vaginal repair with or without graft, perineal repair, and levator plication. The distal or perineal compartment is addressed specifically by perineal repair (26) (Figure 44.2).

When measuring success after a surgical repair, surgeons often use outcomes such as recurrence of symptoms of prolapse after surgery, the prevalence of reoperation for recurrent prolapse, and complications of the original surgery. It is considered the current standard to measure the success of certain surgeries using a composite of both an objective measure of vaginal anatomical failure as defined by the POP-Q exam and a patient-centered measure regarding symptoms or retreatment (1, 27, 28). Common examples of definitions of objective failure include any stage II or greater prolapse, prolapse beyond the hymen, or apical prolapse as measured by a vaginal apex more than 1/3 or 1/2 down its total vaginal length.

The choice of a surgical procedure demands the integration of several individual decisions. The first decision determines if the patient desires insertive vaginal intercourse in the future,

DOI: 10.1201/9781003312109-44

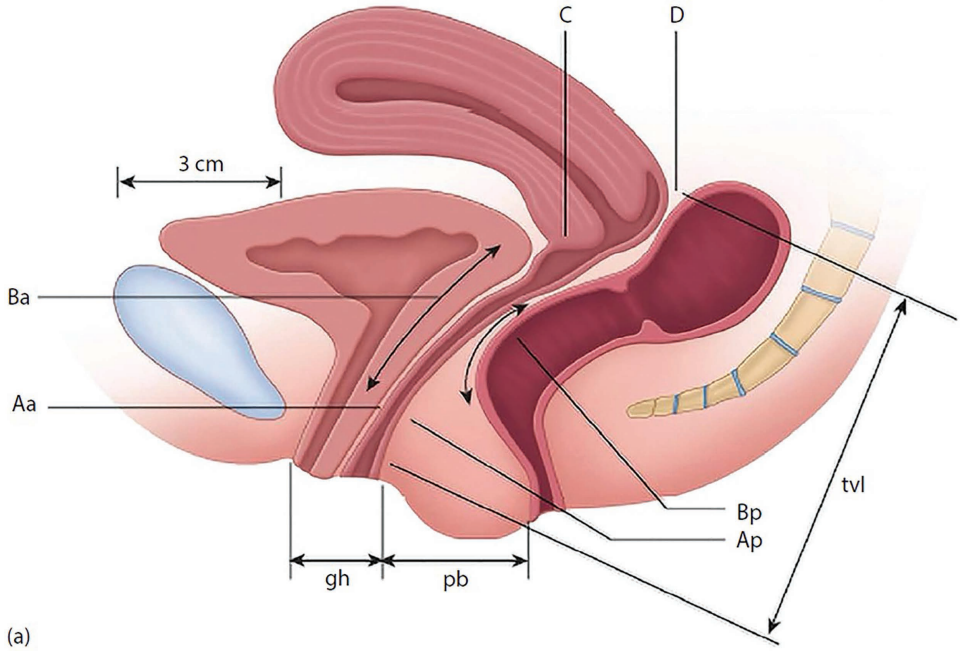


FIGURE 44.1 Pelvic organ prolapse quantification (POP-Q) exam points and documentation:

- A anterior (Aa): A point on the anterior vaginal wall 3 cm above the hymeneal ring
- B anterior (Ba): Most dependent or distal point on the anterior vaginal wall segment between A anterior and point C or the cuff if subject is status posthysterectomy
- C: Anterior lip of the cervix or the cuff if subject is status posthysterectomy
- A posterior (Ap): A point on the posterior vaginal wall 3 cm above the hymeneal ring
- B posterior (Bp): Most dependent or distal point on the posterior vaginal wall segment between A posterior and point D or the cuff if subject is status posthysterectomy
- D: Posterior fornix (this space is left blank in the subject who is status posthysterectomy)
- Genital hiatus (GH): Middle of external urethral meatus to posterior midline hymeneal remnant
- Perineal body (PB): Posterior midline hymeneal remnant to middle of anal opening
- Total vaginal length (TVL): Hymeneal ring to vaginal apex

(From Swift SE et al., Classification and Epidemiology of Pelvic Organ Prolapse. In: Cardozo L et al., eds. *Textbook of Female Urology and Urogynecology*, 6th edn., Vol. 2, Boca Raton, FL: CRC Press; 2023, with permission.)

as lack of this desire makes women possible candidates for a colpocleisis, a surgery that shortens the vaginal length substantially. As colpocleisis has very low risk of prolapse recurrence and is a safe and minimally invasive procedure (29); most women should be made aware of this option.

In the case of women with a uterus still in place, the next decision to be discussed with the patient is the option of uterine preservation (hysteropexy) or hysterectomy at the time of POP surgery. Uterine preservation shortens operating room time, reduces blood loss, and decreases exposure risk in procedures involving permanent mesh grafts compared to hysterectomy (30, 31), but contraindications to uterine preservation include elevated risk of pelvic cancers (including genetic cancer syndromes), inability to comply with recommended pelvic cancer screening, and current or suspected uterine or adnexal pathology (32).

For women opting for a reconstructive procedure, a controversial decision faced by women choosing a POP surgery involves use of a graft versus native tissue repair. Graft reconstruction is less likely to result in prolapse recurrence (33), but the reoperation rate for POP recurrence and subjective relief of POP symptoms is similar between native tissue and graft procedures, and the overall reoperation rate may be higher due to graft-related complications (34, 35). Restrictions have been imposed by the United States Food and Drug Administration (FDA) on what synthetic grafts can be used for POP (36). Biological grafts do not improve outcomes and can have complication rates as high as those of synthetic grafts (33, 37). Therefore, synthetic grafts are typically offered for POP repair in the form of sacrocolpopexy.

Once the selection is made on the type of repair planned, the surgeon and patient arrive on a chosen route of surgery.

TABLE 44.1 Validated Outcome Measures Used to Measure the Impact of Pelvic Organ Prolapse (POP) on a Patient

Outcome	Number of Questions	Detailed Definition and Scoring
Pelvic Floor Distress Inventory (PFDI) (7, 8)	Long form: 61 questions (UDI subscale 28; CRADI subscale 17; POP-DI subscale 16) Short form: 20 (UDI 6; CRADI 8; POPDI 6)	Score ranges from 0 (least distress) to 300 (most distress) and is a sum of the three subscale scores (Pelvic Organ Prolapse Distress Inventory [POP-DI], Urogenital Distress Inventory [UDI], and Colorectal Anal Distress Inventory [CRADI]), each ranging from 0 (least distress) to 100 (most distress)
Pelvic Floor Impact Questionnaire (PFIQ) (7, 8)	Long form: 93 (31 each for IIQ, CRAIQ, and POPIQ subscales) Short form: 7 (each question with bladder, bowel, and vaginal components)	Score ranges from 0 (least impact) to 300 (most adverse impact) and is a sum of three subscale scores (Pelvic Organ Prolapse Impact Questionnaire [POPIQ], Incontinence Impact Questionnaire [IIQ], and Colorectal Anal Impact Questionnaire [CRAIQ]), each ranging from 0 (least impact) to 100 (most adverse impact). A midrange score for these subscales implies bother from prolapse, urinary incontinence, or fecal incontinence
Pelvic organ prolapse/incontinence sexual function questionnaire, International Urogynecologic Society (IUGA) revision (PISQ-IR) (9, 139)	6 for nonsexually active; 15 for sexually active with or without a partner	For nonsexually active patients, there are four domains (partner related, condition specific, global quality, condition impact), where higher scores indicate more impact of the conditions on sexual function For sexually active women, there are six domains (four above plus arousal-orgasm and desire), with higher scores indicating better sexual function.

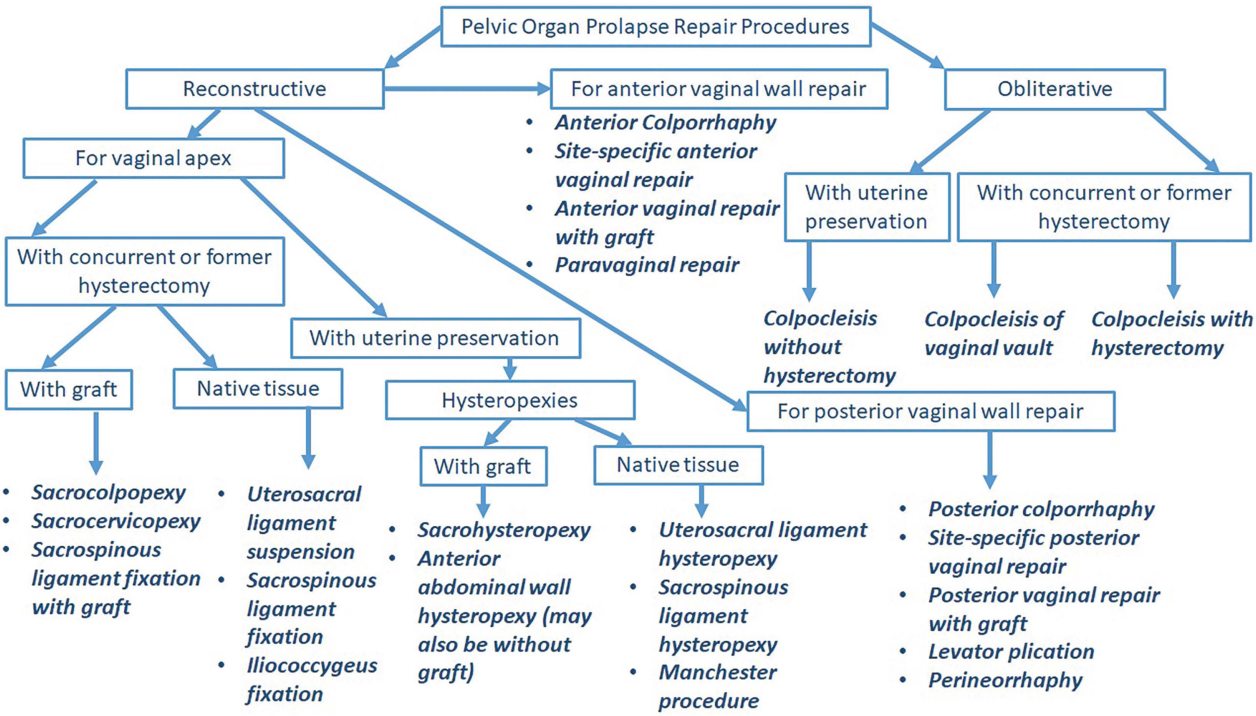


FIGURE 44.2 Surgical procedures for repair of pelvic organ prolapse by approach and appropriate definition (From ref 26 with permission).

Experience of the surgeon certainly affects the choice of a route, but ideal routes are either through the vagina or laparoscopically/robotically, as these minimally invasive routes decrease blood loss, recovery time, and pain compared to open abdominal procedures, despite longer operating room times in some surgical settings (38). Patient contraindications to Trendelenburg positioning, abdominal distension, or longer operating room times may argue for the vaginal route. Regardless of the route, the surgery should address the components of the vagina that are prolapsed and give serious consideration to apical or level I repair (39). Routes of surgical repair are distinguished by both their efficacy for relief of prolapse symptoms and secondary complications or effects (Table 44.2).

44.1.4 Graft POP Surgery for Level I

The current "gold standard" for apical reconstruction of the vagina is the sacrocolopexy. This surgery attaches synthetic mesh to the anterior and posterior vaginal walls on the abdominal side, and then attaches the cephalad end of this

TABLE 44.2 Overall Comparisons between Level I/Apical Pelvic Organ Prolapse Surgical Repair Routes

Surgery	Outcomes in Rigorous Trials	Evidence-Based Comparison to Other Procedures	Important Complications
Sacrocolpopexy/sacrohysteropexy	Success: 73%–100%	• Similar outcomes between sacrocolpopexy and uterine preservation (sacrohysteropexy) (30) • More durable than vaginal native tissue repair bases on less reoperation for prolapse (140) • Better sexual function outcomes than vaginal graft procedures (141)	• Mesh exposure 3.8% with hysterectomy versus 0.4% with cervix/uterus in place (142) • Most common infection urinary tract infection (2%–4%) (143, 144) • Reoperation for complications uncommon (3.6%) (145) and total reoperation 7.1% (140) • Bowel obstruction rare (1.2%) (145)
Uterosacral ligament suspension	Failure: 62%–70% at 5 years	• Nearly double the rate of reoperation compared to sacrocolpopexy with synthetic mesh (140) • Similar outcomes to sacrospinous ligament fixation (54) • Lack of comparative data about uterine preservation, but similar outcomes in existing studies (30)	• Ureteral kinking up to 11% (146), with actual injury typically lower (3.7%) (147) • Neurological pain from sutures rare (> 0.5%) (140) but can be severe • Most common infectious morbidity urinary tract infection (15%) (144)
Sacrospinous ligament fixation	Failure: 62%–70% at 5 years	• Nearly double the rate of reoperation compared to sacrocolpopexy with synthetic mesh (140) • Similar outcomes with uterine preservation (30) • Similar outcomes to uterosacral ligament fixation (54)	• Buttock pain is common (15%) (58), but disabling neurological injury rare (> 0.5%) (140) • Some studies show higher rate of perioperative complications than uterosacral (58), but less granulation tissue and ureteral injury rate (148)
Manchester procedure	98% no repeat treatment/ symptoms at 5 years (149)	• Less prolapse recurrence than with vaginal hysterectomy with uterosacral suspension (150) • Less cost, blood loss, and OR time than uterosacral suspension (61) • 62 minute mean operative time, 15 minutes shorter than vaginal hysterectomy with uterosacral suspension (149)	• 1% risk of hematometria/ pyometria (61) • Transfusion risk around 4% (150)
Colpocleisis	Success: 98.9%–100%	• Few comparative data on success with or without uterine preservation (30), but similar satisfaction and efficacy (89) and fewer complications with uterine preservation (90) • Highest durability and success of POP procedures (87, 151)	• Cannot have insertive vaginal intercourse following; regret rate up to 13.8% (29, 85, 152) • Risk of subsequent malignancy (0.5% at 10 years) (153) • Temporary urinary retention common (11.4%) (85) • Due to population, up to 9.6% prevalence of a complication (90)

mesh to the anterior longitudinal ligament (ALL) over the S1 level of the sacrum (26, 40). There is debate about this "gold standard" label due to failure rate up to 27% at 7 years (41). However, it remains the surgery of choice for patients that are younger, healthier, and want a more durable surgery that does not shorten the vagina. Similar outcomes have been demonstrated for sacrohysteropexy, the same surgery that preserves the uterus, and mesh exposure rates are lower with uterine or cervical preservation than with concomitant hysterectomy (30, 31). The sacrohysteropexy passes mesh from the anterior compartment through the right or bilateral round ligaments to attach to the ALL, thereby making the surgery only minimally different from the sacrocolpopexy in technical performance (Figure 44.3). Minimally invasive routes involve, less time to recovery, and shorter hospital stay, despite early studies when these platforms were emerging demonstrating more operating room time (42, 43). The sacrocolpopexy is a perfect opportunity for the gynecologist with minimally invasive skills to offer a service to the patient population that needs it, particularly with future increased workforce demands for these services (44). As there is no established difference in outcomes comparing laparoscopic to robotic-assisted sacrocolpopexy, either platform is feasible based on surgeon and patient factor, although the robotic approach is associated with higher costs (45).

Sacrocolpopexy or sacrohysteropexy have higher durability than vaginal native tissue repair, with less recurrence in symptoms or reoperation with longer duration following the surgery (46). However, these surgeries have a higher prevalence of complications than transvaginal native tissue repairs (34, 35, 46). Sacrocolpopexy and sacrohysteropexy have similar patient satisfaction and symptom relief to native tissue vaginal repairs for the apex, but have lower vaginal graft exposure rates than graft placed through the vagina (33, 47, 48). This increased durability combined with relatively low rates of graft complications with sacrocolopexy, particularly with cervical or uterine preservation, is the primary reason that sacrocolpopexy survived the United States FDA ban on "transvaginal mesh" for POP repair (36).

Although products to perform SSLF with synthetic graft materials are no longer able to be marketed in the United States (36), there are some former kits and present surgeon-created products that suspend the vagina to the sacrospinous ligament with graft materials attached from the sacrospinous to the vaginal apex or cervix.

44.1.5 Native Tissue POP Surgery for Level I

Uterosacral ligament suspension (USLS) and sacrospinous ligament fixation (SSLF) are the mainstays of transvaginal native tissue repair. USLS can be performed either by plicating the lateral vaginal apex to the ipsilateral uterosacral ligament bilaterally (Figure 44.4) or by plicating the ligaments with circular sutures across the midline (49, 50), methods that seem to have similar outcomes (51, 52). Both methods show good symptom relief in the short term (53), but failure is as high as 62%–70% at 5 years (54).

Sacrospinous ligament fixation has a similar general success rate to uterosacral ligament suspension (53, 54). However, it can be performed unilaterally or bilaterally with similar results (55), and may result in less operating time and lower complications, particularly less bladder and ureteral injury, than USLS. SSLF does not require peritoneal entry and can provide a quick and effective suspension of the apex through the vagina (56, 57). However, the SSLF has a high risk of postoperative buttock pain (up to 15%) and occasionally neurological injury (58).

Native tissue suspension of the uterus, or native tissue hysteropexy, involves either uterosacral or sacrospinous hysteropexy or a Manchester procedure (59, 60). The Manchester operation involves amputation of the cervix and plication of

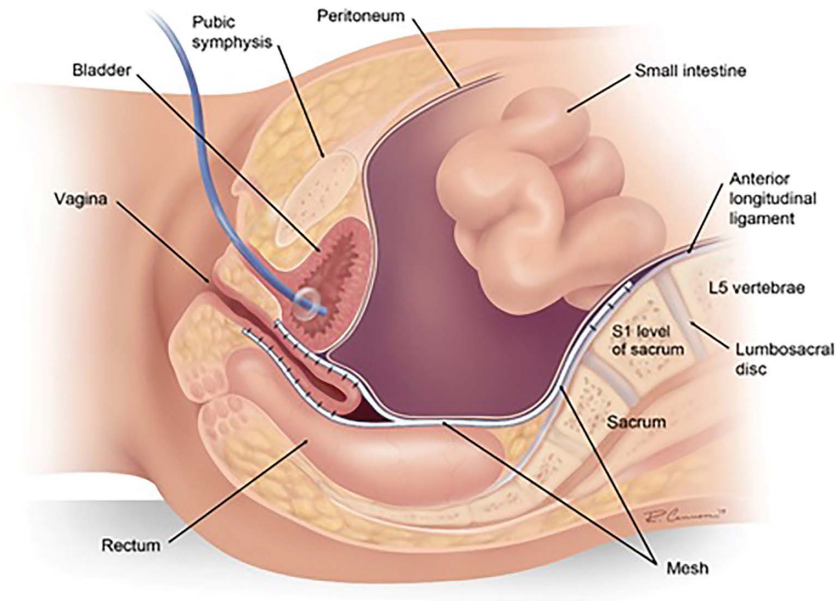


FIGURE 44.3 Sacrocolpopexy, suspending the anterior and posterior vaginal walls with mesh with mesh attachment to the S1 level of the anterior longitudinal ligament of the sacrum, shown here for a patient without a uterus in place (From ref 26 with permission).

the uterosacral ligaments extraperitoneally in front of the uterine stump for suspension, followed by closure of the vaginal apex over this wound and leaving a small opening for uterine mucous drainage (26). Recurrence and reoperation rates for uterosacral or sacrospinous hysteropexy are similar to the corresponding procedures involving a hysterectomy or the vaginal vault (30, 31). The Manchester has been compared extensively to vaginal hysterectomy with USLS and found to involve less recurrent prolapse (7.3%) as well as less operative time, bleeding, and cost (61).

44.1.6 Native Tissue Vaginal Procedures for Level II and Level III Support

Anterior vaginal repair, the plication of the anterior vaginal wall, has widely ranging success rates in rigorous trials, varying from 30% to 82% (62). The addition of graft to anterior repairs has not been shown to improve patient satisfaction or decrease reoperation, despite improved anatomic outcomes (63, 64). Due to this, the typical performance of this operation involves opening the vaginal epithelium, plicating the muscularis layer of the anterior vaginal wall with sutures, and closing the epithelium again after trimming for redundancy (26).

Anterior vaginal repair can also be accomplished by paravaginal repair, which places sutures from the arcus tendinous fascia pelvis, starting about 1–2 cm distal to the ischial spine, to the endopelvic fascia of the lateral anterior vaginal wall (Figure 44.5). Paravaginal repair can be accomplished vaginally or abdominally, either through open abdominal or minimally invasive routes, and minimally invasive abdominal routes are often preferred due to the high risk of bleeding and transfusion with vaginal approach to the retropubic space without ability to see and control venous bleeding (65). Success varies widely from 29% to 98% in months to 1 year (66, 67), with laparoscopic/robotic paravaginal repair showing upwards of 60% success (68).

Similar to anterior vaginal repair, posterior vaginal repair also demonstrates a wide range of success varying from 54% to 93% in trials (69–71). While transperineal or transvaginal repair is preferred over transanal repair due to improved outcomes (72, 73), and there is no advantage to adding synthetic or biological graft in posterior repairs (70, 74–77). Also, similar to anterior repair, all suture techniques including site-specific repair and global repair are acceptable and have similar outcomes.

Surgeons perform perineal repairs in a wide variety of ways (78), but all techniques are intended to restore the muscular tendons of the perineal body toward the central conjoined tendon (26) (Figure 44.6). There are little data for the role of perineal repair in prolapse outcomes, but they improve body image when added to apical prolapse surgery (79) and are more effective than physical therapy at relieving prolapse symptoms after obstetrical lacerations (80). Although there is some evidence that a smaller genital hiatus (< 4 cm) is protective for prolapse recurrence following prolapse surgery (81–83), little is known about long-term outcomes of prolapse surgeries when perineal repair is performed.

Another surgical procedure for level III support is levator plication, which pulls the most medial levator ani muscles (puborectalis and pubococcygeus) toward the midline between the vagina and rectum. This is performed by placing sutures laterally from midline on either side of the perineal body, seeking to form a muscular shelf dividing the levator hiatus (26).

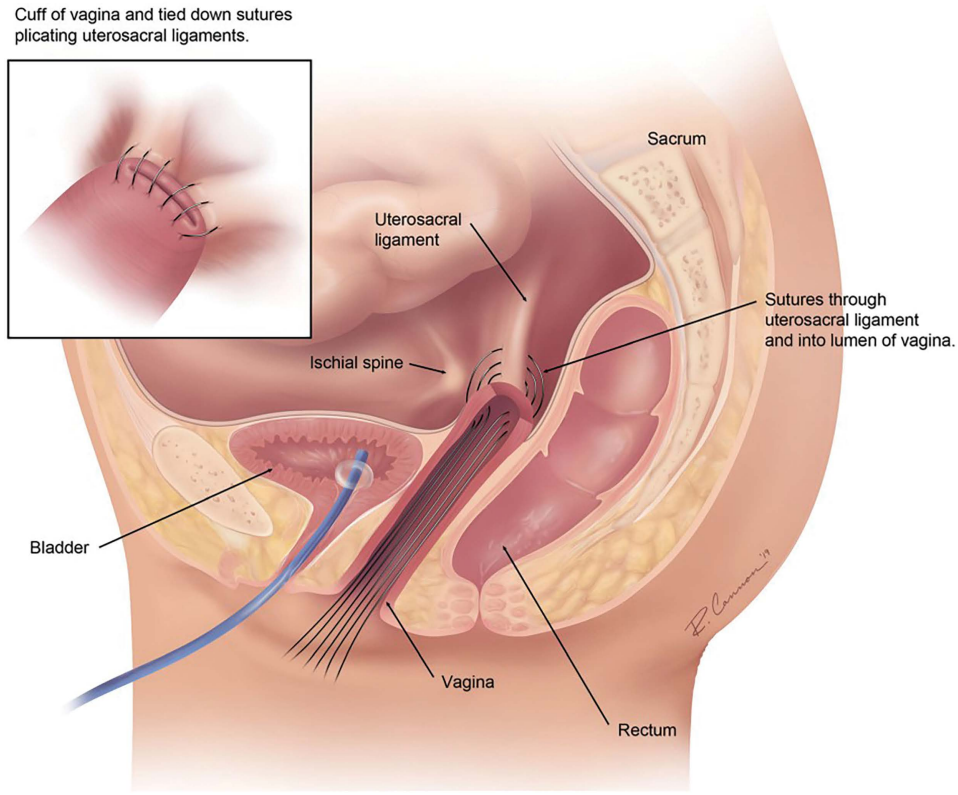


FIGURE 44.4 Uterosacral ligament suspension (USLS) bilaterally, suspending each side of the vagina to the ipsilateral uterosacral ligament (From ref 26 with permission).

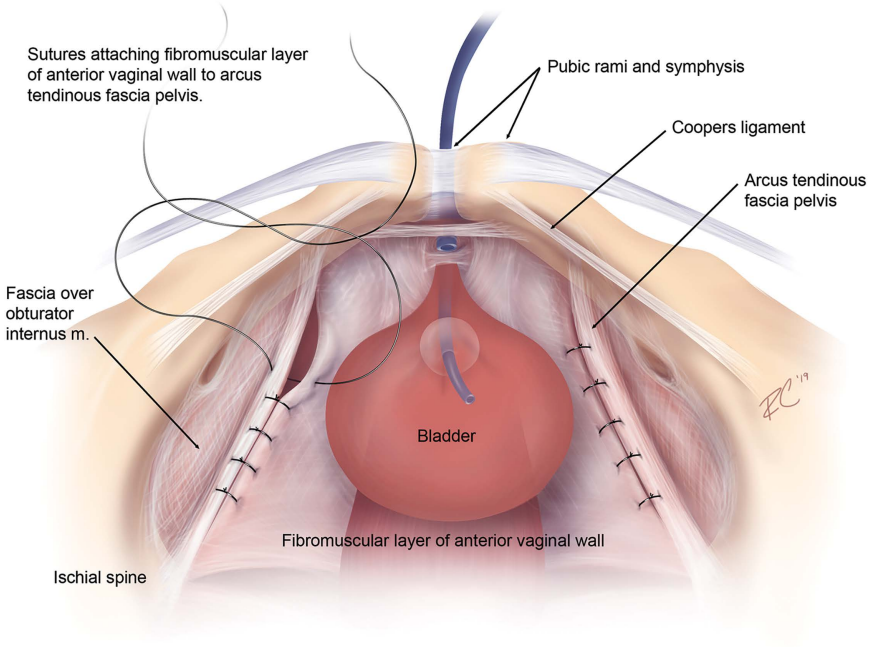


FIGURE 44.5 Paravaginal repair, as seen from the abdominal cavity, in the repair of lateral anterior vaginal wall defects (From ref 26 with permission).

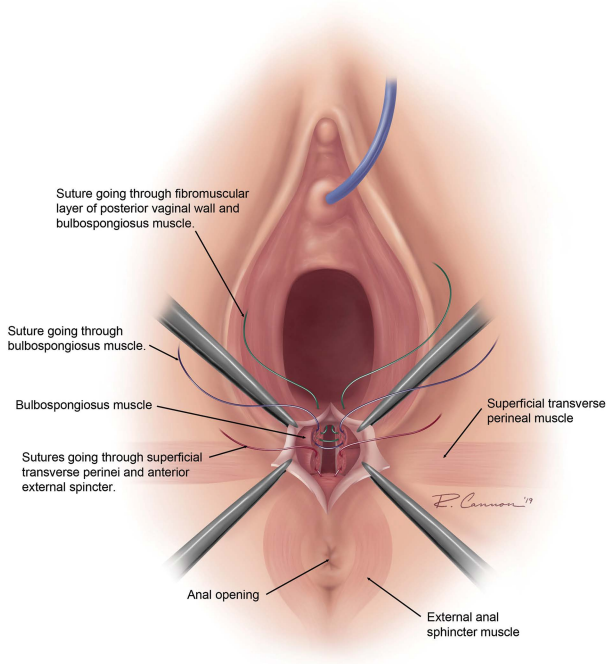


FIGURE 44.6 Perineal repair, with reattachment and/or plication of all the muscular components of the perineal body, including the rectovaginal septum, the bulbocavernosus muscles, the superficial transverse perinei muscles, and the anterior fibers of the external anal sphincter, toward the conjoined tendon of the perineal body (From ref 26 with permission).

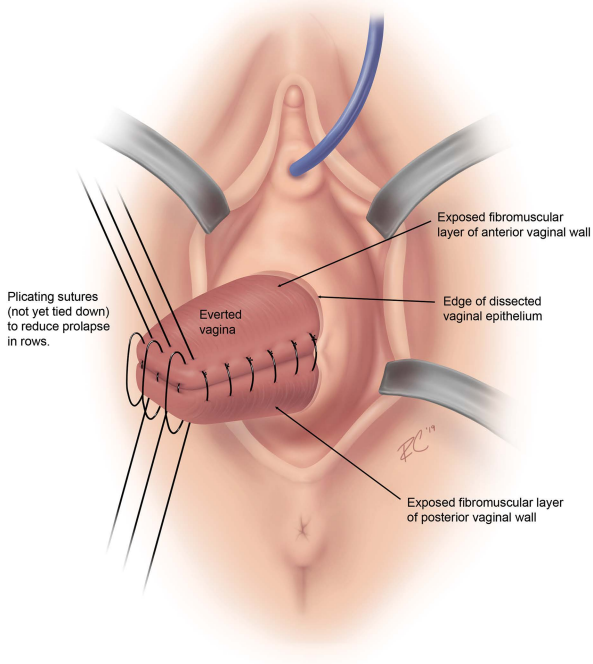


FIGURE 44.7 Colpocleisis with uterine preservation, or "LeFort" colpocleisis, with removal of epithelium from two vaginal rectangles on the anterior and posterior wall and the systematic sewing of these two rectangles together, leaving lateral epithelial channels laterally and closing the inside of the vaginal vault (From ref 26 with permission).

Given how this narrows the vaginal hiatus, this is performed concurrently with procedures like colpocleisis and/or in the setting of reducing the anal hiatus following repair of a large rectal prolapse (29, 84).

44.1.7 Colpocleisis Surgery

Colpocleisis, which involves closure of the proximal vaginal walls, is an excellent choice for women who no longer desire sexual activity that involves insertive vaginal intercourse. Colpocleisis that preserves the uterus, traditionally called a LeFort colpocleisis, involves the removal of two rectangular "panels" of epithelium from the anterior and posterior vaginal wall and sewing these panels to one another, leaving the lateral epithelium rolled into two lateral vaginal channels for mucous drainage (26) (Figure 44.7). This surgery has high anatomical success of 98.9%–100% (85, 86) and relatively few complications given the elderly populations on which this is usually performed (87, 88). Colpocleisis of the vaginal vault or colpocleisis with a hysterectomy appears to have similar outcomes for satisfaction and prolapse (89, 90). Unfortunately, patient regret after colpocleisis is as high as 13.8% (29) so patients must be carefully counseled and selected.

44.2 Stress Urinary Incontinence

44.2.1 Evaluation of Stress Urinary Incontinence

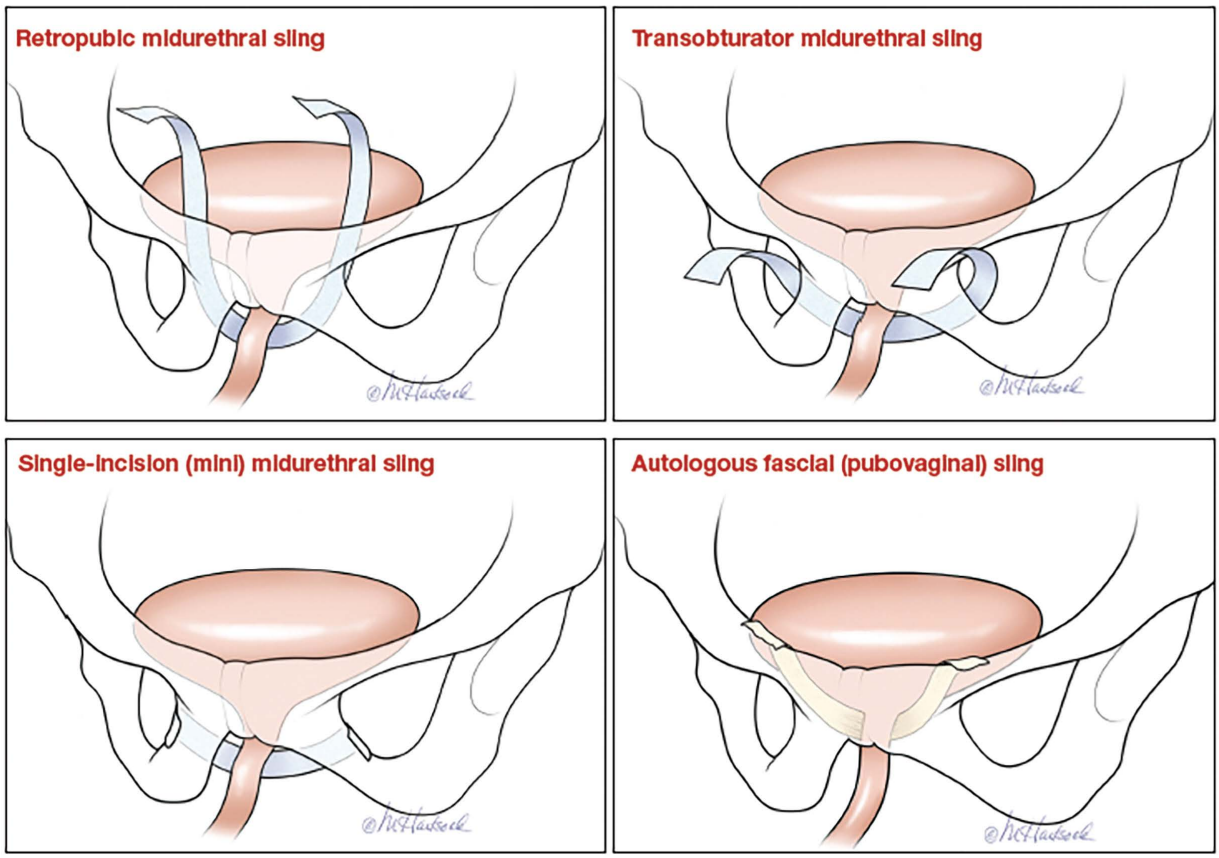
Urinary incontinence affects at least 15% of women (44). Stress urinary incontinence (SUI), defined as the complaint of involuntary loss of urine on effort or physical exertion or on sneezing or coughing (91), is the most prevalent subtype of urinary incontinence, affecting up to 46% of all United States women (92). The lifetime risk of surgery for SUI is 13.6% and climbing each time this figure is re-estimated (2, 93).

The evaluation of SUI can involve history, clinical examination, formal urodynamic testing, or some combination of these. In the uncomplicated form, SUI can be diagnosed by a patient history clearly indicative of leaking of urine with physical impact on the bladder combined with demonstration of normal bladder emptying (post-void residual < 150 mL), leakage of urine from the urethra on cough or Valsalva with a full or empty bladder, and lack of any complicating anatomical issue such as current urinary tract infection, urinary fistula, prolapse beyond the hymen, or neurological dysfunction (94). This indicates that, at a minimum, women should have a thorough medical and urinary symptom history as well as a targeted clinical exam that includes a vaginal exam, POP-Q assessment, cough stress test (supine or upright) with an ideally fully or partially full bladder, measurement of post-void residual (PVR), and a urinalysis and/or urine culture. Women that do demonstrate uncomplicated SUI, however, have the option of proceeding to surgical management without formal urodynamic testing, as this testing does not improve outcomes and increases healthcare costs (95, 96). Women that cannot demonstrate SUI with this office evaluation, have had past failed invasive treatment (such as prior surgery or urethral operations), or have a more complicated or unclear history may need formal urodynamics testing.

TABLE 44.3 Validated Outcome Measures That Can Be Used to Evaluate Stress Urinary Incontinence (SUI) Symptoms and Effect of Treatment

Outcome	Number of Questions	Detailed Definition and Scoring
Medical, Epidemiologic, and Social Aspects of Aging (MESA) questionnaire (154, 155)	15 (9 on SUI and 6 on urgency or urgency urinary incontinence [UUI] symptoms)	Each item scored 0 to 3, with higher scores indicating more symptoms. A ratio called the "urge/stress index" is utilized to determine the proportion of SUI and UUI in their symptoms, where each index (SUI and UUI) is determined by the score for those questions divided by the total possible score (27 for SUI and 18 for UUI). If the SUI is greater than the UUI index, it is considered "stress-predominant MUI," and vice versa.
Incontinence Severity Index (ISI) (156)	2 (1 on frequency of incontinence and 1 on amount of leakage per incontinence episode)	Frequency of leakage scored 1–4 and amount scored 1–3, and the total score is determined by multiplying the two item scores. The total score then determines the incontinence severity of "slight" (1–2), "moderate" (3–6), "severe" (8–9), "very severe" (10–12).
International Consultation on Incontinence Questionnaire – Urinary Incontinence Short Form (ICIQ-UI SF) (157)	3 (1 on frequency of leakage, 1 on amount leaked per incontinence episode, and 1 on level of interference with life)	Frequency of leakage scored 0–5; leakage amount scored 0, 2, 4, or 6, and level of interference with life scored on a VAS scale 0–10. Scores from each of the three items are summed for a score of 0–21, with higher scores indicating more severe incontinence.
Urinary Distress Inventory (UDI or UDI-6) of the Pelvic Floor Distress Inventory (PFDI) (7, 8)	Long form: 28 for UDI subscale Short form: 6 for UDI subscale	Score ranges from 0 (least distress) to 100 (most distress) for the Urogenital Distress Inventory (UDI).
Incontinence Impact Questionnaire (IIQ), a subscale of the Pelvic Floor Impact Questionnaire (PFIQ) (7, 8)	Long form: 31 for IIQ Short form: 7 for bladder component	Score ranges from 0 (least impact) to 100 (most adverse impact) for the Incontinence Impact Questionnaire (IIQ) subscale.

FIGURE 1 Types of slings used in surgical management of SUI



Type	Retropubic midurethral sling	Transobturator midurethral sling	Single-incision (mini) midurethral sling	Autologous fascial (pubovaginal) sling
Description	Mesh sling placed beneath the midurethra with arms extending behind the pubic bone	Mesh sling placed beneath the midurethra with arms through the obturator foramen	Mesh sling placed beneath the midurethra with arms to the obturator foramen	Fascial sling placed beneath the urethra at the level of the bladder neck with arms or suture passing behind the pubic bone
Incisions	Anterior vaginal wall Suprapubic	Anterior vaginal wall Groin	Anterior vaginal wall	Anterior vaginal wall Pfannenstiel Lateral thigh (if using fascia lata)
Conditions in which to consider use	Uncomplicated SUI Occult SUI Recurrent SUI after prior sling Intrinsic sphincter deficiency	Uncomplicated SUI Occult SUI A need to avoid the retropubic space (eg, patients with renal transplants)	Occult SUI A need to avoid the retropubic space (eg, patients with renal transplants) Desire to minimize incisions	A need to avoid mesh A preference to avoid mesh

Abbreviation: SUI, stress urinary incontinence.

ILLUSTRATIONS: MARCIA HARTSOCK FOR OBG MANAGEMENT

FIGURE 44.8 Types of midurethral slings for stress urinary incontinence treatment (From Ringel Net al. Using slings for the surgical management of urinary incontinence: a safe, effective, evidence-based approach. *OBG Manag.* 2019;31(10):42–48, with permission).

TABLE 44.4 Overall Comparisons between Surgeries for Treatment of Stress Urinary Incontinence (SUI)

Surgery	Outcomes in Rigorous Trials	Evidence-Based Comparison to Other Procedures	Important Complications (124, 158)
Retropubic midurethral sling	87% subjective cure and 90% objective cure at 17 years later (159)	• Superior to transobturator slings and single-incision in risk of reoperation, objective and subjective cure (113, 160) • Superior to periurethral bulking agents • Similar to Burch retropubic colposuspension	• Urinary tract infection 11% (higher than other procedures) • 3.6% bladder perforation (more than transobturator or single-incision) • Overactive bladder 6.9% • Major vascular injury 0.8% • 1%–2% mesh exposure or return to OR for mesh exposure, less than transobturator
Transobturator midurethral sling	Subjective cure 60%; and objective cure 70% at 8 years (161)	• At 12 months outcomes equivalent to retropubic slings (162); 3–5 years no longer meeting equivalence (inferior) (163) • Lower risk of complications than retropubic midurethral slings, including retropubic having higher intraoperative bladder or vaginal perforation (OR: 2.4), pelvic hematoma (OR: 2.61), urinary tract infections (OR: 1.31), and voiding symptoms (OR: 1.66) (160)	• Up to 16% leg pain and 6.5% groin pain, more than retropubic or single-incision sling (124) • More neurological symptoms that retropubic midurethral sling (9.4% vs 4%) (162) • 2.8% vaginal perforation, more than other sling types • Similar mesh exposure to other slings (2.2%) but more return to OR for mesh exposure (2.7% • Ureteral injury 1.22% (more than retropubic or single-incision) • Nerve injury 0.61% (more than retropubic or single-incision)
Single-incision sling	81% objective cure 76% subjective cure (164)	• Similar short-term efficacy and shorter operating time than traditional slings (164)	• 2.7% urethral perforation, more than other sling types • UTI 3.6% • Overactive bladder/urgency 5.4% • 1.3% vaginal perforation; 1.4% mesh exposure
Pubovaginal sling (autologous fascial sling with rectus abdominus or fascia lata harvest)	90% success short-term; 75.4% at 10 years 50.8% dry at 10 years (165)	• Slightly better "dry" rates than midurethral slings (165) • Superior to Burch retropubic colposuspension in up to 5 years in RCT (128)	• Bladder perforation 2.3% • 3% return to OR for urinary retention and 7.5% urinary retention past 6 weeks • Overactive bladder 8.6% • 5.4% sling exposure (more than other SUI surgeries) but less return to OR for this (1.6%)
Burch procedure or retropubic colposuspension (open or minimally invasive)	69%–88% cure (166) 59% success at 1–5 years (167)	• Similar success to slings as a whole up to 5 years (166) • Less success than retropubic sling in the medium term (OR 1.70 for success favoring sling) (167) • Less success than sling when performed at the time of prolapse surgery (129) • Fewer intraoperative complications than a sling, but more postoperative complications and recovery time (168)	• Bladder perforation 2.8% • 7.6% urinary retention past 6 weeks • Bowel injury 3.13% (more than other SUI surgeries) • Urinary tract infection 5.9% • 0.58% deep vein thrombosis (more than other SUI surgeries)
Periurethral bulking agent (various agents)	71% cure at 1 year (167) Cure or improvement 84% Bulkamid; 80% macroplastique (135)	• Less effective than slings overall (RR 0.7) (158) and in largest RCT of PAHG versus slings (137, 138) • Less effective than slings for repeat SUI surgery after failed sling (133)	• UTI up to 8.7% • 3%–18% transient urinary retention; complete retention rare (< 2%) • Up to 12% transient hematuria

Another common type of urinary incontinence is mixed urinary incontinence (MUI), in which women have SUI in combination with leakage that happens with detrusor overactivity, either with or without perception of urinary urgency prior. Women with MUI may benefit from many of the same or overlapping treatments that are options for women with SUI but also may benefit from additional treatments for the urgency component. Therefore, it is key to establish the level of bother from both SUI and non-SUI components of incontinence, perform a thorough office evaluation, and consider what other pelvic floor issues may need attention alongside SUI. Many validated instruments used for SUI overlap with questionnaires on other pelvic floor disorders such as POP or have embedded components that also ask other pelvic floor symptoms (Table 44.3).

It is important to note, particularly when treating POP with rare or absent SUI symptoms, that women can develop worsened or new SUI symptoms after treatment of POP, often termed "occult incontinence." This is due to anatomic change in the anterior vaginal wall, straightening the urethra from its formerly "bent" state in POP. Women who present for POP treatment should be counseled about and evaluated for a risk of occult SUI. Without an anti-incontinence procedure at the time of POP surgery, this risk varies from 50% to 57% (97, 98). Anti-incontinence surgery at the time of concurrent POP surgery substantially reduces the risk of postoperative SUI to 23%–34% in women without prior SUI complaints (97, 98), so evaluation of women with reduction of prolapse and a cough stress test (CST) to evaluate incontinence is merited prior to planning a POP surgery. However, SUI does persist or worsen after repair of POP, regardless of whether anti-incontinence surgery was done at the same time. Women should be aware of the full myriad of nonsurgical and surgical treatment options for occult SUI as they would for SUI presenting prior to a POP surgery.

44.2.2 Nonsurgical Treatment for SUI

As with POP, modification of risk factors is a possible intervention that is low risk and accessible for most patients. The established risk factors for SUI are similar to POP, including parity, age, BMI, menopausal status, a history of a hysterectomy, and birth factors such as fetal weight and operative births (99). The risk factors most often modifiable at the time women present for SUI evaluation and treatment is their BMI, and interventions ranging from behavioral education to bariatric surgery meant to reduce weight or BMI are found effective (100). Efficacious interventions include caloric restriction to 800 kcal/day, exercise from 175–200 minutes per week, motivational education, and loss of only 5%–10% of body weight is associated with a 47% reduction in UI risk (101–103).

Also similar to POP, pelvic floor physical therapy is effective for reducing SUI. This is particularly true if PFPT is more intensive and frequent, has more healthcare provider contact/supervision, is combined with an adherence strategy, or is combined with certain other therapies like electrical stimulation or pessaries (104). Patients have better outcomes with PFPT than with incontinence pessaries in the short term (3 months), with 49% having no bothersome incontinence symptoms and 75% noting satisfaction (105). There are also a wide variety of mobile apps, biofeedback devices for home use, and motivational texting systems available to augment pelvic floor training for women, mostly focused on the peripartum period, but more evidence is needed to support most of these (106).

Pessaries utilized for SUI usually include knobs, and the knob sits at the distal anterior vaginal wall, behind the pubic arch, at the level the proximal or midurethra. The vast majority of women (92%) can be fitted with a pessary for SUI treatment (107). At 12 months of use in a randomized trial, pessary became as effective and PFPT for SUI treatment (105), and analysis of a large Medicare claims database revealed that patients who opted for pessary use had less treatment failure than PFPT or surgery (108). However, it is also known that pessaries are the most likely of the nonsurgical treatments to need repeat visits, making them the least cost-effective (109). Furthermore, around 26% of women discontinue the incontinence pessaries at 3 months (105). Many brands of disposable intravaginal continence devices have also been marketed as a discreet way for women to obtain SUI treatment. Although few studies compare these to traditional pessaries, it appears they may have similar short-term success but more risk of needing other treatments over time (110).

44.2.3 Surgical Treatments for SUI

Similar to POP, the patient should be made aware of the wide array of ways in which the industry defined "success" of SUI surgeries. Most SUI treatments have high likelihood of the patient improving or being satisfied, with somewhat lower rates of objective cure (111). Fortunately, it is now the industry standard for rigorous trials of surgical interventions for SUI to investigate at least one outcome from the patient point of view (112). Patient-centered outcome measures may include validated questionnaires such as the ones discussed earlier in this chapter or a composite outcome incorporating symptom bother or severity with objective measures of success such as negative cough stress tests or lack of repeat treatment for SUI.

The dominant treatment for SUI in the current surgical realm is midurethral slings (MUS). These devices have long been the most cost-effective treatment for SUI treatment due to their high efficacy and low complication rate (109) (Table 44.4). MUS involves passage of a trocar, a curved needle 3–7 mm in width, from or into the periurethral space after dissection of this space via a vaginal incision. The surgeon then typically performs cystourethroscopy to ensure no bladder or urethral perforation and uses the trocars to guide the sling arms into place, leaving a strap of 1 cm wide polypropylene, type I synthetic mesh posterior to and lateral to the middle third of the urethra. Care is taken to tension the sling so it does not compress the urethra and allows for contraction of the mesh during healing. Slings can be placed into the retropubic or the obturator space, and several "single-incisions slings" exist that anchor into the obturator internus fascial or the obturator internus muscle without exiting the skin (Figure 44.8). Symptom cure after MUS ranges from 62% to 98% in the short term and appears to be slightly higher with retropubic approaches, particularly in the longer term (113). It is vital to note that subjective success and patient satisfaction is also very high in women with MUI, with overall improvement in both SUI and UUI symptoms and only 5%–11% having worsening of urgency after sling placement (114).

Sling routes differ substantially in morbidity, with 1%–2% urinary retention and 4.5% bladder perforation with retropubic slings (< 1% for each in transobturator routes), and groin pain prevalence of 6.4% after transobturator slings (1.3% retropubic). Vaginal mesh exposure is rare at 21–24/1000 cases (115). Revision or removal of slings is uncommon (3.8%) but is higher with any pain-associated diagnosis (5.6%) (116). Reoperation in the years following sling placement, for either ongoing stress

incontinence or complications, is around 4% (117). Slings demonstrate excellent durability of effect, with the reoperation rate for ongoing or recurrent SUI 15 years later being around 18% (118).

Slings can also be made utilizing the patient's autologous fascia, either from the patient's anterior rectus abdominus fascia or the fascia lata of the leg. Usually, after graft harvest, the sling is attached to permanent sutures, a perivaginal dissection is created similarly to with a midurethral sling, and trocars or threadable needles are utilized to pass the permanent sutures from the vagina space into the lower abdominal wall retropubically. These sutures are then used to tighten the fascial sling at the level of the bladder next or urethra-vaginal junction. Fascia lata and rectus fascia harvest sites have similar composite morbidity (119, 120), although rectus fascia may have more wound comorbidities due to risk of nerve damage, herniation in the abdominal wall, infection, or bleeding (120). With fascia lata harvest, the patient is placed in the left lateral decubitus position and an incision that starts 4 cm above the lateral knee and extends 3–4 cm cephalad along the fascia lata. A 1–2 cm wide by 9 cm long graft is harvested (120, 121). When harvesting from the abdominal rectus fascia, the patient is placed in supine or dorsal lithotomy and a transverse low abdominal incision is made 4–6 centimeters above the pubic bone, ideally in the "safe zone" located about 5.4 cm superior to the symphysis pubis which avoids the inferior epigastric arteries and ilioinguinal and iliohypogastric nerves in the anterior abdominal wall (122). Closure of rectus fascia ideally involves delayed absorbable suture in careful approximation to avoid herniation or dehiscence (120, 121).

Fascial slings are quite effective, with 76%–82% cure at 1 month and 55%–64% cure at 1 year, even in modern populations where the majority of women have had and failed a previous incontinence surgery prior to the fascial sling (120). At 5 years, despite only a 30.8% continence rate, the fascial sling has higher cure than the Burch procedure and has 83% satisfaction (123). However, the Clavien Dindo Type 2 complication rate ranges from 5% to 20%, with common examples being new or worsening urgency, harvest site wound infections or herniations (particularly in the rectus fascial harvest), and bleeding or hematoma (120). Urinary retention at ≥ 6 weeks is around 7.5% after these surgeries (124), and 6%–11% of patients who were not voiding via catheter prior to the surgery were still self-catheterizing 1 year after (120). Although sling loosening in the initial 1–2 months after the surgery can resolve most cases of retention, this issue is still quite common (120, 121).

A less effective but also less morbid option for SUI surgery without synthetic mesh is the Burch procedure. Introduced in the 1960s and developed into a minimally invasive method (125, 126), the Burch procedure is a type of retropubic colposuspension in which permanent suture material from the anterior endopelvic fascia of the distal anterior vaginal wall and attached the pectineal ligament (Cooper's ligament) in the retropubic space, utilizing 2–3 sutures per side of the urethra (Figure 44.9). In general, either open or laparoscopic Burch appears to have cure rates around 49% dropping to 24% at 5 years, which was lower than autologous fascial slings with similar adverse event rates (123, 127). However, only 11% of women have bothersome SUI at 4–8 years (128). The Burch procedures are performed similarly to sling procedures in most trials of efficacy (125, 126, 129–131), but have longer operating times (130) and may decrease in efficacy over time (129).

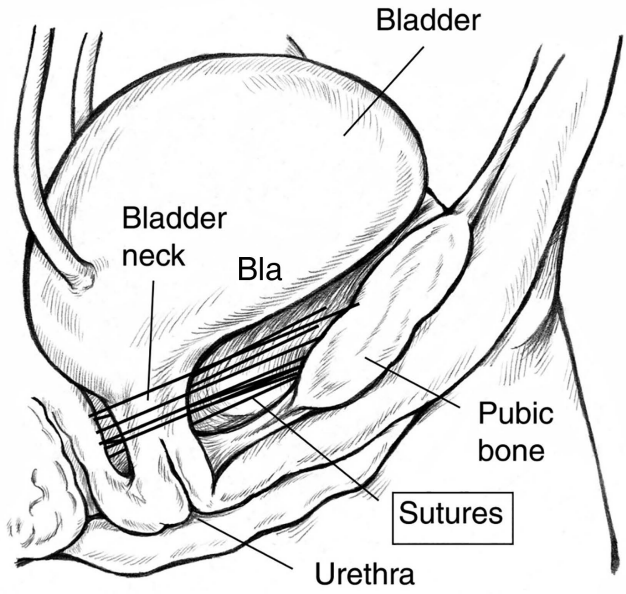


FIGURE 44.9 Burch procedure with two sutures per site, placing one suture at the level of the midurethra and one at the level of the bladder neck to attach the periurethral anterior vaginal wall muscularis to the pectineal ligament (From Wikipedia Commons – https://commons.wikimedia.org/wiki/File:Urinary_Incontinence_Burch.jpg – under Creative Commons Attribution-Share Alike 4.0 International license).

The least morbid of procedures for SUI is the group of periurethral bulking (PUB) agents. Unfortunately, PUB agents are difficult to succinctly describe in efficacy due to the myriads of products, shifting products on the market, and rapidly emerging evidence. Overall, PUB agents are injected into the periurethral space, typically at the proximal urethra, with a needle either under direct visualization with a urethroscope or utilizing anatomical landmarks. Sadly, the historically low efficacy of PUB makes them dominated by other SUI surgeries in cost-efficacy despite their low morbidity (109), but PUB are cost-effective as a rescue surgery after a failed MUS despite having lower efficacy than a repeat MUS (132, 133). Subjective success or improvement in quality of life range from 66% to 90% at 1 year, objective improvements range from 25% to 73% (134), and there is a pooled failure rate of 32% (135). The most efficacious product currently on the market, polyacrylamide hydrogel (PAHG), is a homogenous gel that shows 67% cure/improvement and only 20% repeat incontinence procedures at 7 years (136). Although still underperforming compared to slings, women getting PAHG had 68% satisfaction and 78% negative cough stress test at 3 years, with less complications than in the sling group (24% versus 43.5%) (137, 138). In the future, PUB injection may emerge as the first-line procedural therapy for women with complications of a synthetic sling.

44.3 Conclusion

As the population ages, nonsurgical and surgical treatments of pelvic organ prolapse and stress urinary incontinence will become increasingly in demand, and the ability to offer minimally invasive surgical routes for surgical correction of POP and SUI will be a key element of the future gynecologic

workforce. There are excellent and cost-effective nonsurgical treatments for both conditions, such as behavioral alterations, physical therapy, and vaginal pessaries, and women should be offered nonsurgical management. That being said, surgical treatments for POP and SUI have high patient satisfaction rates and a low-risk profile, particularly when performed vaginally or through minimally invasive abdominal routes.

Surgery selection for POP involves balancing patient considerations of goals, desire for future sexual activity types and/or keeping or removing the uterus, considerations for occult SUI in the future, and the risk profile of the surgery. Surgical choices most often elected in the modern field include colpocleisis, transvaginal native tissue suspension, and sacrocolpopexy with synthetic mesh. Colpocleisis is the most safe and efficacious surgery for prolapse correction but precludes future insertive vaginal intercourse. While minimally invasive sacrocolpopexy with synthetic mesh is the most efficacious and durable POP surgery that leaves normal vaginal anatomy, the increased morbidity of this surgery and surgical skill required to perform this makes it a suboptimal choice for certain patients and surgeons. In all POP surgeries, eligible women can elect to keep the uterus to minimize blood loss, operative time, and synthetic mesh exposure risk.

In the same manner, surgical treatments for SUI balance efficacy against risk considerations related to route (abdominal or vaginal), use of synthetic mesh, and anatomical spaces involved. Midurethral slings, particularly retropubic, offer the highest efficacy in SUI surgery for the lowest risk, but the synthetic mesh involved in this may steer some patients to other procedures that are more morbid but similarly efficacious (Burch or autologous fascial slings) or less morbid but less efficacious at present (periurethral bulking injection).

References

1. Barber MD et al. Epidemiology and outcome assessment of pelvic organ prolapse. *Int Urogynecol J*. 2013;24(11):1783–1790.
2. Wu JM et al. Lifetime risk of stress urinary incontinence or pelvic organ prolapse surgery. *Obstet Gynecol*. 2014;123(6):1201–1206.
3. Wu JM et al. Forecasting the prevalence of pelvic floor disorders in U.S. Women: 2010 to 2050. *Obstet Gynecol*. 2009;114(6):1278–1283.
4. DeLancey JO. Anatomic aspects of vaginal eversion after hysterectomy. *Am J Obstet Gynecol*. 1992;166(6 Pt 1):1717–1724; discussion 1724.
5. Barber MD et al. Can we screen for pelvic organ prolapse without a physical examination in epidemiologic studies? *Am J Obstet Gynecol*. 2006;195(4):942–948.
6. Bump RC et al. The standardization of terminology of female pelvic organ prolapse and pelvic floor dysfunction. *Am J Obstet Gynecol*. 1996;175(1):10–17.
7. Barber MD et al. Psychometric evaluation of 2 comprehensive condition-specific quality of life instruments for women with pelvic floor disorders. *Am J Obstet Gynecol*. 2001;185(6):1388–1395.
8. Barber MD et al. Short forms of two condition-specific quality-of-life questionnaires for women with pelvic floor disorders (PFDI-20 and PFIQ-7). *Am J Obstet Gynecol*. 2005;193(1):103–113.
9. Rogers RG et al. The pelvic organ prolapse incontinence sexual questionnaire, IUGA-revised (PISQ-IR). *Int Urogynecol J*. 2013;24(7):1063–1064.
10. Vergeldt TFM et al. Risk factors for pelvic organ prolapse and its recurrence: a systematic review. *Int Urogynecol J*. 2015;26(11):1559–1573.
11. Schulten SFM et al. Risk factors for primary pelvic organ prolapse and prolapse recurrence: an updated systematic review and meta-analysis. *Am J Obstet Gynecol*. 2022;227(2):192–208.
12. Fitz FF et al. PEOPLE: lifestyle and comorbidities as risk factors for pelvic organ prolapse - a systematic review and meta-analysis PEOPLE: PElvic Organ Prolapse Lifestyle comorbiditiEs. *Int Urogynecol J*. 2023;34(9):2007–2032.
13. Hagen S et al. Individualised pelvic floor muscle training in women with pelvic organ prolapse (POPPY): a multicentre randomised controlled trial. *Lancet*. 2014;383(9919):796–806.
14. Limbutara W et al. Patient-reported goal achievements after pelvic floor muscle training versus pessary in women with pelvic organ prolapse. A randomised controlled trial. *J Obstet Gynaecol*. 2023;43(1):2181061.
15. Braekken IH et al. Can pelvic floor muscle training reverse pelvic organ prolapse and reduce prolapse symptoms? An assessor-blinded, randomized, controlled trial. *Am J Obstet Gynecol*. 2010;203(2):170.e1–170.e7.
16. Oliver R et al. The history and usage of the vaginal pessary: a review. *Eur J Obstet Gynecol Reprod Biol*. 2011;156(2):125–130.
17. Geoffrion R et al. Clinical characteristics associated with unsuccessful pessary fitting outcomes. *Female Pelvic Med Reconstr Surg*. 2013;19(6):339–345.
18. Ding J et al. Successful use of ring pessary with support for advanced pelvic organ prolapse. *Int Urogynecol J*. 2015;26(10):1517–1523.
19. Markle D et al. Patient characteristics associated with a successful pessary fitting. *Female Pelvic Med Reconstr Surg*. 2011;17(5):249–252.
20. Poma PA. Nonsurgical management of genital prolapse. A review and recommendations for clinical practice. *J Reprod Med*. 2000;45(10):789–797.
21. Palumbo MV. Pessary placement and management. *Ostomy Wound Manage*. 2000;46(12):40–45.
22. Brandt CH et al. Adherence to support pessary in the treatment of pelvic organ prolapse: a retrospective study conducted among 1,371 women. *Int Urogynecol J*. 2024;35(1):69–75. https://doi.org/10.1007/s00192-023-05616-z. Epub 2023 Aug 7. PMID: 37548745; PMCID: PMC10810921.
23. Mao M et al. Changes in the symptoms and quality of life of women with symptomatic pelvic organ prolapse fitted with a ring with support pessary. *Maturitas*. 2018;117:51–56.
24. Alperin M et al. Patterns of pessary care and outcomes for medicare beneficiaries with pelvic organ prolapse. *Female Pelvic Med Reconstr Surg*. 2013;19(3):142–147.
25. Bugge C et al. Pessaries (mechanical devices) for managing pelvic organ prolapse in women. *Cochrane Database Syst Rev*. 2020;11(11):CD004010.
26. Developed by the Joint Writing Group of the American Urogynecologic Society and the International Urogynecological Association. Joint report on terminology for surgical procedures to treat pelvic organ prolapse. *Int Urogynecol J*. 2020;31(3):429–463.
27. Barber MD et al. Defining success after surgery for pelvic organ prolapse. *Obstet Gynecol*. 2009;114(3):600–609.
28. de Mattos Lourenço TR et al. A systematic review of reported outcomes and outcome measures in randomized controlled trials on apical prolapse surgery. *Int J Gynaecol Obstet*. 2019;145(1):4–11.
29. Buchsbaum GM et al. Vaginal obliterative procedures for pelvic organ prolapse: a systematic review. *Obstet Gynecol Surv*. 2017;72(3):175–183.
30. Meriwether KV et al. Uterine preservation vs hysterectomy in pelvic organ prolapse surgery: a systematic review with meta-analysis and clinical practice guidelines. *Am J Obstet Gynecol*. 2018;219(2):129–146.e2.
31. Meriwether KV et al. Uterine-preserving surgeries for the repair of pelvic organ prolapse: a systematic review with meta-analysis and clinical practice guidelines. *Int Urogynecol J*. 2019;30(4):505–522.
32. Gutman R et al. Uterine-preserving POP surgery. *Int Urogynecol J*. 2013;24(11):1803–1813.
33. Schimpf MO et al. Graft and mesh use in transvaginal prolapse repair: a systematic review. *Obstet Gynecol*. 2016;128(1):81–91.

34. Coolen A-LWM et al. The treatment of post-hysterectomy vaginal vault prolapse: a systematic review and meta-analysis. *Int Urogynecol J*. 2017;28(12):1767–1783.
35. Siddiqui NY et al. Mesh sacrocolpopexy compared with native tissue vaginal repair: a systematic review and meta-analysis. *Obstet Gynecol*. 2015;125(1):44–55.
36. Urogynecologic surgical mesh implants. *FDA*. Available at: www.fda.gov/medical-devices/implants-and-prosthetics/urogynecologic-surgical-mesh-implants (Accessed Aug 14, 2023).
37. Abed H et al. Incidence and management of graft erosion, wound granulation, and dyspareunia following vaginal prolapse repair with graft materials: a systematic review. *Int Urogynecol J*. 2011;22(7):789–798.
38. Pelvic organ prolapse: ACOG practice bulletin 214. *Obstet Gynecol*. 2019;134(5):e126–e142.
39. Walters MD et al. Surgical treatment of vaginal apex prolapse. *Obstet Gynecol*. 2013;121(2 Pt 1):354–374.
40. Florian-Rodriguez ME et al. First sacral nerve and anterior longitudinal ligament anatomy: clinical applications during sacrocolpopexy. *Am J Obstet Gynecol*. 2017;217(5):607.e1–607.e4.
41. Nygaard I et al. Long-term outcomes following abdominal sacrocolpopexy for pelvic organ prolapse. *JAMA*. 2013;309(19):2016–2024.
42. De Gouveia De Sa M et al. Laparoscopic versus open sacrocolpopexy for treatment of prolapse of the apical segment of the vagina: a systematic review and meta-analysis. *Int Urogynecol J*. 2016;27(1):3–17.
43. Chang C-L et al. An updated systematic review and network meta-analysis comparing open, laparoscopic and robotic-assisted sacrocolpopexy for managing pelvic organ prolapse. *J Robot Surg*. 2022;16(5):1037–1045.
44. Dieter AA et al. Epidemiological trends and future care needs for pelvic floor disorders. *Curr Opin Obstet Gynecol*. 2015;27(5):380–384.
45. Callewaert G et al. Laparoscopic versus robotic-assisted sacrocolpopexy for pelvic organ prolapse: a systematic review. *Gynecol Surg*. 2016;13:115–123.
46. Rogers RG et al. Open sacrocolpopexy and vaginal apical repair: retrospective comparison of success and serious complications. *Int Urogynecol J*. 2018;29(8):1101–1110.
47. Jambusaria LH et al. One-year functional and anatomic outcomes of robotic sacrocolpopexy versus vaginal extraperitoneal colpopexy with mesh. *Female Pelvic Med Reconstr Surg*. 2015;21(2):87–92.
48. Nager CW et al. Effect of sacrospinous hysteropexy with graft vs vaginal hysterectomy with uterosacral ligament suspension on treatment failure in women with uterovaginal prolapse: 5-year results of a randomized clinical trial. *Am J Obstet Gynecol*. 2021;225(2):153.e1–153.e31.
49. Shull BL et al. A transvaginal approach to repair of apical and other associated sites of pelvic organ prolapse with uterosacral ligaments. *Am J Obstet Gynecol*. 2000;183(6):1365–1373; discussion 1373.
50. Wall LL. A technique for modified McCall culdeplasty at the time of abdominal hysterectomy. *J Am Coll Surg*. 1994;178(5):507–509.
51. Parisi S et al. Traditional McCall culdoplasty compared to a modified McCall technique with double ligament suspension: anatomical and clinical outcomes. *Int Urogynecol J*. 2020;31(10):2147–2153.
52. Spelzini F et al. Modified McCall culdoplasty versus Shull suspension in pelvic prolapse primary repair: a retrospective study. *Int Urogynecol J*. 2017;28(1):65–71.
53. Barber MD et al. Comparison of 2 transvaginal surgical approaches and perioperative behavioral therapy for apical vaginal prolapse: the OPTIMAL randomized trial. *JAMA*. 2014;311(10):1023–1034.
54. Jelovsek JE et al. Effect of uterosacral ligament suspension vs sacrospinous ligament fixation with or without perioperative behavioral therapy for pelvic organ vaginal prolapse on surgical outcomes and prolapse symptoms at 5 years in the OPTIMAL randomized clinical trial. *JAMA*. 2018;319(15):1554–1565.
55. Salman S et al. Comparison of unilateral and bilateral sacrospinous ligament fixation using minimally invasive anchorage. *Geburtshilfe Frauenheilkd*. 2019;79(9):976–982.
56. Morgan DM et al. Uterosacral and sacrospinous ligament suspension for restoration of apical vaginal support. *Clin Obstet Gynecol*. 2010;53(1):72–85.
57. Doğanay M et al. Minimally invasive sacrospinous ligament suspension: perioperative morbidity and review of the literature. *Arch Gynecol Obstet*. 2014;289(2):235.
58. Hajhashemi M et al. Comparison of high uterosacral and sacrospinous ligament suspension surgeries for the treatment of pelvic organ prolapse in women. *Adv Biomed Res*. 2023;12:164.
59. Detollenaere RJ et al. Sacrospinous hysteropexy versus vaginal hysterectomy with suspension of the uterosacral ligaments in women with uterine prolapse stage 2 or higher: multicentre randomised non-inferiority trial. *BMJ*. 2015;351:h3717.
60. Schulten SFM et al. Evaluation of two vaginal, uterus sparing operations for pelvic organ prolapse: modified Manchester operation (MM) and sacrospinous hysteropexy (SSH), a study protocol for a multicentre randomized non-inferiority trial (the SAM study). *BMC Womens Health*. 2019;19(1):49.
61. Tolstrup CK et al. The Manchester-Fothergill procedure versus vaginal hysterectomy with uterosacral ligament suspension: a matched historical cohort study. *Int Urogynecol J*. 2018;29(3):431–440.
62. Maher C et al. Surgery for women with anterior compartment prolapse. *Cochrane Database Syst Rev*. 2016;11(11):CD004014.
63. Gutman RE et al. Three-year outcomes of vaginal mesh for prolapse: a randomized controlled trial. *Obstet Gynecol*. 2013;122(4):770–777.
64. Menefee SA et al. Colporrhaphy compared with mesh or graft-reinforced vaginal paravaginal repair for anterior vaginal wall prolapse: a randomized controlled trial. *Obstet Gynecol*. 2011;118(6):1337–1344.
65. Mallipeddi P et al. Vaginal paravaginal repair in the surgical treatment of anterior vaginal wall prolapse. *Prim Care Update Ob Gyns*. 1998;5(4):199–200.
66. Young SB et al. Vaginal paravaginal repair: one-year outcomes. *Am J Obstet Gynecol*. 2001;185(6):1360–1366; discussion 1366.
67. Benson JT et al. Vaginal versus abdominal reconstructive surgery for the treatment of pelvic support defects: a prospective randomized study with long-term outcome evaluation. *Am J Obstet Gynecol*. 1996;175(6):1418–1421; discussion 1421.
68. Chinthakanan O et al. Laparoscopic paravaginal defect repair: surgical technique and a literature review. *Surg Technol Int*. 2015;27:173–183.
69. Lourenço TRM et al. A systematic review of reported outcomes and outcome measures in randomized trials evaluating surgical interventions for posterior vaginal prolapse to aid development of a core outcome set. *Int J Gynaecol Obstet*. 2020;148(3):271–281.
70. Paraiso MFR et al. Rectocele repair: a randomized trial of three surgical techniques including graft augmentation. *Am J Obstet Gynecol*. 2006;195(6):1762–1771.
71. Mowat A et al. Surgery for women with posterior compartment prolapse. *Cochrane Database Syst Rev*. 2018;3(3):CD012975.
72. Nieminen K et al. Transanal or vaginal approach to rectocele repair: a prospective, randomized pilot study. *Dis Colon Rectum*. 2004;47(10):1636–1642.
73. Farid M et al. Randomized controlled trial between perineal and anal repairs of rectocele in obstructed defecation. *World J Surg*. 2010;34(4):822–829.
74. Gustilo-Ashby AM et al. Bowel symptoms 1 year after surgery for prolapse: further analysis of a randomized trial of rectocele repair. *Am J Obstet Gynecol*. 2007;197(1):76.e1–76.e5.
75. Sung VW et al. Porcine subintestinal submucosal graft augmentation for rectocele repair: a randomized controlled trial. *Obstet Gynecol*. 2012;119(1):125–133.
76. Nüssler E et al. Repair of recurrent rectocele with posterior colporrhaphy or non-absorbable polypropylene mesh-patient-reported outcomes at 1-year follow-up. *Int Urogynecol J*. 2019;30(10):1679–1687.

77. Madsen LD et al. Native-tissue repair of isolated primary rectocele compared with nonabsorbable mesh: patient-reported outcomes. *Int Urogynecol J*. 2017;28(1):49–57.
78. Kanter G et al. Perineorrhaphy: commonly performed yet poorly understood. A survey of surgeons. *Int Urogynecol J*. 2015;26(12):1797–1801.
79. Ninivaggio CS et al. Perineorrhaphy outcomes related to body imagery: a randomized trial of body image perception. *Female Pelvic Med Reconstr Surg*. 2021;27(5):281–288.
80. Bergman I et al. Perineorrhaphy compared with pelvic floor muscle therapy in women with late consequences of a poorly healed second-degree perineal tear: a randomized controlled trial. *Obstet Gynecol*. 2020;135(2):341–351.
81. Hill AM et al. Associating genital hiatus size with long-term outcomes after apical suspension. *Int Urogynecol J*. 2020;31(8):1537–1544.
82. Medina CA et al. Wide genital hiatus is a risk factor for recurrence following anterior vaginal repair. *Int J Gynaecol Obstet*. 2008;101(2):184–187.
83. Bradley MS et al. Robotic-assisted sacrocolpopexy: early postoperative outcomes after surgical reduction of enlarged genital hiatus. *Am J Obstet Gynecol*. 2018;218(5):514.e1–514.e8.
84. Habr-Gama A et al. Rectal procidentia treatment by perineal rectosigmoidectomy combined with levator ani repair. *Hepatogastroenterology*. 2006;53(68):213–217.
85. Song X et al. Long-term follow-up after LeFort colpocleisis: patient satisfaction, regret rate, and pelvic symptoms. *Menopause*. 2016;23(6):621–625.
86. Park JY et al. Le Fort partial colpocleisis as an effective treatment option for advanced apical prolapse in elderly women. *Taiwan J Obstet Gynecol*. 2019;58(2):206–211.
87. Mueller MG et al. Colpocleisis: a safe, minimally invasive option for pelvic organ prolapse. *Female Pelvic Med Reconstr Surg*. 2015;21(1):30–33.
88. Catanzarite T et al. Risk factors for 30-day perioperative complications after Le Fort colpocleisis. *J Urol*. 2014;192(3):788–792.
89. Lu M et al. Long-term clinical outcomes, recurrence, satisfaction, and regret after total colpocleisis with concomitant vaginal hysterectomy: a retrospective single-center study. *Female Pelvic Med Reconstr Surg*. 2021;27(4):e510–e515.
90. Raina J et al. Perioperative complication rates of colpocleisis performed with or without concomitant hysterectomy: a large population-based study. *Int Urogynecol J*. 2023;34(5):1111–1118.
91. Haylen BT et al. An International Urogynecological Association (IUGA)/International Continence Society (ICS) joint report on the terminology for female pelvic floor dysfunction. *Neurourol Urodyn*. 2010;29(1):4–20.
92. Kupfer N et al. Prevalence and risk factors for urinary incontinence in nulliparous women: a contemporary, population-based cohort study. *Urogynecology*. 2023;29(5):520–527.
93. Wilkins MF et al. Lifetime risk of surgery for stress urinary incontinence or pelvic organ prolapse. *Minerva Ginecol*. 2017;69(2):171–177.
94. ACOG Committee opinion no. 603: Evaluation of uncomplicated stress urinary incontinence in women before surgical treatment. *Obstet Gynecol*. 2014;123(6):1403–1407.
95. Nager CW et al. A randomized trial of urodynamic testing before stress-incontinence surgery. *N Engl J Med*. 2012;366(21):1987–1997.
96. Lor KY et al. Does pre-operative urodynamics lead to better outcomes in management of urinary incontinence in women? A linked systematic review and meta-analysis. *Eur J Obstet Gynecol Reprod Biol*. 2020;244:141–153.
97. Brubaker L et al. Abdominal sacrocolpopexy with Burch colposuspension to reduce urinary stress incontinence. *N Engl J Med*. 2006;354(15):1557–1566.
98. Wei JT et al. A midurethral sling to reduce incontinence after vaginal prolapse repair. *N Engl J Med*. 2012;366(25):2358–2367.
99. Seshan V et al. Risk factors of urinary incontinence in women: a literature review. *Int J Urol Nurs*. 2016;10(3):118–126.
100. Sheridan W et al. Weight loss with bariatric surgery or behaviour modification and the impact on female obesity-related urine incontinence: a comprehensive systematic review and meta-analysis. *Clin Obes*. 2021;11(4):e12450.
101. Subak LL et al. Weight loss: a novel and effective treatment for urinary incontinence. *J Urol*. 2005;174(1):190–195.
102. Subak LL et al. Weight loss to treat urinary incontinence in overweight and obese women. *N Engl J Med*. 2009;360(5):481–490.
103. Phelan S et al. Weight loss prevents urinary incontinence in women with type 2 diabetes: results from the Look AHEAD trial. *J Urol*. 2012;187(3):939–944.
104. Todhunter-Brown A et al. Conservative interventions for treating urinary incontinence in women: an Overview of Cochrane systematic reviews. *Cochrane Database Syst Rev*. 2022;9(9):CD012337.
105. Richter HE et al. Continence pessary compared with behavioral therapy or combined therapy for stress incontinence: a randomized controlled trial. *Obstet Gynecol*. 2010;115(3):609–617.
106. Woodley SJ et al. Digital technologies for women's pelvic floor muscle training to manage urinary incontinence across their life course: scoping review. *JMIR Mhealth Uhealth*. 2023;11:e44929.
107. Nager CW et al. Incontinence pessaries: size, POPQ measures, and successful fitting. *Int Urogynecol J Pelvic Floor Dysfunct*. 2009;20(9):1023–1028.
108. Hall EF et al. Medium-term outcomes of conservative and surgical treatments for stress urinary incontinence: a medicare claims analysis: developed by the AUGS payment reform committee. *Urogynecology* (Phila). 2023;29(6):536–544.
109. Chang OH et al. Impact of the availability of midurethral slings on treatment strategies for stress urinary incontinence: a cost-effectiveness analysis. *BJOG*. 2022;129(3):500–508.
110. Nekkanti S et al. A randomized trial comparing continence pessary to continence device (Poise Impressa®) for stress incontinence. *Int Urogynecol J*. 2022;33(4):861–868.
111. Călinescu BC et al. Surgical treatments for women with stress urinary incontinence: a systematic review. *Life* (Basel). 2023;13(7).
112. Lim R et al. Which outcome measures should be used in stress urinary incontinence trials? *BJU Int*. 2018;121(5):805–810.
113. Trabuco EC et al. Reoperation for urinary incontinence after retropubic and transobturator sling procedures. *Obstet Gynecol*. 2019;134(2):333–342.
114. Sung VW et al. Effect of behavioral and pelvic floor muscle therapy combined with surgery vs surgery alone on incontinence symptoms among women with mixed urinary incontinence: the ESTEEM randomized clinical trial. *JAMA*. 2019;322(11):1066–1076.
115. Ford AA et al. Mid-urethral sling operations for stress urinary incontinence in women. *Cochrane Database Syst Rev*. 2015;(7):CD006375.
116. Rockefeller NF et al. Midurethral sling removal or revision in women with chronic pain. *Female Pelvic Med Reconstr Surg*. 2022;28(5):e149–e153.
117. Berger AA et al. Surgeon volume and reoperation risk after midurethral sling surgery. *Am J Obstet Gynecol*. 2019;221(5):523.e1–523.e8.
118. Dejene SZ et al. Long-term outcomes after midurethral mesh sling surgery for stress urinary incontinence. *Female Pelvic Med Reconstr Surg*. 2022;28(4):188–193.
119. Cardenas-Trowers OO et al. Comparison of perioperative outcomes of autologous bladder neck fascial slings based on fascial harvest site: a secondary analysis of the national surgical quality improvement program database. *Female Pelvic Med Reconstr Surg*. 2020;26(8):526–529.
120. Peng M et al. Rectus fascia versus fascia lata for autologous fascial pubovaginal sling: a single-center comparison of perioperative and functional outcomes. *Female Pelvic Med Reconstr Surg*. 2020;26(8):493–497.
121. Shaw JS et al. Minimally invasive autologous fascia sling at the midurethra: a case series. *J Minim Invasive Gynecol*. 2022;29(10):1165–1169.

122. Cardenas-Trowers OO et al. Development of a safety zone for rectus abdominis fascia graft harvest based on dissections of the ilioinguinal and iliohypogastric nerves. *Am J Obstet Gynecol*. 2020;222(5):480.e1–480.e7.
123. Brubaker L et al. 5-year continence rates, satisfaction and adverse events of burch urethropexy and fascial sling surgery for urinary incontinence. *J Urol*. 2012;187(4):1324–1330.
124. Schimpf MO et al. Sling surgery for stress urinary incontinence in women: a systematic review and metaanalysis. *Am J Obstet Gynecol*. 2014;211(1):71.e1–71.e27.
125. Paraiso MFR et al. Laparoscopic Burch colposuspension versus tension-free vaginal tape: a randomized trial. *Obstet Gynecol*. 2004;104(6):1249–1258.
126. Asıcıoglu O et al. A 5-year follow-up study comparing Burch colposuspension and transobturator tape for the surgical treatment of stress urinary incontinence. *Int J Gynaecol Obstet*. 2014;125(1):73–77.
127. Albo ME et al. Burch colposuspension versus fascial sling to reduce urinary stress incontinence. *N Engl J Med*. 2007;356(21):2143–2155.
128. Jelovsek JE et al. Randomised trial of laparoscopic Burch colposuspension versus tension-free vaginal tape: long-term follow up. *BJOG*. 2008;115(2):219–225; discussion 225.
129. Trabuco EC et al. Two-year results of Burch compared with midurethral sling with sacrocolpopexy: a randomized controlled trial. *Obstet Gynecol*. 2018;131(1):31–38.
130. Tong J et al. [Effects of laparoscopic Burch colposuspension and tension-free vaginal tape in treatment of female stress urinary incontinence: a comparative study]. *Zhonghua Yi Xue Za Zhi*. 2008;88(45):3192–3194.
131. Téllez Martínez-Fornés M et al. A three year follow-up of a prospective open randomized trial to compare tension-free vaginal tape with Burch colposuspension for treatment of female stress urinary incontinence. *Actas Urol Esp*. 2009;33(10):1088–1096.
132. Kirchin V et al. Urethral injection therapy for urinary incontinence in women. *Cochrane Database Syst Rev*. 2017;7(7):CD003881.
133. Gaddi A et al. Repeat midurethral sling compared with urethral bulking for recurrent stress urinary incontinence. *Obstet Gynecol*. 2014;123(6):1207–1212.
134. Siddique SA et al. Relationship of the uterosacral ligament to the sacral plexus and to the pudendal nerve. *Int Urogynecol J Pelvic Floor Dysfunct*. 2006;17(6):642–645.
135. Braga A et al. Urethral bulking agents for the treatment of recurrent stress urinary incontinence: a systematic review and meta-analysis. *Maturitas*. 2022;163:28–37.
136. Brosche T et al. Seven-year efficacy and safety outcomes of Bulkamid for the treatment of stress urinary incontinence. *Neurourol Urodyn*. 2021;40(1):502–508.
137. Itkonen Freitas A-M et al. Tension-free vaginal tape surgery versus polyacrylamide hydrogel injection for primary stress urinary incontinence: a randomized clinical trial. *J Urol*. 2020;203(2):372–378.
138. Itkonen Freitas A-M et al. Tension-free vaginal tape and polyacrylamide hydrogel injection for primary stress urinary incontinence: 3-year followup from a randomized clinical trial. *J Urol*. 2022;208(3):658–667.
139. Constantine ML. Validation of a single summary score for the Prolapse/Incontinence Sexual Questionnaire-IUGA revised (PISQ-IR). *Int Urogynecol J*. 2017;28(12):1901–1907.
140. Diwadkar GB et al. Complication and reoperation rates after apical vaginal prolapse surgical repair: a systematic review. *Obstet Gynecol*. 2009;113(2 Pt 1):367–373.
141. Antosh DD et al. Sexual function after pelvic organ prolapse surgery: a systematic review comparing different approaches to pelvic floor repair. *Am J Obstet Gynecol*. 2021;225(5):475.e1–475.e19.
142. Nassif J et al. Rate of mesh erosion after sacrocolpopexy with concurrent supracervical compared with total hysterectomy: a systematic review and meta-analysis. *Obstet Gynecol*. 2022;140(3):412–420.
143. Boysen WR et al. Thirty-day morbidity of abdominal sacrocolpopexy is influenced by additional surgical treatment for stress urinary incontinence. *Urology*. 2017;109:82–87.
144. Yadav GS et al. A comparison of perioperative outcomes, readmission, and reoperation for sacrospinous ligament fixation, uterosacral ligament suspension, and minimally invasive sacrocolpopexy. *Female Pelvic Med Reconstr Surg*. 2021;27(3):133–139.
145. Alsahabi JA et al. The outcome of sacrocolpopexy/sacrohysteropexy for patients with pelvic organ prolapse and predictors of anatomical failure. *Int J Womens Health*. 2023;15:1093–1105.
146. Barber MD et al. Bilateral uterosacral ligament vaginal vault suspension with site-specific endopelvic fascia defect repair for treatment of pelvic organ prolapse. *Am J Obstet Gynecol*. 2000;183(6):1402–1410; discussion 1410.
147. Sanses TVD et al. Readmission and prolapse recurrence after abdominal and vaginal apical suspensions in older women. *Obstet Gynecol*. 2016;128(6):1369–1377.
148. Chen Y et al. Sacrospinous ligament fixation vs uterosacral ligaments suspension for pelvic organ prolapse: a systematic review and meta-analysis. *Urology*. 2022;166:133–139.
149. Ünlübilgin E et al. Which one is the appropriate approach for uterine prolapse: Manchester procedure or vaginal hysterectomy? *Turkiye Klinikleri J Med Sci*. 2013;33(2):321–325.
150. Tolstrup CK et al. The Manchester-Fothergill procedure versus vaginal hysterectomy with uterosacral ligament suspension: a matched historical cohort study. *Int Urogynecol J*. 2018;29(3):431–440.
151. Fitzgerald MP et al. Pelvic support, pelvic symptoms, and patient satisfaction after colpocleisis. *Int Urogynecol J Pelvic Floor Dysfunct*. 2008;19(12):1603–1609.
152. Crisp CC et al. Body image, regret, and satisfaction following colpocleisis. *Am J Obstet Gynecol*. 2013;209(5):473.e1–473.e7.
153. Hammerbak-Andersen M et al. Colpocleisis: reoperation risk and risk of uterine and vaginal cancer: a nationwide cohort study. *Int Urogynecol J*. 2023;34(10):2495–2500.
154. Diokno AC et al. Prevalence of urinary incontinence and other urological symptoms in the noninstitutionalized elderly. *J Urol*. 1986;136(5):1022–1025.
155. Diokno AC et al. Office assessment of patient outcome of pharmacologic therapy for urge incontinence. *Int Urogynecol J Pelvic Floor Dysfunct*. 2002;13(5):334–338.
156. Sandvik H et al. Validity of the incontinence severity index: comparison with pad-weighing tests. *Int Urogynecol J Pelvic Floor Dysfunct*. 2006;17(5):520–524.
157. Klovning A et al. Comparison of two questionnaires for assessing the severity of urinary incontinence: the ICIQ-UI SF versus the incontinence severity index. *Neurourol Urodyn*. 2009;28(5):411–415.
158. Pivazyan L et al. Effectiveness and safety of bulking agents versus surgical methods in women with stress urinary incontinence: a systematic review and meta-analysis. *Int Urogynecol J*. 2022;33(4):777–787.
159. Nilsson CG et al. Seventeen years' follow-up of the tension-free vaginal tape procedure for female stress urinary incontinence. *Int Urogynecol J*. 2013;24(8):1265–1269.
160. Fusco F et al. Updated systematic review and meta-analysis of the comparative data on colposuspensions, pubovaginal slings, and midurethral tapes in the surgical treatment of female stress urinary incontinence. *Eur Urol*. 2017;72(4):567–591.
161. Costantini E et al. Long-term efficacy of the trans-obturator and retropubic mid-urethral slings for stress urinary incontinence: update from a randomized clinical trial. *World J Urol*. 2016;34(4):585–593.
162. Richter HE et al. Retropubic versus transobturator midurethral slings for stress incontinence. *N Engl J Med*. 2010;362(22):2066–2076.
163. Kenton K et al. 5-year longitudinal followup after retropubic and transobturator mid urethral slings. *J Urol*. 2015;193(1):203–210.

164. Patel T et al. Single incision mini-sling versus mid-urethral sling (transobturator/retropubic) in females with stress urinary incontinence: a systematic review and meta-analysis. *Cureus*. 2023;15(4):e37773.
165. Khan ZA et al. Long-term follow-up of a multicentre randomised controlled trial comparing tension-free vaginal tape, xenograft and autologous fascial slings for the treatment of stress urinary incontinence in women. *BJU Int*. 2015;115(6):968–977.
166. Lapitan MCM et al. Open retropubic colposuspension for urinary incontinence in women. *Cochrane Database Syst Rev*. 2016;2:CD002912.
167. Saraswat L et al. Traditional suburethral sling operations for urinary incontinence in women. *Cochrane Database Syst Rev*. 2020;1(1):CD001754.
168. Ward K et al. Prospective multicentre randomised trial of tension-free vaginal tape and colposuspension as primary treatment for stress incontinence. *BMJ*. 2002;325(7355):67.

45 PELVIC FLOOR DYSFUNCTION

Rodger Rothenberger, Sean Francis, and Ankita Gupta

45.1 Urinary Incontinence

Urinary incontinence can be a symptom, a sign demonstrated on a physical exam, or a diagnosis confirmed by definitive studies. It can affect 25% of young women and as many as 75% of older women (1–3). Due to this prevalence, the estimated direct cost of urinary incontinence care in the United States is $19.5 billion (4). Despite being a prevalent problem, only 45% of women with weekly incontinence report ever having sought care (5). There are three main types of incontinence: urge incontinence, stress incontinence, and mixed incontinence; however, other definitions have also been proposed (Box 45.1).

45.1.1 Evaluation

A detailed history is the first step in the evaluation of urinary incontinence. Frequency of urinary leakage, severity of the leakage, degree of bother experienced, and goals for treatment should be queried. Reversible causes of urinary incontinence can be identified through a targeted history and physical examination including gynecological examination (Box 45.2) (6).

45.1.1.1 Bladder Diary

A bladder diary is a record that patients can collect which documents daily symptoms. This can include timing and volume of micturition, incontinence episodes, and urgency episodes (7). A bladder diary can be used to better understand the type and severity of urinary incontinence. It can also capture symptoms such as urgency, frequency, and the type and amount of fluid intake. Bladder diaries can be used to review the circumstances around incontinence episodes with the patient and help facilitate an understanding of the relationship between symptoms and behaviors. They can also be used to determine the treatment efficacy and help guide further treatment (8, 9).

45.1.1.2 Validated Questionnaires

Questionnaires can be used to collect information on patient-reported outcomes. Patient-reported outcomes are specific questions that describe how a patient feels, functions, or survives and are used in both clinical practice and research. These questionnaires can be used in the clinical setting to evaluate the effect of a treatment or objectively understand the

BOX 45.1 TYPES OF URINARY INCONTINENCE IN WOMEN. UNDERSTANDING THE NUANCES OF EACH URINARY INCONTINENCE TYPE IS CRUCIAL FOR ACCURATE DIAGNOSIS AND TARGETED MANAGEMENT STRATEGIES.

- *Chronic urinary retention*: Involuntary loss of urine when the bladder does not empty completely; associated with high residual urine volumes*
- *Coital urinary incontinence*: Involuntary loss of urine with sexual intercourse
- *Continuous urinary incontinence*: Continuous involuntary loss of urine
- *Extraurethral urinary incontinence*: Urine leakage through channels other than the urethral meatus (e.g., vesicovaginal, urethrovaginal or ureterovaginal genitourinary fistulas, ectopic ureter)
- *Functional urinary incontinence*: Involuntary loss of urine that is due to cognitive, functional, or mobility impairments in the presence of an intact lower urinary tract system*
- *Insensible urinary incontinence*: Involuntary loss of urine associated with urgency and with physical exertion, sneezing, or coughing
- *Nocturnal enuresis*: Involuntary loss of urine that occurs during sleep
- *Occult stress incontinence*: Stress urinary incontinence that is observed only after the reduction of coexistent pelvic organ prolapse
- *Overactive bladder*: Urinary urgency, typically accompanied by frequency and nocturia, with and without urge urinary incontinence in the absence of urinary tract infection or other obvious pathology
- *Postmicturition leakage*: Involuntary passage of urine after the completion of micturition
- *Postural urinary incontinence*: Involuntary loss of urine associated with change of body position
- *Stress urinary incontinence*: Involuntary loss of urine with effort or physical exertion (e.g., sporting activities) or when sneezing or coughing
- *Urgency urinary incontinence*: Involuntary loss of urine associated with urgency or a sudden, compelling desire to void that is difficult to defer

Data from Abrams P et al. Recommendations of the International Scientific Committee. In: Abrams P et al., eds. *Incontinence*, 5th edn. Paris: ICUD-EAU, 2013:1895–1956. (From ref 4 with permission; data from ref 22.)

DOI: 10.1201/9781003312109-45

BOX 45.2 REVERSIBLE CAUSES OF URINARY INCONTINENCE – DIAPPERS

- **D**elirium, dementia, or other cognitive impairments
- **I**nfection (urinary tract infection)
- **A**trophic vaginitis or urethritis
- **P**harmaceuticals or substances (e.g., diuretics, caffeine, alcohol)
- **P**sychological disorder
- **E**xcessive urine output (e.g., diabetes, diabetes insipidus)
- **R**educed mobility or reversible urinary retention
- **S**tool impaction

impact of a condition on a patient's life (10). They can also be used to aid patients in explaining their symptoms and concerns which might otherwise not be communicated due to the sensitive nature of the symptoms, the constraints of a conventional history, or a lack of understanding of the interrelatedness of symptoms (11, 12).

Questionnaires can be divided into symptom-based questionnaires, quality-of-life questionnaires, and global questionnaires (13). Within the context of urinary incontinence, we will only discuss symptom-based and quality-of-life questionnaires.

Symptom-based questionnaires can range from simple, like the two-question Sandvik Severity Index, to complex, like the Pelvic Floor Distress Inventory (PFDI), which is 46 questions in length and obtains information on urinary incontinence, fecal incontinence (FI), and pelvic organ prolapse (POP) (14, 15). The short form of this questionnaire, the PFDI-20, consists of 20 questions. Both the long and short forms of the PFDI are validated and responsive to changes in measuring pelvic floor disorders.

One of the more widely used urinary incontinence specific questionnaires is the urogenital distress inventory (UDI) (16). This questionnaire determines the presence of irritative symptoms, obstructive or discomfort symptoms, and stress symptoms, and gradates the extent of these symptoms. A six-question short form of the UDI (UDI-6) has demonstrated good correlation with the long form and is commonly used due to ease of administration (16, 17).

Quality of life is vitally affected by urinary incontinence, making questionnaires that assess this metric important. Healthcare-related quality-of-life questionnaires can range from general to condition specific (18). Within pelvic floor disorders as a whole, general questionnaires are poorly responsive to changes in patient symptoms (19). In urinary incontinence, the Incontinence Impact Questionnaire (IIQ) is a condition-specific quality-of-life questionnaire that assesses the impact of urinary incontinence on travel, social activities, emotional state, and physical activity (16). There is a short form of this questionnaire, the IIQ-7, which is often used as the companion questionnaire to the UDI-6 (17). These questionnaires can detect both the impact of urinary incontinence on a patient's life and responsiveness to improvement with treatment or worsening with time (17).

45.1.1.3 Physical Examination

The examination for all pelvic floor disorders, including urinary incontinence, should include a thorough general medical, gynecologic, and neurologic examination with a rectal examination as indicated.

The gynecological exam begins with inspection of the external genitalia assessing for vulvar abnormalities such as skin irritation, atrophy, and vulvar changes. After visual inspection of the vulvovaginal area is completed, speculum and a bimanual examination should be performed to further evaluate the pelvis. Inspection using a bivalved speculum is performed assessing for vaginal atrophy or cervical and vaginal lesions. Bimanual exam should be performed to evaluate for pelvic mass and to assess for areas of tenderness with accompanying pelvic floor muscular examination.

Neurologic conditions can also present with new onset or worsening urinary symptoms (20). One should first assess the sacral reflex, which determines the integrity of the pudendal nerve. The sacral reflex can be assessed in two ways: through the anal reflex, which is examined through lightly stroking the skin near the anus and determining if a contraction of the anal sphincter occurs, or through the bulbocavernosus reflex, which is examined through the tapping or squeezing of the clitoris lightly and looking for contraction of the bulbocavernosus muscle and/or external anal sphincter. The absence of one or both of these reflexes is indicative of lower motor neuron/pudendal nerve injury (21).

Perineal sensation should be assessed during a neurologic examination as well. The sensory dermatomes overlying the mons pubis and upper labia majora (L1–2), perineal and perianal skin (S2–4), front of the knees (L3–4), and the lateral part of the feet (S1) should be assessed for the sensation of light touch, sharp touch, and temperature (21).

The pelvic floor plays an integral role in continence and should be evaluated. Factors to be assessed can include muscle strength, voluntary muscle relaxation, muscular endurance, repeatability, duration, coordination, and displacement (22, 23). The standardized pelvic floor muscle examination published by Meister et al. is a systematic method of evaluating the pelvic floor. It first assesses the bilateral sacroiliac joints, the medial edge of the anterior superior iliac spine, and the cephalad edge of the pubic symphysis. This is followed by an internal exam with palpation of the right obturator internus, right levator ani, left levator ani, and left obturator internus in the center of the muscle with clarification of any discomfort encountered on a 10-point pain scale (24).

Fistulous tracts within the genitourinary tract should also be investigated during the physical examination. Urethral diverticulum can be palpated along the urethra and cause postvoid dribbling and incontinence. Ureteral, vesical, and urethral fistulas can also be a cause of incontinence and may be seen on a careful physical exam.

In patients with urinary incontinence, a rectal examination can be useful once appropriate consent is obtained (4). Rectal examination should assess anal sphincter tone and strength, prior anal sphincter tears, fecal impaction, rectovaginal fistula, tumor, hemorrhoids, and/or fissures. An assessment of resting tone and squeeze pressure of the anal sphincter should be determined during the rectal examination and reported using the Oxford scale (25). The resolution of concerns such as fecal impaction can have a positive impact on urinary and fecal incontinence symptoms (26).

45.1.1.4 Urodynamics

Urodynamics refers to a series of tests performed with bladder filling and voiding, with or without video, to examine the vesicourethral process of micturition. Cystometry reveals relative fluid volumes and pressures during the process of bladder filling, storage, and voiding. This can help determine bladder compliance, capacity, and detrusor activity. Uroflowmetry and pressure flow studies can then be performed during the act of micturition to measure the flow of urine and the mechanism of void (whether completed by the detrusor muscle of the bladder or assisted by Valsalva/abdominal musculature) (4). Urethral pressures can also be determined; however, the reliability of this test has been questioned and its use will not be discussed here (27).

Urodynamics can be used when office evaluation and patient history or reported symptoms do not correlate (for example, negative cough stress test). It can also be of value in those with an unclear diagnosis, in those who do not improve with treatment, or in those with prior procedures for incontinence. Urodynamics does not predict which patients will benefit from nonsurgical treatments for incontinence and is not recommended or cost-effective for uncomplicated urinary incontinence. Examples of complicated urinary incontinence include those with elevated post-void residual volumes, prolapse, and a suspected neurologic component (1, 28).

45.1.2 Management

Management of urinary incontinence can be conservative, medical, or surgical.

45.1.2.1 Nonoperative (Conservative) Management

The first-line intervention for urinary urgency, with or without incontinence, includes behavioral modification, bladder retraining, pelvic floor physical therapy with muscle exercises, and biofeedback.

45.1.2.1.1 Behavioral Modification Including Bladder Retraining

Bladder retraining has been used for urgency, stress, and mixed urinary incontinence although it is most often used in urge urinary incontinence. It involves a systematic approach to voiding in which a voiding schedule is employed. A Cochrane review found that, despite trials being limited by varied outcomes, small sample size, wide confidence intervals, and lack of significance to primary outcome variables, bladder training may be useful in the treatment of urinary incontinence (29). It can be effective in reducing the number of episodes of incontinence and symptom severity and can improve incontinence-related quality of life. It is most effective in younger, cognitively intact women with higher education status (30). This is the first-line treatment for urge urinary incontinence and may be prescribed after ruling out reversible causes of incontinence (17).

45.1.2.1.2 Pelvic Floor Physical Therapy and Biofeedback

Pelvic floor muscle exercises and pelvic floor physical therapy can have a role in the treatment of urinary incontinence. The Kegel exercise (an intentional contraction of the levator ani and voluntary periurethral muscles) has long been a staple of conservative treatment of urinary incontinence. Pelvic floor muscle exercises and therapy as a whole are theorized as effective in the setting of urgency symptoms through a reflexive inhibition of the detrusor muscle with muscle contraction (31).

A 2011 Cochrane review highlighted some pitfalls that may be commonly encountered by patients undergoing pelvic floor physical therapy and muscle training (32). There are many methods and programs for performing pelvic floor physical therapy including variations in training supervision (individual versus group), the actual exercises themselves, the type of contraction, and the frequency of the exercises. None of these have been shown to be superior to another, though some data did show that women may have improved outcomes with frequent provider visits during their pelvic floor muscle training intervention period (32).

45.1.2.2 Pharmacologic (Medical) Management

While medications can be used either alone or in combination with behavioral modification strategies, the use of medical and behavioral interventions together has not shown benefit (33). Medication management is only recommended for the treatment of overactive bladder (OAB) and has not shown benefit in the treatment of stress urinary incontinence. Available medical management strategies include antimuscarinics, beta-adrenergic, and estrogen.

45.1.2.2.1 Antimuscarinic

Antimuscarinic medications are some of the oldest medications used in the management of urgency urinary incontinence. They act through the blockage of the M3 muscarinic receptor of the detrusor muscle in the bladder. Antimuscarinics reduced the number of voids per day by 2.06 and the episodes of incontinence by 1.73 when compared to 1.2 and 1.06 by placebo (34). No antimuscarinic medication has demonstrated superiority over the others.

Despite the availability of bladder specific antimuscarinics (such as solfenacin), common side effects include dry eyes, dry mouth, blurred vision, and constipation. Some studies have quoted stoppage rates as high as 50% secondary to side effects. In recent years, the association of anticholinergic medications with cognitive impairment, dementia, and Alzheimer's disease has been better studied. In an examination of several population-based and cohort studies, a significant increase in risk of dementia and Alzheimer's disease does exist with high cholinergic loads, and this was specifically found within populations receiving anticholinergics for OAB (hazard ratio ranging from 1.54 to 2.47).

In this light, the American Urogynecologic Society recommends using the lowest effective dose and ensuring that patients are appropriately counseled on the risks associated with antimuscarinic use (35). Consideration should be given to beta-3 adrenergic medications instead of antimuscarinic medications when possible. Some antimuscarinic medications have

theoretically limited passage through the blood–brain barrier (such as solfenacin, tolterodine, and trospium), and these should be prescribed over other medications when able (36). Prescription of antimuscarinics in women over 70 should be avoided. Finally, in patients who wish to forgo the side effects of medical management of OAB, one should consider third-line options such as intradetrusor onabotulinum toxin A and neuromodulation.

45.1.2.2.2 Beta-3 Adrenergic

Beta-3 adrenergic medications can also be utilized in the management of OAB. Beta-3 agonist medications, such as mirabegron, cause relief of OAB symptoms through the activation of the beta-3 receptors. The efficacy of mirabegron has been demonstrated in 12-week dose range trials. The mean number of micturitions per 24-hour period was significantly reduced by 1.9, 2.1, 2.1, and 2.2 voids in the mirabegron 25, 50, 100, and 200 mg once-daily dosage groups (placebo was reduced by 1.4). In short-term randomized trials, mirabegron demonstrated adverse event rates (most commonly, tachycardia, headache, and diarrhea) similar to those for placebo (37, 38). Mirabegron is not recommended for patients with severe uncontrolled hypertension, end-stage renal disease, or significant liver impairment. This is despite 12-month studies involving mirabegron having approximately similar pulse rates and blood pressures when compared to baseline (39). Vibegron is a newer beta-3 agonist with more bladder-specific activity and is often used in patients with blood pressure concerns (with the continued contraindications of severe uncontrolled hypertension, end-stage renal disease, and significant liver impairment) (40).

45.1.2.2.3 Estrogen

Systemic estrogen and intravaginal estrogen have paradoxical effects on urinary incontinence symptoms. Systemic estrogen, when given to women for reasons other than incontinence, causes urinary incontinence symptoms to develop or worsen (41). In contrast, intravaginal estrogen was found to improve urinary incontinence (RR of 0.74, overall equating to one to two fewer voids per 24 hour period). Specifically, for patients with urge incontinence, estrogen receptors within the bladder trigone aid in increasing the sensory threshold within the bladder and treatment of atrophy can therefore improve urge

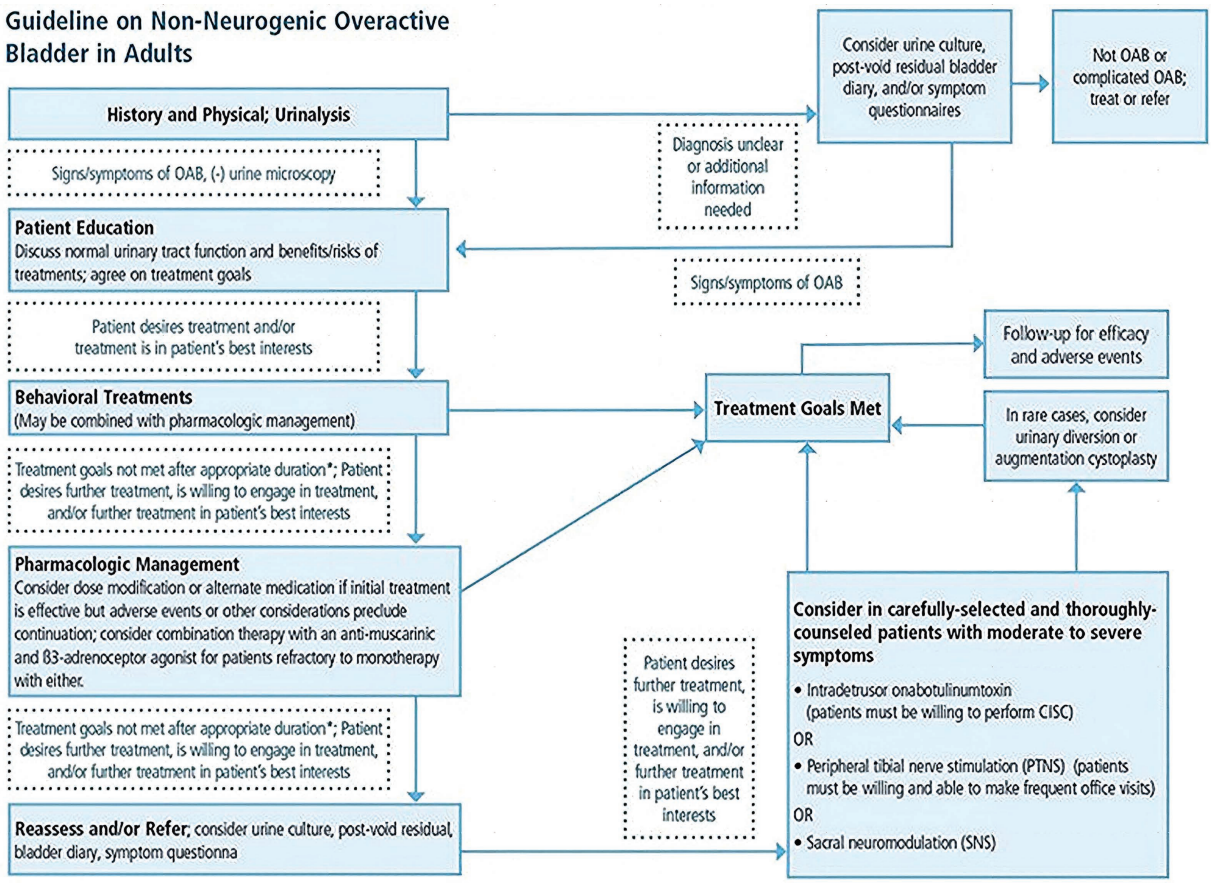


FIGURE 45.1 Diagnosis and treatment algorithm: AUA/SUFU guideline on non-neurogenic overactive bladder in adults (From ref 43 with permission). *Appropriate duration is 8–12 weeks for behavioral therapies and 4–8 weeks for pharmacological therapies Note: This figure outlines a comprehensive management algorithm for non-neurogenic overactive bladder in adults. The algorithm is designed to guide healthcare professionals in the systematic approach to diagnosis, treatment initiation, and ongoing management of patients with this condition.

symptoms (42). There is little or no data on the long-term effect of topical estrogen on incontinence and incontinence symptoms after discontinuation of intravaginal estrogen (41).

45.1.2.3 Procedural Management of Refractory Overactive Bladder

Refractory OAB is defined as overactive bladder refractory to first- and second-line therapy (43). There are three commonly used third-line treatment options: intradetrusor onabotulinumtoxin A, sacral neuromodulation, and posterior tibial nerve stimulation (PTNS) (Figure 45.1).

45.1.2.3.1 Onabotulinum Toxin A

Cystoscopic injection of onabotulinum toxin A is approved by the Food and Drug Administration (FDA) for the treatment of OAB and can be performed in the office or in a surgical setting. When compared with antimuscarinic medications, intradetrusor injection of 100 U of onabotulinum toxin A was found to have a similar reduction in voids per day but higher complete resolution (27% vs 13%) at 6 months (44). Further, per a 2011 Cochrane review, a significant clinical response may be seen in up to 60%–90% of patients, and up to 66% may achieve complete continence (45). Patients must be counseled about the adverse event profile: a relative risk of 1.47 for urinary tract infections, 5.58 for urinary retention, and 1.7 for hematuria (46).

45.1.2.3.2 Sacral Neuromodulation

Sacral neuromodulation (SNM) is indicated for the treatment of urinary and fecal dysfunction. It typically involves the implantation of a programmable device which uses a lead to deliver a low-amplitude electrical signal to the sacral nerve at the level of S3 and occasionally S4. The exact mechanism of action is not well understood although several theories have been postulated. It is thought that SNM inhibits the detrusor muscle without directly influencing urethral sphincter activity or detrusor contractility during the voiding phase. The most widely accepted theory is that this effect is achieved through the modulation of spinal cord reflexes and brain networks by peripheral afferent nerves (47, 48). By inhibiting the afferent input to the spinal cord, detrusor overactivity is also interfered with, and clinical relief is experienced (49). However, alternate suggested mechanisms indicate efferent nervous innervation to the pelvic floor may also be affected by this stimulation (47, 50).

SNM is a minimally invasive option with eligibility determined through a percutaneous nerve evaluation (PNE) procedure (in which a temporary lead is placed, often in an outpatient setting and with placement based on anatomic landmarks) or a staged procedure (in which a quadripolar, tined lead is placed in the operating room with X-ray guidance) (51). Each lead is connected to a stimulator. A typical trial period is 1 to 3 weeks, after which symptoms of incontinence, urge, and frequency of voids will be examined with a bladder diary. Success is defined as a greater than or equal to 50% improvement in symptoms (4, 51). If successful, a permanent battery (accompanied by permanent lead if PNE was performed) is placed beneath the subcutaneous fat of the buttock in the operating room (52, 53). SNM has been approved for the indications of urgency urinary incontinence, urinary frequency, nonobstructive urinary retention, and fecal incontinence. It is also used in the management of constipation in some countries.

SNM is a safe and effective means of treating refractory OAB. A Cochrane review found that 39%–50% of patients achieved complete continence and 67%–87% of patients had a greater than 50% reduction of incontinence symptoms (54). Common adverse events include pain at stimulator or lead sites, lead site migration, infection, irritation, and sensation of electric shock. Removal of device or lead modification requires further surgery, which can occur in as many as 30% of patients (52, 54, 55).

45.1.2.3.3 Posterior Tibial Nerve Stimulation

The goal for PTNS is similar to SNM in the delivery of electrical impulses to the nerves that innervate the urinary tract. In the case of PTNS, this occurs by stimulation of the posterior tibial nerve – which will then deliver retrograde stimulation to the sacral nerve plexus that controls bladder function (56). There are currently three methods of stimulation in PTNS: percutaneous needle electrode, transcutaneous surface electrode, and wireless implantable tibial nerve stimulators.

In the transcutaneous needle electrode procedure, a 34-gauge needle is inserted 4–5 cm cephalad to the medial malleolus. After a current is applied to the needle, correct placement over the posterior tibial nerve is confirmed with toe movement, namely the flexion of the great toe and fanning out of digits 2–5 (57). Stimulation of the posterior tibial nerve occurs over 30 minutes with a frequency of 200 Hz and an intensity of current determined by the patient's comfort. This is performed weekly in the office for 12 weeks and monthly thereafter.

The transcutaneous electrode procedure involves placement of two 5 × 5 cm electrode pads – a live pad posterior and superior to the medial malleolus and a grounding pad 10 cm cephalad to the live pad. Current is applied at a frequency of 10 Hz and with an amplitude determined by tolerable sensory stimulation to the ipsilateral foot. Stimulation again occurs for 30 minutes weekly for 12 weeks and monthly thereafter.

Implantable PTNS devices are a newer invention, with the first device being described in 2006 (58). Implants typically consist of a small cylinder with two bipolar electrodes that are placed surgically over the tibial nerve. Current implants are controlled with an external battery and control unit that can intermittently be applied to the lower extremity. Frequencies, pulse widths, and amplitudes vary by patient, and stimulation only occurs with the use of the external control unit (56).

Side effects of nonimplantable PTNS are limited to pain at the site of the placed needle or lead and are self-limited to the procedure. The implantable PTNS device's primary risks are primarily limited to the surgical site. This makes PTNS, especially nonimplantable PTNS, a remarkably low-risk intervention and very amenable to patients with comorbidities precluding other interventions (59).

45.2 Incontinence Related to Urinary Retention

Chronic urinary retention and the inability to adequately empty the bladder can result in incontinence when volumes within the bladder exceed the storage capacity and involuntary loss of urine occurs. The term "overflow incontinence" is no longer recommended due to its lack of a clear definition (60). Determining the underlying condition causing this urinary retention should be the next step in management. Central or peripheral impairments in the brain–bladder micturition pathway may cause a lack of adequate voiding and urinary retention (60). Conditions such as bladder injury, reduced urethral function, detrusor over/under activity, low bladder compliance, and urinary obstruction can also cause retention and should be evaluated (61). Urodynamics is commonly performed to determine where an aberration of normal is occurring during the process of micturition (4).

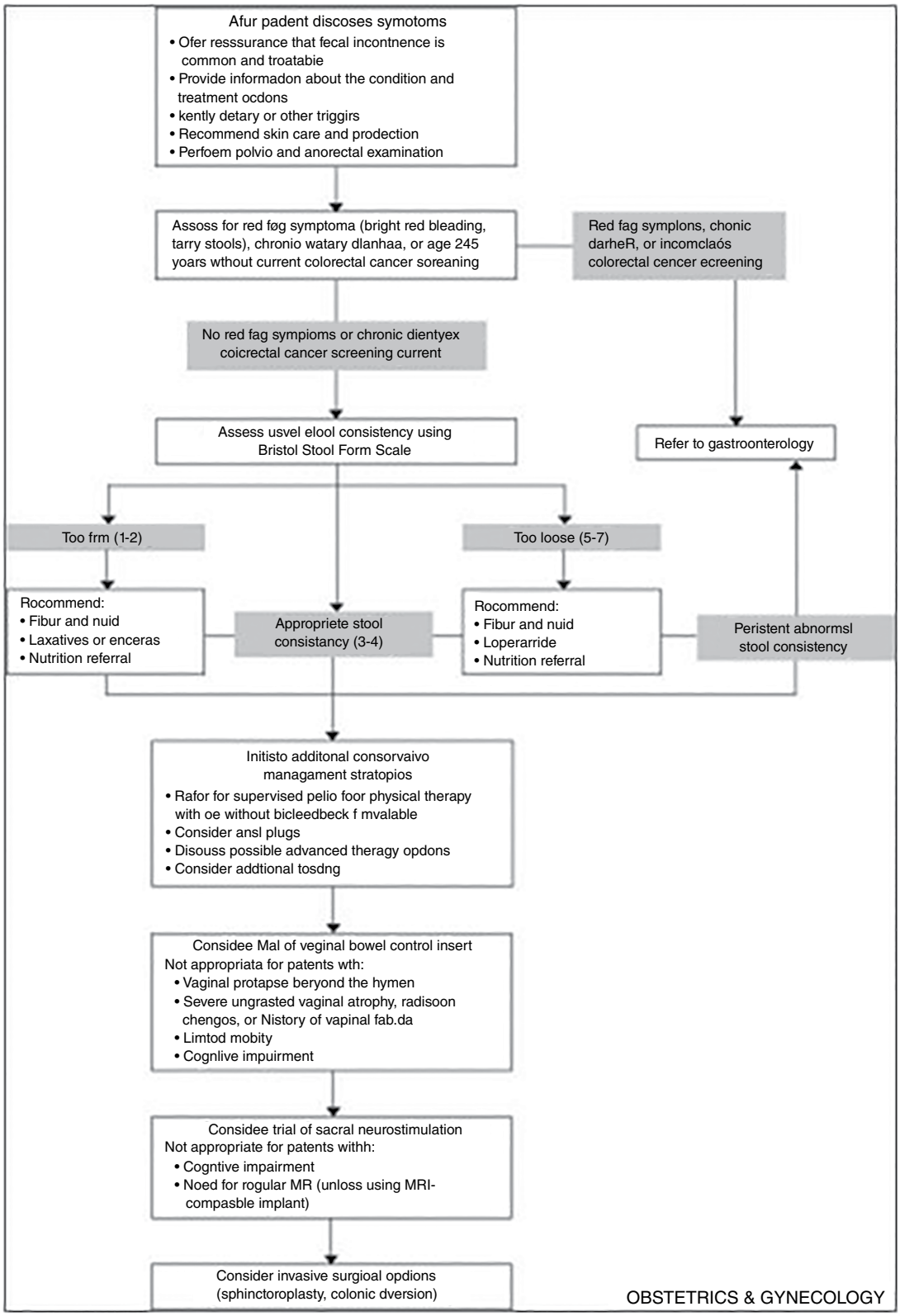


FIGURE 45.2 Fecal incontinence (From ref 67 with permission). Note: This algorithm provides a structured framework for the diagnosis and management of fecal incontinence, fostering a patient-centered and evidence-based approach to optimize clinical outcomes.

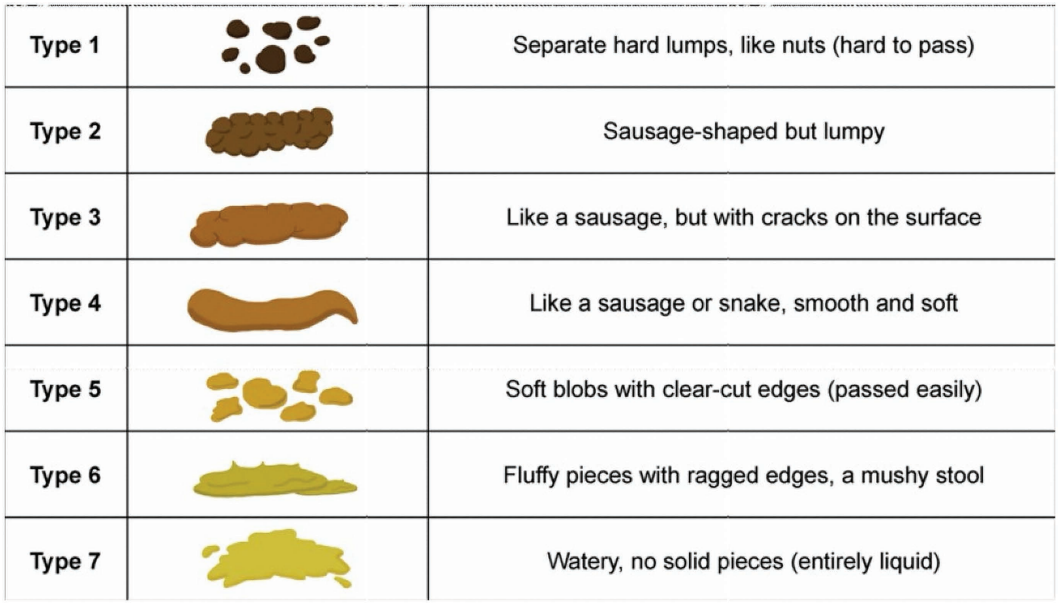


FIGURE 45.3 Bristol Stool Form Scale (From Maruyama M et al. The Management of Constipation: Current Status and Future Prospects. In: Mozsik G., ed., *Constipation*. London: IntechOpen: 2019:1–16, under Creative Commons Attribution license.)

Central to the long-term health of patients with incomplete bladder emptying is the protection of the upper urinary tract from harm as vesicoureteral reflux can occur at high pressures and result in damage over time. Post-void residual (PVR) measurements less than 300 cc are considered normal in an asymptomatic patient (62). If over 300 cc, one can obtain a second, interval measurement or consider the immediate placement of a urinary catheter to relieve potential pressure on the kidneys (62). Pelvic organ prolapse can cause reversible obstruction, but the finding of an elevated PVR is otherwise uncommon in women in the absence of pathology. Storage pressures approaching 40 cm H_2O should be a signal to evaluate for harm to the upper urinary tract and should result in a renal ultrasound for hydronephrosis (63). In the setting of long-term dysfunction, one can also perform renal scintigraphy to evaluate for scarring and obstructive pathologies (64).

45.2.1 Lower Urinary Tract Dysfunction Due to Neurologic Disease (Neurogenic Bladder)

Neurogenic bladder is another form of incontinence where disruptions in the nervous system or the bladder's structure can result in alterations in function. Spinal cord injuries, vascular disease, congenital disorders, diabetes, and demyelinating disorders, among others, can disrupt the communication between the brain and the bladder and cause decreased bladder compliance, sphincter spasticity and dyssynergia, increased detrusor tone, sphincter deficiency, and detrusor areflexia. Separating neurogenic bladder into these subtypes based on history and urodynamics findings can help guide management (65).

Autonomic dysreflexia can be experienced in neurogenic bladder patients with spinal cord abnormalities (characteristically at a level of T6 or higher) undergoing procedures such as urodynamics. This is characterized by hypertension, flushing, diaphoresis, and bradycardia. If this is encountered during bladder filling, the bladder should be emptied immediately. Repositioning of the patient to an upright, seated position should be attempted. Pharmacologic agents such as immediate release nifedipine or sublingual nitrate should be used to treat hypertension, with nitrate paste being the most effective, and the patient should be transferred to a nearby emergency department (65).

Treatment of neurogenic bladder is primarily focused on minimizing the damage to the upper urinary tract. Oral medications such as anticholinergics and beta-3 agonists can be used in conjunction with intermittent catheterization to improve bladder compliance (66). Injection of onabotulinum toxin A can also be used and has been shown to improve maximum cystometric capacity and decrease maximum detrusor voiding pressure (67). Surgical interventions such as SNM and augmentation cystoplasty have been shown to improve some parameters as well.

45.3 Fecal Incontinence

45.3.1 Evaluation

A comprehensive history and physical exam are critical to the evaluation and management of fecal incontinence (FI) (Figure 45.2). A detailed history should include bowel habits, consistency of stools, and triggers of FI. Bowel diaries, validated instruments, and the Bristol Stool Form Scale (Figure 45.3) can be used (68). Validated questionnaires include the Fecal Incontinence Severity Index, St. Mark's Incontinence Score, Fecal Incontinence Quality-of-Life Scale, and Cleveland Clinic Florida Fecal Incontinence Score (69). Risk factors for FI include age over 50 years, nursing home residence, prior

anal trauma (such as prior obstetric anal sphincter injury, anal intercourse, and anorectal trauma), urinary incontinence, pelvic floor disorders, disorders of chronic bowel disturbance, diabetes, obesity, neurologic disorders, prior cholecystectomy, and radiation (70).

45.3.1.1 Physical Exam

Physical examination should include abdominal, pelvic, and rectal examinations. An abdominal exam is performed to examine for masses or stool burden. Perineal sensation should be assessed and Valsalva maneuver should be performed to evaluate for vaginal or rectal prolapse. Pelvic and rectal exams should include a gross examination for masses, hemorrhoids, fistula, and manual muscle testing (69). The digital rectal exam (DRE) should be performed with palpation and maneuvers to provide a rough estimate of the activity of the external and internal anal sphincters. During the Valsalva maneuver a reflexive relaxation of the internal and external anal sphincters should be noted on DRE. Resting muscle tone can be assessed followed by squeeze tone. Lack of reflexive relaxation or lack of muscle strength can be a cause of fecal incontinence (68, 69).

Though further workup can be pursued, it is often acceptable to trial a patient on conservative management such as diet and lifestyle modification, pelvic floor muscle training, and biofeedback.

45.3.1.2 Colonoscopy

Colonoscopy is indicated in the setting of new onset fecal incontinence especially in the setting of new onset diarrhea or hematochezia to rule out malignant pathology or inflammatory bowel disease. Red flag symptoms such as weight loss, family or personal history of colorectal cancer, anemia, and rectal bleeding should also prompt colonoscopy. Additionally, all average-risk adults should have colorectal cancer screening starting at 45 years old (69, 71).

45.3.1.3 Ultrasound

In the setting of suspected anal sphincter injury, endoanal ultrasound can be used to determine if a defect exists in the external or internal anal sphincter (72). This is performed through the insertion of a probe into the anal canal and slow withdrawal of the probe providing a 360-degree view and allowing for examination of the sphincter muscles. While a sphincter defect does not predict functional defect, as many patients are asymptomatic in the setting of anal sphincter defect, a defect has been shown to correlate with symptoms and can be used to guide management (73). Endoanal ultrasound should be performed in patients considering anal sphincteroplasty (68, 69). Other imaging modalities such as magnetic resonance imaging (MRI) have substantial intraobserver variability and are likely inferior to ultrasound imaging. MRI can provide information if endoanal ultrasound is unavailable (74).

45.3.2 Treatment

45.3.2.1 Dietary Interventions

The initial dietary interventions vary with the Bristol score, and fiber and dietary changes are the mainstay of initial conservative treatment (Figure 45.3). These changes are low risk with reasonable opportunity for benefit, even in the setting of sphincter defects, making them ideal first-line interventions (75).

The importance of fiber should be discussed. The required daily intake of dietary fiber is 25 g if less than 50 years of age and 21 g in patients older than 50 (76). Dietary fiber acts by regulating the water-holding capacity of stool and regulating stool bulk, making stool more likely to be within the ideal middle range of the Bristol stool scale. The main side effect of fiber is bloating and flatulence, which can be overcome by incremental increase in dietary fiber. If stools are watery, then fiber is recommended in conjunction with antidiarrheal medications such as loperamide. If stools are firm, then fiber can be used with increased fluid intake and laxative or enema use. A randomized controlled trial of 16 g of psyllium husk daily found that fiber can decrease daily incontinence episodes by 50% (77).

45.3.2.2 Nonsurgical Management

Physical therapy along with biofeedback is recommended as a first-line therapy (68). The nonstandardization of biofeedback techniques has limited its widespread dissemination but should be offered to all patients where available (68, 69). Devices that physically block the unintentional passage of stool have also been studied. Anally and vaginally placed plugs that obstruct the anal canal can offer benefit but are limited by discomfort with use.

The injection of bulking agents perianally has also been used to treat FI. A 2010 Cochrane review found four eligible randomized controlled trials with a total of 176 patients undergoing injection of a bulking agent into the anal submucosa or the perianal space. The injected substances varied from autologous fat to synthetic products. There was not enough data to suggest that bulking agents were effective at that time (78). A systematic review in 2022 included trials from 2015–2020 and found possible benefit in incontinence scores and quality-of-life scores after bulking for FI. However, there was a high adverse event rate related to these synthetic products. Of the 166 patients included, 16 experienced procedure-related complications such as anal discomfort and intraoperative complications. Bulking material–related complications occurred in 48 of 166 patients including material dislodgement, removal, and extrusion. Studies had a moderate to high risk of bias and a very low strength of evidence (79).

45.3.2.3 Surgical Interventions

45.3.2.3.1 Sacral Neuromodulation

SNM, as previously discussed in this chapter, can be utilized in the treatment of FI. A 2015 Cochrane review showed improvement in patients with FI but not with constipation (80). Long-term data suggests that this is a durable intervention with approximately 90% of patients noting a greater than or equal to 50% improvement in FI at 5 years after device implantation. Further, 36% of patients can expect complete resolution of incontinence. Long-term adverse events include a 10.8% infection rate and a 24.4% rate of at least one revision or replacement (81). The presence of anal sphincter injury does not seem to impact SNM results in FI (68, 69).

45.3.2.3.2 Sphincteropasty

Anal sphincter disruption may occur through several means such as obstetric anal sphincter injury, pelvic trauma, and prior surgery and can lead to fecal incontinence. In the short term, improvements in fecal continence are reported in as high as 85% of patients. However, this is not a durable increase in continence with a 50% failure rate 40–60 months postoperatively. In the last decade, SNM has become the more popular surgical intervention for FI while sphincteroplasty is reserved for patients with anal sphincter injury and FI shortly after vaginal delivery or pelvic trauma (82).

45.3.2.3.3 Colostomy/Ileostomy

A very successful but morbid option for managing FI is the creation of an ostomy, and this is usually the last resort. In a survey of patients who had undergone colostomy for fecal incontinence, 83% felt that their ostomy restricted their life "a little" or "not at all," median satisfaction was 9/10, and 84% would "probably" or "definitely" choose to have a colostomy again. Although the majority of people liked their ostomy, a minority were strongly dissatisfied with this procedure suggesting that colostomy is an acceptable option in patients who are extensively counseled (83).

45.4 Constipation (Figure 45.4)

45.4.1 Definition

Although constipation has been defined as fewer than three bowel movements per week, patients will frequently present for evaluation with symptoms of bloating, abdominal distension, hard stools, or straining with bowel movements regardless of frequency of bowel movements (84). Therefore, constipation can also be defined as the complaint that bowel movements are infrequent or incomplete with or without the need for frequent straining or manual assistance to defecate (85). Chronic constipation is when these persist for greater than 6 months. Constipation is extremely common and affects approximately 16% of adults overall and 33% of adults older than 60 years (84). Diseases of the colon, metabolic disturbances, neurologic disorders, and functional causes can all contribute to constipation. Symptomatic patients can be organized into the three subgroups of defecatory disorders, normal transit constipation, and slow-transit constipation (Box 45.3), and this can help guide treatment (84).

45.4.2 Evaluation

The initial evaluation should include a detailed history and physical examination. History elements such as the frequency and consistency of bowel movements, abdominal or anorectal pain related to the bowel movement and the timing thereof, rectal bleeding, and the need to strain or the use of additional maneuvers with defecation should be elicited. A patient may also report the need for manual evacuation of stool or other manipulation to assist with bowel movements as well (86).

When constipation is discussed in the setting of pelvic floor disorders, the history finding that is often discussed is splinting. Splinting is the application of pressure on the vagina, perineum, or anus to facilitate bowel movements, presumably against posterior vaginal prolapse or perineal decent and is the only patient-reported symptom that is reliably associated with posterior pelvic organ prolapse (87).

Physical examination should include an abdominal exam along with an assessment of pelvic floor similar to that

BOX 45.3 DIAGNOSTIC CRITERIA FOR SUBGROUPS OF DEFECATORY DISORDERS (FROM REF 85 WITH PERMISSION). THE FIGURE DETAILS THE SUBGROUPS OF DEFECATORY DISORDERS, EACH CHARACTERIZED BY DISTINCT CLINICAL FEATURES. UNDERSTANDING THESE SUBGROUPS IS CRUCIAL FOR ACCURATE DIAGNOSIS AND TAILORED MANAGEMENT STRATEGIES.

FUNCTIONAL CONSTIPATION

1. Must include ≥2 of the following:
   a. straining during at least 25% of defecations
   b. lumpy or hard stools in at least 25% of defecations
   c. sensation of anorectal evacuation for at last 25% of defecations
   d. sensation of anorectal obstruction/blockage for at least 25% of defecations
   e. manual maneuvers to facilitate at least 25% of defecations (e.g., digital evacuation and support of the pelvic floor)
   f. fewer than three defecations per week
2. Loose stools are rarely present without the use of laxatives
3. Insufficient criteria for irritable bowel syndrome

FUNCTIONAL DEFECATION DISORDERS

1. The patient must satisfy diagnostic criteria for functional constipation (see above)
2. During repeated attempts to defecate must have ≥ 2 of the following:
   a. evidence of impaired evacuation, based on balloon expulsion test or imaging
   b. inappropriate contract of the pelvic floor muscles (i.e., anal sphincter or puborectalis) or < 20% relaxation of basal resting sphincter pressure by manometry, imaging, or EMG
   c. inadequate propulsive forces accessed by manometry or imaging

DYSSYNERGIC DEFECATION

1. Inappropriate contraction of the pelvis floor or < 20% relaxation of basal resting sphincter pressure with adequate propulsive forces during attempted defecation

INADEQUATE DEFECATORY PROPULSION

1. Inadequate propulsive forces with or without inappropriate contraction or < 20% relaxation of the anal sphincter pressure during attempted defecation

Criteria fulfilled for the last 3 months with symptom onset at least 6 months before diagnosis.

described for FI. In addition, palpation of the rectovaginal septum should be performed to examine for the presence of rectal pockets or areas of weakness or laxity in the vagina or perineum occupied by the rectum (84, 86).

45.4.2.1 Laboratory Testing

Laboratory testing can be obtained to rule out medical conditions as a cause of constipation. A complete blood count, thyroid-stimulating hormone, glucose, HbA1c, renal function, and serum potassium, among others, are often recommended to be performed in this setting depending on the clinical history. The efficacy of laboratory testing in constipation has not been determined and is likely of low value (86).

45.4.2.2 Colonoscopy

Colon and rectal cancer can be a cause of constipation. Screening colonoscopy should be performed in patients over 45 years with average risk patients and in those with "red flag" features such as unintentional weight loss, blood in the stool, anemia, and sudden changes in bowel habits or abdominal pain. Routine colonoscopy is not recommended for constipation unless patients meet these criteria (84).

45.4.2.3 Anorectal Manometry

Anorectal manometry can help determine the coordination and effectiveness of the process of defecation, specifically the anal sphincters. This test also rules out Hirschsprung's disease and can be used to identify pelvic floor dyssynergia, if present. Dyssynergic defecation involves failure to relax or paradoxical contraction of the anal sphincters with attempts to defecate and can be treated with biofeedback (85).

Anorectal manometry is performed by placing a small balloon in the rectum which is attached to a catheter and inflated. This balloon is placed approximately 6 cm from the anal verge and slowly withdrawn. While the balloon is in place the patient is asked to squeeze, push, and simulate the process of defecation. This test will determine anal length along with information regarding the resting and squeeze pressures of the anal canal and sphincters. The balloon expulsion test can also be performed and the inability to expel a 50 mL latex balloon within 1 minute is abnormal and concerning for dyssynergic defecation (88).

The rectoanal inhibitory reflex (RAIR) can also be determined through rapid inflation and deflation of the balloon when placed in the distal rectum. This reflex involves a relaxation of the internal anal sphincter with reflex contraction of external anal sphincter in response to rectal distension and is absent in Hirschsprung's disease. This reflex is how rectal content is sensed by the anus and fecal continence is ensured (85, 86). As many as 20% of patients can have falsely nonrelaxing anal sphincters on anal manometry during defecation, likely due to discomfort from the procedure itself (89).

45.4.2.4 Barium and MRI Defecography

Defecography provides a functional assessment of the pelvic anatomy through the process of defecation. Oral contrast

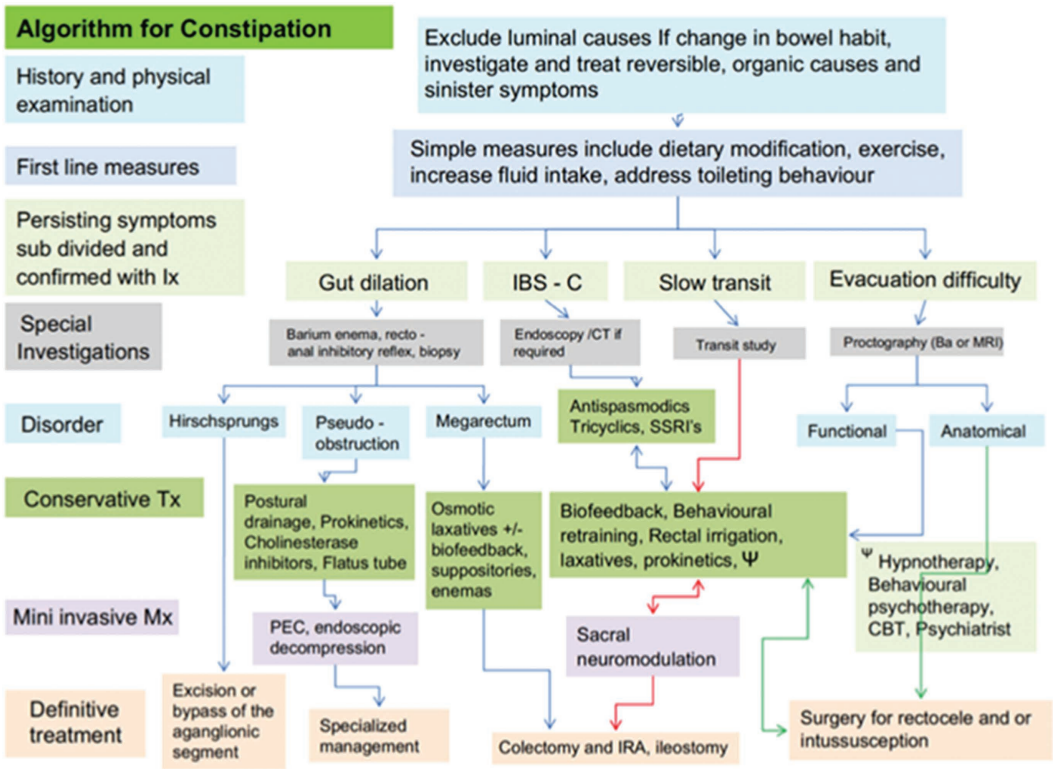


FIGURE 45.4 Algorithm for constipation (From ref 83 with permission). Note: This algorithm serves as a guide for healthcare professionals to navigate the diagnosis and management of constipation in adults.

can be given to visualize the small bowel (~30–45 minutes before imaging) along with vaginal contrast (if desired) and rectal contrast. The patient then sits on a commode on a fluoroscopic table and attempts to defecate while dynamic images are obtained. There are three phases of the assessment – rest, evacuation, and recovery.

The anal canal is closed during the resting phase, and the puborectalis muscle activity can be calculated from the anorectal angle (ARA) and anorectal junction (ARJ) at this phase. With attempts to evacuate, the anorectal junction should migrate caudally as the pelvic floor descends (less than 3.5 cm of caudal migration is considered normal) and the rectum should begin to empty of contrast. A bulge in the anterior rectal wall at this phase is considered normal if less than 2 cm. After the rectum is emptied the extent of possible rectal or vaginal prolapse can be evaluated. There are many grading systems for enteroceles, rectoceles, vaginal prolapse, and rectal prolapse. The recovery phase occurs after straining.

Defecography can be performed fluoroscopically or with MRI – with these two modalities correlating in the identification and degree of prolapse (90). Neither of these modalities of defecography correlate well with physical examination. Radiologic diagnosis of rectocele in this way does not correlate with defecatory symptoms and can commonly be found in asymptomatic patients (91). Defecography images should be interpreted with caution in this setting. Defecography can also be used for a number of other rectoanal conditions such as dyskinetic puborectalis muscle syndrome, intussusception, and rectal prolapse (92).

45.4.2.5 Colon Transit

If a patient's bowel movements are infrequent and refractory to laxative therapy, slow-transit constipation should be suspected. The Sitz Marker Transit Study is the most common study performed in this setting and involves the patient ingesting a gelatin capsule containing 24 precut radiopaque polyvinyl chloride markers on day 0. An abdominal X-ray is obtained on day 5 and if less than 80% of the markers are expelled, the study is considered abnormal. If unexpelled markers are scattered throughout the colon, then slow-transit constipation is diagnosed. If markers are located in the rectosigmoid region, the diagnosis is likely outlet obstruction.

45.4.3 Treatment

45.4.3.1 Medications

If the initial evaluation of the patient is normal, then a trial of fiber and either a stimulant or osmotic laxative is recommended. The use of fiber was discussed previously and is similar to treatment of FI. Bulk-forming, hyperosmotic, or stool-softening laxatives should be trialed first (in conjunction with fiber). If stool is the desired Bristol score, then stimulant laxatives may be attempted (preferably given 30 minutes after a meal).

45.4.3.2 Biofeedback

Biofeedback therapy can improve symptoms of constipation both in conjunction with or following fiber and laxative therapy. Although there are many protocols for biofeedback, it is superior to sham treatments, dietary changes, exercises, and laxatives in the treatment of chronic constipation. Biofeedback has been shown to be inferior to some surgical treatments on the posterior compartment (93).

45.4.3.3 Sacral Neuromodulation

SNM has been attempted in patients with functional constipation. It has irregularly shown some benefit, though often small, in the chronic constipation population, with this small benefit being weighed against the risks of the procedure and the need for permanent implantation of a device (94, 95). The American Gastroenterological Association does not currently recommend SNM in the treatment of chronic constipation (84). The IUGA/ICS guidelines for constipation do mention neuromodulation in their guidelines for the treatment of constipation within the treatment of constipatory irritable bowel syndrome and slow-transit constipation (85). Overall, this method should be pursued with caution, with shared decision making with patients understanding that the benefit has been small and irregular throughout the current literature.

References

1. Shamliyan T. Nonsurgical treatments for urinary incontinence in adult women: diagnosis and comparative effectiveness. *Comp Eff Rev*. 2012;(36).
2. Boyington JE et al. Differences in resident characteristics and prevalence of urinary incontinence in nursing homes in the southeastern United States. *Nurs Res*. 2007;56(2):97–107.
3. Carls C. The prevalence of stress urinary incontinence in high school and college-age female athletes in the midwest: implications for education and prevention. *Urol Nurs Off J Am Urol Assoc Allied*. 2007;27(1):21–25.
4. Urinary incontinence in women: AUGS practice bulletin. *Female Pelvic Med Reconstr Surg*. 2015;21:304–314. https://journals.lww.com/fpmrs/abstract/2015/11000/urinary_incontinence_in_women.3.aspx.
5. Harris SS et al. Care seeking and treatment for urinary incontinence in a diverse population. *J Urol*. 2007;177:680–684.
6. Khandelwal C et al. Diagnosis of urinary incontinence. *Am Fam Physician*. 2013;87(8):543–550.
7. Brown JS et al. Measurement characteristics of a voiding diary for use by men and women with overactive bladder. *Urology*. 2003;61(4):802–809.
8. Amundsen CL et al. Bladder diary measurements in asymptomatic females: functional bladder capacity, frequency, and 24-hr volume cindy. *Neurourol Urodyn*. 2007;26:341–349.
9. Parsons M et al. Bladder diary patterns in detrusor overactivity and urodynamic stress incontinence. *Neurourol Urodyn*. 2007;26:800–806.
10. Rogers RG. Translating patient-reported outcomes to improve patient care and urogynecologic research. *Int Urogynecol J*. 2017;28(12):1765–1766.
11. Cichowski S et al. International urogynecology consultation: patient reported outcome measures (PROs) use in the evaluation of patients with pelvic organ prolapse. *Int Urogynecol J*. 2022;33(10):2603–2631.
12. Gray T et al. What are the concerns and goals of women attending a urogynaecology clinic? Content analysis of free-text data from an electronic pelvic floor assessment questionnaire (ePAQ-PF). *Int Urogynecol J*. 2019;30(1):33–41.
13. Barber MD. Questionnaires for women with pelvic floor disorders. *Int Urogynecol J*. 2007;18(4):461–465.
14. Hanley J et al. Validity study of the severity index, a simple measure of urinary incontinence in women. *Br Med J*. 2001;322(7294):1096–1097.
15. Barber MD et al. Psychometric evaluation of 2 comprehensive condition-specific quality of life instruments for women with pelvic floor disorders. *Am J Obstet Gynecol*. 2001;185(6):1388–1395.
16. Shumaker SA et al. Health-related quality of life measures for women with urinary incontinence: the incontinence impact questionnaire and the urogenital distress inventory. *Qual Life Res*. 1994;3(5):291–306.

17. Uebersax JS et al. Short forms to assess life quality and symptom distress for urinary incontinence in women: the incontinence impact questionnaire and the urogenital distress inventory. *Neurourol Urodyn*. 1995;14(2):131–139.
18. Tang DH et al. Impact of urinary incontinence on healthcare resource utilization, health-related quality of life and productivity in patients with overactive bladder. *BJU Int*. 2014;113:484–491.
19. Naughton MJ et al. Symptom severity and QOL scales for urinary incontinence. *Gastroenterology*. 2004;126(1):114–123.
20. Bientinesi R et al. Neurologic urinary incontinence, lower urinary tract symptoms and sexual dysfunctions in multiple sclerosis: expert opinions based on the review of current evidences. *J Clin Med*. 2022;11(21).
21. Pal M et al. Approach to a woman with urinary incontinence. *Urol Ann*. 2020;12(1):4–8.
22. Haylen BT et al. An International Urogynecological Association (IUGA)/International Continence Society (ICS) joint report on the terminology for female pelvic floor dysfunction. *Neurourol Urodyn*. 2010;29:4–20.
23. Messelink B et al. Standardization of terminology of pelvic floor muscle function and dysfunction: report from the pelvic floor clinical assessment group of the International Continence Society. *Neurourol Urodyn*. 2005;24(4):374–380.
24. Meister MR et al. Development of a standardized, reproducible screening examination for assessment of pelvic floor myofascial pain. *Am J Obstet Gynecol*. 2019;220(3):255.e1–255.e9.
25. Orkin BA et al. The digital rectal examination scoring system (DRESS). *Dis Colon Rectum*. 2010;53(12):1656–1660.
26. Coyne KS et al. The impact of overactive bladder, incontinence and other lower urinary tract symptoms on quality of life, work productivity, sexuality and emotional well-being in men and women: results from the EPIC study. *BJU Int*. 2008;101(11):1388–1395.
27. Rosier PF et al. Executive summary: the international consultation on incontinence 2008 – committee on: '"dynamic testing"'; for urinary incontinence and for fecal incontinence. Part 1: innovations in urodynamic techniques and urodynamic testing for signs and symptoms of Ur. *Neurourol Urodyn*. 2010;29:140–145.
28. Collins CW et al. AUA/SUFU adult urodynamics guideline: a clinical review. *Urol Clin North Am*. 2014;41(3):353–362.
29. Wallace S et al. Bladder training for urinary incontinence in adults. *Cochrane Database Syst Rev*. 2004;2009(1).
30. Yıldız N et al. Factors predicting the treatment success of bladder training for urgency urinary incontinence. *Neurourol Urodyn*. 2022;41(8):1809–1816.
31. Reisch B et al. Cognitive components of behavioral therapy for overactive bladder: a systematic review. *Int Urogynecol J*. 2021;32(10):2619–2629.
32. Hay-Smith E et al. Comparisons of approaches to pelvic floor muscle training for urinary incontinence in women (review). *Cochrane Database Syst Rev*. 2011;(12):CD009508.
33. Burgio KL et al. Combined behavioral and individualized drug therapy versus individualized drug therapy alone for urge urinary incontinence in women. *J Urol*. 2010;184(2):598–603.
34. Reynolds WS et al. Comparative effectiveness of anticholinergic therapy for overactive bladder in women: a systematic review and meta-analysis. *Obstet Gynecol*. 2015;125(6):1423–1432.
35. Thomas TN et al. Clinical consensus statement: association of anticholinergic medication use and cognition in women with overactive bladder. *Female Pelvic Med Reconstr Surg*. 2021;27(27):69–71.
36. Todorova A et al. Effects of tolterodine, trospium chloride, and oxybutynin on the central nervous system. *J Clin Pharmacol*. 2001;41(6):636–644.
37. Chapple CR et al. A phase II dose-ranging study of mirabegron in patients with overactive bladder. *Int Urogynecol J*. 2013;24(9):1447–1458.
38. Sanford M. Mirabegron: A review of its use in patients with overactive bladder syndrome. *Drugs*. 2013;73(11):1213–1225.
39. Chapple CR et al. Randomized double-blind, active-controlled phase 3 study to assess 12-month safety and efficacy of mirabegron, a β3-adrenoceptor agonist, in overactive bladder. *Eur Urol*. 2013;63(2):296–305.
40. Varano S et al. Efficacy and safety of once - daily vibegron for treatment of overactive bladder in patients aged ≥ 65 and ≥ 75 years: subpopulation analysis from the EMPOWUR randomized, international, phase III study. *Drugs Aging*. 2021;38(2):137–146.
41. Cody J et al. Oestrogen therapy for urinary incontinence in post-menopausal women. *Cochrane Database Syst Rev*. 2012;(10):CD001405.
42. Robinson D et al. The role of estrogens in female lower urinary tract dysfunction. *Urology*. 2003;62(4 Suppl 1):45–51.
43. Lightner DJ et al. Diagnosis and treatment of overactive bladder (non-neurogenic) in adults: Aua/sufu guideline amendment 2019. *J Urol*. 2019;202(3):558–563.
44. Visco AG et al. Anticholinergic therapy vs. onabotulinumtoxina for urgency urinary incontinence. *N Engl J Med*. 2012;367(19):1803–1813.
45. Duthie JB et al. Botulinum toxin injections for adults with overactive bladder syndrome (review). *Cochrane Database Syst Rev*. 2011;(12):CD005493.
46. Cheng T et al. Efficacy and safety of onabotulinumtoxina in patients with neurogenic detrusor overactivity: a systematic review and meta-analysis of randomized controlled trials. *PLoS One*. 2016;11(7).
47. DeWachter S et al. Sacral neuromodulation: mechanism of action. *Eur Urol Focus*. 2020;6(5):823–825.
48. Gill BC et al. Real-time changes in brain activity during sacral neuromodulation for overactive bladder. *J Urol*. 2017;196(6):1379–1385.
49. Elkelini MS et al. Mechanisms of action of sacral neuromodulation. *Int Urogynecol J*. 2010;21(Suppl 2):439–446.
50. Vaganée D et al. Behind the scenes: an electromyographic interpretation of the pelvic floor contractions seen by the naked eye upon lead stimulation in sacral neuromodulation patients. *Neurourol Urodyn*. 2019;38.
51. Baxter C et al. Contrasting the percutaneous nerve evaluation versus staged implantation in sacral neuromodulation. *Curr Urol Rep*. 2010;11(5):310–314.
52. Gormley EA et al. Diagnosis and treatment of overactive bladder (non-neurogenic) in adults: AUA/SUFU guideline. *J Urol*. 2012;188(6 Suppl):2455–2463.
53. Elterman D et al. A prospective, multicenter, international study to explore the effect of three different amplitude settings in female subjects with urinary urge incontinence receiving interstim therapy. *Neurourol Urodyn*. 2021;40(3):920–928.
54. Herbison GP et al. Sacral neuromodulation with implanted devices for urinary storage and voiding dysfunction in adults. *Cochrane Database Syst Rev*. 2009;(2):CD004202.
55. Sutherland S et al. Sacral nerve stimulation for voiding dysfunction: one institution's 11-year experience. *Neurourol Urodyn*. 2007;26(1):36.
56. Bhide AA et al. Posterior tibial nerve stimulation for overactive bladder – techniques and efficacy. *Int Urogynecol J*. 2020;31(5):865–870.
57. Zecca C et al. Motor and sensory responses after percutaneous tibial nerve stimulation in multiple sclerosis patients with lower urinary tract symptoms treated in daily practice. *Eur J Neurol*. 2014;21(3):506–511.
58. Van Der Pal F et al. Implant-driven tibial nerve stimulation in the treatment of refractory overactive bladder syndrome: 12-Month follow-up. *Neuromodulation*. 2006;9(2):163–171.
59. Warehime JM et al. Proximity of percutaneous tibial nerve stimulation needle insertion to surrounding anatomic structures: a cadaveric study. *Am J Obstet Gynecol*. 2023. 229(4):430.e1–430.e6.

60. Gajewski JB et al. An International Continence Society (ICS) report on the terminology for adult neurogenic lower urinary tract dysfunction (ANLUTD). *Neurourol Urodyn*. 2018;37(3):1152–1161.
61. D'Ancona C et al. The International Continence Society (ICS) report on the terminology for adult male lower urinary tract and pelvic floor symptoms and dysfunction. *Neurourol Urodyn*. 2019;38(2):433–477.
62. Stoffel JT et al. Nonneurogenic chronic urinary retention: consensus definition, treatment algorithm, and outcome end points. *J Urol*. 2017;198(1):153–160.
63. Damiano R et al. Follow-up in adults with neurogenic bladder dysfunction. In: Esposito C et al., eds. *Pediatric Neurogenic Bladder Dysfunction*. Berlin, Heidelberg: Springer; 2006. https://doi.org/10.1007/3-540-30867-9_49.
64. Peters C et al. Vesicoureteral reflux associated renal damage: congenital reflux nephropathy and acquired renal scarring. *J Urol*. 2010;184(1).
65. Linsenmeyer T et al. Bladder management for adults with spinal cord injury: a clinical practice guideline for health-care providers. *J Spinal Cord Med*. 2006;29(5):527–573.
66. Kamei J et al. Video-urodynamic effects of mirabegron, a β3-adrenoceptor agonist, in patients with low-compliance bladder. *Int J Urol*. 2015;22(10):956–961.
67. Schurch B et al. Botulinum toxin type A is a safe and effective treatment for neurogenic urinary incontinence: results of a single treatment, randomized, placebo controlled 6-month study. *J Urol*. 2005;174:196.
68. Brown HW et al. Management of fecal incontinence. *Obstet Gynecol*. 2020;136(4):811–822.
69. Paquette IM et al. The American Society of Colon and Rectal Surgeons' clinical practice guideline for the treatment of fecal incontinence. *Dis Colon Rectum*. 2015;58(7):623–636.
70. ACOG practice bulletin 210: fecal incontinence. *Obstet Gynecol*. 2017;133(4):202–207.
71. Wolf AMD et al. Colorectal cancer screening for average-risk adults: 2018 guideline update from the American Cancer Society. *CA Cancer J Clin*. 2018;68(4):250–281.
72. Albuquerque A. Endoanal ultrasonography in fecal incontinence: current and future perspectives. *World J Gastrointest Endosc*. 2015;7(6):575.
73. Karoui S et al. Results of sphincteroplasty in 86 patients with anal incontinenc. *Dis Colon Rectum*. 2000;43(6):813–820.
74. Malouf AJ et al. Prospective assessment of accuracy of endoanal MR imaging and endosonography in patients with fecal incontinence. *Am J Roentgenol*. 2000;175(3):741–745.
75. Forte ML et al. Treatments for fecal incontinence. *AHRQ Comp Eff Rev*. 2016;15(16).
76. Turner N et al. Dietary fiber. *Adv Nutr*. 2011;(2):151–152.
77. Bliss DZ et al. Supplementation with dietary fiber improves fecal incontinence. *Nurs Res*. 2001;50(4):203–213.
78. Maeda Y et al. Perianal injectable bulking agents as treatment for faecal incontinence in adults (review). *Cochrane Database Syst Rev*. 2010:CD007959.pub2.
79. Gassner L et al. Clinical effectiveness and safety of self-expandable implantable bulking agents for faecal incontinence: a systematic review. *BMC Gastroenterol*. 2022;22(1).
80. Thaha M et al. Sacral nerve stimulation for faecal incontinence and constipation in adults. *Cochrane Database Syst Rev*. 2015;(8):CD004464.
81. Hull T et al. Long-term durability of sacral nerve stimulation therapy for chronic fecal incontinence. *Dis Colon Rectum*. 2013;56(2):234–245.
82. Wald A et al. ACG clinical guideline: management of benign anorectal disorders. *Am J Gastroenterol*. 2014;109(8):1141–1157.
83. Norton C et al. Patients' views of a colostomy for fecal incontinence. *Dis Colon Rectum*. 2005;48(5):1062–1069.
84. Bharucha AE et al. American gastroenterological association medical position statement on constipation. *Gastroenterology*. 2013;144(1):211–217.
85. Sultan AH et al. An International Urogynecological Association (IUGA)/International Continence Society (ICS) joint report on the terminology for female anorectal dysfunction. *Neurourol Urodyn*. 2017;36:10–34.
86. Ridgeway BM et al. American urogynecologic society best-practice statement on evaluation of obstructed defecation. *Female Pelvic Med Reconstr Surg*. 2016;24(6):383–391.
87. Erekson EA et al. The association between stage II or greater posterior prolapse and bothersome obstructive bowel symptoms. *Female Pelvic Med Reconstr Surg*. 2010;16(1):59–64.
88. Bharucha AE et al. Review of the indications, methods, and clinical utility of anorectal manometry and the rectal balloon expulsion test. *Neurogastroenterol Motil*. 2022;34(9):1–18.
89. Minguez M et al. Predictive value of the balloon expulsion test for excluding the diagnosis of pelvic floor dyssynergia in constipation. *Gastroenterology*. 2004;126(Suppl. 1):57–62.
90. Maglinte DDT et al. Comparison between dynamic cystocolpoproctography and dynamic pelvic floor MRI: pros and cons: which is the "functional" examination for anorectal and pelvic floor dysfunction? *Abdom Imaging*. 2013;38(5):952–973.
91. Shorvon P et al. Defecography in normal volunteers: results and implications. *Gut*. 1989;30(12):1737–1749.
92. Kim AY. How to interpret a functional or motility test – sphincter of oddi manometry. *J Neurogastroenterol Motil*. 2012;18(2):211–217.
93. Woodward S et al. Biofeedback for treatment of chronic idiopathic constipation in adults [Internet]. *Cochrane Library*. 2014:CD008486.pub2.
94. Janssen PTJ et al. Long-term outcome of intractable constipation treated by sacral neuromodulation: a comparison between children and adults. *Colorectal Dis*. 2018;20(2):134–143.
95. Pilkington SA et al. Surgery for constipation: systematic review and practice recommendations results V: sacral nerve stimulation. *Colorectal Dis*. 2017;19:92–100.

46 FISTULAS AND REPAIR OF OBSTETRIC LACERATIONS

Emily E. Weber LeBrun and Veronica O. Demtchouk

46.1 Obstetric Perineal and Vaginal Lacerations

Vaginal and perineal injuries are common events following vaginal delivery and other nonobstetric-related trauma, occurring in 53%–79% of women (1). Risk factors for obstetric injury include nulliparity, fetal weight, vertex malpresentation, prior dystocia, and operative vaginal delivery (2). The routine use of episiotomy during vaginal delivery has diminished following a systematic review showing no benefit, and while vaginal lacerations can occur during well-controlled deliveries, they are more commonly associated with shoulder or other labor dystocia, malpresentation, and precipitous and operative delivery (3, 4). The use of forceps has greatly diminished in favor of vacuum extraction, at least in part due to shorter training time to achieve proficiency. There is insufficient consensus on standard classification of obstetric anal sphincter injuries (OASIS) and wide variation in reported incidence, from 1% to 2% in the United States and United Kingdom to 10% in developing nations (5, 6). Undiagnosed injuries or those due to prolonged labor in developing nations give rise to obstetric fistula, affecting about 1.4 per 1000 women in sub-Saharan Africa and South Asia where access to emergent cesarean delivery is severely limited (7). Prevention strategies include perineal massage, warm compress, and lateral delivery position. Superficial lacerations typically do not require repair, but persistent bleeding, anatomic distortion, and interruption of perineal or vaginal anatomy merit reconstruction.

46.1.1 Anatomy and Classification

Any discussion of pelvic anatomy must acknowledge the disparate history of published nomenclature as both inaccurate, imprecise, and inconsistent. A 2021 study from the Society of Gynecologic Surgeons Pelvic Anatomy Group, aimed at standardizing terminology for gynecologic education and research, identified 486 unique terms for the posterior vagina and vulva, accepting 264 and proposed 12 new terms based on expert consensus (1). It is imperative that students of pelvic anatomy compare publications and that researchers publishing on the topic utilize modern nomenclature to enhance communication and to allow for comparative analyses.

The classification of obstetric lacerations is shown in Table 46.1.

While first- and second-degree lacerations commonly affect the labia minora, periurethral, and vestibule, the perineal body is the most common site of third- and fourth-degree lacerations. The subcutaneous anatomy of the perineum (Figure 46.1) is critical for understanding the principles of vulvovaginal reconstruction following an obstetrical laceration or mature fistula repair.

The perineal body is a midline intersection of the superficial and deep muscles superficial to the perineal membrane including the transverse perineal and the bulbocavernosus (also called bulbospongiosus) muscles. The distal rectal sphincter complex is made up of the circumferential muscles of the internal and external sphincters and extends cephalad about 3–4 cm. The external anal sphincter (EAS) is thicker than and more distal to the internal anal sphincter (IAS), forming a sort of collar around the distal anus whereas the IAS is shaped more like a hollow cylinder. The two sphincters "overlap for about 1.7 cm and the IAS extends cephalad about 1.2 cm from the proximal margin of the EAS" (2). The perineal membrane separates the superficial perineal structures from the deeper muscles of the levator ani, which include pubococcygeus, iliococcygeus, and puborectalis muscles. While the anal sphincter complex is traditionally credited for fecal continence (80% provided by the internal and 20% by the external sphincter), the perineal body and puborectalis muscle play an important role in defecatory function.

Obstetrical lacerations and fistulas can also occur as isolated defects in the upper vagina, cervix, or even lower uterine segment. In a premenopausal woman, the anterior vaginal wall has a continuous thick (2–3 mm) muscularis that separates the vaginal mucosa from the bladder detrusor muscle and intervening adventitia. Sometimes this layer is called the endopelvic fascia, as it is used in reconstruction of anterior prolapse. Posteriorly, the rectovaginal septum is thick, fascia-like connective tissue, extending from the perineal body cephalad about 3–4 cm, at which point it devolves into a thin peritoneal-like membrane between the upper rectosigmoid and the posterior vaginal fornix with intervening adipose tissue. The anterior and posterior endopelvic fascia condense laterally into the arcus tendineous fascia pelvis (ATFP) and arcus tendineous levator ani (ATLA) as they attach to the obturator internus and levator ani muscles. These lateral attachments form the anterior and posterior lateral sulcus on each side where parasagittal obstetric lacerations can be particularly difficult to visualize.

46.1.2 Diagnosis

As evidenced by the previous clinical scenario, a thorough exam may perhaps be the most important element of managing obstetric lacerations. If adequate visualization is not possible in the delivery room setting, the patient should be moved to an operating room with adequate lighting, anesthesia, and retraction assistance. Breisky–Navratil (also called "spade"), Weitlander (with teeth), and Rigby (without teeth) vaginal retractors are extremely helpful for achieving complete visualization of the entire vagina and cervix. The Weitlander and Rigby retractors are particularly handy to assist a solo surgeon.

TABLE 46.1 Classification of Obstetric Perineal Lacerations

First Degree	Perineal skin only
Second Degree	Involving the superficial perineal muscles
Third Degree	Involving the anal sphincter muscles (complex) A. < 50% of the external anal sphincter (EAS) B. > 50% of the EAS C. Involving both the EAS and the internal anal sphincter (IAS)
Fourth Degree	Involving the anal sphincter complex and anal/rectal mucosa

DOI: 10.1201/9781003312109-46

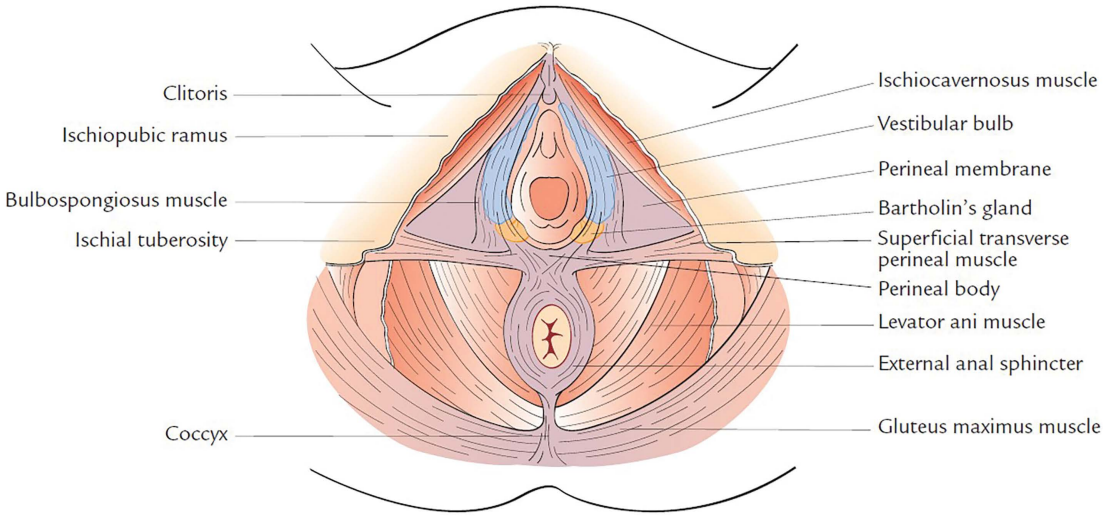


FIGURE 46.1 Structures covering the pelvic outlet, as viewed from below (From Cardozo L et al. *Textbook of Female Urology and Urogynaecology*, 2nd edn., Boca Raton, FL: CRC Press; 2006:77.1, with permission).

A systematic approach to the exam is best, to avoid missing any portion of the vagina or perineum. Check for cervical lacerations by using ring forceps to grasp the cervix and "run it." A digital rectal exam is required to fully assess the posterior vaginal wall and sulcus. Clues that might indicate an occult injury include traumatic or precipitous delivery, persistent bleeding, and the appearance of thinning blood or clear fluid. All posterior and perineal lacerations should be carefully examined for involvement of the rectal sphincter complex. Retrograde 4 to 6 bladder with sterile milk (commonly available as formula in labor and delivery) can help identify an injury to the bladder, as the milk seeps into the vaginal field and is much more visible than urine. In the setting of an anterior lesion consider cystourethroscopy to evaluate bladder involvement. While overt injuries can sometimes be difficult to repair, occult injuries often lead to complications affecting the patient's comfort, continence, and/or sexual function for years.

46.1.3 Instruments, Surgical Techniques, and Timing of Repair

Immediate repair of obstetric lacerations is most appropriate and frequently quite feasible in the delivery suite. Delivery rooms should be equipped with adequate lighting, instruments, and supplies to evaluate and repair most lacerations. Some vaginal surgeons use a Heaney curved needle driver to allow separation and triangulation of their hands during vaginal repair where space is limited.

Repair instruments and supplies for uncomplicated vaginal repair:

- Light mounted on a flexible arm
- Long Graves speculum
- Two ring forceps
- 9-inch needle driver
- 9-inch Russian or toothed forceps
- Suture scissors
- Gauze/lap sponges
- 3–0 polygalactin suture on an SH needle
- 2–0 polygalactin suture on a CT-1 needle
- 2–0 polydiazanone suture on a CT-2 needle for sphincter repair

Once a thorough exam has identified all lesions needing repair, the surgeon begins at the most proximal lesion (the cervix or vaginal apex) and works towards herself. If necessary, local analgesia can be delivered through a single entry point in the open wound in a fan-like distribution. The addition of epinephrine can reduce bleeding through vasoconstriction. First- and second-degree lacerations are repaired by reapproximating the tissue layers. Most descriptions of this repair recommend using continuous suture from the apex of the vaginal laceration and then running it down to close the perineal body. We prefer the technique of interrupted figure-of-eight stitches in the perineum as it provides excellent tissue reapproximation with less chance of tearing out of the friable tissue. The final sutures to close the perineal body are sometimes called "crown stitches." The surgeon begins with the side opposite her dominant hand to allow for burying the knot. As the curved needle is passed through the tissue radially, it captures the rectracted fibers of the bulbocavernosus and transverse perineal muscles. The correct placement of these stitches can reconstruct a strong perineal body, but aggressive suturing here can entrap the deeper pubococcygeus muscle, leading to debilitating pain and dyspareunia. Careful attention to reapproximating the vaginal mucosa and reconstruction of the posterior fourchette with adequate tissue support to form a "right-angle shelf" as the vagina transitions to the perineum will provide adequate support and prevent the creation of a thin membrane of tissue at the posterior introitus. See Figure 46.2.

Third- and fourth-degree lacerations can be tricky, sometimes having noncontinuous lesions. Deep lacerations such as these require an intentional multilayered strategy to adequately separate the anal and vaginal mucosa and reconstruct the anal sphincter complex and intervening layers. In addition to a systematic exam, Dr. Robert Barbieri advocates for a standard checklist to optimize outcomes (8):

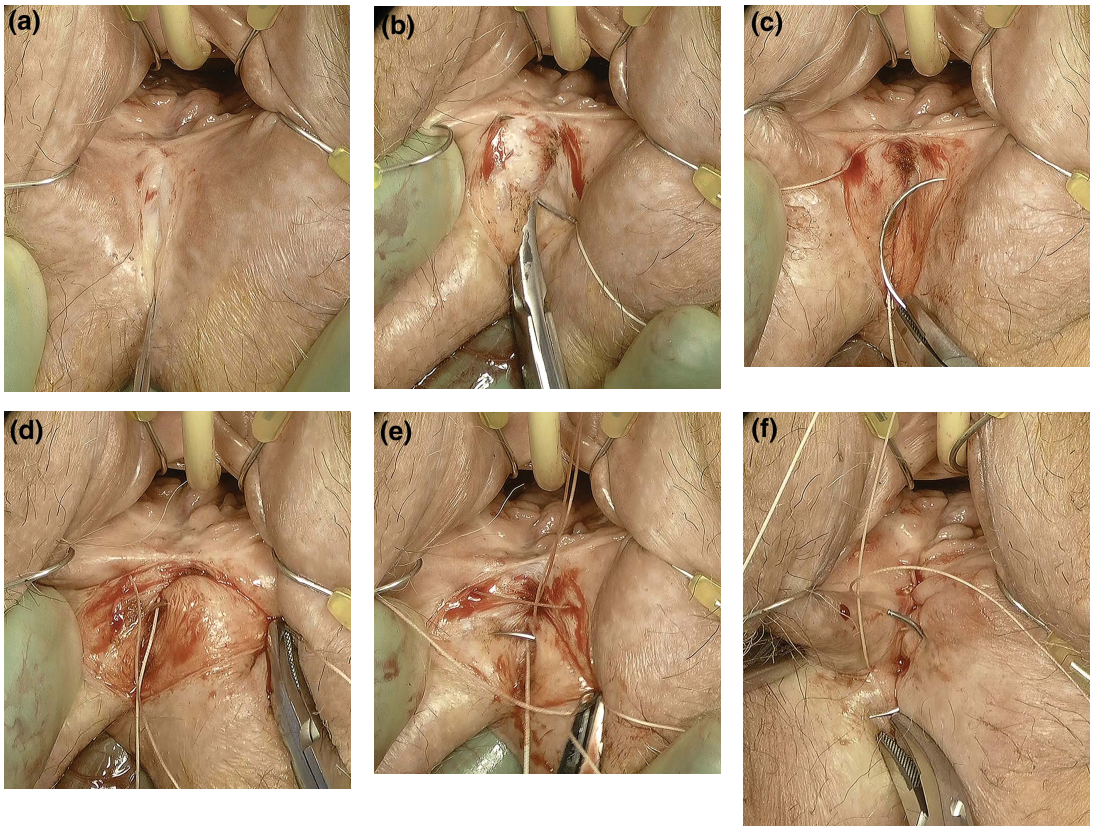


FIGURE 46.2 (a) Perineal repair without lengthening the perineal body involves a midline incision; (b) "crown" stitches are placed to capture the bulbocavernosus and transverse perineal muscles; (c) position the needle vertically and then (d, e) rotate inward to bury the knot; (f) finish with subcuticular closure.

1. Identify the clinician(s) best suited to do the repair. *It can be difficult for junior trainees to ask for assistance on a busy labor unit and thus they are often left repairing lacerations alone. An environment of collegiality allows more experienced obstetricians to assist and train others.*
2. Consider moving the patient from a labor and delivery room to an operating room.
3. Consider administering pre-repair prophylactic antibiotics.
4. Obtain excellent exposure. *Consider arranging for a surgical technician to assist with all deep obstetric repairs.*
5. Define the extent of the perineal laceration with digital rectal exam.
6. Identify the apex of the laceration. *Begin the repair 1 cm above the apex of the laceration to assist with visualization and accuracy. Maintain visualization by holding the apical suture in the mucosa until the lower layers have been closed.*
7. Repair the rectal mucosa with 4–0 polydioxanone or poliglecaprone (Monocryl) suture on a tapered needle.
8. Repair the IAS with a 3–0 suture on a tapered needle. *The internal sphincter is sometimes a light gray color and may be retracted laterally. Well-placed sutures through the thickness of the internal sphincter and sparing the rectal mucosa will best ensure continence. End-to-end repair is appropriate for the IAS.*
9. Repair the EAS with a 2–0 polydioxanone suture using either an end-to-end (preferred) or overlapping technique (if there is limited tissue mobility) (6, 9, 10). *An Allis clamp can be used to grasp the retracted fibers of the EAS on each side. With a finger in the rectum, the two Allis clamps can then be crossed in the midline to confirm compression of the finger, simulating an intact sphincter. Four interrupted sutures placed at 3, 6, 12, and 9 o'clock positions, holding each with a hemostat, allows for burying of the knots and good visualization until each suture is tied in the same order as was placed. End-to-end repairs require 1–1.5 cm of muscle on either end to provide sufficient overlap and, while preferred, should not be attempted without adequate tissue mobility* (Figure 46.3) (1, 2, 9, 10).
10. Fellowship-trained reconstructive pelvic surgeons (urogynecologists) have the most experience and training in repairing these types of injuries (9).
10. Repair the remaining laceration as a typical second-degree injury.
11. Identify the patient as a "high-risk" postpartum patient who warrants extra attention. *Additional administration of antibiotics has not been well-studied for OASIS, but patients receiving antibiotics for other indications have demonstrated lower rates of wound complication after OASIS, suggesting they are beneficial. Episiotomy and OASIS are independent risk factors for postpartum*

voiding dysfunction, discernible by a retrograde voiding trial prior to discharge (2). *Pelvic floor physical therapy, starting as soon as 2 weeks postpartum, enhances the recovery and reduces pelvic floor symptoms following OASIS* (11).

12. Schedule an early return clinical visit to examine the healing process. *Implement an instrument count, as with any other surgical procedure, to prevent retained sponges which can be an avoidable source of infection. The relatively high rate of wound breakdown (25%) or infection (20%) following OASIS repair warrants scheduled visits at 1, 2, and 6 weeks postpartum and an expectation for increased need for pain medications and stool softeners* (1).
13. Assess long-term clinical outcomes. Be mindful of the stages of repair and the various functional demands for the patient. Initially, the focus is on tissue integrity, a closed wound, and infectious precautions. Mild to moderate dyschezia and perineal discomfort is expected for about 3–4 weeks. Women may not participate in sexual activity during the postoperative period and so dyspareunia may go unmanaged for months or years. Providers are encouraged to monitor for full restoration of all functions 3–6 months following the repair.

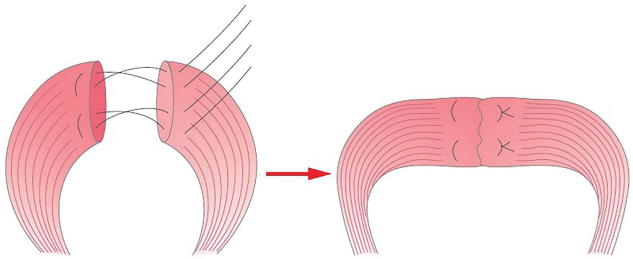


FIGURE 46.3A Diagrammatic illustration demonstrating conventional end-to-end approximation of the disrupted anal sphincter with two figure-of-eight sutures (1).

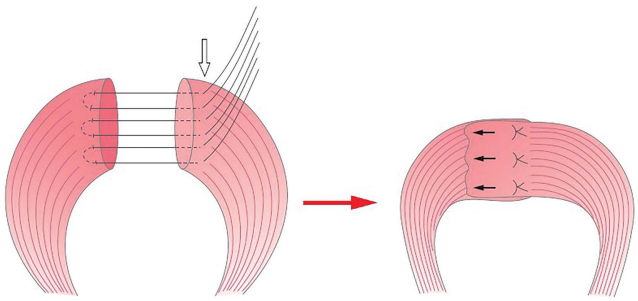


FIGURE 46.3B The technique of overlap repair of the external anal sphincter. The first suture is inserted about 1.5 cm from the torn edge of the muscle (open arrow) and carried through to within 0.5 cm of the edge of the other arm of the external sphincter. A second row of sutures (small arrows) is inserted to attach the loose end of the overlapped muscle (From Cardozo L et al. *Textbook of Female Urology and Urogynaecology*, 2nd edn. Boca Raton, FL: CRC Press; 2006:78.3, 78.9 with permission).

46.2 Obstetrical Uterine Lacerations

Elective cesarean section can reduce a patient's risk of vaginal obstetrical injury in the setting of fetal macrosomia or history of cephalopelvic disproportion. While most obstetric fistulas follow complicated vaginal delivery, cesarean section is not without risk of injury resulting in fistula formation.

A fistula is an abnormal connection between two adjacent epithelial surfaces as a result of trauma or inflammation. As the damaged epithelial cells heal, they migrate towards one another, creating an epithelial bridge between the two viscera. While the unique type of epithelial cell is retained in the adjacent organs (such as transitional cells in the bladder, squamous cells in the vagina, and goblet cells in the rectum), the bridging cells within the fistula are typically flat squamous cells accompanied by inflammatory cells, erythrocytes, and other cellular debris indicative of the harsh environment (12).

Cystotomy and hysterotomy extension are particularly prone to the morbid sequelae of fistula formation during urgent/emergent surgery due to fetal distress, maternal hemorrhage, and hemodynamic instability. An obstetrician's efforts to expedite delivery and close the uterus quickly can result in hysterotomy extension and suture entrapment of the bladder, respectively. Hysterotomy extension can involve the lower uterine segment, uterine vessels, cervix, bladder, and ureters.

46.2.1 Diagnosis and Anatomy

The accurate diagnosis of genitourinary fistulas following cesarean section can be quite tricky, depending on the timing of presentation, the availability of obstetrical history, and the particular symptoms. Classification of injuries with their associated symptoms and findings follow:

Vesicouterine Fistula

Definition – Connection between bladder and uterus
Symptoms – Constant leakage of watery fluid (urine) from vagina
Diagnosis – Test fluid with urinalysis to determine if it is urine. Retrograde filling of the bladder with methylene blue will demonstrate efflux of blue liquid through the cervix. Fluoroscopic cystourethrogram will identify the fistulous connection with classification of simple (single) or complex (multiple).
Repair – Vesicouterine fistula repair requires an abdominal approach to separate the bladder from the lower uterine segment (or cervix) and repair each serosa with an interposition graft. Laparoscopy and robotic surgery enhance visibility over laparotomy.

Ureterouterine Fistula

Definition – Connection between ureter and uterus
Symptoms – Constant leakage of watery fluid (urine) from vagina
Diagnosis – Test fluid with urinalysis to determine if it is urine. Retrograde filling of the bladder with methylene blue will demonstrate efflux of blue liquid through the cervix if there is an additional vesicouterine fistula but will not identify a ureterouterine fistula. Office identification of ureteral fistula requires the patient to take phenazopyridine at least 1 hour prior to the exam. Orange fluid will be seen from the fistulous opening. Fluoroscopic cystourethrogram will identify the

fistulous connection with classification of simple (single) or complex (multiple).

Repair – Ureterouterine fistula repair requires an abdominal approach to perform ureterolysis and reimplantation.

46.2.2 Prevention

Following every cesarean delivery, the obstetrician should perform a preliminary assessment of the hysterotomy to identify any obvious defects that impact closure. Immediate hysterotomy closure can promote uterine contraction and control blood loss. Once the first layer has been closed and bleeding is minimal, a more thorough inspection is advised by following the corners of the hysterotomy laterally and inferiorly. If a bladder flap was not performed or the bladder is in close proximity to the hysterotomy, then it should be dissected away from the fresh uterine closure. This will allow identification of any sutures in the bladder and minimize the adherence of the bladder over the uterine scar. Inadvertent incorporation of the bladder into the hysterotomy closure is one of the more common causes of obstetric fistula in the developing world.

Invasive placentation is becoming an increasing cause of maternal morbidity and mortality due to the high rate of repeat cesarean sections. Placental imaging has improved, however, allowing obstetrical teams to better predict abnormal placentation and thereby plan cesarean hysterectomy. Despite planning, these cases can be very difficult, leading to maternal hemorrhage and surgical rescue. The cardiovascular changes of pregnancy include vasodilation and more rapid development of coagulopathy following high blood loss. The uterine size and Pfannenstiel incision limits visualization of lateral structures, including the ureters. These factors and the pressure of operating quickly can lead to visceral injuries, delayed diagnosis, and fistula formation. As is the case for all surgical procedures, team-based simulation, surgical planning, open communication, and adequate visualization can all contribute to optimal outcomes for our patients.

46.3 Nonobstetric Genitourinary Fistulas

Nonobstetric urogenital fistulas (NOF) can be caused by pelvic trauma (e.g., motor vehicle accident, use of jet skis and rope swings), retained foreign object such as a pessary, sexual assault, pelvic infection (e.g., pelvic inflammatory disease, inflammatory bowel disease, diverticulitis), a medical procedure that is complicated by unrecognized injury to the urogenital tract or inadequate repair, wound breakdown, infection, hematoma, congenital malformation, and malignancy (i.e., in the setting of eroding tumor or pelvic radiation). The vast majority of NOFs in developed countries are due to hysterectomy for benign gynecologic conditions. While vaginal and laparoscopic hysterectomy report lower injury rates compared to laparotomy, this is likely due to less complicated anatomy such as smaller uteri. Except in the hands of master laparoscopic surgeons, laparoscopic hysterectomy results in a higher rate of undiagnosed urogenital injury compared to abdominal and vaginal approaches (13, 14). The urinary tract may be compromised with the use of diathermy, unrecognized cystotomy, or excessive dissection into the vesicovaginal space resulting in tissue devascularization, ischemia, necrosis, and ultimately fistula formation. Table 46.2 lists risk factors for NOFs.

TABLE 46.2 Operative and Patient Risk Factors for Nonobstetric Urogenital Fistulas

Body mass index > 30
Compromised tissue quality (e.g., due to diabetes mellitus, tobacco use, pelvic irradiation)
Intraoperative estimated blood loss > 1 L
Cystotomy involving bladder trigone
Large uterine size (e.g., due to fibroids, adenomyosis)
Pelvic adhesions (e.g., due to prior surgery, pelvic inflammatory disease, endometriosis, diverticulitis)
Laparoscopic approach for hysterectomy
Inflammatory bowel disease (e.g., Crohn's disease)

46.3.1 Diagnosis

While clinical presentation can be variable, the most common complaint for genitourinary fistulas is continuous wetness and odor or urinary incontinence without sensory awareness. Symptoms can also include hematuria, dysuria, suprapubic pain, vaginitis, and vulvar irritation. Fistulas involving the uterus can track into the uterine cavity or the cervix and present with cyclical hematuria or menouria (cyclic passage of urine) or endometritis. Timing of the onset of symptoms is also highly variable, between a few days, weeks (following abdominopelvic surgery), or years (following radiation). Severity of leakage may also vary depending on the size and location of the fistulous tract.

Fistula evaluation starts with a complete history and physical exam. History of intraoperative urinary tract injury with either immediate or delayed recognition, attempted repair, postoperative hematuria, or infection all raise suspicion for urogenital fistula. A thorough speculum exam commonly shows pooling of fluid in the vaginal canal. A defect in the vagina with or without inflammation or granulation tissue may be visualized at the same time, depending on its size and location. A double dye test using a tampon may be performed to isolate the defect and differentiate between bladder (vesicovaginal fistula) and ureteral (ureterovaginal fistula) involvement. For this, the bladder is backfilled with normal saline containing methylene blue dye, the patient is given oral phenazopyridine, and a tampon is placed in the vagina. A Foley catheter may be placed to prevent leakage per urethra and erroneous staining of the distal tampon. Catheter placement may also be beneficial for identifying urethrovaginal fistula if a catheter is visualized or palpated through the urethra. Blue staining of the tampon suggests vesicovaginal fistula whereas orange staining suggests ureterovaginal fistula, and staining with both colors suggests both bladder and ureteral involvement.

Cystourethroscopy, and sometimes vaginoscopy, is performed to further inspect the size, complexity, number, and location of the fistula, particularly its proximity to and involvement of the ureters and the bladder neck. Throughout these evaluations, the surrounding tissue is observed for inflammation, infection, necrosis, and other pathology such as malignancy, all of which should be addressed prior to proceeding with fistula repair. Prolonged bladder catheterization for at least 4 weeks allows for resolution of inflammation and edema, and antibiotics are provided in the setting of infectious cystitis. If malignancy is suspected, a biopsy should be performed at the time of the cystourethroscopy.

Several imaging modalities may be used to better characterize the site and course of the urogenital fistula and the involved organs, especially if physical exam or cystourethroscopy

are inconclusive, and to augment surgical planning. Up to 12% of vesicovaginal fistulas also involve ureters (15). Cystourethroscopy with retrograde pyelogram can isolate both ureteral and bladder fistulas. Voiding cystourethrogram can visualize both bladder and urethral fistulas, but not ureteral fistulas. Intravenous urography with computed tomography (CT) or magnetic resonance imaging (MRI) not only provides comprehensive assessment of the entire urinary tract but also the involved surrounding organs; however, it may be limited if the bladder is poorly distended and the fistula tract is very small (16). Tonolini describes several adjustments to CT urography protocols or additional acquisitions that can be made to identify the fistula tract (2). Lastly, hysterosalpingography is used for identifying vesicouterine fistula. In many cases, an exam under anesthesia offers the unique ability to blend direct visualization modalities (cystoscopy, vaginoscopy) in a setting safe and comfortable for the patient.

46.3.2 Anatomy and Classification

NOFs are classified as either simple or complex based on their size, location, number, and associated pathology (Table 46.3). Obstetrical fistula classification include: (1) urethrovaginal; (2) vesicovaginal involving trigone; (3) vesicovaginal; (4); vesicouterine; (5) vesicocervical; (6) ureterovaginal; (7) rectovaginal (Figure 46.4).

46.3.3 Prevention and Timing of Repair

Fastidious surgical technique in gynecologic surgery can dramatically reduce the risk of iatrogenic genitourinary fistula and their morbid sequalae. During hysterectomy, the bladder must be separated from its attachment to the anterior cervix and uterus. The accurate identification of tissue planes and balanced use of blunt and sharp dissection as well as electrocautery will contribute to injury-free completion of the bladder flap.

During vaginal hysterectomy, the anterior entry is typically the most feared and misunderstood portion of the case. The purpose of the anterior dissection is to separate the bladder from the underlying cervix and uterus by entering the vesicouterine space. In some cases, developing that space provides easy and early intraperitoneal access. However, multiple prior cesarean sections, cervical elongation, an anterior fibroid, or endometriosis can create scar tissue that limits peritoneal access and increases the risk of cystotomy. Contrary to conventional teaching, early and definitive entry into the peritoneal cavity through the vesicouterine space is not required to proceed with vaginal hysterectomy. Once the vesicouterine space is developed and the location of the ureters confirmed by digital palpation, the Deaver retractor can safely protect the bladder while securing the cervical and lower uterine pedicles, including the uterine vessels (see Figure 46.5a–c). Specialized techniques such as cervical amputation, bivalve of the uterus, and vaginal myomectomy can eliminate bulk to allow peritoneal visualization. One favorite technique is to pass a finger from the posterior colpotomy around the fundus of the uterus and into the vesicouterine space, thereby providing a safe target for anterior dissection (see Figure 46.5d and e).

Surgical techniques during hysterectomy to prevent bladder and ureteral injury include (1) appropriate positioning, (2) adequate exposure and lighting, (3) blunt dissection between planes and sharp dissection to enter a space, (4) constant awareness of the course of the ureter, (5) maintaining hemostasis, (6) avoidance of large pedicles, (7) continuous bladder drainage, (8) judicious use of electrocautery, and (9) universal cystoscopy (3). In addition, backfilling the bladder with sterile milk and using indocyanine green to delineate the ureters is helpful. Sterile milk allows identification of the bladder wall as well as helps to diagnose and confirm closure of a cystotomy without staining the nearby tissue, as methylene blue does. Once stained, it is difficult to reassess the watertight seal of a cystorrhaphy.

The identification and separation of the urinary tract from the surgical field will prevent most injuries that can lead to fistula formation. If such injury does occur, then repair should be performed immediately by the most-skilled individual available. Bladder injuries require a multilayered, tension-free closure with nonoverlapping suture lines (Figure 46.6).

An interposition graft of peritoneum or omentum can be used to reduce the likelihood of fistula formation, especially in cases with a nearby healing epithelial surface, such as the vagina or ureter.

Injuries of any size at the bladder base or those > 1 cm at the dome require prolonged catheterization with either Foley or suprapubic tube for 7–14 days. Confirmation of healing with fluoroscopic cystourethrogram is recommended prior to removal of the catheter. Injuries < 1 cm at the dome do not require prolonged catheterization. Ureteral injuries may require ureteral reimplantation to ensure a tension-free repair, especially in the setting of electrocautery-induced injury necessitating removal of nonviable tissue. Ureteral stents are used to promote urine drainage and prevent ureteral stricture formation.

Exam under anesthesia following pelvic trauma is essential to accurately identify and repair all injuries. Most emergency rooms have inadequate positioning, lighting, supplies,

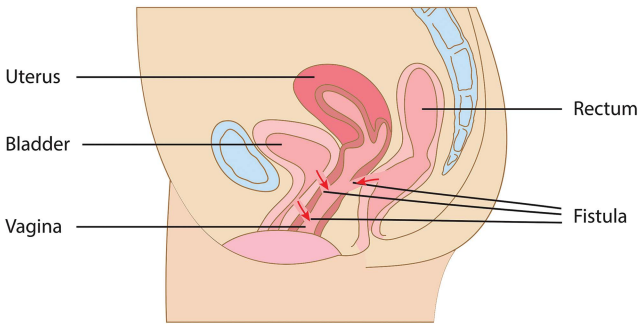


FIGURE 46.4 Rectovaginal, Vesicovaginal and Urethrovaginal fistulas are shown with arrows.

TABLE 46.3 Classification of Urogenital Fistulas

Simple fistula	Complex fistula
Less than 0.5 cm in size	Greater than 3 cm in size
Simple (single) tract	Multiple tracts
Supratrigonal location	Trigone involvement
First attempt to repair	Prior failed repair(s)
Healthy tissue	Poor surrounding tissue
	Involvement of ureter(s), bladder neck, urethra, and/or bowel
	History of pelvic radiation and malignancy

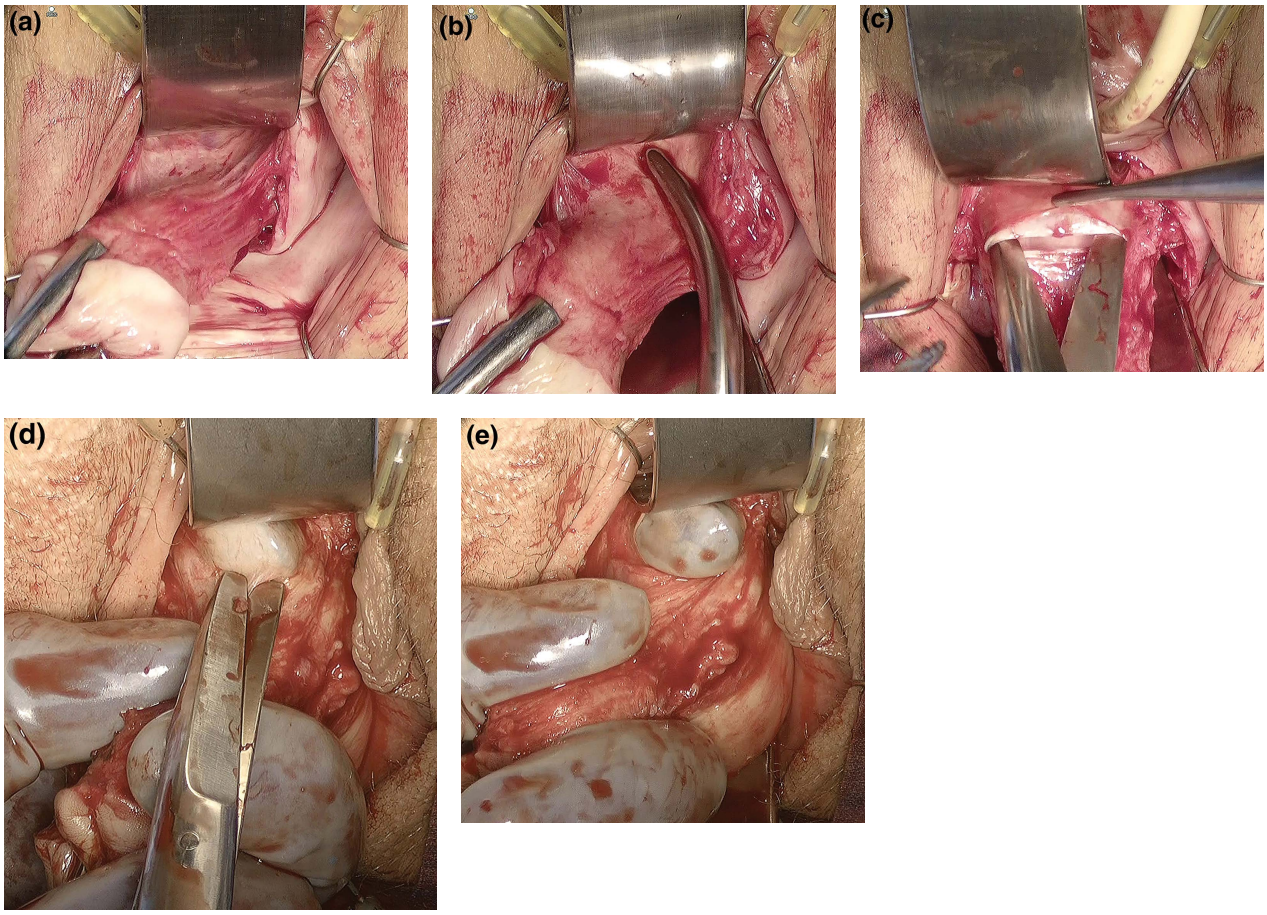


FIGURE 46.5 (a) Placement of Deaver retractor into the vesicouterine space without intraperitoneal access; (b) the Deaver protects the bladder from clamp placement; (c) at this point, the peritoneum is easily identified and opened; (d) in the setting of a small uterus, grasp the uterine corpus and pass the index finger through the posterior colpotomy into the vesicouterine space to delineate the anterior peritoneum; (e) cutting the peritoneum overlying the index finger opens the space for the Deaver retractor.

and analgesia for thorough gynecologic exams following trauma. A standard metal speculum can sometimes obscure a lesion and so the use of Breisky–Navratil (also called spade) retractors can facilitate visualization and access for vaginal repair.

46.3.4 Management

Conservative treatment can be considered for patients with simple fistulas, who are poor surgical candidates, and who desire a less invasive intervention (4). This usually involves prolonged bladder catheterization (at least 4 weeks), which may resolve 10%–15% of simple fistulas that are diagnosed early and have not yet epithelialized. Fibrin glue, bovine collagen, and platelet-rich plasma has also been described as sealants for urogenital injuries and small fistulas to promote fibrosis and neovascularization (17–19). These agents can be applied if the tract has not been epithelialized or after de-epithelializing or fulgurating it, as long as this does not result in a larger defect (> 1 cm). This is then followed by prolonged catheterization.

Ureterovaginal fistulas are predominantly managed with prolonged stenting (at least 3 months), with 90%–100% resolution by 8 to 12 weeks, which should be confirmed with retrograde pyelogram prior to stent removal. These patients may experience urinary tract infection, stone formation, and stricture formation.

Considerations for surgical approach include fistula complexity, location, tissue quality, tissue mobility or rigidity, and access. A narrow vaginal introitus or a long canal with minimal descent or mobility can make a transvaginal approach more challenging, requiring a transabdominal approach (ideally either laparoscopic or robotic). No single approach or technique is considered superior; however, the transvaginal approach is generally associated with lower morbidity, shorter operating time, decreased blood loss, decreased postoperative pain, and shorter hospital stay compared to the transabdominal route. Vaginal approach avoids abdominal and bladder incisions and intraperitoneal entry. Fistula repair may be early or delayed, which is largely dependent on tissue quality, surgeon experience, and available resources. Surgery need not be delayed if there is no infection, inflammation, or necrosis. We recommend consenting patients for both vaginal and abdominal repairs, as findings at the time of exam under anesthesia may alter one's surgical approach.

Leading up to surgery, patients are instructed on perineal care and zinc oxide barrier cream application. They may also be fitted with a vaginal diaphragm connected to a urinary

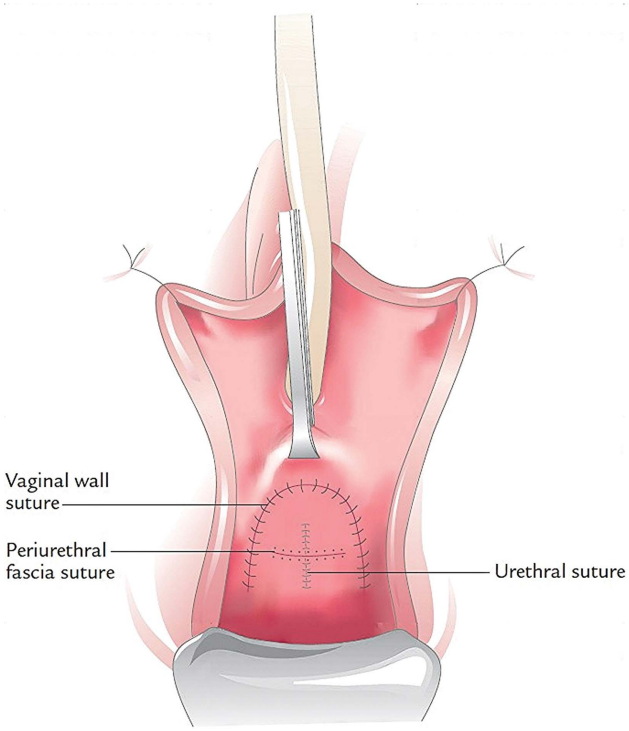


FIGURE 46.6 The vaginal wall flap is closed, resulting in a three-layer closure with no overlapping suture lines (From Cardozo L et al. *Textbook of Female Urology and Urogynaecology*, 2nd edn. Boca Raton, FL: CRC Press; 2006:90.20 with permission).

TABLE 46.4 Principles of Vesicovaginal Fistula Repair

Adequate tissue mobilization
Hemostasis
Multiple nonoverlapping layers
Tension-free closure with absorbable sutures
Watertight closure
Adequate blood supply
Postoperative continuous bladder drainage
Postoperative medical management of bladder spasms

catheter to ameliorate vulvar and perineal dermatitis from constant urinary leakage.

46.3.5 Surgical Techniques

Primary repair of a urogenital fistula, regardless of approach, is generally 90%–100% successful as long as basic principles listed in Table 46.4 are properly applied. Factors contributing to failure include surgeon's lack of experience, poor tissue quality (such as due to radiation), very large defect limiting mobilization of surrounding tissue, and patient's poor health status.

46.3.6 Vesicovaginal Fistula – Vaginal Approach

Vesicovaginal fistula (VVF) repair is initiated with a thorough pelvic exam under anesthesia and cystourethroscopy. Dorsal lithotomy position with steep Trendelenburg provides excellent visualization of the vaginal canal. If the fistula is within 1 cm of one or both ureteral orifices, ureteral stenting is performed. Foley catheter is placed in the urethra. A self-retaining ring retractor with hooks is placed to aid with visualization. To help with the identification of the fistula on the vaginal side, the bladder can be backfilled with saline containing methylene blue. Fistula may also be stented or catheterized to isolate the tract. Stay sutures are placed around the tract to assist with visualization and traction of the fistula. For vesicovaginal fistula repair, we usually use 2–0 or 3–0 delayed absorbable suture such as polyglactin 910 with CT-2 or UR-6 needle.

In the traditional Latzko technique, a circumferential incision is made encompassing the fistula orifice. Surrounding epithelial edges and underlying pubocervical fascia are then mobilized for 2.5 cm. The fistula tract is not excised or denuded or closed on the bladder side. The fascial layer, followed by the epithelium, is then closed using delayed absorbable suture in interrupted fashion.

Another technique is to excise the tract in its entirety if small or denude it until fresh tissue is revealed if large. However, there is no consensus whether this is essential for the success of the repair, and care must be taken to avoid significantly enlarging the defect. Surrounding layers are mobilized, and the defect is closed in multiple layers (bladder mucosa, bladder muscularis, pubocervical fascia, and vaginal epithelium) using interrupted delayed absorbable suture. If the bladder mucosa is not closed, then pubocervical fascia is used to imbricate the suture line. The bladder is backfilled with saline containing methylene blue to confirm watertight closure prior to epithelial closure, and additional interrupted sutures can be placed at the sites of dye extravasation. An interposing flap of fat overlying the bulbocavernosus (Martius flap) can be placed at this time, and the vaginal epithelium is closed.

46.3.7 Urethrovaginal Fistula

The same principles apply to urethrovaginal fistula (UVF) repair as VVF repair; however, the fistula tract is unlikely to be excised completely in order to avoid enlarging the defect and thus forming urethral stricture. The repair is performed over a Foley catheter. The surrounding periurethral tissue and vaginal epithelium are mobilized laterally toward bilateral descending pubic rami to allow for tension-free closure. In the setting of UVFs caused by mesh erosion, successful repair relies on excision of surrounding mesh. The defect is closed in multiple nonoverlapping layers and a watertight closure can be assessed by using a double balloon Trattner catheter or a deflated Foley catheter with the tip retracted into the urethra. An interposing flap of Martius graft can be placed at this time. The vaginal epithelium is then closed (Figure 46.7).

Repair of proximal UVFs may compromise the external urethral sphincter and thus the continence mechanism. In this scenario, an autologous fascial sling may be performed at the time of fistula repair and provides an additional layer of closure. We usually prefer a staged approach to allow for complete healing and vascularization and postoperative assessment of stress urinary incontinence. In this case, synthetic mesh sling can be considered, unless the source UVF was in the setting of mesh complication.

46.3.8 Vesicovaginal Fistula – Abdominal Approach

VVFs that are difficult to access vaginally, those involving the uterus, cervix, and/or ureter(s), and those that have failed prior transvaginal approach can be approached via laparotomy or laparoscopy, depending on the surgeon's skill set.

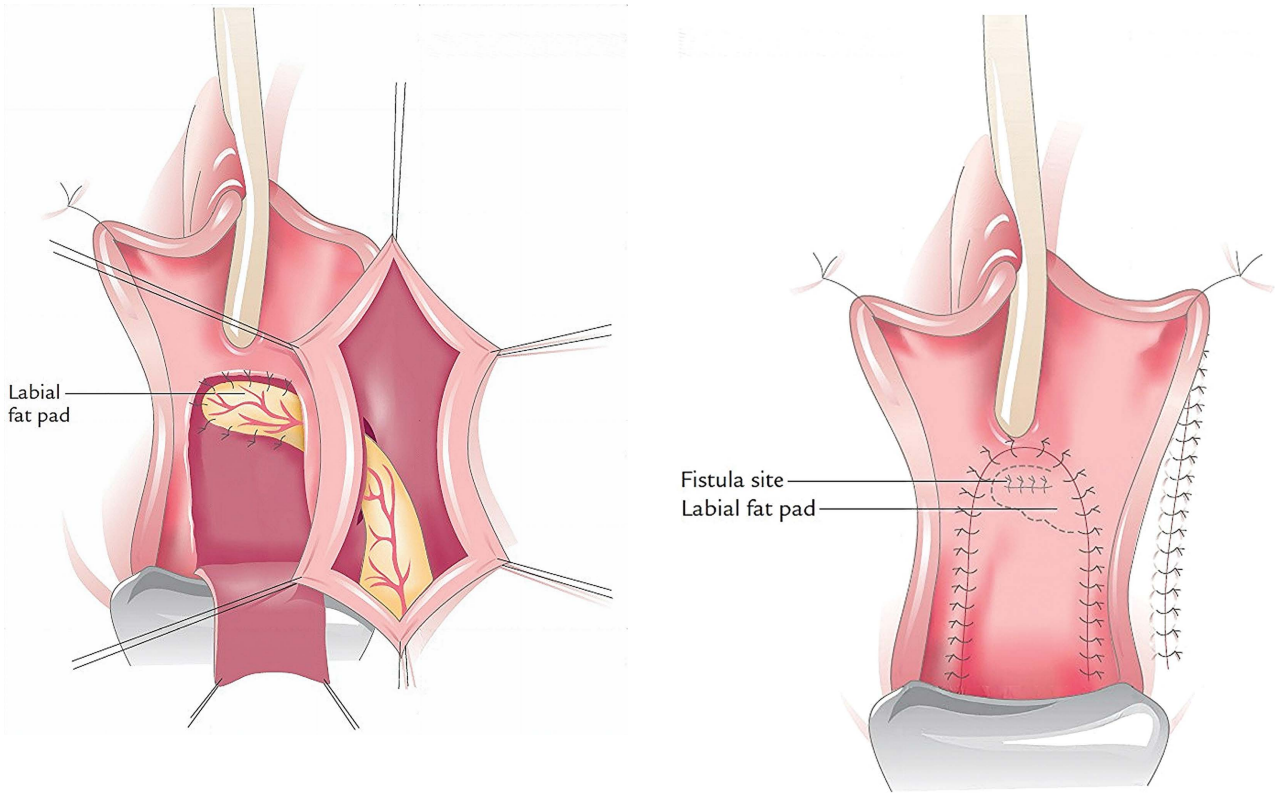


FIGURE 46.7 The labial fat pad is passed through a medial tunnel and secured over the fistula repair site. The vaginal wall flap is advanced over the fat-pad graft, resulting in closure with no overlapping suture lines (From Cardozo L et al. *Textbook of Female Urology and Urogynaecology*, 2nd edn. Boca Raton, FL: CRC Press; 2006:90.28 and 90.29, with permission).

Either midline vertical or transverse skin incision can be used for the open abdominal technique. The fistula tract is stented or catheterized vaginally or cystoscopically to delineate the fistula. Ureters are stented if the ureteral orifices are within 1 cm of the fistula tract. Once the abdominal cavity is entered and the bowel packed cephalad, self-retaining retractors are secured for visualization. The O'Conor technique describes "bivalving" the bladder to create a cystotomy that is then extended to the level of the fistula, at which point a circumferential incision is made to excise the tract. The vesicovaginal space is dissected to divide the defect and close the vagina and the bladder separately. A section of the omentum (or peritoneum) approximately 1 cm larger than the closed fistula can be mobilized and secured between the vagina and bladder at this time. An omental flap with retained blood flow will optimize healing, whereas a peritoneal flap simply provides a thin epithelial barrier to discourage fistula reformation. The modified O'Conor technique involves creation of a high cystotomy in the extraperitoneal portion of the bladder in order to visualize the fistula tract through the bladder dome without extending the cystotomy to the level of the fistula. The fistula tract is then circumferentially excised and the layers are mobilized and closed separately.

Alternatively, a VVF can be repaired without an intentional cystotomy. The vesicovaginal space is dissected until the fistula tract is encountered (usually with the help of a stent or catheter inserted into the tract). It is helpful to insert a vaginal retractor, such as a Breisky or EEA sizer, in the vagina to maintain the correct plane during this dissection. At this point, the tract is circumferentially excised. The bladder is closed longitudinally and the vagina transversely to create nonoverlapping suture lines, both using polyglactin 910 interrupted suture. An omental or peritoneal flap can be secured between the vagina and bladder at this time.

The same techniques can be performed laparoscopically or robotically in the hands of an experienced surgeon, with the advantages of decreased blood loss, pain, and hospital admission. The patient is placed in the dorsal lithotomy position in steep Trendelenburg. The laparoscopic or robotic ports may be placed lower on the abdominal wall to allow for adequate access to the vesicovaginal plane and the bladder.

46.3.9 Vesicouterine and Vesicocervical Fistula Repairs

Patients electing for conservative management of vesicouterine or vesicocervical fistula or those who are not surgical candidates can be offered prolonged bladder catheterization, hormonal menstrual suppression, and antimicrobial therapy to decrease inflammation when small and diagnosed early in the postpartum or postoperative period. Only 5% of such cases may resolve after 4–8 weeks of conservative therapy, while the majority are successfully treated surgically (20, 21). Traditionally, abdominal hysterectomy has been performed as part of vesicouterine or vesicocervical fistula repair. However, recently laparoscopic and robotic approaches have allowed for a uterine-sparing option (22, 23). The techniques for transabdominal VVF repair can be applied to vesicouterine and vesicocervical fistula repairs, with dissection into the vesicovaginal

space, excision of the fistula tract, mobilization of surrounding tissue, and separate closure on the uterine and bladder layers. A transvaginal uterine-sparing approach has also been described (24). In this technique, a transverse colpotomy is made on the anterior vagina similar to the start of a vaginal hysterectomy case. The vesicouterine space is carefully dissected to completely separate the uterus and the bladder. The authors describe the use of Hegar dilators to isolate the fistula openings on each side, but cystoscopic stenting at the beginning of the case could also be considered. The fistula tract is excised or fulgurated on each side and closed in several layers, followed by closure of the vaginal epithelium.

46.3.10 Flaps and Sealants

The use of transposition flaps is recommended for repairs in which tissue is compromised, layers are thin, or closure is in tension. Martius flap using the labial fat pad is ideal for the transvaginal approach to vesicovaginal fistula and urethrovaginal fistula repairs. Omental J flap or peritoneal flap is utilized for the transabdominal approach. The use of interposing layer of fibrin glue has recently been described in a study of 40 patients allocated to either omental flap or fibrin glue placed at the time of their laparoscopic vesicovaginal fistula repair. There were no cases of fistula recurrence at 3 months in the fibrin glue group (18).

46.3.11 Postoperative Care

Following urogenital fistula repair, transurethral 16 French Foley catheter should remain in place for 2 to 4 weeks, depending on fistula size and surgical complexity. An anticholinergic medication can be offered if the patient experiences bladder irritation and bothersome spasms from the catheter. We recommend performing a cystourethrogram to confirm resolution of the fistula prior to catheter removal.

46.4 Nonobstetric Rectovaginal Fistula

Similar to genitourinary fistulas, those involving the bowel are most commonly caused by tissue trauma or inflammation. Rectovaginal fistulas are classified by their location, connecting viscera, size (small < 0.5 cm, medium 0.05–2.5 cm, large > 2.5 cm) and complexity (large, high, or caused by inflammatory bowel disease, diverticulitis, or irradiation). Common causes of rectovaginal fistula are listed in Table 46.5.

46.4.1 Enterovaginal and Colovaginal Fistula

An enterovaginal fistula involves the small intestines and usually the upper portion of the vagina. An enterovaginal fistula can occur as a result of simultaneous denudation or inflammation of the serosa overlying the small intestines and the vagina. The raw surfaces of the adjacent organs fuse during healing and reperitonealize, forming the fistula. Spontaneous enterovaginal fistula is extremely rare, although the inflammation associated with ulcerative colitis, prior pouch procedures, or intestinal tumors contribute (25). Iatrogenic causes of enterovaginal fistula include aggressive lysis of adhesions during complete (uterus and cervix) hysterectomy, pelvic radiation, and a peritoneal dialysis catheter (26, 27).

A colovaginal fistula describes the abnormal communication between the lower portion of the sigmoid colon and the vaginal apex. These fistulae are almost always attributed to perforated diverticulitis, although the acute infection may be subclinical, presenting only once the fistula tract has matured. Other risk factors include concomitant hysterectomy or sacral colpopexy and sigmoid resection rectopexy (28, 29). Essentially, any time two adjacent surfaces are opened, the epithelial surfaces can re epithelialize in such a way to abnormally connect the two adjacent viscera. While the use of synthetic mesh during resection rectopexy does not appear to increase the risk of fistula formation, surgical prudence is strongly advised due to the high morbidity associated with these types of injury (30).

TABLE 46.5 Nonobstetric Causes of Rectovaginal Fistula

Prior surgery or nonsurgical trauma
Inflammatory bowel disease
Infection (diverticulitis, cryptoglandular disease)
Tumor (benign or malignant)
Prior radiation
Prolonged retention of a foreign body

46.4.2 Rectovaginal Fistula

A rectovaginal fistula develops when the rectal (or anal) and vaginal mucosa experience simultaneous injury or inflammation, as previously described during a fourth-degree obstetric laceration. Nonobstetric rectovaginal fistulas are most commonly associated with Crohn's disease with lower incidences related to pelvic radiation, malignancy, and surgical complications (31). Retained foreign body is not a common cause of rectovaginal fistula but has been seen in the setting of a forgotten vaginal pessary used for pelvic organ prolapse.

46.4.3 Diagnosis and Classification

Patients with rectovaginal fistulae may present with a wide variety of symptoms, depending on the size, location, and cause of the fistula. Obvious passage of stool can signal fistula but can also represent anal incontinence with an intact rectovaginal septum. Less obvious symptoms such as recurrent UTI, mild fecal or mucus staining, and vulvar irritation require an astute clinician. As with other types of fistulae, a careful exam is critical for surgical planning. A very small fistula can be difficult to identify as the ostium may be obscured by vaginal rugae, and a distal fistula can hide in the folds of the posterior fourchette. An office-based exam can make use of the patient's mobility to fill the vagina with warm water and insufflate the rectum in various positions (lithotomy or knee–chest) to look for bubbles traveling through the fistulous tract (31). Utilization of an exam under anesthesia is encouraged whenever necessary to permit comprehensive multimodal assessment with cystoscopy, vaginoscopy, anoscopy, and either water or dye testing. Especially in the setting of a regional insult (inflammation or radiation), multiple fistula sites should be excluded during the evaluation. Fistulas are classified as complex if they are large (> 2.5 cm), high (near the vaginal apex), or caused by an inflammatory process (including irradiation). In contrast, fistulae resulting from surgical trauma are best prevented by avoiding simultaneous instrumentation of the rectum and vagina such as concomitant vaginal repair of a rectocele and a transanal Altemeier resection of anal prolapse.

46.4.4 Surgical Repair

Thoughtful and strategic management of rectovaginal fistula contributes greatly to successful resolution. Some small and mild fistulas may resolve spontaneously without intervention. In the setting of infection or local inflammation, antibiotic therapy

will reduce bacterial load and prepare the tissue for surgical manipulation. The surgical principles in fistula repair include:

1. Adequate exposure and hemostasis
2. Tissue mobilization with good blood supply
3. Complete removal of the fistulous tract
4. Multilayered closure with nonoverlapping suture lines
5. Independent and tension-free closure of each epithelial surface

Optional strategies may include colonic diversion and use of an interposition or advancement flap. Active inflammatory bowel disease should be managed medically prior to fistula repair, and persistent disease merits consideration of colectomy and/or proctectomy.

A low rectovaginal fistula can usually be repaired transperineally without the need for stool diversion. A posterior vaginal advancement flap is made by undermining the vaginal mucosa to provide a new, pristine epithelial surface. The base of the advancement flap should be at least 1–2 cm to provide adequate blood perfusion for healing. This is not usually possible in the setting of pelvic irradiation due to the absence of tissue laxity.

High rectovaginal fistulae usually require colonic diversion for a minimum of 3 months to achieve adequate healing. Open, laparoscopic, or robotic approaches should have similar success rates, and the surgical approach is selected to optimize visualization and minimize complications. High fistulae can be a result of an inflammatory process (Crohn's disease or diverticulitis) or pelvic irradiation, and the poor tissue quality frequently demands a vascularized interposition graft. The abdominal omentum usually provides adequate thickness and length to be used as an interposition graft. In the absence of a robust omentum, a variety of tissue transfers can be used (peritoneum, gracilis or Martius flap). In the setting of a rectovaginal fistula, the Martius flap is mobilized away from the ventral blood supply, leaving the dorsal pedicle to enable healing of the fistula repair.

46.5 Conclusion

Obstetric lacerations and genitourinary fistula contribute greatly to maternal and gynecologic morbidity. Prevention of injury is paramount whenever possible. Close partnership between the patient and surgeon is critical to discovering the cause and extent of the injury or fistulous process.

Because repeated attempts at obstetrical laceration and fistula repair are associated with diminishing success, fastidious attention to surgical principles is critical.

References

1. Committee on Practice Bulletins-Obstetrics. ACOG practice bulletin 198: prevention and management of obstetric lacerations at vaginal delivery. *Obstet Gynecol*. 2018;132(3):e87–102.
2. Meister MR et al. Techniques for repair of obstetric anal sphincter injuries. *Obstet Gynecol Surv*. 2018;73(1):33–39.
3. Jiang H et al. Selective versus routine use of episiotomy for vaginal birth. *Cochrane Database Syst Rev*. 2017;2(2):CD000081.
4. Morgan R et al. Classification and evaluation of episiotomy practices from 2004 to 2020 and association with OASIS. *Int J Gynaecol Obstet*. 2022;159(1):237–245.
5. Darmody E et al. Women's experience of obstetric anal sphincter injury following childbirth: an integrated review. *Midwifery*. 2020;91:102820.
6. Ali M et al. Risk factors for obstetric anal sphincter injuries among women delivering at a tertiary hospital in Southwestern Uganda. *Obstet Gynecol Int*. 2020;2020:6035974.
7. Bihon AM et al. Survival modeling on the determinants of time to recovery from obstetric fistula: the case of Mekelle Hamlin Fistula Center, ethiopia. *Int J Reprod Med*. 2022;2022:8313575.
8. Barbier R. Develop and use a checklist for 3rd- and 4th-degree perineal lacerations. *OBG Manag*. 2013;25(8):8–11.
9. Abramov Y et al. Primary repair of advanced obstetric anal sphincter tears: should it be performed by the overlapping sphincteroplasty technique? *Int Urogynecology J*. 2008;19(8):1071–1074.
10. Mongardini FM et al. Short- and long-term outcomes of sphincteroplasty for anal incontinence related to obstetric injury: a systematic review. *Updat Surg*. 2023;75(6):1423–1430.
11. Von Bargen E et al. Evaluation of postpartum pelvic floor physical therapy on obstetrical anal sphincter injury: a randomized controlled trial. *Female Pelvic Med Reconstr Surg*. 2021;27(5):315–321.
12. Siegmund B et al. Results of the fifth scientific workshop of the ECCO (II): pathophysiology of perianal fistulizing disease. *J Crohns Colitis*. 2016;10(4):377–386.
13. Chang EJ et al. Vesicoureteral injury during benign hysterectomy: minimally invasive laparoscopic surgery versus laparotomy. *J Minim Invasive Gynecol*. 2020;27(6):1354–1362.
14. Dallas KB et al. Urologic injury and fistula after hysterectomy for benign indications. *Obstet Gynecol*. 2019;134(2):241–249.
15. Smayra T et al. Vesicouterine fistulas: imaging findings in three cases. *Am J Roentgenol*. 2005;184(1):139–142.
16. Tonolini M. Elucidating vaginal fistulas on CT and MRI. *Insights Imaging*. 2019;10(1):123.
17. Shirvan MK et al. A novel method for iatrogenic vesicovaginal fistula treatment: autologous platelet rich plasma injection and platelet rich fibrin glue interposition. *J Urol*. 2013;189(6):2125–2129.
18. Evans LA et al. Fibrin sealant for the management of genitourinary injuries, fistulas and surgical complications. *J Urol*. 2003;169(4):1360–1362.
19. Shekarriz B et al. The use of fibrin sealant in urology. *J Urol*. 2002;167(3):1218–1225.
20. Porcaro AB et al. Vesicouterine fistulas following cesarean section: report on a case, review and update of the literature. *Int Urol Nephrol*. 2002;34(3):335–344.
21. Rahmita MM et al. Rare cases of vesicouterine fistula. *LUTS Low Urin Tract Symptoms*. 2022;14(5):401–404.
22. Govorov IE et al. Robotic repair of the symptomatic vesicouterine fistula. *Int Urogynecology J*. 2021;32(7):1945–1947.
23. Baker BV et al. Vesicouterine fistula: a robotic approach. *Int Urogynecology J*. 2022;33(6):1685–1687.
24. Milani R et al. Repair of a vesicouterine fistula following cesarean section. *Int Urogynecology J*. 2018;29(2):309–311.
25. Drefs M et al. Predictors of outcome for treatment of enterovaginal fistula: therapeutical strategies for treatment. *Int J Colorectal Dis*. 2023;38(1):187.
26. Harrison RF et al. Repair of vagino-peritoneal fistula caused by vaginal cuff fixation of peritoneal dialysis catheter: a case report. *Perit Dial Int*. 2015;35(3):363–365.
27. Berger MB et al. Colovaginal fistulas – presentation, evaluation and management. *Female Pelvic Med Reconstr Surg*. 2016;22(5):355–358.
28. VanderPas Lamb S et al. Safety of combined abdominal sacral colpopexy and sigmoid resection with suture rectopexy: a retrospective cohort study. *Female Pelvic Med Reconstr Surg*. 2015;21(1):18–24.
29. Adeyemo D. Mesh fistulation into the rectum after laparoscopic ventral mesh rectopexy. *Int J Surg Case Rep*. 2014;5(3):152–154.
30. Wen Y et al. Evaluating surgical management and outcomes of colovaginal fistulas. *Am J Surg*. 2017;213(3):553–557.
31. Das B et al. Rectovaginal fistulae. *Clin Colon Rectal Surg*. 2016;29(1):50–56.

47 URETHRAL DIVERTICULA AND VAGINAL CYSTS

K. Marie Douglass and Tajnoos Yazdany

47.1 Introduction

Urethral and vaginal masses can be difficult to characterize based on symptoms alone. Patients may present with pain, infection, or symptoms of voiding dysfunction. Given that history may fail to elucidate the exact cause of a patient's symptoms, a thorough physical exam and often imaging of the lower urinary tract are key to differentiating and diagnosing any urethral or vaginal mass. This chapter will review several different masses of the vaginal and urethral spaces, including their etiology, incidence, and presentation, and will outline the diagnosis and management of such masses.

47.2 Urethral Masses

47.2.1 Urethral Diverticula

47.2.1.1 Incidence and Etiology

Urethral diverticula are cystic outpouchings of the urethra into the periurethral space. They are most often located posteriolaterally in the mid- to distal urethra (1).

The true incidence of urethral diverticula is unknown; quoted incidence rates range from one to six percent (1, 2). Of the suburethral masses, urethral diverticula are thought to be the most common, representing 84% of reported cases (3).

Female urethral diverticula are most commonly diagnosed in the third to fifth decade of life, and are most often acquired rather than congenital (1). Acquired urethral diverticula are thought to develop from polymicrobial infections which lead to abscess formation within the glands surrounding the urethra, subsequently rupturing into the urethral lumen creating a residual outpouching (4). They may also be caused by trauma after vaginal delivery, or after urethral surgery or instrumentation (1).

Urethral diverticula are often benign, with rare cases of malignancy, usually adenocarcinoma, reported, though these account for only five percent of urethral cancers (5).

47.2.1.2 Presentation

While up to 20% of patients may be asymptomatic with the diverticulum being an incidental finding, the majority of patients will complain of a vaginal mass which can be seen or felt along the anterior vaginal wall and upon palpation may express purulent material (Figure 47.1) (1). Urethral diverticula are prone to urinary stasis from trapping of urine within the sac, and patients may also report recurrent urinary tract infections (in 18%–70% of cases), stress incontinence (12%–60%), or irritative symptoms like urgency, frequency, or urge incontinence (22%–47%) (1, 5–8). Patients may complain of pelvic and urethral pain or dyspareunia (11%–60%) (1, 6–8). While the classic triad of a urethral diverticula is described as "the three Ds" – post-void dribbling, dysuria, and dyspareunia – this is estimated to be found in only five percent of cases (1, 6).

47.2.1.3 Diagnosis and Imaging

A comprehensive exam is key in establishing the diagnosis of a urethral diverticulum. A half-speculum along the posterior vaginal wall will aid in exposing the anterior vaginal wall and urethra. The suburethral surface should be palpated along the anterior vaginal wall to assess for masses, tenderness, or the ability to express purulent material from the urethra.

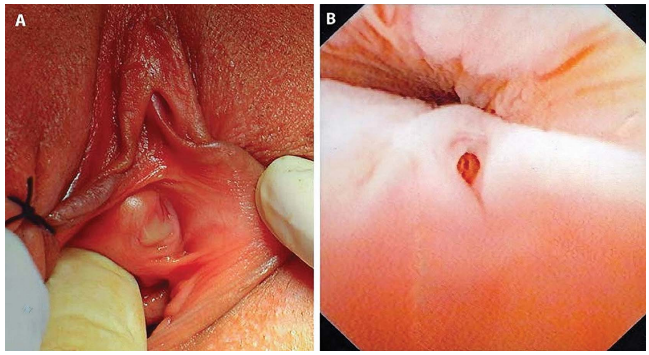


FIGURE 47.1 Urethral diverticulum – clinical photo (From Di Gregorio M et al. Female Urethral Diverticulum: Diagnosis, Treatment and Outcome. *Gynecol Obstet.* 2016;6(4): 1000374 under Open Access).

For those with masses and symptoms of voiding dysfunction, a postvoid residual volume should be measured. For those with irritative voiding symptoms, urinalysis and urine culture should be obtained.

Cystoscopy, and specifically urethroscopy, can be considered to aid in the diagnosis of urethral diverticula, though its utility in visualizing the diverticulum is variable (reported in 15%–89% of cases) (1). Magnetic resonance imaging (MRI) is considered the gold standard for imaging of urethral diverticula, noted to have both sensitivity and specificity of 100% (9). On a T2-weighted image, urine will appear hyperintense within the urethra, and a diverticulum can be identified as a similarly hyperintense sac below and/or extending laterally along the urethra (Figure 47.2).

47.2.1.4 Management

Patients who are asymptomatic or minimally symptomatic can be managed conservatively. Sitz baths and oral analgesics can be prescribed to reduce inflammation and pain. Broad-spectrum antibiotics can be prescribed in case of overlying infection, and overactive bladder medications trialed for irritative symptoms. Data is limited on best practices for conservative management, including the optimal course and duration of observation.

Surgical management most commonly involves excision of the urethral diverticulum itself. A technique for a posterior diverticulum involves making an inverted U-shaped incision in the vaginal epithelium overlying the urethral diverticulum. The entire diverticulum sac is excised from the urethra, and the urethral opening then closed longitudinally in layers over a Foley catheter using interrupted delayed absorbable sutures (10). Historically, marsupialization of distal urethral diverticula, also known as the "Spence procedure," was performed, though it has been reported to carry the risk of urethral shortening and stricture, and thus is less frequently performed (11).

DOI: 10.1201/9781003312109-47

FIGURE 47.2 Urethral diverticulum – axial T2-weighted MRI image shows endoluminal coil (asterisk) placed in vagina. Arrow indicates locally rounded urethral diverticulum on left; A indicates anus (From Dwarkasing RS et al. MRI Evaluation of Urethral Diverticula and Differential Diagnosis in Symptomatic Women. *AJR Am J Roentgenol.* 2011;197(3):676–682 with permission).

After surgery for urethral diverticula, patients should be discharged with a catheter. Though the optimal timing has not been defined, most suggest one to three weeks (1, 10). Before removal of the catheter, imaging such as a voiding cystourethrogram (VCUG) may be performed to rule out extravasation, and a voiding trial is performed to ensure proper emptying of the bladder. Success rates from the transvaginal repair of urethral diverticula range from 84% to 98% (1).

47.2.2 Skene's Gland Cysts

47.2.2.1 Incidence and Etiology

The female urethra is surrounded by several paraurethral ducts and glands, the largest of which are the Skene's glands, the female equivalent to the male prostate (12). They arise from the urogenital sinus and lie adjacent to the distal urethra bilaterally (13). The ducts produce lubrication for the urethral mucosa and vagina and drain primarily into the anterior vagina, while smaller accessory ducts drain into the lumen of the urethra (14).

As these cysts are rare and may be asymptomatic, their exact incidence is unknown. They are occasionally reported as congenital abnormalities, thought to be due to degeneration of embryonic remnants of the paraurethral glands (15, 16). In adults, cysts are typically observed in the third or fourth decade of life, and it is thought that obstruction of these glands due to infection leads to subsequent cyst development (12, 13).

Skene's gland cysts are usually benign, though hyperplasia has been reported. Malignant transformation is exceedingly rare, with only 20 cases, most commonly adenocarcinoma, reported in the literature (17).

47.2.2.2 Presentation

Symptoms of Skene's gland cysts may include a visible or palpable mass along the anterior vaginal wall/urethra, dysuria, dyspareunia, urinary tract infections, and symptoms of voiding dysfunction, including obstructive voiding (13).

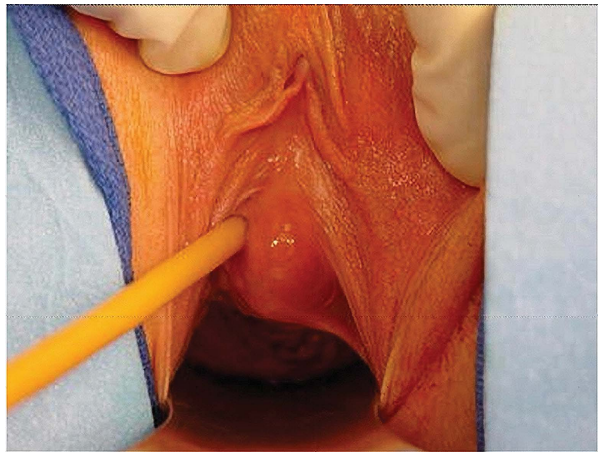


FIGURE 47.3 Skene's gland cysts – clinical image (From Shah SR et al. Surgical management of Skene's gland abscess/infection: a contemporary series. *Int Urogynecol J.* 2012;23:159–164 with permission).

On pelvic exam, these cysts may present as painless cystic masses, but infected cysts or abscesses will present as a painful, erythematous, fluctuant mass inferior and lateral to the urethra. The masses are most commonly unilateral. Pressure on the mass may express clear or purulent fluid from the duct opening. However, distinct from urethral diverticula, compression of a Skene's duct cyst will not result in urine drainage via the urethra, as this cyst does not have direct communication with the urethral meatus (Figure 47.3) (12).

47.2.2.3 Diagnosis and Imaging

Apart from clinical examination, imaging is key in differentiating a Skene's gland cyst from a urethral diverticulum. Thus, most experts advocate for the use of MRI, as this is the gold standard for imaging of urethral diverticula (12).

Histologic reports will show benign squamous-lined mucosa with no urothelium lining, thus differentiating these lesions from urethral diverticula which are continuous with the urethral lumen and will be lined with urothelium (12).

47.2.2.4 Management

There is limited information on the best practices in management of Skene's gland cysts. Asymptomatic masses can likely be conservatively managed. For patients that fail conservative management, or those with large, symptomatic cysts, surgical management may be warranted. Case series describe a range of treatments including needle aspiration, marsupialization, and partial or total excision, though they are limited by small sample sizes and short follow-up time (12, 13).

Complete excision is often described as a definitive approach. The procedure is similar to that described for a urethral diverticulum though is reported to carry a risk of distal urethral-wall injury, which can result in incontinence, urethrovaginal fistula, or urethral stricture (12). Small case series report a recurrence rate of 0%–18% (12, 18, 19).

47.2.3 Urethral Caruncle

47.2.3.1 Incidence and Etiology

A urethral caruncle is a benign solid, fleshy outgrowth at the urethral meatus, most often occurring at the posterior lip of

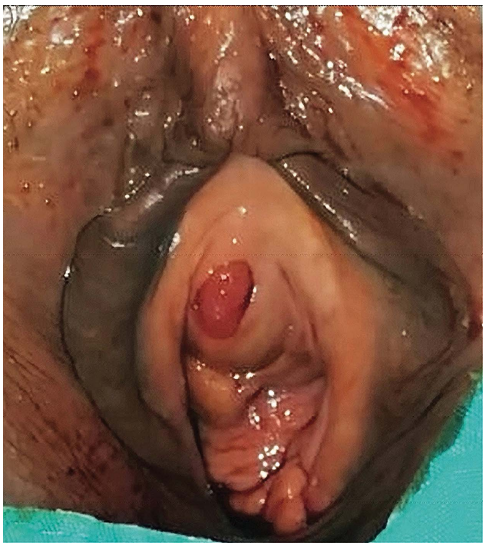


FIGURE 47.4 Urethral caruncle – clinical image (From Kolukcu E et al. A rare cause of urinary retention in women: urethral caruncle. *Kafkas J Med Sci.* 2020;10(3):253–256 with permission).

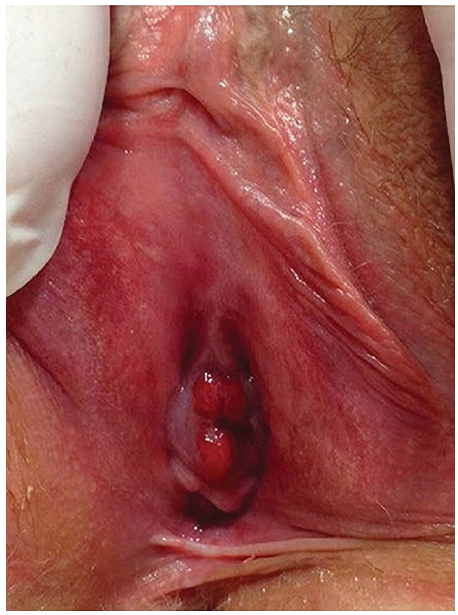


FIGURE 47.5 Urethral prolapse – clinical photo (From Fornari A et al. Urethral prolapse: a case series and literature review. *J Obstet Gynaecol India.* 2020;70(2):158–162 with permission).

the distal urethra. They are sometimes identified as urethral polyps, and these terms are sometimes used interchangeably (20). They are most commonly seen in postmenopausal women, although rare cases have been reported in premenopausal women and girls (21, 22).

The etiology of the urethral caruncle is unknown – urethral congestion, irritation, trauma, and estrogen deficiency have been suggested, though histologic studies suggest chronic inflammation as the most likely etiology (21). They are usually benign, though case reports of squamous cell carcinoma and transitional cell carcinomas have been published (23, 24).

47.2.3.2 Presentation

Urethral caruncles are typically asymptomatic lesions and incidentally noted on exam, though some patients may present with complaints of vaginal bleeding, hematuria, urethral pain, dysuria, or a visible or palpable mass at the urethra (25).

On examination, the lesion will be visible along the posterior edge of the distal urethral meatus (Figure 47.4). It may be sessile or pedunculated.

Urethral caruncles are unlikely to cause issues with incontinence or voiding dysfunction, though these conditions may coexist independently in postmenopausal women and should be evaluated if present.

47.2.3.3 Diagnosis and Imaging

The diagnosis of a urethral caruncle is based on symptoms and physical examination. No additional laboratory imaging studies are necessary, unless the presentation is complex or the diagnosis is uncertain.

47.2.3.4 Management

There is limited evidence regarding treatment for urethral caruncles. In general, asymptomatic patients can be observed. Patients who are symptomatic are often managed conservatively with sitz baths and topical estrogen. Topical estrogen administration follows the same schedule as that of vaginal atrophy, with patients instructed to place a small amount of the cream at the vaginal introitus and urethral meatus nightly for two weeks, followed by two to three nights a week thereafter.

For patients with large symptomatic lesions or those in whom the diagnosis is uncertain, surgical removal is recommended. Various surgical techniques have been described, including simple excision, cauterization, suture ligation, and application of topical agents with the aim of destroying the lesion (20).

Potential complications include development of strictures and voiding dysfunction, as well as recurrence of the caruncle. Recurrence rates from cases series of surgically excised urethral caruncles range from 4.3% to 40% (26–28). It is generally advised that patients with genitourinary symptom of menopause who have undergone surgical excision remain on vaginal estrogen to prevent recurrence, though the effectiveness of this treatment is unknown.

47.2.3.5 Urethral prolapse

Urethral prolapse is a circumferential protrusion of the mucosa surrounding the urethral meatus. It is thought to arise from low estrogen states, and thus is typically seen in either premenarchal girls or postmenopausal women (20, 29). Other suggested etiologies include increased intra-abdominal pressure, perineal or urethral trauma, sexual abuse, and infection (29). While girls are usually asymptomatic, postmenopausal women may present with vaginal bleeding and a painful donut-shaped mass at the urethral meatus which is irreducible (30). It is important to differentiate urethral caruncles from urethral prolapse. Prolapse is circumferential in nature, while caruncles will usually arise from the posterior urethral meatus (Figure 47.5) (31).

The diagnosis is often based on clinical exam alone, and imaging is only indicated if another condition or infection is suspected (29). For those who are asymptomatic or minimally symptomatic, sitz baths and topical estrogen cream may be used. There is no consensus on the optimal duration of treatment, though at least six weeks has been suggested (29, 30). Success rates of conservative management range from 33% to 92%,

though recurrence rates may be up to 67% (29). For patients who fail conservative management, are symptomatic, or present with thrombosis or necrosis of the prolapsed portion of the urethra, surgical excision is indicated (30).

47.2.4 Vaginal Masses

47.2.4.1 Gartner Duct Cysts

47.2.4.1.1 Incidence and Etiology

Gartner duct cysts are vaginal cysts which develop from remnants of the mesonephric (Wolffian) ducts. The developed Wolffian ducts form the male genital tract, but these structures regress in females as the Müllerian ducts continue to develop. However, remnants of the mesonephric ducts may persist alongside the developing Müllerian structures and can form these inclusion cysts (32).

Gartner duct cysts are though to represent 11% of all vaginal cysts, yet the exact incidence of these cysts is unknown as many are asymptomatic. They are most often benign, though malignant transformation has been described (33).

47.2.4.1.2 Presentation

Gartner duct cysts are typically asymptomatic. Symptoms, if present, may include dyspareunia, vaginal pain, and difficulty inserting tampons. Especially large cysts may be associated with incontinence or obstructive voiding symptoms (34).

Pelvic examination may reveal a tense cyst that is palpable or seen to bulge from beneath the vagina wall (32). The cysts are usually small (<2 cm) but can vary greatly in size, with large cysts measuring up 16 cm reported (35, 36). Large cysts may mimic other abnormalities such as prolapse, Bartholin's gland cysts, and urethral diverticula.

Congenital malformations of the ureters and kidneys, including ectopic ureter, renal agenesis, and renal hypoplasia, have been associated with Gartner duct cysts (37). In one study, 21% of surgically managed patients with Gartner duct cysts were found to have concomitant genitourinary malformations (34).

47.2.4.1.3 Diagnosis and Imaging

Diagnosis is based on clinical exam; however, to determine the location and extent of the cyst, to ascertain its relation to the bladder and ureters, and to identify any potential genitourinary anomalies, imaging is recommended prior to proceeding with surgical management. Ultrasound, while cost-effective, may fail to differentiate a Gartner duct cyst from a urethral diverticulum, and thus some experts recommend MRI as first-line imaging (33). Injection of the cyst with contrast medium has also been described to aid in identifying the mass on imaging (34).

The histologic findings of "cuboidal or low columnar, nonciliated, nonmucinous cells" are consistent with the diagnosis of Gartner duct cyst (33, 34).

47.2.4.1.4 Management

Observation is reasonable in most cases, although excision is recommended for symptomatic Gartner duct cysts or those with concerning symptoms like bleeding, irritation, and sensitivity (32, 33).

Cyst excision is the most common surgical technique described, in which sharp and blunt dissection are used to separate and remove the cyst from the vaginal wall (34). The majority of these excisions have been reported as vaginal approaches, though large cysts have removed successfully via the laparoscopic route (38, 39). Other techniques include cyst aspiration with tetracycline injection, marsupialization, CO_2 laser ablation, partial excision, and drainage (34, 38).

47.2.5 Bartholin's Gland Cysts and Abscesses

47.2.5.1 Incidence and Etiology

Bartholin's glands, also called the greater vestibular glands, are found bilaterally in the labia minora at 4 and 8 o'clock (40). Bartholin's glands become active toward puberty and secrete mucous to lubricate the vagina (40, 41). If these glands become obstructed, a Bartholin's gland cyst can develop; if this cyst becomes infected, an abscess may follow (40). Obstruction and subsequent cyst and abscess formation can follow infection or trauma or can be seen with congenitally narrowed ducts (32).

An estimated two to three percent of women will develop a Bartholin's gland cyst or abscess in their lifetime (40–42). The majority of cases are associated with *Escherichia coli* and *Staphylococcus aureus*, with sexually transmitted infections constituting a minority of cases (32, 40).

Bartholin's glands are usually thought to involute towards menopause; thus, Bartholin gland cysts and abscesses are uncommon after this age. Pathology in women older than 40 years should raise suspicion for malignancy (32, 40). Bartholin's gland cancers are rare, with an incidence of 0.1 per 100,000 women and accounting for only five percent of all vulvar cancers; however, a high suspicion should be maintained as these cancers can be aggressive (32, 40, 43). The majority of these cases are squamous cell carcinoma and adenocarcinoma (40, 44).

47.2.5.2 Presentation

While normal Bartholin's glands are typically small and not palpable in the absence of pathology, a cystic gland will present with a typically unilateral mass at 4 or 8 o'clock, protruding medially into the vaginal introitus (Figure 47.6). Cysts may be fluctuant or tense and can measure 3–6 cm in size or even larger. In those with an abscess, the overlying epithelium may be tender and erythematous. While patients with smaller cysts may be asymptomatic or present with minor discomfort, patients with larger cysts may complain of dyspareunia and pain. Fever or drainage of purulent material from the area may be present in those with an abscess (32, 40). Firm, fixed,

FIGURE 47.6 Bartholin's gland cyst – clinic picture (From Griffith WF and Wener CL. Benign disorders of the lower genital tract. In: Hoffman BL et al., eds. *Williams Gynecology*, 3rd edn. New York: McGraw-Hill Education; 2016:101–102 with permission).

irregular-shaped, or recurrent masses should raise suspicion for malignancy, especially in women over 40 (40).

47.2.5.3 Diagnosis and Imaging

Bartholin's gland cysts and abscesses are diagnosed clinically. Typically, no additional imaging is required to make the diagnosis, with the exception of a biopsy in those cases of suspected malignancy, though this is typically performed at the time of treatment. Culture of abscess fluid may be obtained, though the etiology is usually polymicrobial, as well as testing for gonorrhea and chlamydia in patients at risk of sexually transmitted infections (32, 40).

47.2.5.4 Management

Small, asymptomatic Bartholin's gland cysts in women younger than 40 require no intervention. They can be managed conservatively, and sitz baths, warm compresses, and anti-inflammatories can be recommended for symptom relief (32). Antibiotic treatment of Bartholin's gland cysts and simple abscesses is not necessary in the absence of sexually transmitted infection, urinary tract infection, or overlying cellulitis (40).

Techniques for treatment of large, symptomatic cysts or abscesses include incision and drainage (I&D), marsupialization, and Bartholin's gland excision (32). There is little evidence to recommend one approach over the other with few randomized control trials available and systematic reviews showing similar cure rates and recurrence rates between various management strategies (42, 45).

Incision and drainage is performed by creating a small incision just at or inside and parallel to the hymen at 5 or 7 o'clock, in the location of the gland's duct. The cyst or abscess can be left to drain, or a Word catheter, a small, space-filling device meant to allow for drainage and re-epithelialization of the drainage tract, may be placed. If utilized, a Word catheter is typically left in place for at least a week, with some experts recommending 4 to 6 weeks, though there is no clear consensus on the ideal duration (46).

Bartholin's gland cyst I&D does not require antibiotic treatment; however, abscesses are typically surrounded by significant cellulitis, and antibiotics are warranted in these cases. Suitable choices include trimethoprim-sulfamethoxazole, doxycycline, or cephalexin, prescribed for seven days (46).

Marsupialization can be used for primary Bartholin's gland cysts or abscesses, though it is more commonly performed for recurrent infections (44). The procedure involves creation of a vertical or elliptical incision overlying the cyst, in the same location used for I&D. The cyst wall or abscess is then opened, and the cyst wall edges are everted and sutured to adjacent skin edges using a delayed absorbable suture in order to allow for continued drainage (46). Over time, a new outflow tract is formed as the cyst wall shrinks and re-epithelializes (40).

For recurrent infections, duct excision is sometimes performed. In this procedure, the overlying vaginal epithelium is opened and the cyst wall dissected in its entirety; ultimately, the deep vessels are ligated and transected to free the cyst. The remaining cyst bed is closed with delayed-absorbable sutures, and the epithelium reapproximated (46).

For those with recurrent infections or in women over age 40, regardless of the technique chosen, biopsy of the cyst wall should be taken to exclude malignancy (32).

Recurrence rates are comparable between the different approaches, ranging from 6% to 12% in larger studies, though some smaller, older studies quote recurrence rates as high as 30%–40% (41, 42, 45).

47.2.6 Other Vaginal Masses

47.2.6.1 Epidermal Inclusion Cysts

Epidermal inclusion cysts, or sebaceous cysts, are rarely found in the vagina and more typically seen on the vulva. They typically occur due to plugged pilosebaceous glands but can form after implantation of epidermal cells into deeper tissues (such as after surgical repair) with a resulting foreign body type inflammation. They typically present as round or ovoid masses and are filled with viscous, gritty, or caseous foul-smelling material. They may be asymptomatic, in which case they require no intervention. Those with symptomatic or secondarily infected cysts can undergo incision and drainage or excision (32, 47).

47.2.6.2 Leiomyoma and Other Benign Masses

Leiomyomas are common benign smooth muscle tumors of the uterus, affecting up to 70%–80% of women of reproductive age. Around 300 cases of leiomyoma of the vulva and vagina have been reported. These masses are typically singular, benign, and slow-growing, most commonly found on the anterior vaginal wall, and may or may not be associated with leiomyomas elsewhere in the body (48). They may be asymptomatic or may present with pain, vaginal bleeding, dyspareunia, or urinary symptoms including potential urinary obstruction (49). Given the broad potential differential diagnosis, imaging – ultrasound, CT, or MRI – can help confirm the diagnosis of a leiomyoma, though ultimately pathology will confirm the diagnosis. Surgical excision, particularly in rapidly growing lesions, is recommended in order to rule out leiomyosarcoma; though extremely rare, it has high metastatic potential and mortality rates (32, 48, 50).

Fibromas are benign tumors arising from fibroblast proliferation. They are typically also found in the vulva but may present in the vagina. As with leiomyomas, imaging can help guide diagnosis. Surgical excision is indicated for symptomatic lesions or if the diagnosis is unclear (32).

Lipomas are soft, sessile, or pedunculated masses composed of mature adipose cells. As with the other benign lesions, asymptomatic lesions can be observed, but symptomatic or large lesions should be imaged and removed. Lipomas lack a fibrous connective tissue capsule, and thus dissection can require a larger incision and can be technically more complicated (32).

47.3 Conclusion

Urethral and vaginal masses can often represent a diagnostic quandary for the gynecologist given the wide range of potential diagnoses. Patients may present with symptoms ranging from minor irritation to dyspareunia and voiding dysfunction. In order to optimize workup, a thorough urethral, vaginal, and pelvic exam are warranted, and imaging, including MRI and potentially cystoscopy, can be used to aid in making a diagnosis and in surgical planning. For the majority of these masses, there is little high-quality data to guide treatment, especially conservative management. Ultimately, surgical management is indicated for symptomatic lesions or those in which the diagnosis is unclear.

References

1. Greiman AK et al. Urethral diverticulum: a systematic review. *Arab J Urol*. 2019;7(1):49–57.
2. El-Nashar SA et al. Incidence of female urethral diverticulum: a population-based analysis and literature review. *Int Urogynecol J*. 2014;25(1):73–79.

3. Tunitsky E et al. Periurethral mass: a rare and puzzling entity. *Obstet Gynecol*. 2012;120(6):1459–1464.
4. Di Gregorio M et al. Female urethral diverticulum: diagnosis, treatment and outcome. *Gynecol Obstet*. 2016;6(4):1000374.
5. Thomas AA et al. Urethral diverticula in 90 female patients: a study with emphasis on neoplastic alterations. *J Urol*. 2008;180(6):2463–2467.
6. Baradaran N et al. Female urethral diverticula in the contemporary era: is the classic triad of the "3Ds" still relevant? *Urology*. 2016;94:53–56.
7. Vaidya RV et al. Characterization of urethral diverticula in women. *Urogynecology*. 2022;28(1):54–56.
8. Jacox N et al. Periurethral and anterior vaginal wall masses: etiology, presentation, and treatment outcomes. *Obstet Gynecol*. 2022;140(5):778–783.
9. Dwarkasing RS et al. MRI evaluation of urethral diverticula and differential diagnosis in symptomatic women. *Am J Roentgenol*. 2011;197(3):676–682.
10. Karram MM et al. Repair of suburethral diverticulum. In: Baggish MS et al., eds. *Atlas of Pelvic Anatomy and Gynecologic Surgery*, 5th edn. Philadelphia: Elsevier; 2021:1037–1048.
11. Welch ET et al. Urethral diverticulum marsupialization with modified Spence-Duckett procedure. *Urology*. 2023 Jun:176:248.
12. Foster J et al. Skene's gland cyst excision. *Int Urogynecol J*. 2016;27(5):817–820.
13. Shin T et al. Adult-onset Skene's gland cyst following a history of multiple gynecological treatment interventions. *Urol Case Rep*. 2021;36:101586.
14. Slopnick EA et al. Skene's gland malignancy: a case report and systematic review. *Urology*. 2022;165:36–43.
15. Kusama Y et al. Skene's duct cyst. *J Gen Fam Med*. 2017;18:299–300.
16. Sousa P et al. Skene's gland cyst – case report of a 2-year-old girl. *Fetal Pediatr Pathol*. 2023;7:1–5.
17. Gao Q et al. Adenosquamous carcinoma of Skene's gland: a case report and literature review. *Front Oncol*. 2022;12:893980.
18. Shah SR et al. Surgical management of Skene's gland abscess/infection: a contemporary series. *Int Urogynecol J*. 2012;23:159–164.
19. Köse O et al. Experiences with the management of paraurethral cysts in adult women. *Cent Eur J Urol*. 2013;66:477–480.
20. Verma V et al. Management of urethral caruncle – a systematic review of the current literature. *Eur J Obstet Gynecol Reprod Biol*. 2020;248:5–8.
21. Chiba M et al. Urethral caruncle in a 9-year-old girl: a case report and review of the literature. *J Med Case Rep*. 2015;9:71.
22. Ferrier PA. Urethral caruncle. *Cal West Med*. 1926;24(4):500.
23. Kaneko G et al. A case of intraepithelial squamous cell carcinoma arising from urethral caruncle. *Can Urol Assoc J*. 2011;5(1):E14.
24. Walther HWE. Caruncle of the urethra in the female with special reference to the importance of histological examination in the differential diagnosis. *J Urol*. 1943;50(3):380–388.
25. Kolukcu E et al. A rare cause of urinary retention in women: urethral caruncle. *Kafkas J Med Sci*. 2020;10(3):253–256.
26. Conces MR et al. Urethral caruncle: clinicopathologic features of 41 cases. *Hum Pathol*. 2012;43(9):1400–1404.
27. Hall ME et al. Results of surgical excision of urethral prolapse in symptomatic patients. *Neurourol Urodyn*. 2017;36(8):2049–2055.
28. Malpas P. The recurrence rate of urethral caruncles. *BJOG Int J Obstet Gynaecol*. 1945;52(4):367–369.
29. Fornari A et al. Urethral prolapse: a case series and literature review. *J Obstet Gynaecol India*. 2020;70(2):158–162.
30. Muteke JK et al. Urethral prolapse mimicking a uterine prolapse in an eight-year-old girl: a case report. *Int J Surg Case Rep*. 2022;94:107169.
31. Gebhart JB. Surgical repair of urethral prolapse. In: Baggish MS et al., eds. *Atlas of Pelvic Anatomy and Gynecologic Surgery*, 5th edn. Philadelphia: Elsevier; 2021:1029–1030.
32. Griffith WF and Werner CL. Benign disorders of the lower genital tract. In: Hoffman BL et al., eds. *Williams Gynecology*, 3rd edn. New York: McGraw-Hill Education; 2016:101–102.
33. Bats AS et al. Malignant transformation of Gartner cyst. *Int J Gynecol Cancer*. 2009;19(9):1655–1657.
34. Niu S et al. Gartner's duct cysts: a review of surgical management and a new technique using fluorescein dye. *Int Urogynecol J*. 2020;31(1):55–61.
35. Thapa BD et al. Gartner's duct cyst of the vagina: a case report. *JNMA J Nepal Med Assoc*. 2020;58(227):505–507.
36. Mikos T et al. Vaginal excision of a large gartner duct cyst. *J Minim Invasive Gynecol*. 2018;25(7):1132–1133.
37. Dwyer PL et al. Congenital urogenital anomalies that are associated with the persistence of Gartner's duct: a review. *Am J Obstet Gynecol*. 2006;195(2):354–359.
38. Baggish MS. Benign lesions of the vaginal wall. In: Baggish MS et al., eds. *Atlas of Pelvic Anatomy and Gynecologic Surgery*, 5th edn. Philadelphia: Elsevier; 2021:779–787.
39. Lin PH et al. Laparoscopic excision of a large Gartner's duct cyst. *J Minim Invasive Gynecol*. 2022;29(12):1285–1286.
40. Omole F et al. Bartholin duct cyst and gland abscess: office management. *Am Fam Physician*. 2019;99(12):760–766.
41. Rotem R et al. Surgical treatment of Bartholin's gland abscess: is word catheter superior to marsupialization? *J Minim Invasive Gynecol*. 2021;28(6):1211–1215.
42. Illingworth B et al. Evaluation of treatments for Bartholin's cyst or abscess: a systematic review. *BJOG*. 2020;127(6):671–678.
43. Akhtar M et al. Bartholin gland carcinoma in a young female: a rare disease in an unusual age group. *BMJ Case Rep*. 2021;14(1):e236821.
44. Yahaya JJ. Bartholin's gland hyperplasia with dysplastic changes: a rare case report. *J Surg Case Rep*. 2020;2020(9):rjaa312.
45. Karabük E et al. Marsupialization versus word catheter in the treatment of Bartholin cyst or abscess: retrospective cohort study. *J Turk Ger Gynecol Assoc*. 2022;23(2):71–74.
46. Corton MM and Hoffman BL. Surgeries for benign gynecologic disorders. In: Hoffman BL et al., eds. *Williams Gynecology*, 3rd edn. New York: McGraw-Hill Education; 2016:980–985.
47. Margesson LJ et al. Vulvar lesions: differential diagnosis of red lesions [Internet]. *UpToDate*, 2022. [cited Mar 2022]. Available at: www.uptodate.com/contents/vulvar-lesions-differential-diagnosis-of-red-lesions?search=vagina%20Epidermal%20inclusion%20cyst&source=search_result&selectedTitle=3~150&usage_type=default&display_rank=3#H1916434939.
48. Shah M et al. Vaginal leiomyoma: a case report. *JNMA J Nepal Med Assoc*. 2021;59(237):504–505.
49. Touimi Benjelloun A et al. Vaginal leiomyoma mimicking a cystocele (report case). *Int J Surg Case Rep*. 2022;93:106955.
50. Reinicke T et al. Vulvar leiomyosarcoma masquerading as a Bartholin's gland cyst in an adolescent. *Cureus*. 2022;14(1):e21674.

48 CYSTOSCOPY, URINARY STENTS, AND SUPRAPUBIC TUBES TO ASSIST WITH PELVIC SURGERY

Paige K. Kuhlmann, Kris E. Gaston, and Philippe Zimmern

48.1 Cystoscopy/Vaginoscopy

48.1.1 Female Urethrocystoscopy

There is an important technical distinction needed to be made between a male and a female cystoscope to evaluate the urethra (1). Both scopes are equivalent for bladder evaluation. However, a male cystoscope has a curved beak at the end and the fluid throughput exits at the bottom of the inferior groove (Figures 48.1 and 48.2). As such the male scope is not intended to distend or evaluate the short female urethra. In fact, by the time there is enough fluid irrigation traversing the sheath to distend the female urethra, the scope is already located in the proximal urethra or bladder neck area. So urethral pathology that is mid- or distally located will be overlooked (Figure 48.3).

Several female urethrocystoscopes exist. The smallest one made by Wolff is a 17.5 Fr scope (Figure 48.2). There are larger ones, such as a 21 Fr intended for injection of bulking agents. They all have an obturator sheath in case the meatus is too tight for introduction and the tip gets caught at the meatal lip. These cystoscope sheaths can accommodate a 30-degree lens as well as a 70-degree lens to carefully inspect the anterior bladder wall and dome.

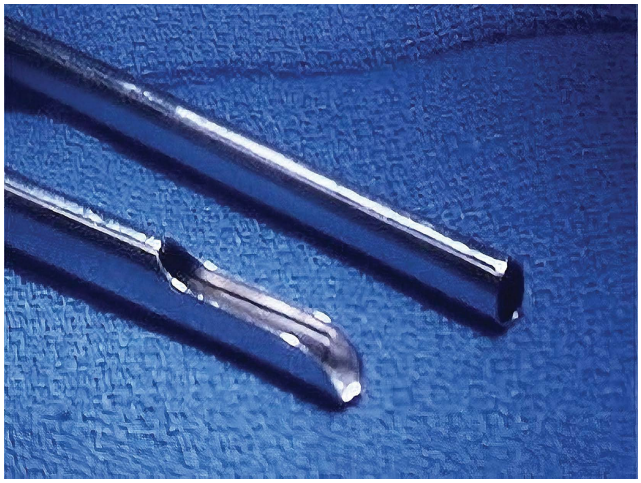


FIGURE 48.1 Male versus female cystourethroscope tip comparison. The female tip prevents escape of irrigant and allows better urethral lumen distension (From ref 1 with permission).

A flexible scope can also be used to inspect the urethra. This is generally employed more for diagnostic purposes in the clinic setting. The flexible scope can also help in visualizing sutures or mesh exposed along the anterior bladder wall or bladder neck by using its retroflex feature, or to identify the site of a small fistula and its relationship to the trigone and ureteric orifices.

Both flexible and rigid scopes can be used to detect small areas of exposed mesh in the vagina and provide documentation of such (2). This procedure, called vaginoscopy, can also be useful in some very elongated vaginas after open or laparoscopic/robotic mesh sacrocolpopexy when it is difficult to reach the upper vagina to locate the site of extrusion (3).

In some rare instances of mesh excision around the urethra, or whenever the mesh fragments are difficult to localize when imbedded in scar tissue (especially clear mesh material), a transvaginal retropubic cystoscopy can be performed using a rigid female scope to explore that area and look for mesh remnants.

For bladder biopsies, we recommend using a common urology set with Olympus for example, which provides a 21 Fr sheath and a biopsy forceps. A 12-degree cystoscope sheath is needed to clearly see the site being biopsied (instead of a 30-degree). The biopsy sites can be fulgurated with the same cystoscopy sheath or with the smaller 17.5 Fr female urethroscope which can accommodate a fine-tip Bugbee electrode to do so (Figure 48.4).

48.1.2 Ureteral Stents for Gynecologic Surgery

The pelvic ureters are in proximity to the uterus and adnexa and may be encountered during gynecologic pelvic surgery. While the overall incidence of ureteral injury during gynecologic surgery is low, damage to the ureters can lead to significant morbidity and mortality.

48.1.3 Types of Ureteral Injury

There are a variety of possible mechanisms of iatrogenic injury to the ureter during gynecologic surgery. These include transection (partial vs complete), ligation, thermal injury with delayed perforation, crush injury, and devascularization. The most common type is partial transection. However, with the

FIGURE 48.2 Female urethrocystoscope (From ref 1 with permission).

DOI: 10.1201/9781003312109-48

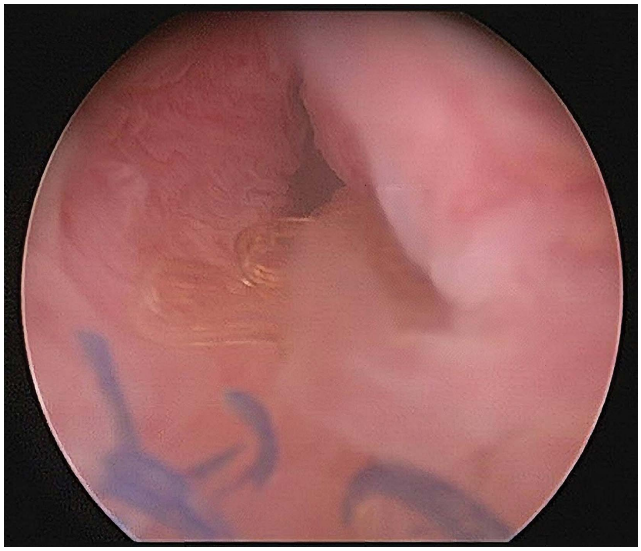


FIGURE 48.3 Pathology such as sling mesh erosion in the female urethra can be missed without the superior distention allowed by the female urethrocystoscope (From ref 1 with permission).

FIGURE 48.4 Fine-tip Bugbee electrode at the end of the 17.5 Fr Wolf scope for fulguration of bleeding sites or chronic cystitis areas.

popularization of bipolar energy tools, thermal injuries have been increasing in frequency.

Examples of ureteral injury during pelvic surgery include:

- Transection during sharp or blunt dissection
- Crushed with a clamp
- Kinked or ligated with a suture or staple
- Thermal spread when using monopolar or bipolar cautery (Ligasure™) for hemostasis on nearby structures
- Devascularization during ureterolysis

Depending on the mechanism of injury, the resultant presentation may be a urine leak with urinoma formation, ureteral stricture or complete obliteration of the lumen, or ureterovaginal or other type of fistula formation. These injuries can lead to urinary tract infection, pyelonephritis, sepsis, and potential renal loss.

48.1.4 Risk Factors for Iatrogenic Ureteral Injury

The chance of ureteral injury during gynecologic surgery may be impacted by the presence of distorted pelvic anatomy, anatomic issues leading to poor visualization, and conditions causing obliteration of natural tissue planes. Specific risk factors include endometriosis, fibroids, genitourinary anomalies (e.g., duplicated ureter, pelvic kidney), obesity, presence of a large pelvic mass, prior pelvic surgery (including cesarean section), and prior pelvic radiation.

48.1.5 Indications for Ureteral Stenting

Pertinent indications for ureteral stenting in gynecologic surgery can be grouped into three general categories: relieving preoperative ureteral obstruction, assisting with intraoperative localization of the ureters, and facilitating healing of ureteral injury.

48.1.6 Obstruction

If a large pelvic mass is causing ureteral compression with resultant hydronephrosis, acute kidney injury, and/or flank pain, an indwelling ureteral stent may be placed to temporize this issue while awaiting definitive surgery (4).

48.1.7 Intraoperative Localization

Whether prophylactic stents actually prevent ureteral injuries is controversial, but they do allow for better recognition of injury allowing for immediate repair. Selection of appropriate candidates for ureteral stent placement immediately prior to gynecologic surgery is left to the discretion of each individual gynecologist. However, it is generally recommended to strongly consider preoperative stent placement for patients with a history of pelvic radiation or surgery (in whom tissue planes may be obliterated or there may be a high adhesion burden), severe endometriosis, and large fibroids (particularly if located near the cervix or in the broad ligaments). It is a minor procedure much easier performed preoperatively (compared to intraoperatively) that adds a relatively short amount of time to the case.

If the surgery is begun without preoperative stent placement and the dissection proves to be especially challenging (unexpected periureteral scarring, adhesions, endometriosis, distorted anatomy), stents can and should be inserted at this time. To be prepared for this possibility, it is suggested to place all patients in dorsal lithotomy position for these surgeries.

48.1.8 Ureteral Injury

If a ureteral injury does happen to occur intraoperatively, strong consideration should be given to obtaining an intraoperative urology consult. If ureteral repair is undertaken, a stent will be left in place as the repair heals. If there is a strong suspicion for ureteral injury (i.e., temporary clamping or concern for thermal injury), a stent should be placed.

48.1.9 Ureteral Stents

Modern indwelling ureteral stents are typically made of silicone with a hydrogel coating. They have a curl on each end to hold the stent in place in the renal collecting system and the bladder (Gibbons or double J stent; Figure 48.5). The sizes most commonly used are diameter 6 Fr and length 18–30 cm

FIGURE 48.5 Example of double J ureteral stent (by courtesy of Boston Scientific Contour Ureteral Stent™).

FIGURE 48.6 Example of 5 Fr open-ended ureteral catheter (by courtesy of Cook Medical™ Open-End Ureteral Catheter).

depending on length of the ureter. While there are a variety of methods to determine the correct stent length, one equation that generally works is to subtract 42 from a patient's height in inches (e.g., a 5'6" woman would get a 24 cm stent).

Another option for ureteral stenting for the purpose of intraoperative localization is to insert a 5 Fr open-ended catheter (Figure 48.6). This is a straight, flexible catheter, usually 70 cm in length, that should be placed with one end in the renal collecting system and the other internalized into a Foley bag. It can be removed at the end of the procedure or on postoperative day 1 when the Foley catheter is removed.

One newer alternative for intraoperative localization of the ureter, specific to robotic-assisted surgery, is injection of indocyanine green (ICG) into the ureter at the beginning of the procedure. This then causes the ureter to glow green when viewed through a specific filter on the robotic console.

48.1.10 Procedure Steps

1. Place the patient in dorsal lithotomy position and sterilely prep the genitalia.
2. Insert a 21 Fr or larger rigid cystoscope with a 30-degree lens into the bladder.
3. Identify the ureteral orifices.
4. Cannulate one ureteral orifice with a guidewire and advance it into the ipsilateral renal collecting system, stopping when light resistance is met.
   a. If fluoroscopy is available and the operating table is compatible, it is helpful to perform this and the next step under fluoroscopic guidance.
5. Advance the stent over the wire into the renal collecting system.
   a. If using an indwelling stent, advance it with the pusher until the large black mark is encountered, marking the distal end of the stent. Take care to not advance the distal end of the stent into the ureter, especially if the string has been removed. Once the distal mark is in view, remove the wire and ensure the distal end of the stent curls in the bladder.
   b. If using a 5 Fr open-ended ureteral catheter, advance it over the wire 15–20 cm (marked on the catheter). Once it has been advanced far enough, remove the scope while leaving the catheter in place. Take care to not pull the catheter out as you back the scope out.
6. Repeat these steps on the contralateral side if bilateral ureteral localization is desired.
7. Remove the cystoscope.
8. Insert a Foley catheter.
   a. If using 5 Fr open-ended catheters, secure them to the Foley with a silk suture to prevent them from falling out. Then internalize them into the Foley immediately proximal to where it attaches to the drainage bag. This allows the stents to drain the collecting systems during the surgery and to prevent urine spillage.

48.1.11 Important Stent Considerations

- If leaving indwelling stents, obtain a kidney, ureter and bladder x-ray in the recovery room to ensure correct stent placement (Figure 48.7).
- If unable to place a stent intraoperatively due to complete obstruction of the ureter, consult urology and plan for nephrostomy tube placement and potential antegrade stent placement per interventional radiation postoperatively.
- Placing all patients in dorsal lithotomy position on fluoroscopy compatible operative bed (i.e., slider), even if not planning on placing preoperative ureteral stents, will facilitate intraoperative ureteral stent placement should the need arise.

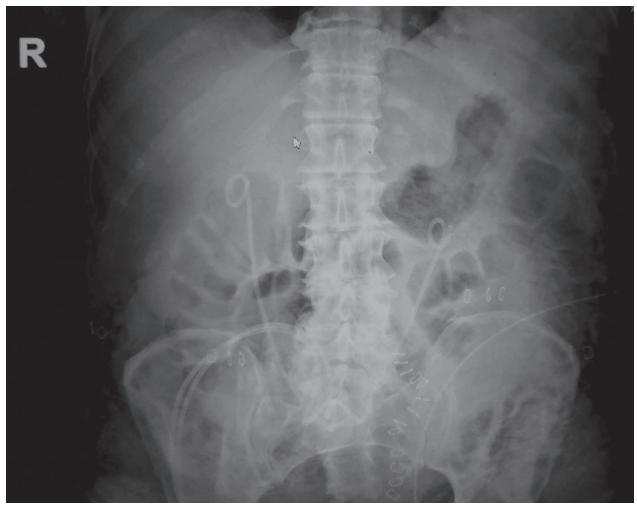


FIGURE 48.7 KUB showing correct ureteral stent placement.

48.1.12 Postoperative Management

Duration of the stent depends on the intraoperative findings. If there was no injury to the ureters, stents can be removed immediately postoperatively. If there was an injury, stents are often left in place for generally 6 weeks while the ureter heals. Some practitioners opt to leave a Foley catheter in place in this setting as well, to prevent reflux. Stent removal is typically performed with a flexible cystoscope and flexible grasper in the office setting.

Patients should be counseled that light gross hematuria while a stent is in place is normal. They also may experience flank pain or bladder spasms, especially during voiding.

48.1.13 Complications of Stents

The most common postoperative issues with stents include pain, bladder spasms, and urinary tract infections. Stent pain can be managed with NSAIDs, an alpha blocker, and/or phenazopyridine. Bladder spasms can be treated with oxybutynin. It is not routine to prescribe prophylactic antibiotics while a stent is in place.

If the stent migrates, it can cause obstruction with resultant flank pain. Initial evaluation if there is concern for stent migration includes a KUB to assess stent position and a renal US to assess for significant hydronephrosis.

Other rarer complications include renal hemorrhage and stent encrustation, for which a urology consult should be obtained.

48.2 Suprapubic Cystostomy

Urinary drainage with the use of some type of urethral catheter for urinary retention was described as far back as 3500 BC. Suprapubic cystostomy tubes were an invention of the 20th century. Two main ways to place a cystostomy tube directly into the bladder is by (1) an open surgical approach or (2) a percutaneous approach. The percutaneous approach is by far the most common way to place a cystostomy tube unless the patient is already undergoing major open surgery. The first percutaneous suprapubic cystostomy technique described was the trocar cystostomy tube (Figure 48.8). Initially described by gynecologists in 1966 with Taylor and Nickel, the first study of its use was reported by Hodgkinson and Hodari at the Cleveland Clinic for postoperative urinary management after gynecologic surgery (5, 6).

FIGURE 48.8 Metal suprapubic trocars.

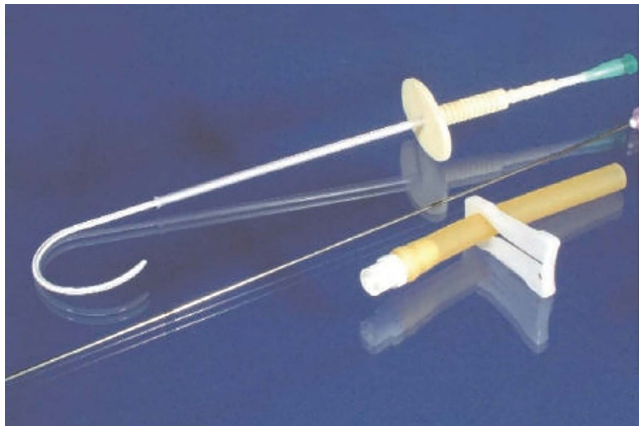


FIGURE 48.9 Bonanno suprapubic cystostomy set (by courtesy of Becton Dickinson).

48.2.1 Bonanno Cystostomy

Many practitioners found these metal trocars intimidating and a potential for major complication. Further urogynecological innovation was by Bonanno and colleges in 1970 who described a Seldinger technique placement by needle aspiration and catheter placement over the needle in the bladder (Figure 48.9) (7).

48.2.2 Stamey Malecot Cystostomy

The Bonanno cystostomy tube is technically easier to place as it is only a 14-gauge catheter and can be performed in the awake patient; however, the major criticism is the small diameter of the cystostomy tube which can easily obstruct with minor sediment or blood. The Stamey Malecot cystostomy tube uses the same needle guidance and aspiration with a catheter sliding over the needle into the bladder by Seldinger technique but is a larger bore needle and allows for a 12 F Malecot catheter to be placed (Figure 48.10).

48.2.3 Supra-Foley Cystostomy™

The 12 French catheter is still considered a pediatric size and still can have problems with obstruction. As most suprapubic catheters are placed in gynecologic surgery under general anesthesia, large bore catheters can be placed with modern plastic trocars safely using percutaneous placement (Figure 48.11). As the Supra-Foley™ is available in 12 F and 16 F, a 10 to 18 Fr Foley catheter can be placed and can negate the obstruction issue related to the smaller diameter needle guided cystostomy tubes. Additionally with the blunt "pencil-like" tip, surgeons can feel more control and comfort with the placement versus the sharp metal trocars.

48.2.4 Indications for Cystostomy Tube Placement

Common gynecologic considerations for cystostomy tube placement urinary diversion include:

1. Pubovaginal sling placement due to potential urinary retention (also at time of urethral diverticulum repair)
2. Vesicovaginal fistula repair
3. Urethral trauma, especially if associated with vaginal lacerations requiring repair
4. Neurogenic causes of urinary retention

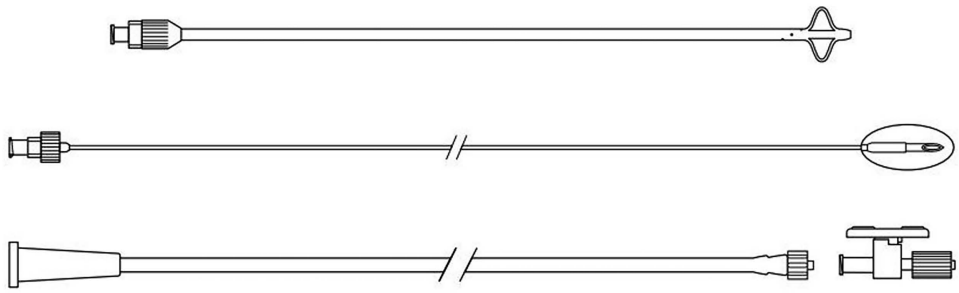


FIGURE 48.10 Malecot (Stamey) Cystostomy kit™ (by courtesy of Cook Medical).

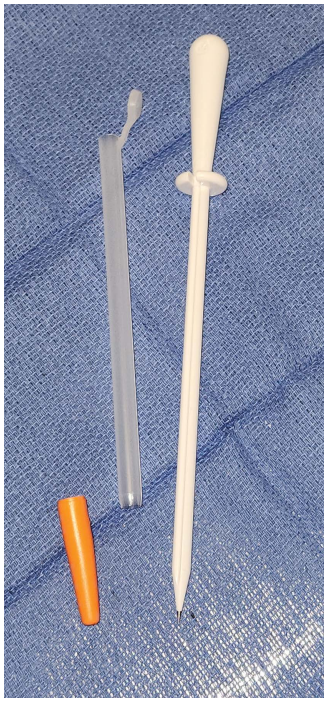


FIGURE 48.11 Supra-Foley™ (Utah Medical).

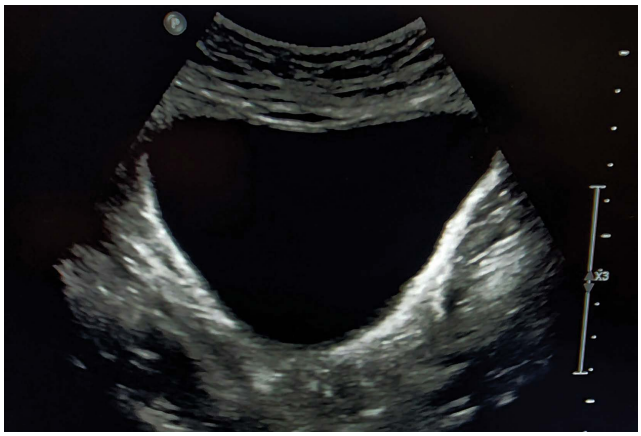


FIGURE 48.12 Bladder ultrasound, transabdominal.

48.2.5 Procedural Steps

Regardless of the operation being performed gynecologically, percutaneous placement of suprapubic cystostomy has the same general steps.

1. Make sure the abdominal wall is surgically prepped in the field.
2. Position the patient in as much Trendelenburg as it is safe regarding the patient being optimally secured to the table to allow the intestines to move to the mid- to upper abdomen to help prevent bowel injury.
3. Measure about two fingers breadth above the pubic bone in the midline to be marked out for target placement.
4. Maximally fill the bladder (consider using a cystoscope for filling and direct vision placement of the trocar/needle and catheter).
5. If ultrasound is available, take a quick bladder ultrasound, as when the bladder is filled with fluid you should see not more than bladder and anterior wall. If there are any concerns of bowel in the space, consider a urologic consultation or send the patient postoperatively to interventional radiology for image-guided catheter placement.
6. Once the catheter is placed and confirmed, irrigate the catheter with a catheter tip syringe to make sure it is irrigating properly. If the catheter does not irrigate, be concerned the catheter is not in the bladder and consider cystoscopy.
7. Secure the catheter to the skin with a nylon drain type suture and place a gauze dressing over the surgical site.

48.2.6 Complications

1. *Early* complications include bowel injury, catheter misplacement/dislodgement, hematuria, bladder spasms, and wound infection
2. *Late* complications include bladder stones, urinary tract infections, sepsis, decreased bladder capacity, and potential for squamous cell cancer of the bladder

Bowel injuries can be potentially avoided by placing the patient into Trendelenburg position, filling the bladder maximally, and using an intraoperative ultrasound (Figure 48.12) to confirm no anterior structures to the bladder. A 16 or 18 Fr spinal needle can be used to aspirate the bladder contents and reassure you are in the correct space. If you do not have ultrasound available, still optimally position the patient in Trendelenburg and cystoscopically maximally fill the bladder and place the suprapubic tube under direct vision with a cystoscope if possible, as you will additionally have final confirmation of the correct position. Be cautious when placing a suprapubic tube in any patient who has had prior bowel surgery, especially in the lower GI cavity as the space of Retzius may have been violated and bowel could be potentially within the space. Consider ordering a noncontrast CT scan of the abdomen and pelvis, preoperatively surveying for bowel in the space of Retzius if concerns exist prior to procedure. If there is

bowel preoperatively in the space, you can consult with your interventional radiologist about image-guided placement of the catheter prior to the procedure.

References

1. De EJB et al. Instrumentation for native tissue repair reconstructive procedures. In: Zimmern PE et al., eds. *Native Tissue Repair for Incontinence and Prolapse*. Springer; 2017:2:37–50.
2. Patel RS et al. Role of office-based vaginoscopy in a tertiary care center. *Urology Practice*. 2022;9:80–86.
3. Chen JY et al. Vaginoscopy with laser treatment of symptomatic upper vaginal mesh exposure after prior mesh sacrocolpopexy. *Urology*. 2003;176:69–73.
4. Di Muzio B et al. *Ureteric stent* [Internet]. Available at: www.Radiopaedia.org (Accessed Jul 2023).
5. Hodgkinson CP et al. Trocar suprapubic cystostomy for postoperative bladder drainage in the female. *Am J Obstet Gynecol*. 1966;96(6):773–783.
6. Taylor BD et al. Suprapubic cystostomy and the use of polyethylene tubing. I. *Obstet Gynecol*. 1966;28:854–856.
7. Bonanno PJ et al. Bladder drainage with the suprapubic catheter needle. *Obstet Gynecol*. 1970 May;35(5):807–812.

49 COSMETIC GYNECOLOGY

Bayley Clarke, Cheryl Iglesia, and Wakako Horiuchi

49.1 Introduction

Cosmetic gynecology is a broad category of elective interventions to alter the aesthetic appearance of the external genitalia or functional vaginal procedures in the absence of pathology (1). The scope of cosmetic gynecology addresses both aesthetic and functional concerns aimed at enhancing sexual wellness. The definition of cosmetic gynecology is distinct from reconstructive pelvic surgery performed for medical pathology, such as symptomatic pelvic organ prolapse and urinary incontinence. Cosmetic gynecologic procedures are typically performed by general gynecologists, urogynecologists, urologists, dermatologists, and plastic surgeons.

The field of cosmetic gynecology is controversial. The American College of Obstetricians and Gynecologists (ACOG) stated concerns in a committee opinion about cosmetic procedures not being medically indicated or supported by enough evidence regarding safety and effectiveness (2). The Royal College of Obstetrician and Gynecologists published a statement of similar opinion (3).

Despite its controversy, interest in cosmetic gynecology has increased for both patients and providers. The number of cosmetic procedures being performed increased by 55% from 2020 to 2021, with over 30,000 procedures in total (4), which is a greater increase than any other cosmetic surgical field. The procedural volume increase is thought to be secondary to increased social media exposure, the increasing number of women who are grooming or removing pubic hair allowing for increased awareness of genitalia asymmetries with idealization of perfect genitalia, and increased access to pornographic images (5).

49.2 Preoperative Counseling

Before undergoing any cosmetic procedure, a woman's motivation for getting surgery must be explored. Patients considering elective cosmetic gynecologic procedures should be assessed for possible body dysmorphic disorder. Body dysmorphic disorder (BDD) is a psychiatric disorder that is characterized by extreme preoccupation of self-perceived defects in one's appearance. Patients with BDD make up about 8% of patients undergoing cosmetic procedures in the United States. There is no evidence that surgery will help improve the mental well-being of patients with BDD. Patients can be screened for BDD with a screening questionnaire such as the Cosmetic Procedure Screening Scale (COPS) (6). The COPS questionnaire is a nine-item questionnaire that asks for the feature(s) that the person dislikes, the nature of the cosmetic procedure they are seeking, and diagnostic criteria of BDD. The items are scored from 0 (least impaired) to 8 (most impaired). The total range is from 0 to 72, with a higher score reflecting greater impairment. A score of 40 or above is suggestive of BDD. If a diagnosis of BDD is made during the preoperative evaluation, the patient should be referred to a mental health provider prior to any surgical intervention.

It is important that the normal range of vulvovaginal anatomy and all the various aspects of female sexual function and dysfunction are discussed in detail with any patient interested in cosmetic gynecology. Patients must be aware that these procedures are elective and are not entirely risk-free. Additionally, it is important to explore a woman's autonomy when regarding her decision to pursue cosmetic surgery. The surgeon must fully rule out the possibility of exploitation, force, or external influence as the driving factor.

Patients must be made aware that there is a paucity of data regarding cosmetic gynecology procedures. There is no ideal shape or size of external female genitalia, so efficacy of aesthetic improvement is difficult to determine. The few studies that do report on patient satisfaction following cosmetic vulvovaginal procedures and sexual function are retrospective studies, with most not utilizing validated questionnaires, and therefore must be interpreted with caution (7). Complication rates are not well published for any of the procedures and are widely variable from paper to paper. Potential complications include pain, bleeding, infection, adhesions, dyspareunia, changes in sexual function or sensation including difficulty with orgasmic function, reoperation, and dissatisfaction with the cosmetic appearance. It is important to note that elective cosmetic gynecologic procedures performed on patients under the age of 18 are prohibited in the United States unless there are medical indications (8).

49.3 Terminology

In an effort to clarify the ambiguous cosmetic gynecology terminology, Garcia et al. recently recommended formal terminology to utilize when describing research and when conversing within the medical community (9). The format of *anatomic region + therapeutic descriptor + therapeutic approach* should be used.

TABLE 49.1 Cosmetic Gynecology Terminology

Therapeutic Descriptor	Definition
Reduction	Removal of tissue to make smaller or less apparent
Tightening	To decrease the appearance of loose tissue or feeling of laxity
Augmentation	To make larger or change shape/appearance
Amplification	To enlarge via increase in surface area or functional stimulation effect
Depigmentation	Decreasing pigmentation
Therapeutic Approach	
Surgical	The use of scalpel, scissors, electrocautery, and/or sutures
Energy-based	Application of an energy-based source in one or more sessions
Lipectomy	The use of cannulas to remove excess adipose tissue
Filler	Injection of biological or supplementary medium
Topical	Application of a chemical cream or ointment

Source: Compiled from Ref. 9.

DOI: 10.1201/9781003312109-49

49.4 Cosmetic Procedures

49.4.1 Clitoris and Clitoral Prepuce

The clitoris is an organ that includes the glans, body, root, crura, suspensory ligament, and vestibular bulbs. The clitoral prepuce (or clitoral hood) is keratinized squamous epithelium on the cephalad portion of the clitoris that may partially cover it. The size is variable; Kreklau et al. took measurements in almost 700 women and found the clitoris to have a mean size of 4.62°±°2.5 mm × 6.89°±°4.9 mm (10). It is innervated by the dorsal nerves of the clitoris (branches of the pudendal nerve), which are encountered at 11 and 1 o'clock along the body of the clitoris.

Clitoral procedures are most often done in conjunction with labia minora procedures. A clitoral frenulum reduction procedure refers to when a portion of the epithelial folds containing the frenulum is surgically removed, frequently to achieve symmetry after a labia minora procedure. A clitoral prepuce reduction has two primary surgical techniques (Figure 49.1). It may be performed as a "lift," in which a triangular portion of epithelium at the anterior aspect of the clitoral prepuce is resected and reapproximated. It may also be performed by resecting epithelium in the shape of vertical ellipses on either side of the clitoris (11).

To date, there is only one study looking at outcome measurements, which showed no change in sensitivity after a clitoral hood reduction (11).

49.5 Labia Minora

The labia minora are non-hair-bearing keratinized squamous epithelium that originate at the clitoral prepuce and extend to the posterior fourchette. There is significant variation in labia minora length (5–100 mm) and width (1–60 mm), and protruding labia minora beyond the labia majora were more common than recessed labia minora (12).

Because of this variation, there is no numeric definition of labia minora hypertrophy or elongation. There are several systems that classify the labia minora anatomy. Garcia et al. adapted three accepted systems: Smarrito (classification based on the most prominent aspect of labia), Franco (measurement of the introitus to the distal edge), and Motakef (measurement of the lateral aspect of the labia majora to the distal edge of the labia minora) (1). See Table 49.2 for this classification. Stage is determined by the largest measured side if asymmetry is present.

Labia minora reduction-surgical, or "labiaplasty," is the most common cosmetic gynecologic procedure (4). There are several different techniques published for surgical reduction of the labia minora (Figure 49.2).

De-epithelization involves resecting aspects of the medial and lateral labia minora epithelium and then closing with sutures, without disturbing the underlying subcutaneous tissue (13, 14). A central wedge excision removes a triangular portion of tissue from the central (15) or inferior/posterior portion of the labia minora (16–18). A Z-plasty entails two Z-shaped incisions that are made spanning from the base of the central portion of the labia minora to the distal edge, with the two Zs pointed 90 degrees apart. The central wedge is then resected and the edges are reapproximated (8). A direct excision is simply removal of the distal edge of the labia minora (11, 19). A composite reduction is a more extensive version of a direct excision of superior flaps and clitoral prepuce reduction (20). A W-plasty utilizes two intersecting W-shaped lines are made on the lateral and medial labia majora. The epithelium is resected on either side on the incision, and then it is reapproximated (21, 22).

Overall evidence regarding outcomes and complications is limited. The rates of complications are highly variable from study to study. Surgical revision rates range from 0% to 17.6% (1). There is no uniform subjective or objective outcome measurement in place, making a high-quality meta-analysis difficult.

TABLE 49.2 Labia Minora Classification

Stage 0	Labia minora absent
Stage I	< 2 cm
Stage II	2.1–4 cm
Stage III	4.1–6 cm
Stage IV	> 6 cm
Suffixes	
A	Asymmetrical labia minor (must denote larger side)
B	Cosmetic bother
C	Clitoral prepuce involvement
D	Dyspareunia or discomfort with physical activity due to labia minora

Source: Adapted from Ref. 1.

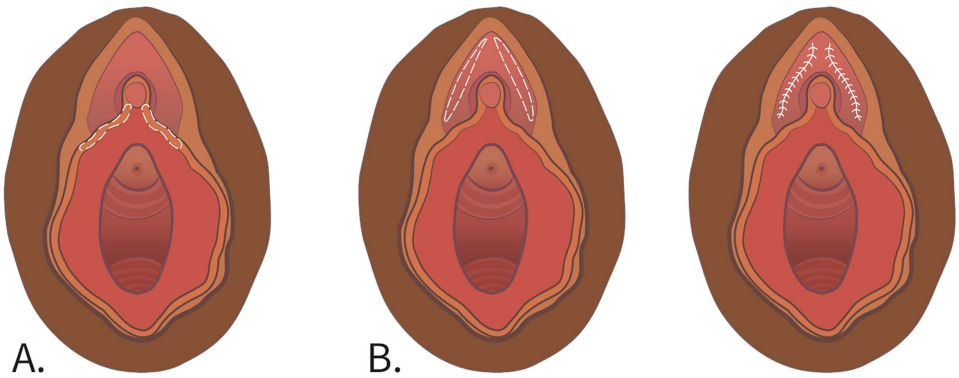


FIGURE 49.1 (A) Clitoral frenulum reduction – excision (white dotted lines) of the epithelial folds containing the clitoral frenulum; (B) clitoral prepuce reduction – resection of the clitoral epithelium in the elliptical technique (left: white dotted lines) and "lift" technique (right: white lines, proposed suture lines).

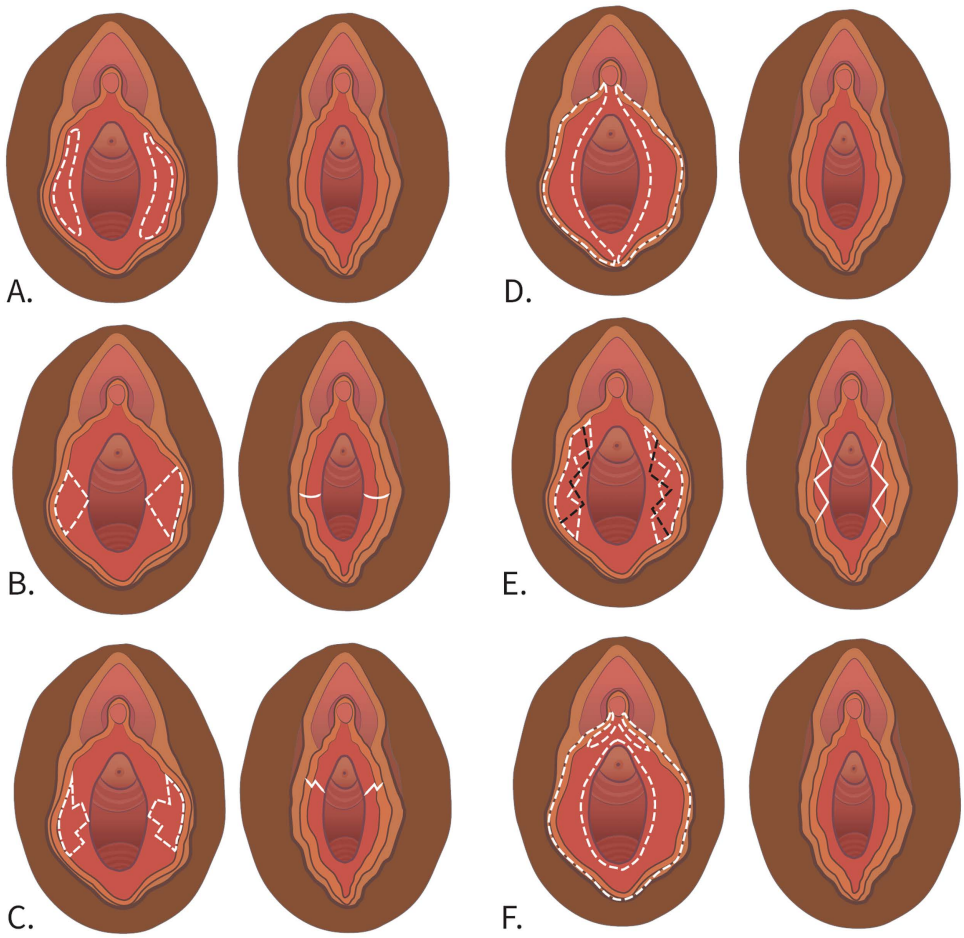


FIGURE 49.2 Labia minora reduction: (A) De-epithelization; (B) central wedge; (C) Z-plasty; (D) direct excision; (E) W-plasty; (F) complete reduction.

49.6 Labia Majora

The labia majora are cutaneous skin folds that begin at the mons pubis and extend posteriorly to the perineum, forming the lateral longitudinal borders or the vulvar clefts. The medial aspect is hairless, while the lateral aspect has hair. As with all other genitalia, there is wide variation in size, about 80°±°15°mm (10).

There are established classifications of labia majora hypotrophy, but these are all in relation to pathologies such as genitourinary symptoms of menopause. There are no classifications for normal, nonpathological variations. Garcia et al. proposed describing labia as stage 0 – desires no alteration, stage I – desires augmentation, and stage II – desires reduction.

Labia majora reductions can be performed in three ways (Figure 49.3): (1) labia majora reduction-surgical, which entails an elliptical or bow-shaped incision in the inner labia majora to excise unwanted epithelium and adipose tissue; (2) labia majora liposuction ("lipectomy"), to remove excess adipose tissue, although many patients require surgical removal of redundant epithelium after a lipectomy (15); and (3) energy-based laser or radiofrequency therapy to tighten the labia, which is discussed in Chapter 37.

Labia majora augmentations are relatively new, first described in 2007. They may be performed surgically or with filler. Labia majora augmentation-surgical may be done using a dermal graft, which entails creating tunnels bluntly on the medial aspect of the labia majora, and then inserting two de-epithelialized dermal fat grafts (23). It may also be performed using an adipofascial flap, in which a de-epithelialized adipofascial flap from the inner thigh is raised to the labia majora (24). Finally, it may be achieved by taking a de-epithelized portion of the labia minora and transposing it to a pocket in the labia majora (25).

Labia majora augmentation-filler may be performed with autologous fat grafts ("lipofilling") (26, 27) or with hyaluronic acid filling (28). Both inject into the subcutaneous tissue of the labia majora.

49.7 Vagina

The vagina is a muscular tube that begins proximally at the cervix and extends to the vulva vestibule distally. The function of the vagina is for both sexual intercourse and childbirth. Vaginal laxity is associated with excessive vaginal looseness, especially noticed at the introitus. It may or may not be associated with symptoms of pelvic organ prolapse (POP) or sexual dysfunction; if associated POP exists, vaginal laxity surgery would not be considered cosmetic.

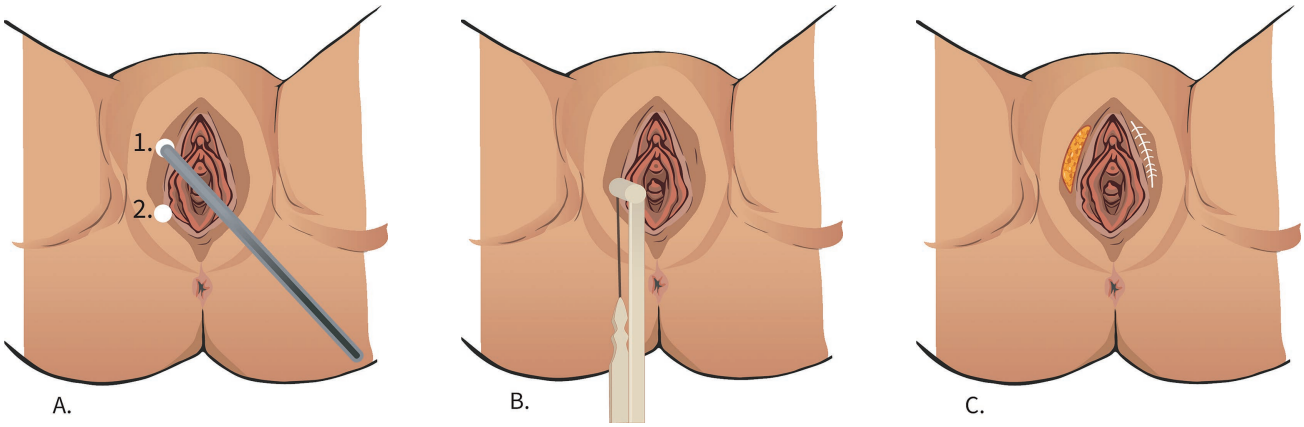


FIGURE 49.3 Labia majora reduction – (A) lipectomy (1, 2: proposed locations of liposuction; a liposuction canula is inserted in the area of fat removal); (B) energy-based/radiofrequency; (C) surgical (on the contralateral side, a white line depicting the reapproximated edges is illustrated on the labia majora).

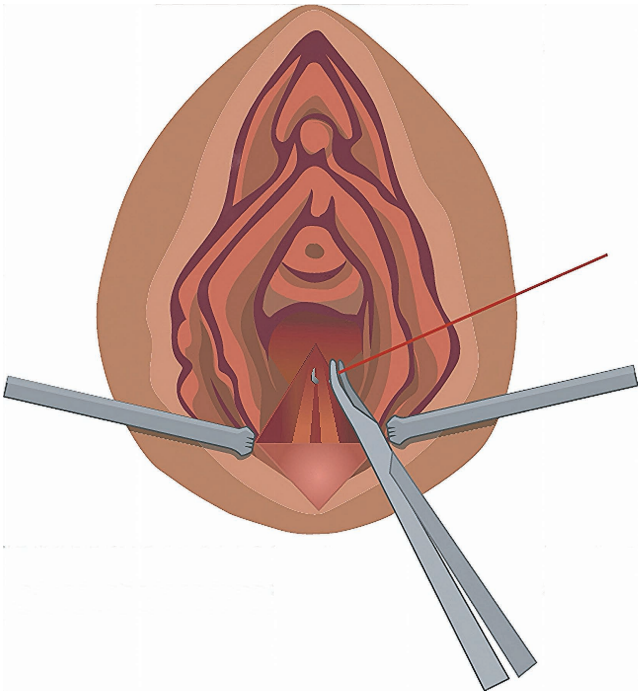


FIGURE 49.4 Vaginal reduction by posterior vaginal colporrhaphy.

The symptom of vaginal laxity does not correlate with physical exam findings of POP or sexual function (29). Indeed, the relationship between laxity and sexual function is not well understood. There is no standardized, objective measurement of vaginal laxity.

Vaginal reduction-surgical (Figure 49.4) is performed to narrow either the genital hiatus or the entire vagina in the absence of POP. The surgical repairs are performed in the same manner as for POP: anterior/posterior vaginal colporrhaphy, perineal repair, or levator plication. These may be performed in isolation or together. Additionally, a lateral colporrhaphy has been described as an excision of vaginal epithelium on the posterior lateral wall (30). Vaginal tightening–energy based is described in Chapter 36.

49.8 Mons Pubis

The mons pubis is a fat pad located directly anterior to the pubic bone. It is usually covered in pubic hair and functions as a cushion during sexual intercourse. Mons pubis hypertrophy can be associated with ptosis, laxity, and redundancy and can be caused by weight loss or gain, pregnancy, and familial fat distribution (31).

Plastic surgery literature has well-established classifications of mons pubis hypertrophy. The El Khatib grading system is graded on a four-point scale based on the degree of mons pubis bulge and extent of external genitalia coverage (32). The Pittsburg Rating Scale is a four-point scale intended for use after extreme weight loss that grades contour deformities (33).

Mons pubis reduction is performed with the intent to achieve a smooth transition from the lower abdomen to the vulva. It is often performed in conjunction with an abdominoplasty or a panniculectomy (Figure 49.5).

Liposuction of the mons pubis may be performed. In a suction-assisted lipectomy, adipose tissue is aspirated using a suction cannula. Ultrasound-assisted lipectomy is a technique that liquifies adipose tissue prior to removal with the suction cannula.

Surgical reduction of the mons pubis, or monsplasty, removes excessive skin and fat from the mons. This is achieved by a wedge resection from the pubic symphysis to the superior border of the mons, down to the level of the mons pubis fascia. The shape of the wedge is variable but may be triangular, trapezoidal, circular, or crescent. The mons pubis is subsequently sutured to the abdominal fascia.

49.9 Genital Depigmentation

Hyperpigmentation of the anogenital area can result from pregnancy, medical conditions, or chronic irritation secondary to activities like waxing. There are procedures that may be performed with the aim of achieving a skin color consistent with surrounding areas. This may be done with energy-based treatments such as fractional CO_2 laser or radiofrequency. It may also be done with topical treatments such as a chemical peel or glycolic acid peels. However, at this time, there is very minimal data on safety or efficacy regarding these treatments.

TABLE 49.3: Mons Pubis Hypertrophy Scales

Classification	Definition	Recommended Intervention
El Khatib Grading System		
Grade 1	Mild bulging with minimal or no covering of external genitalia	Liposuction
Grade 2	Moderate bulging with partial covering of external genitalia	Liposuction-assisted panniculectomy
Grade 3	Marked bulging with complete covering of external genitalia	Liposuction-assisted panniculectomy and fascial-dermal suspension suture ± vertical wedge excision to address
Grade 4	No bulging with partial or complete covering of external genitalia	Panniculectomy-assisted dermal-fascial suspension sutures and vertical wedge excision to address the horizontal
Pittsburgh Rating Scale		
Score 0	No visible abnormality	No intervention
Score 1	Excessive adiposity	Ultrasound assisted lipectomy or suction-assisted lipectomy
Score 2	Ptosis	Monsplasty
Score 3	Significant overhand below symphysis	Monsplasty

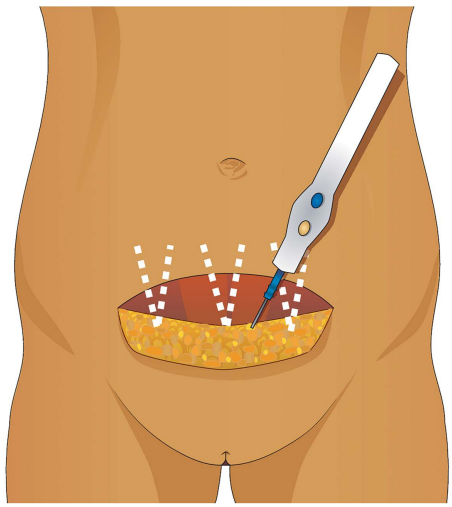


FIGURE 49.5 Mons pubis reduction: excess skin and adipose tissue is excised and sutures are placed to elevate the mons pubis.

49.10 Sexual Function Procedures

Filler procedures have been marketed to improve sexual experience. However, they are not an approved treatment option for female sexual dysfunction (FSD) but are rather marketed for sexual enhancement. There is minimal data on the efficacy of these procedures.

Platelet-rich plasma (PRP) is an autologous injection in which whole blood is removed from a patient and centrifuged down to isolate the PRP. It is then activated with calcium, resulting in platelet degranulation. The proposed mechanism of action is that it causes the release of cytokines and growth factors, which are transferred to the target tissue. The target tissue then has a stimulation of cell proliferation from the growth factors. It is FDA approved for orthopedic procedures but has been used off label for other intents, including sexual function. It is used as an injection into the anterior vaginal wall and periclitoral region to help increase growth factors and stimulate cell proliferation to augment the sexual experience. This can be done as an in-office procedure with no down time for the patient.

Other biologic fillers such as hyaluronic acid and collagen have been proposed for theoretically enhancing sexual function, but there is minimal data that exists to support its use.

49.11 Conclusion

Cosmetic gynecology is an emerging and controversial field. For patients seeking cosmetic procedures, extensive counseling must be provided. Patients must be made aware that all procedures are elective and not medically indicated. As the procedures continue to become more popular and widespread, it will be important to investigate their efficacy and safety.

References

1. Garcia B et al. Cosmetic gynecology - a systematic review and call for standardized outcome measures. *Int Urogynecol J*. 2020;31(10):1979–1995.
2. ACOG Committee opinion 795: elective female genital cosmetic surgery. *Obstet Gynecol*. 2020;135(1):e36–e42.
3. Royal Collage of Obstetricians and Gynaecologists. Ethical opinion paper. *RCOG Ethics Committee*, 2013. Available at: www.yumpu.com/en/document/view/24721817/rcog-fgcs-ethical-opinion-paper.
4. Aesthetic plastic surgery national databank report [internet]. *The Aesthetic Society*, 2022. Available at: www.plasticsurgery.org/news/plastic-surgery-statistics.
5. Grossman SL et al. Risky business: is pubic hair removal by women associated with body image and sexual health? *Sex Health*. 2018;15:269–275.
6. Veale D et al. Development of a Cosmetic Procedure Screening Questionnaire (COPS) for body dysmorphic disorder. *J Plast Reconstr Aesthet Surg*. 2012;65(4):530–532.
7. Miao LM et al. Labial surgery for well women: a review of the literature. *BJOG*. 2010;117:20–25.
8. Giraldo F et al. Central wedge nymphectomy with a 90-degree Z-plasty for aesthetic reduction of the labia minora. *Plast Reconstr Surg*. 2004;113(6):1820–1827.
9. Joint Writing Group of the International Urogynecological Association and the American Urogynecologic Society. Joint report on terminology for cosmetic gynecology. *Int Urogynecol J*. 2022;33(6):1367–1386.
10. Kreklau A et al. Measurements of a 'normal vulva' in women aged 15–84: a cross-sectional prospective single-Centre study. *BJOG*. 2018;125(13):1656–1661.

11. Placik OJ et al. A prospective evaluation of female external genitalia sensitivity to pressure following Labia minora reduction and clitoral Hood reduction. *Plast Reconstr Surg*. 2015;136(4):442e–452e.
12. Hayes JA et al. What is the anatomical basis of labia- plasty? A review of normative datasets for female genital anatomy. *Aust New Zeal J Obstet Gynaecol*. 2020:1–8.
13. Choi HY et al. A new method for aesthetic reduction of labia minora (the deepithelialized reduction of labioplasty). *Plast Reconstr Surg*. 2000;105(1):414–419.
14. Cao YJ et al. A modified method of labia minora reduction: the de-epithelialised reduction of the central and posterior labia minora. *J Plast Reconstr Aesthet Surg*. 2012;65(8): 1096–1102.
15. Alter GJ. Management of the Mons Pubis and Labia Majora in the massive weight loss patient. *Aesthet Surg J*. 2009;29(5):432–442.
16. Rouzier R et al. Hypertrophy of labia minora: experience with 163 reductions. *Am J Obstet Gynecol*. 2000;182(1 Pt 1):35–40.
17. Munhoz AM et al. Aesthetic labia minora reduction with inferior wedge resection and superior pedicle flap reconstruction. *Plast Reconstr Surg*. 2006;118(5):1237–1247.
18. Kelishadi SS et al. Posterior wedge resection: a more aesthetic labiaplasty. *Aesthet Surg J*. 2013;33(6):847–853.
19. Pardo J et al. Laser labioplasty of labia minora. *Int J Gynaecol Obstet*. 2006;93(1):38–43.
20. Gress S. Composite reduction labiaplasty. *Aesthet Plast Surg*. 2013;37(4):674–683.
21. Maas SM et al. Functional and aesthetic labia minora reduction. *Plast Reconstr Surg*. 2000;105(4):1453–1456.
22. Solanki NS et al. Aesthetic and functional reduction of the labia minora using the Maas and Hage technique. *J Plast Reconstr Aesthetic Surg*. 2010;63(7):1181–1185.
23. Salgado CJ et al. Use of dermal fat graft for augmentation of the labia majora. *J Plast Reconstr Aesthet Surg*. 2012;65(2):267–270.
24. Karabagli Y et al. Labia majora augmentation with De-epithelialized labial rim (minora) flaps as an auxiliary procedure for Labia minora reduction. *Aesthet Plast Surg*. 2015;39:289–293.
25. El Danaf AAH. Deepithelized fasciocutaneous flap for labia majora augmentation during thigh lift. *Eur J Plast Surg*. 2010;33(6):373–376.
26. de Alencar Felicio Y. Labial surgery. *Aesthet Surg J*. 2007;27(3): 322–328.
27. Vogt PM et al. Autologous fat transplantation for labia majora reconstruction. *Aesthet Plast Surg*. 2011;35(5):913–915.
28. Hexsel D et al. Soft-tissue augmentation with hyaluronic acid filler for Labia majora and Mons pubis. *Dermatologic Surg*. 2016;42(7):911–914.
29. Polland A et al. Description of vaginal laxity and prolapse and correlation with sexual function (DeVeLoPS). *Sex Med*. 2021;9(6):100443.
30. Adamo C et al. Cosmetic mucosal vaginal tightening (lateral colporrhaphy): improving sexual sensitivity in women with a sensation of a wide vagina. *Plast Reconstr Surg*. 2009;123(6): 212e–213e.
31. Rahman AA. Monsplasty: new technique. *Plast Reconstr Surg*. 2013;37(1):107–109.
32. El-Khatib HA. Mons pubis ptosis: classification and strategy for treatment. *Aesthet Plast Surg*. 2011;35(1):24–30.
33. Song AY et al. A classification of contour deformities after bariatric weight loss: the Pittsburgh rating scale. *Plast Reconstr Surg*. 2005;116(5):1535–1544.
34. ACOG. Committee opinion 686. Breast and labial surgery in adolescents. *Obstet Gynecol*. 2017;129:17–19.

50 AVOIDANCE AND MANAGEMENT OF LAPAROSCOPIC COMPLICATIONS

Shivani Parikh, Hosam Hanna, and Resad Paya Pasic

50.1 Introduction

Minimally invasive surgery is becoming the preferred surgical route for many specialties, especially in gynecology. While laparoscopy provides advantageous benefits compared to open surgery, it is not impervious to complications. In the literature, a review of laparoscopic operations worldwide showed an overall complication rate ranging from 0.2% to 10.3% (1). Thus, in this chapter, we will discuss not only common complications experienced in laparoscopy but also methods for avoiding and recognizing these complications by considering preoperative, intraoperative, and postoperative factors.

50.2 Preoperative Considerations

A properly performed preoperative evaluation is important as it uncovers comorbidities that require further evaluation and management to avoid perioperative complications. Additionally, it allows the surgery team to effectively prepare and use the operative room and resources.

50.2.1 Patient Selection

In appropriately selected patients, laparoscopy has many advantages compared to laparotomy, such as faster recovery time, improved cosmesis, less postoperative pain, diminished adhesion formation, and equivalent surgical results. The decision to perform laparoscopy is based on several parameters. Primary among these are patient characteristics, availability of appropriate instrumentation, and the surgeon's skill set. Patient characteristics such as age, body mass index (BMI), comorbidities, previous abdominal surgeries, and anatomical considerations play a significant role in determining candidacy. A comprehensive evaluation involving medical history, physical examination, and diagnostic imaging is crucial to assess the patient's suitability for the procedure. Various scoring systems, such as the American Society of Anesthesiologists (ASA) classification and the physiological and operative severity score for the enumeration of mortality and morbidity (POSSUM) score, aid in predicting surgical outcomes and identifying high-risk patients.

50.2.2 History and Physical

A thorough patient history is necessary for preoperative surgical risk assessment. Any history of previous abdominal or pelvic surgeries, pelvic inflammatory disease (PID), peritonitis, and endometriosis may increase the complexity of any case. Medical comorbidities, especially cardiovascular and pulmonary disease, should be thoroughly investigated before the procedure and appropriate consultation to specialists or primary care providers can be placed. Previous complications with anesthesia should be carefully evaluated and documented with an anesthesiologist. Patients with higher BMI or weight over 350 pounds require special preoperative planning such as a bariatric operating table and equipment, special pneumatic compression boots, and anesthesia (20).

50.2.3 Prior Surgeries and Surgical Planning

Previous surgeries increase the likelihood of adhesive disease, risk of bowel and vascular injury during abdominal entry, and higher rates of converting to laparotomy (Table 50.1). Thus, preoperative physical examination should include abdominal evaluation of prior surgical scars to plan for abdominal entry. Additionally, a history of endometriosis, PID, or radiation treatment may predispose a patient to adhesions. Abdominal wall hernias or hernia repairs with possible mesh should be noted prior to the patient's surgery.

50.2.4 Preoperative Imaging

Ultrasonography: Ultrasound is a foundational imaging technique in gynecology. Transabdominal and transvaginal ultrasound provide real-time visualization of the pelvic structures, enabling the assessment of uterine abnormalities, ovarian masses, and other pelvic pathology. Doppler ultrasound aids in assessing blood flow patterns, which is valuable for diagnosing conditions such as ovarian torsion, ectopic pregnancy, and endometrial polyps (25).

Magnetic Resonance Imaging (MRI): MRI offers unparalleled soft tissue contrast and detailed anatomical information, playing a vital role in the evaluation of complex gynecologic conditions. Preoperative pelvic MRI provides insights into pathologies such as endometriosis, adenomyosis, deep infiltrating lesions, and enlarged fibroid uteri. It aids in surgical planning by elucidating anatomical relationships and identifying potential surgical challenges (19, 37).

Computed Tomography (CT): Although CT is infrequently used in gynecology due to radiation exposure concerns, it can be useful in specific scenarios. It is valuable for assessing certain pelvic masses, identifying lymph node involvement, evaluating potential invasion of advanced gynecologic malignancies, and postoperatively for assessing possible bowel injury (36).

Multimodal Imaging: In cases of intricate pathologies, a multimodal imaging approach can provide comprehensive information. Combination of pelvic ultrasound, MRI, and/or

TABLE 50.1 Frequency of Umbilical Adhesions in Patients with and without Previous Surgery

	N/Previous Surgery	No Prior Surgery	Prior Laparoscopy	Prior Low Transverse Incision	Prior Midline Incision
Agarwala	918/Surgery	None	16%	22%	62%
Brill	360/Laparotomy	None	None	27%	55%–67%
Audebert	814/Laparoscopy	0.68%	1.6%	19.8%	51.7%
Sepilian	151/Laparoscopy	None	21%	None	None

DOI: 10.1201/9781003312109-50

CT can offer a holistic understanding of the patient's condition, facilitating accurate diagnosis and surgical planning.

While imaging is an invaluable asset, it has its limitations. False positives, false negatives, and artifacts can occur. It is crucial to consider patient factors, such as body habitus, in the interpretation of imaging results. Additionally, the potential for radiation exposure and contrast-related reactions in CT imaging must be acknowledged. Effective communication about surgical goals and concerns between radiologists and gynecologic surgeons is paramount to ensure that imaging protocols are tailored to the specific clinical context.

50.2.5 Surgical Clearance and Consent

Surgical clearance involves assessing a patient's overall health status to determine their suitability for undergoing laparoscopic surgery. A comprehensive medical history and physical examination are conducted to identify preexisting medical conditions, medications, allergies, and potential contraindications. Chronic medical conditions such as hypertension, diabetes, cardiac disorders, and respiratory diseases are assessed for their impact on surgical risk and postoperative outcomes. Optimization of anemia and diabetes should occur prior to surgery with goals of hemoglobin > 8 g/dL and random blood sugar < 200 mg/dL, respectively, to limit perioperative complications. Depending on the patient's medical history, age, and procedure complexity, additional laboratory tests, imaging studies, and consultations with specialists might be required, as discussed previously.

Informed consent is a fundamental ethical and legal obligation that ensures patients are fully aware of the procedure and its associated risks, benefits, and alternatives. Surgeons must engage in a thorough discussion with patients, explaining the nature of the laparoscopic procedure, anticipated outcomes, potential complications, and any alternatives. Potential risks, benefits, and alternatives of the surgery should be discussed with the patient prior to the procedure (24, 35).

50.3 Intraoperative Considerations

Before beginning the planned surgery, the surgeon must be aware of all contents of the operating room (OR), which includes the patient, operating room staff team, surgical team, anesthesia team, and the location and workings of all surgical instruments and equipment. This allows the surgeon to assess the situation and troubleshoot accordingly if a problem arises. Additionally, while the surgeon may be the leader in the operating room, each patient and surgery should be handled with a team-based approach to help avoid any unnecessary complications. Moreso, communication is imperative between the surgical team, anesthesia, and OR supporting and nursing staff to address problems swiftly when they arise.

50.3.1 Patient Positioning

Proper patient positioning is important to the technical aspects of the surgery and in limiting neurovascular and muscular injuries to the patient. The patient must be positioned optimally for anesthesia to have access to the airway, circulation, and administration of fluids and medications throughout the procedure and for the surgeon to have access to the surgical site to operate efficiently and effectively.

For most pelvic surgeries, the patient must be positioned in a manner to withstand Trendelenburg and lithotomy positioning for the duration of the surgical time. With prolonged operative times, this type of positioning can cause compression or stretch events that lead to ischemia of muscle and neurovascular structures. The patient may experience transient neuropathies, tissue breakdown, compartment syndrome, and rhabdomyolysis. The overall incidence of nerve injuries is relatively uncommon and not well documented, likely as most are transient. In the literature, improper positioning accounts for the most common cause of peripheral neuropathy in gynecologic surgery, with reported rates of 0.02%–0.16% in the upper limbs and 1.5%–1.8% in the lower limbs. Major risk factors to cause such injuries include prolonged operative times, extreme of body mass index, and the ASA physical status classification (2–5).

There are four aspects for optimal patient positioning to limit these potential complications: (1) pressure redistribution, (2) deep vein thrombosis (DVT) prevention, (3) upper extremities positioning, and (4) lower extremities positioning. The use of padding material to disperse focal pressure on bony prominences of the body can prevent pressure-induced skin and tissue breakdown during long operating times. The use of sequential compression devices or stockings is recommended to minimize the risk of DVT, especially with the inherent factors of laparoscopy that contribute to this risk. For the upper extremities, the arms should be secured carefully at the patient's sides in supination with enough padding around the posteromedial elbows to avoid a brachial plexus injury and protect the ulnar nerve. Generally, shoulder braces should be avoided, and the use of steep Trendelenburg should be minimized if possible. If shoulder braces are used, apply gel, egg crate, or foam mattress pads to the acromioclavicular joint. For the lower extremities, the amount of hip flexion, abduction, and external rotation should be limited to avoid excessive strain on these nerves. Padded boot stirrups should be used instead of candy cane stirrups. Additionally, the knees should be adequately padded to avoid common peroneal nerve injury (Figure 50.1).

50.3.1.1 Abdominal Entry

Most serious complications related to laparoscopy are often due to initial abdominal entry, and the literature estimates that about 50% of inadvertent laparoscopic injuries to vital organs and vessels occur at the time of initial trocar entry (7, 8). While these injuries are rare, the most serious complications include major vascular, bowel, and visceral injury. The reported incidence rates of bowel wall and major vessel injuries are 0%–0.5% and 0.01%–1.0% of cases, respectively (9, 10).

Entry techniques include open (Hasson), closed (Veress), and direct or direct optical entry. A 2019 Cochrane systematic review concluded that there was insufficient evidence to show support for one method over another or differences in visceral or vascular injuries (9). However, most of these studies included low-risk patients and excluded high BMI and prior abdominal surgery. Thus, the choice of initial abdominal entry should be dependent on the surgeon's preference and the patient's characteristics.

Careful consideration of initial trocar placement can avoid damage to major vasculature and organs. Knowledge of abdominal and pelvic anatomy is crucial in considering entry point. Initial abdominal entry during laparoscopy is dependent on the patient's body habitus and surgical history, the surgeon's experience and preference of entry technique, and expected intra-abdominal pathology. Common entry points include the umbilicus, left upper quadrant or Palmer's point, right upper quadrant, mid-abdomen (Lee Huang point), vaginal or uterine fundus, and Jain's point (Figure 50.2) (33).

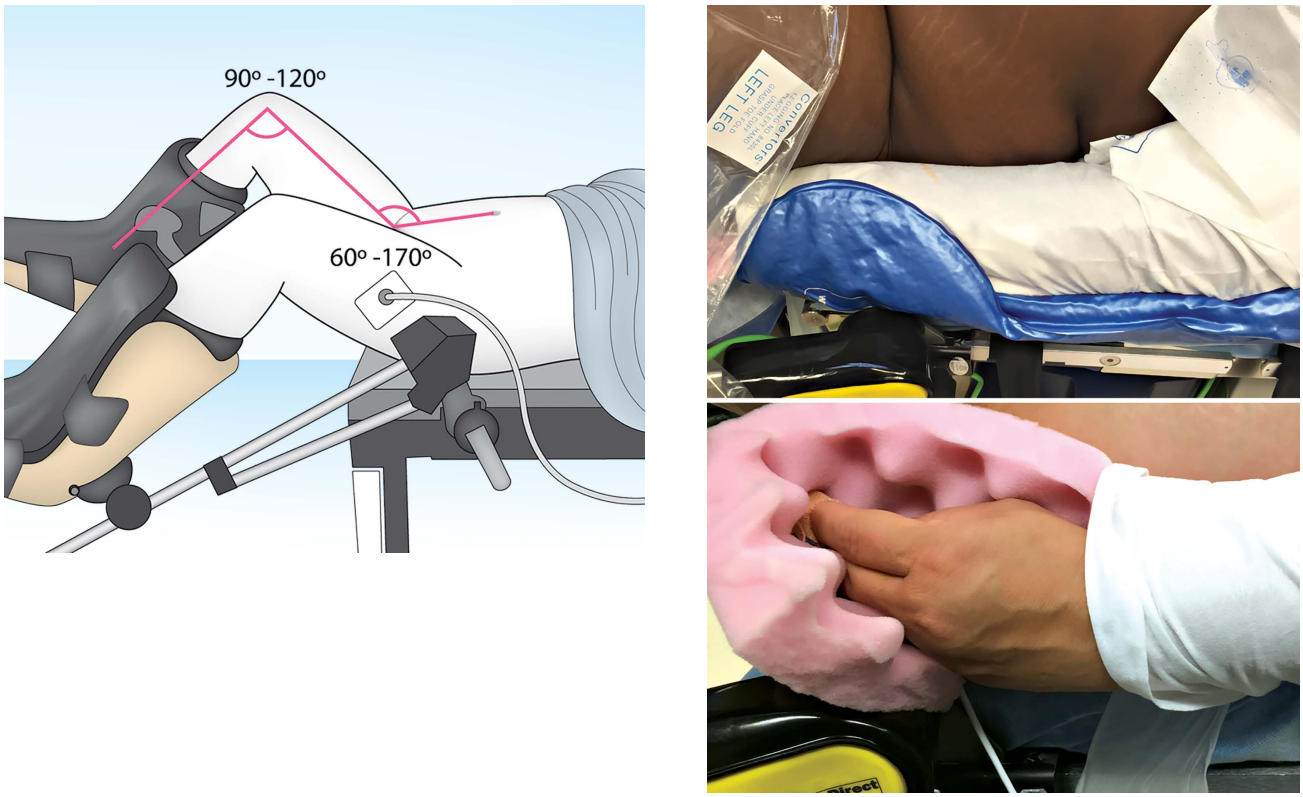


FIGURE 50.1 Patient positioning (From Biscette S et al. Patient Preparation. In: Pasic RP et al., eds. *Practical Manual of Minimally Invasive Gynecologic and Robotic Surgery*, Boca Raton, FL: CRC Press; 2018, with permission).

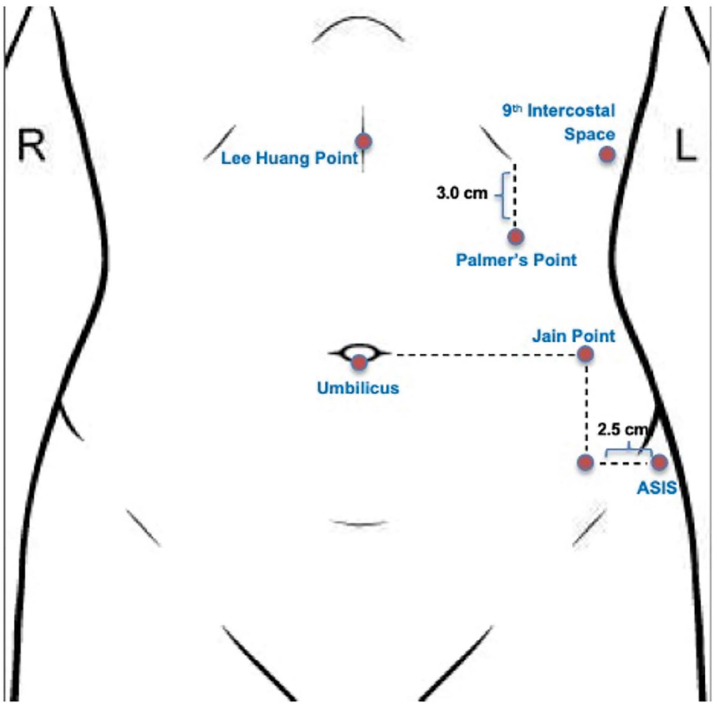


FIGURE 50.2 Laparoscopic entry points.

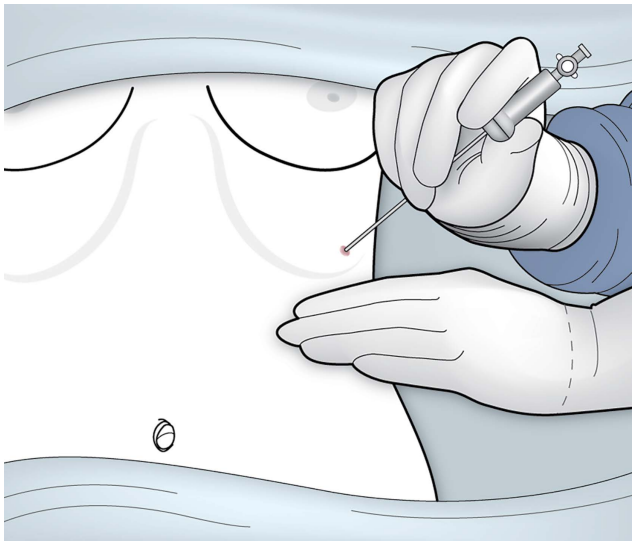


FIGURE 50.3 Left upper quadrant (Palmer's point) entry (From Reich H et al. Laparoscopic Surgery for Adhesions. In: Pasic RP et al., eds. *Practical Manual of Minimally Invasive Gynecologic and Robatic Surgery*. Boca Raton, FL: CRC Press; 2018, with permission).

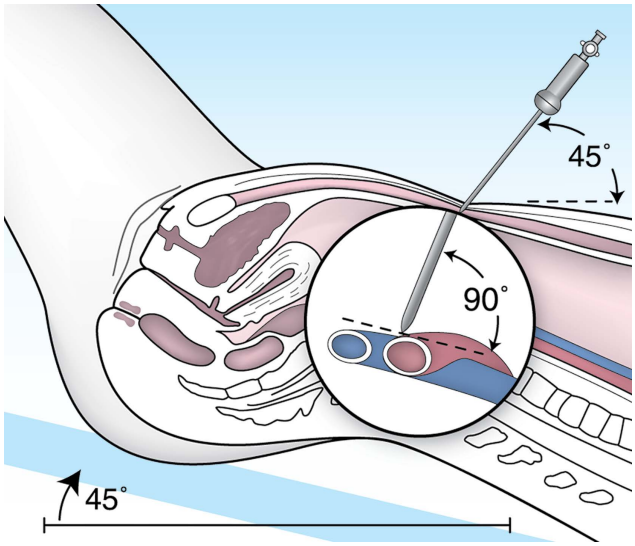


FIGURE 50.4 Veress entry. Avoid premature Trendelenburg positioning as it increases risk of vascular injury (From Lang TG et al. Creation of Pneumoperitoneum and Trocar Insertion Techniques. In: Pasic RP et al., eds. *Practical Manual of Minimally Invasive Gynecologic and Robotic Surgery*, Boca Raton, FL: CRC Press; 2018, with permission).

In patients with prior laparotomy or midline vertical incisions, the risk of intra-abdominal adhesions is approximately 50%, and approximately 30% of these patients will have severe umbilical adhesions with increased potential for bowel injury (11). With the rising rates of complex surgical patients and obesity, umbilical entry may not be ideal. In these cases, the left upper quadrant entry point should be considered, as it is generally a safe entry point for patients with previous laparotomies, abdominal mesh or umbilical hernia repair, abdominal or pelvic adhesions, and extremes in BMI (7) (Figure 50.3).

Methods to avoid injury during initial laparoscopic entry include the following:

1. Patient should lie flat in supine position as any degree of angulation can increase the risk of vascular or visceral injury (Figure 50.4).
2. Avoid multiple passes with the Veress needle or trocar. Once entry has been accomplished, inspect the area underneath the entry site to assess for blood, debris, discoloration of tissue, or bowel contents.
3. The abdomen should be insufflated at least 20–25 mmHg for a short period of time to maximize peritoneal volume and allow maximal counterpressure on the anterior abdominal wall when inserting additional trocars, which should be placed under direct visualization.
4. After placing a secondary port, the laparoscope can "port hop" to assess initial trocar entry for bleeding or unintentional insertion into the bowel. This technique can also be used to assess intra-abdominal or peritoneal adhesions.
5. Remove trocars under direct visualization at the conclusion of the procedure.

50.3.1.2 Pneumoperitoneum

Creation of pneumoperitoneum is essential in performing laparoscopic surgery as it enables visualization and mobilization within the operating field. Carbon dioxide (CO_2) is commonly used for pneumoperitoneum due to low cost, solubility, and nonflammability. The physiologic effects of pneumoperitoneum include systemic absorption of CO_2 and alterations in the hemodynamics and physiology of a variety of organs due to increased intra-abdominal pressure. Increased systemic absorption of CO_2 can cause hypercarbia and systemic acidosis, which may require changes in ventilation during surgery. Increased abdominal pressures decrease respiratory compliance and cardiac output by 30% and increase systemic vascular resistance and airway pressures (31). Appropriate patient selection is important as not all patients will tolerate pneumoperitoneum. Patients with cardiac history should have appropriate preoperative evaluation to assess cardiac risk with pneumoperitoneum (39).

During the procedure, reduced intra-abdominal pressures should be utilized when possible. The use of sequential compression devices during laparoscopy has shown to be beneficial in reversing the adverse effects of pneumoperitoneum on venous flow in the lower extremities and prevent DVT. Serious, but rare, complications of pneumoperitoneum include subcutaneous emphysema, pneumomediastinum and pneumothorax, and gas embolism for direct entry of gas into the arterial or venous system. Postoperative shoulder pain is common due to diaphragmatic irritation from CO_2, stretching of phrenic nerves, or pressure from abdominal organs in Trendelenburg positioning. Persistence of pneumoperitoneum can occur for up to 7 days.

50.3.1.3 Electrosurgery Complications

Electrosurgery is the use of high-frequency electrical current to create a desired clinical tissue effect. It is one of the

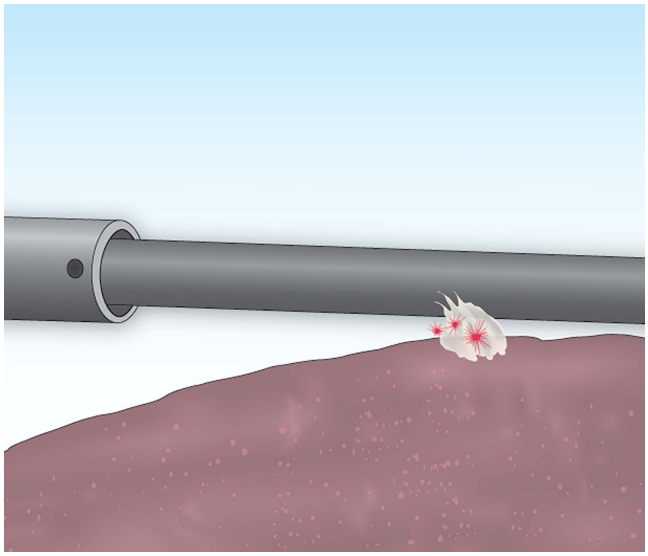


FIGURE 50.5 Direct coupling due to insulation defect of laparoscopic instrument (From Brill AI, Energy Systems in Laparoscopy. In: Pasic RP et al., eds. *Practical Manual of Minimally Invasive Gynecologic and Robotic Surgery*. Boca Raton, FL: CRC Press; 2018, with permission).

most common energy systems used during laparoscopic surgery. Complications related to electrosurgery are typically due to misidentification of anatomic structures, mechanical trauma, or electrothermal injury from unrecognized energy transfer. While the true incidence of electrosurgery injuries is known, the most serious complication is inadvertent bowel injury. Approximately 75% of bowel injuries due to electrosurgery are unrecognized at the time of occurrence, and the injury to small bowel is most common (12). Symptoms of bowel perforation following electrothermal injury are typically seen within 3 to 6 days postoperatively.

Electrothermal injuries result from direct application, insulation failure, direct coupling, or capacitive coupling. Remember, current always flows in pathways of least resistance. For additional information, please refer to the Chapter 8, "Energy Systems in Laparoscopy."

50.3.2 Direct Application: Unintended Activation of the Electrosurgical Probe on a Non-Target Tissue

- *Insulation failure*: Equipment defect to the insulating cover of the active electrode, allowing the current to contact non-target tissue. All instruments should be carefully inspected preoperatively as major causes of insulation failure are due to use of high-voltage current and frequent resterilization of instruments.
- *Direct coupling*: Unintended contact of an uninsulated instrument by active electrode within the abdomen (Figure 50.5)
- *Capacitive coupling*: Electric current is transferred from one conductor to adjacent conductive material without direct contact

Prevention of electrosurgical injuries is dependent on the knowledge of electrosurgical properties and use of monopolar and bipolar energy; training of operative staff; regular equipment maintenance; and the surgeon's hand–eye coordination using laparoscopic instruments. Alternate site burns can be avoided by ensuring the dispersive pad has sufficient contact with the patient's skin. The electrosurgical dispersive pad should be placed over clean, dry skin over a large muscle mass. Choose a proper current waveform mode when using monopolar energy. When applying energy during laparoscopic surgery, keep the tips of the instruments in the center of the operative field. Do not activate the electrode in the air when not in use as this can create an "open circuit." Finally, avoid using multiple energy sources in the abdomen at the same time.

If an electrosurgical injury to the bowel is not recognized at the time of surgery, there should be high alert of possible peritonitis within the first postoperative week. The severity of peritonitis is dependent on time between the bowel perforation and exploration and spillage of contents. Early intervention is crucial, and increasing abdominal pain postoperatively should prompt immediate surgical evaluation if necessary. Laboratory tests, such as complete blood count, comprehensive metabolic panel, C-reactive protein (CRP), and CT imaging with oral and intravenous contrast are recommended if there is suspicion for a bowel injury.

50.3.2.1 Vascular Injury

Vascular injuries at the time of laparoscopic surgery are associated with high morbidity and mortality, emergent laparotomy, blood transfusion, and vascular graft. The overall rate of reported vascular injuries during laparoscopy ranges from 0.02% to 0.64% (13). Due to this low incidence, there is limited ability to accurately assess risk factors. Yet, the greatest risk of vascular injury occurs at the time of initial abdominal entry.

The most common vessels injured at the time of trocar insertion are the right common iliac vessels and aorta. These injuries can be unrecognized due to the retroperitoneal location of these vessels. However, prompt intervention is critical. Consider placing the patient in steep Trendelenburg to evaluate the promontory for possible signs of vascular injury. The patient may require immediate fluid and blood resuscitation. Manual pressure on the aorta should be applied, and an experienced vascular surgeon should be contacted for urgent assessment.

Other locations common for vascular injury during gynecologic laparoscopy include the pelvic side wall, intraperitoneal structures (ovarian and uterine vessels), and retroperitoneum. Veins are at greater risk for injury during dissection and resection due to thinner walls. Bleeding from vasculature may be concealed due to temporary tamponade effect from the increased abdominal pressures and pneumoperitoneum. Thus, prior to closure, all surgical sites should be carefully evaluated for bleeding under lower abdominal pressures after releasing pneumoperitoneum.

Some vascular injuries can be managed laparoscopically depending on surgeon experience and location of the bleeding vessel. The following steps should be considered in the management of a possible vascular injury or uncontrolled bleeding:

1. Vessel occlusion with an atraumatic grasper to stop active bleeding
2. Suction irrigation to identify bleeding vessel
3. Laparoscopic vascular clip, bipolar energy, or suture to ligate bleeding vessel
4. Ray-Tac sponge for mechanical pressure or hemostatic agents consisting of thrombin and gelatin matrix (Figure 50.6).

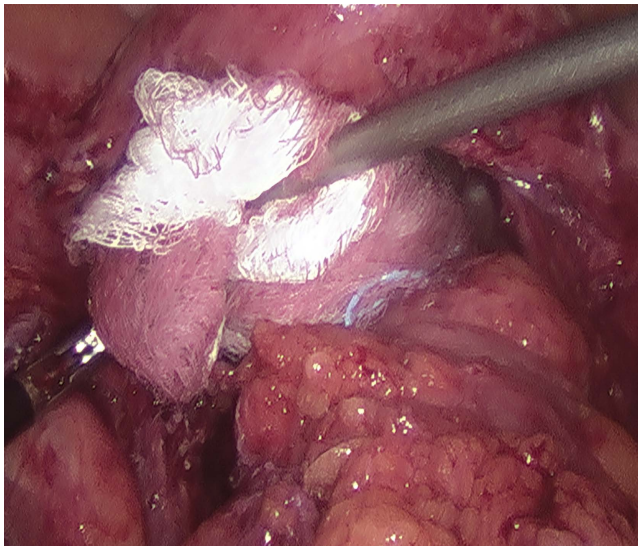


FIGURE 50.6 Ray-Tac sponge for mechanical pressure for control of bleeding (From Dun EC et al. Complications of Laparoscopic Surgery. In: Pasic RP et al., eds. *Practical Manual of Minimally Invasive Gynecologic and Robotic Surgery*. Boca Raton, FL: CRC Press; 2018, with permission).

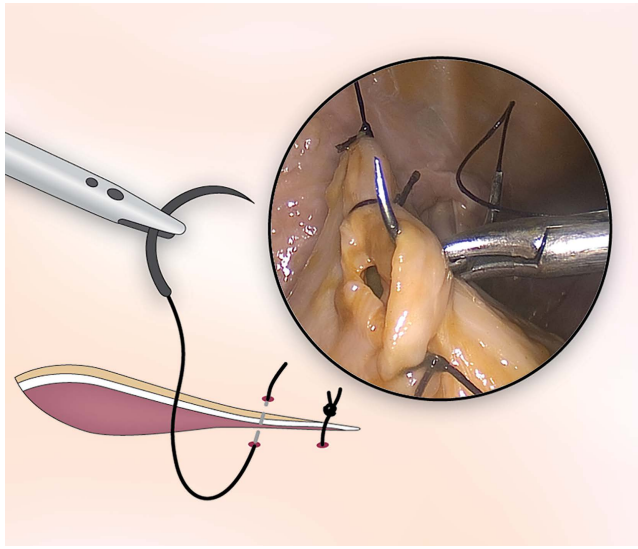


FIGURE 50.7 Bowel repair (From Dun EC et al. Complications of Laparoscopic Surgery. In: Pasic RP et al., eds. *Practical Manual of Minimally Invasive Gynecologic and Robotic Surgery*. Boca Raton, FL: CRC Press; 2018, with permission).

50.3.2.2 Bowel Injury

The risk of bowel injury during laparoscopic procedures is less than 1%. The most common causes of bowel injuries are initial abdominal entry and electrosurgery. About 40% of bowel injuries are unrecognized, and the sequela of complications can be catastrophic to a patient, with a mortality rate of up to 20%. The average time of diagnosis is approximately 3–7 days postoperatively. Small bowel and full-thickness colon injuries may take longer to develop significant symptoms due to the neutral pH of small bowel content and retroperitoneal position of portions of the bowel. Electrosurgical injuries may present 10–12 days postoperatively (14, 15).

Typical symptoms include abdominal pain, peritonitis, fever, nausea and vomiting, and abdominal distention. Patients who present later with symptoms generally have delayed necrosis of damaged bowel or a bowel leak, sepsis, abscess formation, and peritonitis. Exam findings may show acute abdomen or decreased bowel sounds. Chest and abdominal imaging should be ordered with either X-ray or CT scan. Imaging may show free air in the abdomen, extraluminal gas, extravasation of contrast, or characteristics of intra-abdominal abscess. Additionally, antibiotic therapy should be considered in these cases.

Surgical management of bowel injuries is dependent on the size and type of injury. Management options include primary repair, bowel resection with or without anastomosis, and stoma. With some larger injuries, the bowel can be laparoscopically managed by primary repair, reapproximating the defect with a 3–0 delayed-absorbable suture in two layers and perpendicular to the longitudinal axis of the bowel to prevent narrowing of the lumen (Figure 50.7). A bowel integrity test should be completed to assess the repair. Contraindications to primary closure of bowel injuries are > 50% disruption of bowel circumference and mesenteric devascularization with bowel ischemia, which may require a resection. Those with electrothermal bowel injuries may also require a resection. Thus, general or colorectal surgery should be considered for intraoperative evaluation whenever the surgeon has limited surgical experience with bowel injuries or complications (18, 34).

50.3.2.3 Genitourinary Complications

The bladder is the most common site of injury in gynecologic surgery, especially the bladder dome. Reported incidence of bladder injuries during laparoscopy range from 0.05% to 0.66% across all procedure types (16). Fortunately, the bladder is a very forgiving organ and can be repaired laparoscopically if identified intraoperatively. A two-layer running stich with absorbable 2–0 or 3–0 suture should be used to repair a bladder defect (Figure 50.8). Backfilling the bladder with 200 mL of sterile water or diluted methylene blue should be performed with cystoscopy to assess the integrity of the repair. Depending on the size of the cystotomy, a Foley catheter may need to be placed to decompress the bladder for at least 10 days to allow it to heal. The patient may need a retrograde cystourethrogram prior to catheter removal to ensure that the bladder has healed well without any defects.

Ureteral injuries occur at a higher incidence with laparoscopy than open surgeries, about 0.3%–2.0% (17). The ureter is particularly vulnerable to injury at three locations during gynecologic procedures: (1) the pelvic brim, (2) ovarian fossa, and (3) lateral to the cervix, uterosacral ligaments, or the cardinal ligament. Therefore, the ureters should be identified at the beginning of the procedure and ureterolysis should be considered in cases with severe fibrosis or distorted pelvic anatomy.

If a suspected or confirmed ureteral injury occurs, cystoscopy should be the next step to assess for ureteral efflux. Indigo carmine can be administered intravenously to identify the site of injury under laparoscopy by visualizing spillage of blue-colored urine. Retrograde ureteral stent placement with or without a pyelogram may be placed to evaluate for obstruction.

Repair of the ureter is dependent on the location and extent of the injury. For a partial ureteral injury, 6–0 Vicryl suture

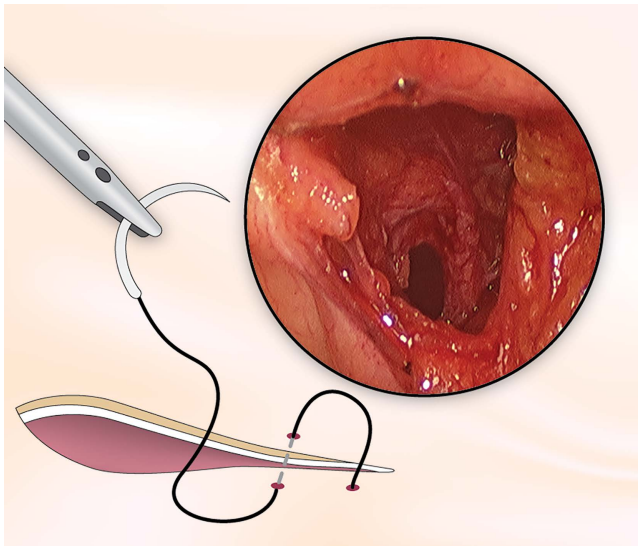


FIGURE 50.8 Bladder repair (From Dun EC et al. Complications of Laparoscopic Surgery. In: Pasic RP et al., eds. *Practical Manual of Minimally Invasive Gynecologic and Robotic Surgery*. Boca Raton, FL: CRC Press; 2018, with permission).

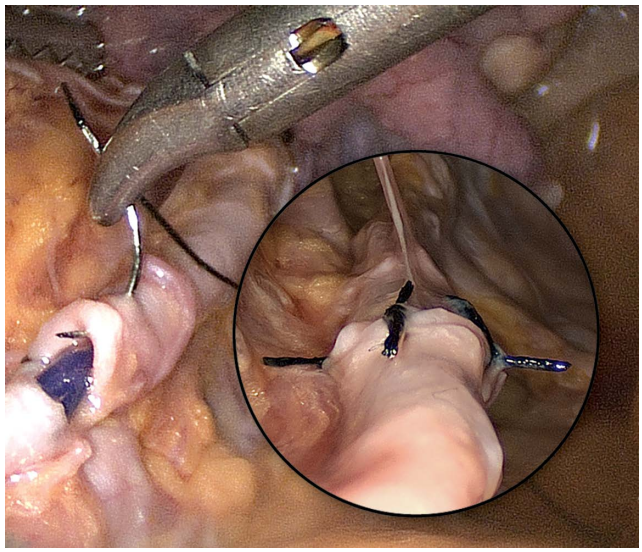


FIGURE 50.9 Ureter repair (From Dun EC et al. Complications of Laparoscopic Surgery. In: Pasic RP et al., eds. *Practical Manual of Minimally Invasive Gynecologic and Robotic Surgery*. Boca Raton, FL: CRC Press; 2018, with permission).

can be used laparoscopically after a stent has passed through the ureter. With complete ureteral transection, a ureteroureterostomy is preferred if the upper or middle third of the ureter is injured. Ureterolysis should be performed to free the ureter from any tension. A ureteral stent can be passed under direct visualization and a 3–0 Vicryl suture is passed through the adventitia and muscularis tissue to reapproximate the cut ends. The final repair is performed with a 5–0 or 6–0 absorbable suture with full thickness stitches at 3-, 6-, 9-, and 12 o'clock positions to reconnect the ureter (Figure 50.9). Ureteral stents should stay in place for 4–6 weeks after the repair.

It should be noted that thermal injuries, although rare, may not be noted until 10–14 days postoperatively. Injuries recognized intraoperatively have the best results as up to 25% of unrecognized ureteral injuries may result in loss of the ipsilateral kidney. Thus, knowledge of pelvic anatomy, identification of the ureter during difficult dissection, and recognition of injury are essential in preventing further complications.

50.4 Postoperative Considerations

Proper postoperative counseling should detail postoperative pain expectations, utilization of postoperative medications, and concerning signs and symptoms that should be communicated to the provider if necessary. Regular postoperative appointments can facilitate early detection and management of postoperative complications. For complex cases, a multidisciplinary approach with various specialists may be necessary during the postoperative period.

50.4.1 Wound Infection

Wound infections can be distressing for patients and lead to prolonged recovery times. Preventing, identifying, and managing wound infections are paramount for optimal postoperative care. Risk factors for wound infections are obesity, diabetes, smoking, and lengthy surgical duration. Adherence to sterile techniques during surgery, timely administration of prophylactic antibiotics, and meticulous wound care are methods in limiting wound infections. Finally, a patient that presents with a wound infection should have wound exploration and appropriate antibiotic therapy (30).

50.4.2 Venous Thromboembolism (VTE)

VTE is a serious and potentially life-threatening postoperative complication, and appropriate preoperative assessment should be completed for prophylaxis. Risk factors for VTE include obesity, prior history of VTE, and immobility. Early ambulation and postoperative chemoprophylaxis can help reduce the risk of developing a VTE (23).

50.4.3 Hernia Prevention

While incidence of incisional hernia is 12% for major open abdominal surgery, the risk is greatly reduced with laparoscopy, about 0.02%–5% for major laparoscopic surgeries. The most important risk factor in developing port-site hernias is trocar size. Thus, all fascial tissue of port sites > 10 mm should be meticulously closed with delayed-absorbable suture. It should also be noted that not all trocar sizes will create similar size fascial defects. For example, a 10–12 mm non-bladed trocar will produce fascial defects less than 6–8 mm in diameter, while 8 mm pyramidal trocars may produce fascial defects as large as 12 mm. The most common location of incisional hernias after laparoscopy are at the umbilicus due to its inherent anatomical weakness (28, 29, 32).

50.5 Conclusion

In this chapter, perioperative considerations and common complications related to laparoscopy were discussed to aid the surgeon in preventing and recognizing problems that may arise during laparoscopic surgery. Effective surgical planning is imperative for successful outcomes of gynecologic laparoscopic surgery. Prompt recognition and diagnosis of surgical complication are essential for patient safety and overall well-being.

References

1. Magrina JF. Complications of laparoscopic surgery. *Clin Obstet Gynecol*. 2002;45(2):469–480.
2. Abdalmageed OS et al. Nerve injuries in gynecologic laparoscopy. *J Minim Invasive Gynecol*. 2017;24(1):16–27.
3. Agostini J et al. Patient positioning in laparoscopic surgery: tricks and tips. *J Visc Surg*. 2010;147(4):e227–e232.
4. Barnett JC et al. Laparoscopic positioning and nerve injuries. *J Minim Invasive Gynecol*. 2007;14(5):664–673.
5. Lee-Ong A et al. *Operating Room Setup and Patient Positioning in MIS. Mastering Endo-Laparoscopic and Thoracoscopic Surgery*. Singapore: Springer. 2022:61–67.
6. Zillioux JM et al. Patient positioning during minimally invasive surgery: what is current best practice? *Robot Surg*. 2017;4:69–76.
7. Dun E et al. Complications of laparoscopic surgery. In: Pasic RP, Brill A, eds. *Practical Manual of Minimally Invasive Gynecologic and Robotic Surgery*, 3rd edn. CRC Press; 2018:355–366.
8. Lang T et al. Creation of pneumoperitoneum and trocar insertion techniques. In: Pasic RP, Brill A, eds. *Practical Manual of Minimally Invasive Gynecologic and Robotic Surgery*, 3rd edn. Boca Raton, FL: CRC Press; 2018;3:43–54.
9. Ahmad G et al. Laparoscopic entry techniques. *Cochrane Database Syst Rev*. 2019;1(1):CD006583.
10. Raimondo D et al. Laparoscopic entry techniques: which should you prefer? *Int J Gynaecol Obstet*. 2023;160(3):742–750. https://doi.org/10.1002/ijgo.14412.
11. Audebart A et al. Role of microlaparoscopy in the diagnosis of peritoneal and visceral adhesions and in the prevention of bowel injury associated with blind trocar insertion. *Fertil Steril*. 2000;3(3):631–635.
12. Alkatout I et al. Principles and safety measures of electrosurgery in laparoscopy. *JSLS*. 2012;16(1):130–139.
13. King NR et al. Laparoscopic major vascular injuries in gynecologic surgery for benign indications: a systematic review. *Obstet Gynecol*. 2021;137(3):434–442.
14. Llarena NC et al. Bowel injury in gynecologic laparoscopy: a systematic review. *Obstet Gynecol*. 2015;125(6):1407–1417.
15. Smyth L et al. WSES guidelines on blunt and penetrating bowel injury: diagnosis, investigations, and treatment. *World J Emerg Surg*. 2022;17(13).
16. Adelman MR et al. Urinary tract injuries in laparoscopic hysterectomy: a systematic review. *J Minim Invasive Gynecol*. 2014;21(4):558–566.
17. Shinohara S et al. Delayed detection of ureteral thermal injury in laparoscopic surgery. *Gynecol Minim Invasive Ther*. 2017;6(1):45.
18. Agresta F et al. Laparoscopic approach to acute abdomen from the Consensus Development Conference of SICE, ACOI, SIC, SICUT, SICOP, and EAES. *Surg Endosc*. 2012;26(8):2134–2164.
19. Bazot M et al. Value of magnetic resonance imaging for the diagnosis of ovarian tumors: a review. *J Comput Assist Tomogr*. 2008;32(5):712–723.
20. Geerts WH et al. Prevention of venous thromboembolism: the seventh ACCP conference on antithrombotic and thrombolytic therapy. *Chest*. 2004;126(3):338S–400S.
21. Goldstein RE. The importance of informed consent in surgery. *AMA J Ethics*. 2016;18(11):1175–1181.
22. Goldstein SR. Ultrasonography in the diagnosis of abnormal uterine bleeding. *Best Pract Res Clin Obstet Gynaecol*. 2007;21(6):893–903.
23. Kim Y et al. Risk factors of incisional hernia after laparoscopic colorectal surgery with periumbilical minilaparotomy incision: a propensity score matching analysis. *J Minim Invasive Surg*. 2022;25(1):24–31.
24. LeBlanc KA et al. Laparoscopic incisional and ventral hernia repair: complications – how to avoid and handle. *Hernia*. 2012;16(4):389–397.
25. Mangram AJ et al. Guideline for prevention of surgical site infection. *Infection Control & Hospital Epidemiol*. 1999;20(4):247–280.
26. Nguyen NT et al. The physiologic effects of pneumoperitoneum in the morbidly obese. *Ann Surg*. 2005;241(2):219–226.
27. Pulle MV et al. Port site hernia in laparoscopic surgery: mechanism, prevention and management. *Current Medicine Res Pract*. 2015;5(3):130–137.
28. Recknagel JD et al. Clinical perspective concerning abdominal entry techniques. *J Minim Invasive Gynecol*. 2021;28(3):467–474.
29. Schrenk P et al. Mechanism, management, and prevention of laparoscopic bowel injuries. Gastrointest Endosc. 1996;43(6):572–574.
30. Statement on principles underlying perioperative responsibility. American College of Surgeons. *Bull Am Coll Surg*. 1996;81(9):39–40.
31. Thomassin-Naggara I et al. Contribution of computed tomography in the diagnosis of pelvic recurrence in patients with gynecological malignancies. *Eur Radiol*. 2007;17(4):1045–1051.
32. Thomassin-Naggara I et al. How to differentiate benign from malignant myometrial tumours using MR imaging. *Eur Radiol*. 2013;23(8):2306–2314.
33. Wu MP et al. Complications and recommended practices for electrosurgery in laparoscopy. *Am J Surg*. 2000;179(1):67–73.

51 HEMOSTATIC AGENTS IN GYNECOLOGIC SURGERY

Traci Ito

51.1 Background

Achieving hemostasis in any surgery is paramount for patient safety. In the realm of gynecology, there has been a major shift over the last two decades towards increasing rates of minimally invasive laparoscopic surgeries compared to open procedures. While more complicated cases can be completed using a minimally invasive approach, an inability to maintain hemostasis can potentially lead to longer operating times and possible conversion to laparotomy (1, 2).

When it comes to hemostasis, the basic surgical principles of pressure, electrosurgery, suturing, and use of clips should always be employed. However, in situations with diffuse small vessel bleeding or bleeding near vital structures, like larger vessels or ureters, these techniques may not be suitable. Topical hemostatic agents (THAs) could serve as an alternative option to reduce thermal damage, devascularization, and tissue necrosis while also reducing blood loss (3, 4). Therefore, understanding the mechanism, proper application, contraindications, and general cost of each of these agents is critical to our role as gynecologic surgeons. Studies in other specialties have shown that THAs can effectively achieve hemostasis, reduce blood loss, shorten operative times, and reduce perioperative transfusion (5, 6).

51.2 Mechanism of Hemostasis

Prior to addressing the categories and types of topical hemostatic agents, it is crucial to understand the mechanism of hemostasis. The process of hemostasis involves vasoconstriction, platelet plug formation, and activation of the coagulation cascade. When injury or damage to a blood vessel occurs, there is vascular spasm which helps decrease blood flow to the area. Platelets in circulation then gather to form a platelet plug (primary hemostasis). For secondary hemostasis to occur the clotting cascade must be activated to allow for cross-linking of platelet plugs. Activation of the intrinsic and extrinsic pathway results in the conversion of prothrombin to thrombin. Thrombin catalyzes the conversion of fibrinogen to fibrin, which polymerizes and forms a cross-linked fibrin clot (7).

51.3 Topical Hemostatic Agents

Knowledge of THAs is important when basic surgical principles are not feasible. Adjunctive treatment with THAs is useful when there is diffuse bleeding or friable tissue or when patients have abnormal clotting status. The four main categories of these agents are mechanical agents, biologic agents, flowable agents, and fibrin sealants.

51.3.1 Mechanical Agents

Mechanical agents provide a passive substrate to provide a scaffold for clot formation. It is important to note that some of these agents also activate the clotting cascade, while others do not. The most common agents within each category are discussed as follows.

51.3.1.1 Oxidized Regenerated Cellulose (ORC)

Examples of commonly used agents in this category are Surgicel® (Ethicon, Inc, Cincinnati, OH), which comes in several forms: Original, NuKnit®, Fibrillar™, and SNoW™. These are all plant-based products that create a platform that promotes platelet aggregation. The composition of these agents exerts bactericidal properties, due to its low pH, and minimal tissue reaction. The acidic pH also activates the clotting cascade and induces vasoconstriction. The disadvantage of the acidic pH is that this may inactivate other biologic agents like thrombin (8).

While they are all in the same family, each one has properties that allow application in a variety of settings. The original is sheer, NuKnit is still pliable but may be more effective in areas of heavier bleeding. Fibrillar is also impressionable and can be peeled off in layers to allow placement of as little or as much as needed. Finally, SNoW is marketed with a 43% faster time to hemostasis compared to the original. It also indicated for better adherence to the bleeding site with minimal attachment to laparoscopic instruments, allowing easy placement (9).

These agents come in sheets of material that are easy to handle. Surgicel® Original may be cut or placed whole through laparoscopic trocars. This is shown in Figure 51.1 where it was placed over an area of uterine perforation. Placement through a 5 mm trocar is possible, but care is taken to make sure the cannula is clean and dry prior to insertion since efficacy is greatest when the agent is applied dry. After placement into the abdominal cavity is achieved, pressure should be exerted on the agent in the place of concern for approximately 2 minutes. Excess should be removed once hemostasis is achieved to prevent foreign body reaction. Complete absorption of the material ranges widely from 2 to 6 weeks (3).

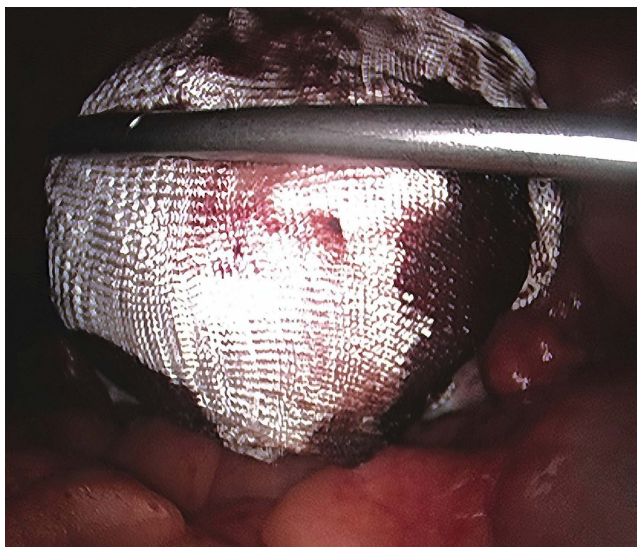


FIGURE 51.1 Surgicel Original (by Ethicon, Inc., Cincinnati, OH).

DOI: 10.1201/9781003312109-51

51.3.1.2 Microfibrillar Collagen (MFC)

Microfibrillar collagen is made from bovine collagen and can exist in a powder or sponge sheet form. Powder forms include Avitene® (Bard Davol Warwick, RI) and Helitene® (Integra Lifesciences, Plainsboro, NJ). The sponge sheet forms on the market include Avitene Ultrafoam, Avitene UltraWrap, Endo-Avitene, and Helistat (Integra Lifesciences, Plainsboro, New Jersey). The advantage of this agent is the large surface area that provides a scaffold for platelets allowing for their aggregation and thrombus formation (3, 10). Due to the need for platelets, this is not considered in patients suffering from thrombocytopenia but can be a useful resource in patients who are heparinized (5).

MFC is appropriate in situations of diffuse oozing as it conforms and adheres to irregular spaces. Only placement of the amount needed to achieve hemostasis is advised, and the process can take anywhere from 2 to 5 minutes. Unlike some other agents, MFC does not have a significant increase in volume and is absorbed in less than 8 weeks (3).

51.3.1.3 Microporous Polysaccharide

Arista™ (Bard Davol Inc., Warwick, Rhode Island) is an example of MPH that is produced from potato starch. This agent does not activate the clotting cascade but absorbs water and other compounds of low molecular weight from the blood to concentrate the components to promote platelet clot formation. Given its mechanism of action, this agent is not effective in heparinized patients or patients with brisk and severe bleeding (11, 12).

Figure 51.2 shows Arista in the top left circle, Arista with a laparoscopic applicator in the middle, and guidance of the applicator with a laparoscopic grasper into the pelvis on the bottom right. The properties of MPH cause it to be degraded as quickly as 6 hours after application due to the presence of alpha amylase. Therefore, there are concerns for potential postoperative bleeding if the platelet plug created by Arista is transient and provides no benefit (13). An additional thing to consider while using this agent in surgery is the application of greater than 50 g affecting glucose load in a diabetic patient.

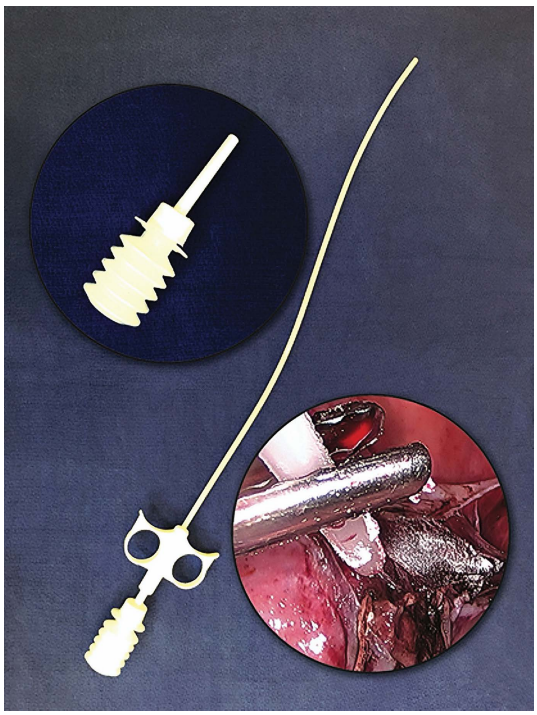


FIGURE 51.2 Arista AH Absorbable Hemostat (by Bard Davol Inc., Warwick, RI).

51.3.2 Biologic Agents

Biologically active agents rely on the enzyme thrombin, which allows for the conversion from fibrinogen to fibrin promoting clot formation. Stand-alone thrombin was previously available as a product derived from bovine plasma. However, the bovine-derived thrombin produced immune response when used in humans. Patients can develop antibodies against thrombin, prothrombin, factor V, and cardiolipin. These concerns led researchers to develop human plasma–derived thrombin (Evithrom, Omrix, Johnson & Johnson) and recombinant human thrombin (rhThrombin) (Recothrom®, Bristol-Myers Squibb, Princeton, New Jersey) (3). Currently, thrombin is more commonly combined with another agent in the categories of flowable agents and fibrin sealants and will be addressed in the following categories.

51.3.3 Flowable Agents

51.3.3.1 Floseal

Floseal® consists of a bovine-derived gelatin matrix and a thrombin matrix prepared from pooled human plasma and is shown in Figure 51.3. The gelatin matrix provides a scaffold for platelets while the thrombin portion directly stimulates the coagulation cascade. This agent can be beneficial for spontaneous bleeding episodes and surgical interventions for patients with hemophilia A or B (3, 14).

51.3.3.2 SURGIFLO

SURGIFLO® (Ethicon) is a flowable agent composed of porcine gelatin and human thrombin. This functions similarly to Floseal with its two components and is typically absorbed within 4–6 weeks.

51.3.4 Fibrin Sealants

Fibrin sealants are composed of thrombin and plasma-derived fibrinogen. These agents can be beneficial in heparinized patients. Since they provide their own fibrinogen, this may

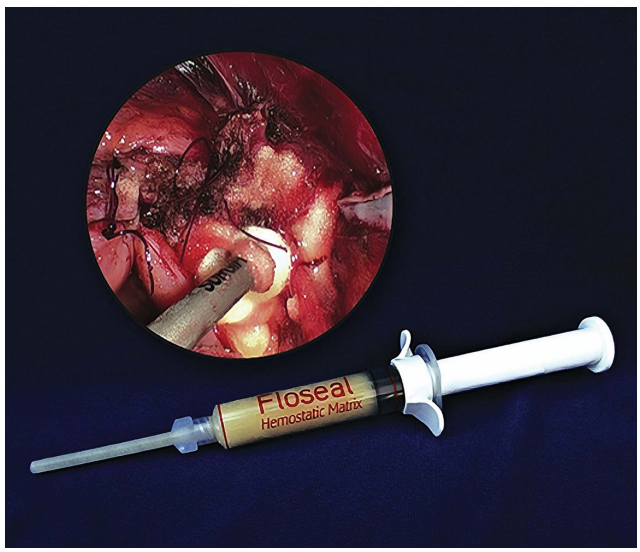


FIGURE 51.3 Floseal (by Baxter, Deerfield, IL).

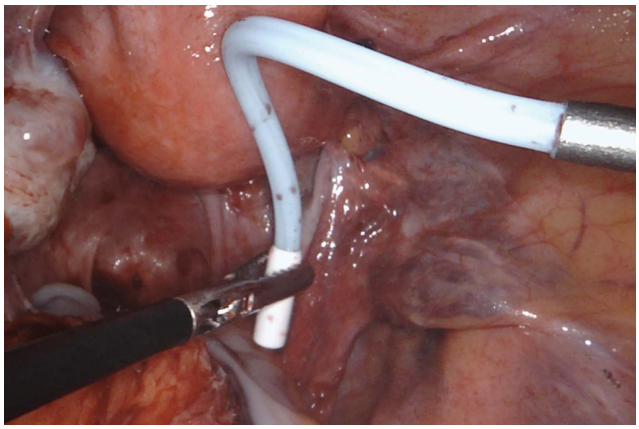


FIGURE 51.4 TISSEEL application (by Baxter, Deerfield, IL).

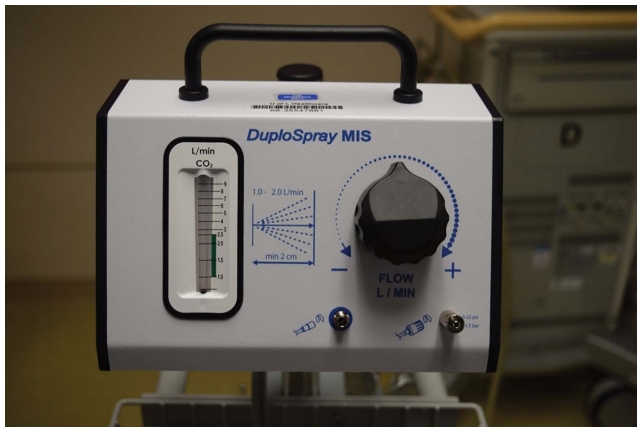


FIGURE 51.5 DuploSpray System for proper laparoscopic application.

be effective in patients with altered bleeding profiles. This is effective in areas of diffuse venous oozing. Studies have investigated their efficacy for surgeries in the retroperitoneal space, myomectomy, and posthysterectomy. The components of this THA are separated using a dual-syringe delivery system.

51.3.4.1 TISSEEL

TISSEEL® is an example of a two-component fibrin sealant. The first component is a sealer protein solution which contains a synthetic aprotinin, factor XIII, and fibrinogen. The second component is the thrombin solution that has human thrombin and calcium chloride (15). The solutions are frozen and therefore must be defrosted prior to use. Proper application involves thawing then warming to 37°C. The two components work symbiotically at the time of application.

TISSEEL® is effective because thrombin transforms the fibrinogen in the sealer protein solution into fibrin monomers that cross-link to form a fibrin clot. In addition to this, the synthetic aprotinin is a protease inhibitor that delays degradation of fibrin. These unique properties make TISSEEL® an attractive option in patients on anticoagulation and those with coagulopathy (15).

Contraindications for application include patients with a known hypersensitivity to synthetic aprotinin or brisk arterial or venous bleeding. TISSEEL is denatured when exposed to alcohol, iodine, or heavy metals. It also cannot function in the presence of oxidized regenerated.

Application of this product is supported in laparoscopic surgery. This is achieved by use of the DuploSpray system. The system includes a disposable laparoscopic applicator (20, 30, or 40 cm in length), dual lumen tubing, and two disposable spray tips. A pressure regulator pedal is used to assist in application. Once the disposable laparoscopic applicator is connected to the TISSEEL® Duplojet syringe, the one component of the double lumen tubing is connected to this unit and the other component to the trocar. The other end of this tubing is then attached to the regulator to allow flow of CO_2 gas. Once proper gas flow is verified, application involves slow and steady pressure on the TISSEEL® applicator while pressing on the pedal (Figures 51.4 and 51.5). A laparoscopic instrument can be used to guide the tip to the desired area of application. Starting and stopping will facilitate clot formation in the disposable tip, and this part may need to be replaced to continue proper placement of this agent.

51.3.4.2 VISTASEAL

VISTASEAL is composed of human fibrinogen and human thrombin. This agent also requires thawing. Like TISSEEL, laparoscopic application is supported but does not require the Duplojet spray system. This agent also requires thawing.

51.4 Conclusion

Topical hemostatic agents have been cited in the literature as early as 1978 (16). Since then, several subtypes and brands of the various agents leave the surgeon with a multitude of options. Besides basic surgical techniques, topical hemostatic agents should be added to a surgeon's surgical armamentarium. Knowledge of the types of agents, their respective mechanisms of action, contraindications, potential complications, and cost is necessary for proper utilization and application.

References

1. Uccella S et al. Laparoscopic hysterectomy in case of uteri weighing ≥1 kilogram: a series of 71 cases and review of the literature. *J Minim Invas Gynecol*. 2014;21(3):460–465.
2. Walsh CA et al. Total abdominal hysterectomy versus total laparoscopic hysterectomy for benign disease: a meta-analysis. *European J Obstet Gynecol Reprod Biol*. 2009;144(1):3–7.
3. Achneck HE et al. A comprehensive review of topical hemostatic agents: efficacy and recommendations for use. *Ann Surg*. 2010;251(2):217–228.
4. Tomizawa Y. Clinical benefits and risk analysis of topical hemostats: a review. *J Artif Organs*. 2005;8(3):137–142.
5. Abbott WM et al. The effectiveness and mechanism of collagen-induced topical hemostasis. *Surgery*. 1975;78(6):723–729.
6. Nasso G et al. Prospective, randomized clinical trial of the FloSeal matrix sealant in cardiac surgery. *Ann Thorac Surg*. 2009;88(5):1520–1526.
7. LaPelusa A et al. Physiology, hemostasis [Updated 2023 May 1]. In: *StatPearls* [Internet]. Treasure Island: StatPearls Publishing; 2024. Available at: www.ncbi.nlm.nih.gov/books/NBK545263/
8. Spangler D et al. In vitro antimicrobial activity of oxidized regenerated cellulose against antibiotic-resistant microorganisms. *Surg Infect*. 2003;4(3):255–262.
9. Ethicon I. *Surgicel® Family of Absorbable Hemostats [Brochure]*. San Lorenzo, Puerto Rico: Ethicon, Inc.; 2012.
10. Bard D, Inc. *Avitene™ Microfibrillar Collagen Hemostat [Brochure]*. Warwick, RI: C.R. Bard, Inc.; 2016.

11. Lewis KM et al. Efficacy of hemostatic matrix and microporous polysaccharide hemospheres. *J Surg Res*. 2015;193(2):825–830.
12. Wolberg AS et al. A systematic evaluation of the effect of temperature on coagulation enzyme activity and platelet function. *J Trauma*. 2004;56(6):1221–1228.
13. Ereth MH et al. Microporous polysaccharide hemospheres do not enhance abdominal infection in a rat model compared with gelatin matrix. *Surg Infect*. 2009;10(3):273–276.
14. Baxter H, Inc. *Floseal® Hemostatic Matrix [Brochure]*. Hayward, CA: Baxter Healthcare Corporation; 2008.
15. Baxter H, Inc. *TISSEEL® Fibrin Sealant [Brochure]*. Westlake Village, CA: Baxter Healthcare Corporation; 2014.
16. Cameron WJ. A new topical hemostatic agent in gynecologic surgery. *Obstet Gynecol*. 1978;51(1):118–122.

52 ANESTHESIA IN LAPAROSCOPY

Daisy Sangroula, Jeremy Haysley, Alexander Bautista, and Laura Clark

52.1 Introduction

Minimally invasive laparoscopic surgery, including newer techniques utilizing surgical robotic platforms, has revolutionized gynecologic care by providing numerous benefits over traditional open surgical procedures. The anesthesiology team plays a crucial role in ensuring patient comfort and safety during all procedures by providing adequate analgesia, amnesia, and muscle relaxation. Proper physiological monitoring is essential to allow the surgical procedure to be performed safely, without causing pain or discomfort to the patient. The medications used to achieve this goal impact the native physiology of the patient, but in combination with further derangements caused by laparoscopy, the physiologic imbalance can be accentuated. The primary mission of the anesthesiology team is to maintain a state of physiological homeostasis, ensuring patient safety. Optimal preprocedural patient preparation, choice of anesthetic technique, and the variety of pharmacological agents used can significantly impact patient outcome and the overall success of the surgery.

52.2 Preoperative Concerns

Preoperative considerations for gynecologic procedures involve assessments and preparations to ensure the safety and optimal outcome of the surgery. Identifying significant comorbid conditions that require consideration and/or treatment throughout the perioperative period and gauging the patients' functional status prior to surgery minimizes risk of complications. Certain comorbidities may have ramifications magnified by laparoscopy and should be optimized preoperatively. Key factors for consideration are the following:

- *Medical evaluation*: A thorough medical evaluation assesses the patient's overall health and identifies preexisting medical conditions which may affect the surgery, choice of anesthetic technique, or complications anticipated during delivery of anesthesia. This evaluation may include a review of medical history; focused physical examination of the airway, neurologic, and cardiopulmonary systems; laboratory tests; and other diagnostic imaging studies.
- *Anesthesia assessment*: An anesthesiologist will evaluate patients' suitability for anesthesia, including previous anesthesia experiences, allergies, current medications, and any known anesthesia-related complications in the patient or family. This assessment helps determine the most appropriate anesthetic technique for the patient.
- *Preoperative testing*: Depending on the patient's medical history and complexity of the planned procedure, additional preoperative blood tests, updated electrocardiogram (ECG), chest X-ray, and/or other investigations may be ordered. Cardiology consultation may be warranted in patients with a major clinical predictor of cardiac risks such as evolving myocardial infarction or unstable coronary syndrome. Risk stratification in terms of benefits of any further diagnostic testing or therapeutic steps and postoperative follow-up plan should be addressed (1). Cardiac implantable electronic devices should be interrogated, or the team should review the most recent interrogation report. This should be done if the interrogation has not occurred in the past 6 months per American Society of Anesthesiologists (ASA) standards. The anesthesiologist should determine whether intraoperative electromagnetic interference is likely to occur and ensure temporary pacing and defibrillation equipment are immediately available in procedures with electromagnetic interference potential (2).
- *Medication review*: All current medications, including prescription drugs, over-the-counter medications, and herbal supplements, are reviewed. Certain medications, such as antihypertensives or anticoagulants, may need adjustment or temporary discontinuation before surgery to minimize the risk of complications, such as bleeding or adverse drug interactions.

Angiotensin-converting enzymes (ACE), angiotensin II receptor blockers (ARBs), and lisinopril should be held 24 hours before major surgeries to prevent profound hypotension refractory to phenylephrine (3).

Glucagon-like peptide-1 (GLP-1) receptor agonists are used for treatment of type 2 diabetes mellitus, for cardiovascular risk reduction, and for weight loss. These patients may be at higher risk of aspiration. The ASA consensus guideline recommends holding GLP-1 agonists on the day of the procedure or surgery for patients on daily dosing and for one week prior to a procedure for patients on weekly dosing. If gastrointestinal (GI) symptoms such as severe nausea and vomiting, abdominal bloating, and abdominal pain are present, an elective procedure should be delayed, and concerns of potential risk of regurgitation and pulmonary aspiration of gastric contents should be discussed with the surgeon and the patient. A gastric ultrasound can also be performed to help determine if stomach contents warrant delaying surgery.

Patients who have been taking prednisone for more than 20 mg/day or its equivalent for more than 3 weeks may have a suppressed hypothalamic–pituitary axis and may not be able to physiologically cope with perioperative stress. These patients may need a preoperative stress dose of steroids followed by continued maintenance dosing (4).

- *Allergy assessment*: Any known allergies, especially to medications or latex, are identified and considered to ensure appropriate precautions are taken throughout the surgery and administration of anesthesia. Penicillin (PCN) allergy is one of the most common drug allergies, and it can cause a range of allergic reactions from mild skin rashes to severe anaphylaxis. Cephalosporins are a class of antibiotics that are structurally like penicillin, and there is a possibility of cross-reactivity between the two. However, studies have shown that the risk of cross-reactivity between penicillins and cephalosporins is relatively low, ranging from 1% to 10% among individuals with a documented penicillin allergy. The risk may

DOI: 10.1201/9781003312109-52

be higher for those with a history of severe reactions to penicillin or those with an allergy to a specific type of penicillin (e.g., amoxicillin). The risk can vary depending on the specific cephalosporin being considered, and over 80% of people lose their sensitivity after 10 years. If the penicillin reaction was not anaphylaxis or throat swelling, or if they were told they reacted as a child and cannot recall a reaction, cephalosporins are usually well tolerated.

- *Preoperative counseling*: On the day of surgery, patients refrain from eating or drinking anything for a period (ranging from 2 hours for clear liquids and up to 8 hours for solid foods) before the procedure to minimize the risk of aspiration.
- *Tobacco and alcohol use*: Patients who smoke or consume alcohol regularly should discontinue or reduce their habits before surgery. Smoking cessation and minimizing alcohol intake reduce perioperative complication risk and promote better surgical outcomes.

Note that these preoperative considerations may vary depending on the specific gynecologic procedure and individual patient factors.

52.3 Physiologic Changes Associated with Laparoscopic Surgery

Laparoscopic surgery causes unique alterations that are mechanical and/or physiologic. Homeostatic changes are due to the mechanical effects of increased abdominal pressure with insufflation of intra-abdominal gas and positioning. Systemic absorption of carbon dioxide also causes physiologic effects. Young, healthy patients may tolerate these changes well, but elderly or deconditioned patients with limited physiologic reserve may experience significant instability.

If a patient becomes unstable during laparoscopic surgery, the first intervention is to decrease the mechanical effects of insufflation, deflating the pneumoperitoneum to decrease the intra-abdominal pressure. The pressure goal is less than 15 mmHg, or the least amount required to safely perform the procedure.

Key physiologic changes of laparoscopic surgery are summarized in Table 52.1.

52.3.1 Cardiovascular System

- *Hemodynamic changes*: An increase in intra-abdominal pressure due to CO_2 insufflation can cause increased systemic vascular resistance and decreased venous return, leading to a temporary rise in blood pressure (5, 6). Insufflation pressure may also cause profound bradycardia. Adequate fluid management and careful patient monitoring are necessary to maintain cardiovascular stability.
- *Cardiac output*: Depending on patient preexisting conditions and the specific surgical procedure, cardiac output may increase or decrease during laparoscopic surgery. Monitoring of heart rate, blood pressure (sometimes invasive with an arterial catheter), and oxygen saturation guides anesthetic management.

TABLE 52.1 Summary of Physiologic Changes during Laparoscopy

Physiological Change	Description
Increased Heart Rate	Laparoscopic surgery can stimulate the sympathetic nervous system, leading to an increase in heart rate. The body's response to stress and the release of stress hormones can contribute to this effect.
Elevated Blood Pressure	Like heart rate, blood pressure may rise due to the body's stress response during surgery. The release of stress hormones, such as adrenaline, can cause vasoconstriction and increased peripheral resistance, leading to elevated blood pressure.
Increased Respiratory Rate	The stress response during laparoscopic surgery can also affect the respiratory system. The body may initiate faster and shallow breathing to meet the increased oxygen demand resulting from the surgical procedure.
Changes in Blood Oxygen Saturation	Surgical procedures, including laparoscopic gynecologic surgery, can influence blood oxygen saturation levels. Anesthesia, positioning of the patient, and alterations in lung mechanics due to pneumoperitoneum may impact oxygen exchange in the lungs and consequently affect blood oxygen levels.
Reduced End-Tidal Carbon Dioxide ($ETCO_2$)	During laparoscopic surgery, carbon dioxide gas is used to inflate the abdominal cavity, creating the pneumoperitoneum. As a result, there can be a decrease in end-tidal carbon dioxide levels, which is measured to monitor the effectiveness of ventilation.
Metabolic Changes	The body's metabolism may be affected during laparoscopic surgery due to the stress response and anesthesia. Changes in glucose levels, electrolyte imbalances, and alterations in the body's energy expenditure can occur.
Temperature Regulation	Laparoscopic surgery can impact body temperature regulation. Surgical exposure, the use of cold insufflation gas, and exposure to a cold operating room environment may lead to heat loss and a decrease in core body temperature.
Fluid and Electrolyte Imbalances	Surgical procedures, including laparoscopy, can result in fluid shifts and electrolyte imbalances due to factors like fluid loss, changes in fluid distribution, and the administration of intravenous fluids. Close monitoring is necessary to maintain homeostasis.
Surgical Stress Response	Laparoscopic gynecologic surgery induces a systemic stress response, which involves the release of stress hormones such as cortisol and catecholamines. This response can affect various physiological processes and organ systems, including the immune system and blood clotting mechanisms.
Pain and Analgesia	Postoperative pain is common after laparoscopic surgery. Effective pain management strategies, including the administration of analgesic medications, should be implemented to ensure patient comfort and aid in the recovery process.

52.3.2 Respiratory System

- *Ventilation–perfusion (V/Q) mismatch*: Pneumoperitoneum can cause a decrease in lung compliance and functional residual capacity (FRC), leading to V/Q mismatch and hypoxemia. Adequate ventilation strategies and monitoring of end-tidal CO_2 levels are important to optimize gas exchange.
- *Hypercapnia and acid-base changes*: Systemic absorption of CO_2 from the peritoneal cavity, subcutaneous deposited CO_2, or subcutaneous emphysema into the bloodstream can lead to varying degrees of hypercapnia (7). This causes respiratory acidosis and its sequelae if not effectively managed. Increasing minute ventilation by 30% with close monitoring of arterial blood gases is crucial (8).

52.3.3 Renal System

- *Fluid balance and renal perfusion*: Increased intra-abdominal pressure can affect renal blood flow and urine output. Adequate hydration and monitoring of urine output help to optimize renal perfusion and function (9). Vigilant monitoring of blood pressure and intraoperative blood loss, with maintenance of normotension in coordination with the surgical team, is imperative for adequate renal perfusion pressure during abdominal insufflation.
- *Metabolic system*: Surgery, including laparoscopic procedures, triggers a systemic response leading to increased stress hormones, including cortisol, catecholamines, and glucagon. Appropriate pain management and stress reduction techniques help mitigate this response (9).

Note that the anesthesiologist closely monitors and manages these physiologic changes throughout the procedure, aiming to maintain stable vital signs, adequate tissue perfusion, and optimal patient outcomes. Permissive hypercapnia is the normal approach in laparoscopic surgery.

52.4 Enhanced Recovery After Surgery (ERAS) Protocols

Enhanced recovery after surgery (ERAS) protocols focus on the avoidance of preoperative bowel preparation and the use of preadmission counseling, opioid-sparing multimodal analgesia techniques, intraoperative goal-directed fluid therapy (GDT), and minimally invasive surgical techniques. Routine use of nasogastric tubes, drains, and/or catheters is avoided. Postoperative recovery includes early feeding, early mobilization, timely removal of tubes and drains when present, and function-oriented multimodal analgesia regimens (10).

52.5 Intraoperative Considerations

52.5.1 Monitoring

During laparoscopic gynecologic surgery, vital signs and depth of anesthesia are continuously monitored. This involves instrumentation and techniques to monitor adequacy of ventilation, assess endotracheal tube placement, and identify potential issues that could cause hypo- or hyperventilation.

In addition to standard monitoring, monitoring of anesthetic depth includes bispectral index (BIS) monitoring, which uses electroencephalography (EEG) to measure the patient's level of consciousness. These monitors avoid under- or overanesthetizing patients. Neuromuscular blockade is monitored to optimize surgical conditions, emergence from anesthesia, and readiness for extubation. This monitor should be placed prior to tucking the arms because the placement over the ulnar nerve is more accurate than on the forehead.

Monitoring intravenous access ensures ability to administer fluids, medications, and blood products during surgery. Laparoscopic and robotic-assisted laparoscopic procedures require specific considerations due to lack of intraprocedural access with arms tucked beneath drapes. Therefore, two intravenous catheters should be standard in all patients.

52.5.2 Fluid Management

Increased intra-abdominal pressure and absorption of CO_2 during laparoscopic surgeries can affect the patient's respiratory and circulatory systems. Proper fluid management is essential for adequate hydration, hemodynamics, and electrolyte balance.

Additionally, the anesthesiologist will closely observe the overall well-being of the patient throughout the procedure, considering factors like facial color, muscle relaxation, and response to surgical stimuli. Continuous monitoring identifies any deviations from normal parameters, allowing prompt intervention and adjustment of anesthesia as needed to maintain patient safety.

52.5.3 Patient Positioning

Trendelenburg position can aggravate cardiovascular and respiratory effects brought about by pneumoperitoneum during laparoscopic surgery. The increased intra-abdominal pressure can cause compression of the inferior vena cava, reducing venous return. This, in turn, can decrease cardiac output and blood pressure. The heart rate may increase to compensate for these changes. Increased respiratory effort is due to decreased lung compliance and increased work of breathing. The patient may require adjustments in ventilation parameters to maintain adequate oxygenation and ventilation.

Reverse Trendelenburg position can impede cardiac output due to decreased preload if the patient has underlying heart disease, pulmonary hypertension, or a history of congestive heart failure. This can be impacted not only by preoperative condition but by the intraoperative administration of cardiac depressants. This can all lead to a greater risk of hypotension in reverse Trendelenburg position in a patient with congestive heart failure.

Steep Trendelenburg position can also be problematic in a patient with congestive heart failure and can overload the myocardium. Some patients may not be candidates for this position and will need open surgery. This should be a team decision between the surgeon, anesthesiologist, and the patients' cardiologist.

52.6 Maintenance of Anesthesia

General anesthesia (GA) involves the administration of medications that induce a state of unconsciousness, ensuring that the patient feels no pain or discomfort during the procedure. GA ensures a secure airway via use of an endotracheal tube and facilitates better surgical condition utilizing muscle relaxation medications. Research has shown that keeping a patient fully paralyzed will create optimum surgical conditions. This can best be achieved by using an accelerometer placed before the arms are tucked.

Regional anesthesia involves blocking sensation in specific areas of the body, typically by injecting local anesthetic (LA) agents near nerves. Some common regional anesthesia options for laparoscopic gynecological procedures include:

- *Epidural anesthesia*: LA is injected into the epidural space surrounding the spinal cord. It can be used with GA for pain relief intraoperatively and postoperatively. Guidelines exist to manage anticoagulants in the presence of an epidural catheter. The epidural should be kept in place until signs of bowel function return, and it can be adjusted daily to meet individual pain needs. If placed in the thoracic region, it rarely interferes with bladder function, so the Foley catheter can be removed.
- *Peripheral nerve block*: LA is injected around specific nerves and/or nerve bundles or within fascial planes to provide targeted pain relief to a specific area. In gynecological procedures, nerve blocks can be used to numb specific pelvic nerves, providing analgesia during and after surgery.
- *Local anesthesia*: LA is directly infiltrated into the area where the procedure will be performed. LA can be injected at incision sites to help with postoperative pain control.

52.6.1 Regional Anesthesia

Multiple options exist for regional anesthesia. These include:

Transverse abdominis plane (TAP) block: LA is injected into the fascial plane between the transversus abdominis and internal oblique muscles. TAP blocks provide somatic anesthesia for the abdominal wall and parietal peritoneum, and they depend on interfascial spread. TAP blocks can be used for any surgery involving the abdominal wall, including bowel surgery, cesarean section, appendectomy, hernia repair, umbilical surgery, and gynecological surgery.

Anatomy: The sensory supply of the skin, muscles, and parietal peritoneum of the anterolateral abdominal wall is derived from ventral rami of the thoracoabdominal intercostal nerves (T7–11), the subcostal nerve (T12), and the L1 spinal nerve. Cutaneous branches of these nerves travel through the transversus abdominis and internal oblique muscles to course within the transversus abdominis fascial plane (11).

Technique: TAP blocks are performed with ultrasound guidance and can be placed before or after induction of anesthesia prior to the incision, more commonly after skin closure while the patient is still under GA, or in the recovery room after emergence. The combination of subcostal and classical TAP injections with rectus sheath injections provide coverage for incisions above and below the umbilicus. The duration of analgesia associated with a TAP block is governed by the duration of action of LA, which is typically 10–12 hours with analgesia (Figure 52.1).

TAP blocks have demonstrated clinically significant reductions in postoperative opioid requirements and postoperative pain and some effect on opioid-related side effects (12). TAP blocks also decrease postoperative nausea and vomiting (PONV), length of hospital stay (1.45 vs 2.2 days), and lower total perioperative opioid use when compared to those without a TAP block in laparoscopic gynecological cases (13).

TAP catheters can be placed in the same anatomical locations as single shot blocks and are used for a continuous infusion of LA, including as an outpatient for several days postoperatively, when longer postoperative pain control is anticipated. TAP catheters can provide prolonged analgesia and decreased opioid consumption compared to a single shot (14).

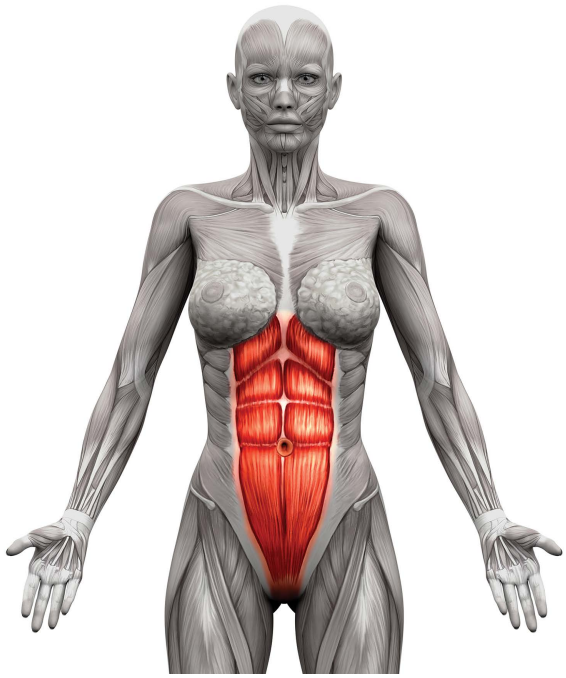


FIGURE 52.1 Gynecological laparoscopic procedures would require TAP bilaterally (red) if ports are above the umbilicus, a subcostal TAP block would be indicated and rectus sheath block depending on the port site.

Use of liposomal bupivacaine yields a slow release at the site of injection, and when added to a standard multimodal analgesic regimen prolongs the duration of pain control, decreases opioid consumption, and decreases median length of hospital stay. Cohen compared the economic impact of a liposomal bupivacaine-based multimodal analgesic regimen with an opioid-based regimen in open colectomy patients and demonstrated less opioid consumption with decreased median hospital stay (4.9 versus 2.0 days) (15).

TAP blocks have an excellent safety profile. Although complications have been reported, they are rare and consist of punctures of the abdomen, bowel, pneumothorax, hematoma, and liver. Ultrasound guided approaches minimize these complications.

Quadratus lumborum (QL) block: The QL block gives more consistent somatic coverage with the addition of visceral analgesia of the abdomen and wider, longer sensory blocks compared to TAP blocks. LA is deposited under ultrasound guidance into the posterior thoracolumbar fascia. QL blocks may work by the spread of LA through the diaphragm to reach the paravertebral space via the endothoracic pathway, resulting in a block of visceral components (16). QL blocks may also result in LA distribution to the lumbar plexus and prolong motor blockade, potentially delaying postoperative mobilization and contributing to hypotension due to spread to the paravertebral space, resulting in presumed sympathetic blockade. QL blocks can be more challenging to place due to the posterior location of the injection site and the depth of the anatomic structures.

Rectus sheath block: LA is injected between the posterior aspect of the rectus muscle and rectus sheath resulting in somatic anesthesia only to the midline of the abdomen. It is a useful adjunct block for midline incisions, such as umbilical herniorrhaphy. The injection does not spread well and often covers only two dermatomes; this would require multiple injections for any incision larger than an umbilical hernia. TAP blocks are therefore preferred for larger midline incisions. Complications are rare and similar to TAP blocks.

Medications used for nerve block: Long-acting LAs, such as 0.5% or 0.25% ropivacaine, levobupivacaine, and bupivacaine, are used to perform nerve blocks. Analgesic efficacy relies on appropriately injecting adequate volume, rather than a high concentration of LA solution. When performing multiple TAP blocks, the total dose of all sites of injection must be calculated not to exceed the maximum allowable dose. Both full concentration and half concentration are effective. When full concentrations are used, the amount of LA should be 2.5–3 mg/kg.

52.7 Postoperative Concerns

Postoperative anesthesia concerns regarding laparoscopic surgeries primarily revolve around pain management, monitoring, and potential complications. Common considerations include pain management and prevention of postoperative nausea and vomiting.

Laparoscopic surgery, while minimally invasive, can still cause varying degrees of postoperative pain. Adequate pain control is crucial to promote patient comfort and facilitate early mobilization. Pain management strategies include a combination of oral or intravenous analgesics, patient-controlled analgesia (PCA), epidural and regional analgesic blocks, and local anesthetic infiltration at the surgical site. The choice of pain management technique depends on the patient's condition, surgical procedure, and the anesthesiologist's recommendation.

Patients undergoing laparoscopic surgeries usually have multiple risk factors for PONV, such as female gender, smoking, previous history of PONV, and postoperative use of opioids. PONV can cause discomfort, delay recovery, warrant unplanned admission, and increase healthcare costs. It is standard to give two different types of antiemetics such as ondansetron and dexamethasone; a third antiemetic is added to high-risk patients (17).

52.8 Complications

Many potential complications can occur during or after laparoscopic surgery. These include:

- Pulmonary embolism, while rare, may be due to venous stasis resulting from obstruction of flow secondary to pneumoperitoneum.
- Venous gas embolism is common during laparoscopy, but clinically significant embolism is rare. Gas embolism can occur due to direct venous injection of CO_2 with a Veress needle or via CO_2 entrainment if a vein is severed or disrupted, allowing gas under pressure to access the systemic circulation. Gas embolism causes unexplained tachycardia, hypotension, abrupt reduction of end tidal CO_2, hypoxemia, arrhythmias, mill-wheel murmur, and EKG signs of right heart strain. This is more common during hysteroscopy than laparoscopy. The volume of gas necessary to produce symptoms is 25 mL/kg of CO_2, compared with 5 mL/kg of air. Aspiration of gas, foamy blood from a central venous line, or air bubbles demonstrated on transesophageal echocardiography (TEE) provide definitive diagnosis. To help reverse the symptoms, deflate the abdomen with the patient placed in the head down and left lateral position, administer 100% oxygen, and aspirate as much gas as possible. Although gas embolism may be fatal, rapid diagnosis and treatment is highly successful if blood pressure is supported.
- Subcutaneous emphysema occurs due to insufflation of an improperly positioned pneumoperitoneum needle or port, as CO_2 dissects through peritoneal defects into the subcutaneous tissue. Any increase in end tidal CO_2, especially above 50 mmHg, that does not respond to increased minute ventilation should lead to suspicion of subcutaneous emphysema. A correlation exists with more than six ports and prolonged operative time. Subcutaneous emphysema is usually superficial and does not compromise the airway lumen. Severe swelling should call for an assessment of airway edema, and patency should be assessed before extubation. The patient may require mechanical ventilation, with the patient positioned head up, until CO_2 levels return to normal.
- Capnothorax, capnomediastinum, and capnopericardium: Risk factors are similar to subcutaneous emphysema. Intraperitoneal gas may find its way through openings in the diaphragm and esophageal hiatus that are congenital or surgically created inadvertently. Pneumothorax is the most common of these issues and can occur solely from positive pressure ventilation, which should be noted as higher ventilator pressures are typically needed to overcome abdominal insufflation.
- Tension pneumothorax should always be considered as a possibility in patients with high airway pressure, unstable hemodynamics, and unilaterally diminished air entry. Treatment consists of identifying the cause and supporting the patient by increasing the pressure in the alveoli to decrease the tendency for compression. If the patient does not respond to supportive treatments, a chest tube is indicated.

Key Points

1. Physiologic changes during laparoscopic procedures are due to positioning, mechanical changes, and carbon dioxide absorption.
2. The most commonly affected organ systems are the pulmonary and cardiovascular systems.
3. Benefits of laparoscopic procedures include less pain, early mobilization, and decreased hospital stay.
4. Extremely sick patients may not be candidates because they cannot compensate for physiologic changes that occur during laparoscopy.
5. Cardiovascular changes manifested during laparoscopic surgeries are due to compression of the inferior vena cava and aorta, increased systemic vascular resistance and preload, followed by a

decrease in preload, CO_2, and increased heart rate. This can follow profound bradycardia including asystole during insufflation.
6. Pulmonary effects during laparoscopic surgeries include decreased pulmonary compliance, increased airway pressure, decreased functional residual capacity and vital capacity, and concern for endobronchial intubation.
7. A small decrease in intra-abdominal pressure may rapidly resolve hemodynamic instability.
8. Unnecessary Trendelenburg position should be avoided.
9. Minute ventilation should be increased by at least 30% to compensate for CO_2 absorption.
10. Arterial lines may be necessary to monitor pH in patients who would not need one in an open procedure.
11. The goal of the preoperative visit is to identify and optimize patient medical conditions, with a focus on the pulmonary and cardiovascular systems.
12. Multimodal pain control therapy with the use of peripheral nerve blocks helps limit the total dose of narcotic, decrease PONV, and shorten the hospital stay.

52.9 Conclusion

Laparoscopic surgery has obvious benefits to the patient and will continue to develop, as better instruments, greater experience, and more knowledge about the effects on the body are further elucidated. Sound knowledge regarding physiological changes associated with laparoscopic procedures and inclusion of ERAS protocols, multimodal pain control, and appropriate prevention or treatment of PONV improves patient outcome. Communication and understanding between the surgery and anesthesia teams is paramount in improving perioperative care.

References

1. Park KW. Preoperative cardiology consultation. *Anesthesiology*. 2003;98(3):754–762.
2. Practice advisory for the perioperative management of patients with cardiac implantable electronic devices: pacemakers and implantable cardioverter – defibrillators 2020. *Anesthesiology*. 2020;132(2):225–252.
3. Roshanov PS et al. Withholding versus continuing angiotensin-converting enzyme inhibitors or angiotensin II receptor blockers before noncardiac surgery. *Anesthesiology*. 2017;126(1):16–27.
4. Hamrahian AH et al. The management of the surgical patient taking glucocorticoids [Internet]. *UpToDate*, 2025.
5. Atkinson TM et al. Cardiovascular and ventilatory consequences of laparoscopic surgery. *Circulation*. 2017;135(7):700–710.
6. Giebler RM et al. Intraperitoneal and retroperitoneal carbon dioxide insufflation evoke different effects on caval vein pressure gradients in humans. *Anesthesiology*. 2000;92(6):1568–1580.
7. Gutt CN et al. Circulatory and respiratory complications of carbon dioxide insufflation. *Dig Surg*. 2004;21(2):95–105.
8. Llorens J et al. Adaptive support ventilation for gynaecological laparoscopic surgery in Trendelenburg position: bringing ICU modes of mechanical ventilation to the operating room. *Eur J Anaesthesiol*. 2009;26(2):135–139.
9. Myre K et al. Plasma catecholamines and haemodynamic changes during pneumoperitoneum. *Acta Anaesthesiol Scand*. 1998;42(3):343–347.
10. Miralpeix E et al. A call for new standard of care in perioperative gynecologic oncology practice: impact of enhanced recovery after surgery (ERAS) programs. *Gynecol Oncol*. 2016;141(2):371–378.
11. Finnerty O et al. Trunk blocks for abdominal surgery. *Anaesthesia*. 2010;65(Suppl 1):76–83.
12. Petersen PL et al. The transversus abdominis plane block: a valuable option for postoperative analgesia? A topical review. *Acta Anaesthesiol Scand*. 2010;54(5):529–535.
13. Pather S et al. The role of transversus abdominis plane blocks in women undergoing total laparoscopic hysterectomy: a retrospective review. *Aust N Z J Obstet Gynaecol*. 2011;51(6):544–547.
14. Yoshida T et al. Analgesic efficacy of bilateral continuous transversus abdominis plane blocks using an oblique subcostal approach in patients undergoing laparotomy for gynaecological cancer. *Br J Anaesth*. 2016;117(6):812–820.
15. Cohen SM. Extended pain relief trial utilizing infiltration of Exparel((R)), a long-acting multivesicular liposome formulation of bupivacaine. *J Pain Res*. 2012;5:567–572.
16. Elsharkawy H et al. Quadratus lumborum block: anatomical concepts, mechanisms, and techniques. *Anesthesiology*. 2019;130(2):322–335.
17. Kienbaum P et al. Update on PONV-What is new in prophylaxis and treatment of postoperative nausea and vomiting? *Anaesthesist*. 2022;71(2):123–128.

53 TRANSABDOMINAL CERCLAGE

Jamal Mourad

53.1 Introduction

Cervical insufficiency is defined by the American College of Obstetricians and Gynecologists as the inability to keep a pregnancy to term even in the absence of contractions or labor (1). It usually presents as painless dilatation of the cervix, followed by preterm premature rupture of membranes (PPROM) and subsequent delivery of a nonviable or a premature infant. Cervical insufficiency is estimated to complicate 0.1%–1.0% of all pregnancies (2) leading to profound implications for both maternal and neonatal outcomes. Preterm delivery and low birth weight remain the leading causes of neonatal morbidity and mortality (3, 4) with an estimated incidence of 5% to 11% of all pregnancies, ranging from as low as 4.5% in Ireland and as high as 15% in the United States (5). If an infant is born preterm, the risk of death in the first year of life is 40-fold greater compared with an infant born at term (5). Although the pathophysiology of cervical insufficiency remains poorly understood, there are certain conditions that may play an important role in its causation. Important factors to consider include uterine malformations, history of surgical manipulation, or trauma to the cervix such as precipitous deliveries and cervical cone biopsies due to dysplastic lesions. Ongoing efforts to elicit a better understanding of possible etiologies for cervical insufficiency have prompted more scientific investigations suggesting that fetal and maternal inflammatory processes may play a more significant role leading to premature cervical dilatation and subsequent preterm birth (6).

Conventional treatment often includes expectant management with or without placement of a cerclage. Transvaginal cerclage procedures and their outcomes were first described by Shirodkar in 1955 (7) and McDonald in 1957 (8). This was shortly followed by the first report of transabdominal cerclage placement by Benson and Durfee in 1965 reserved for women where a vaginal approach was not feasible or recommended (9). Transabdominal cerclage is often considered a procedure that carries higher morbidity due to its laparotomic approach and the fact that it will always require two separate open procedures, cerclage placement and a cesarean section for delivery, placing a significant burden on maternal health in a relatively short period of time. Today, advancements in surgical technique and instrumentation allow for most gynecologic procedures to be performed in a minimally invasive manner. In 1998 the first laparoscopic approach to transabdominal cerclage placement was described (10), and more recently there have been several reports of robotic transabdominal cerclage placement in both the preconceptual and the pregnant state (11–13). Today, the surgical landscape dictates a minimally invasive approach to be considered when possible when counseling patients for a transabdominal cerclage. This chapter will discuss the robotic approach for transabdominal cerclage placement in more detail.

53.2 Surgical Management Strategies for Cervical Insufficiency

Transvaginal Cerclage: Transvaginal cerclage was first described in the mid-1950s, initially by Dr. Vithal Nagesh Shirodkar in 1955 (7) and later by Dr. Ian McDonald in 1957 (8). The two main approaches to transvaginal cerclage include a purse-string suture placed around the cervix, although there are many variations to this procedure (14). Transvaginal cerclage is typically performed under regional anesthesia. The perineum and vagina are prepped, typically with povidone-iodine, with special care if protruding/prolapsing membranes are present in cases of physical examination-indicated cerclage (15). Preoperative antibiotics are not routinely indicated. To ensure optimal exposure of the cervix during the procedure, surgical assistants provide continuous retraction of the lateral vaginal walls and anterior vaginal wall, while a weighted speculum is frequently used in the posterior vagina (16). The McDonald approach is completed with four to six bites of suture placed circumferentially around the cervix, just distal to the vesicocervical reflection and the vaginal-rectal reflection (17). Experts recommend the suture should be placed as high as possible, less than 1 cm should be between bites, and bites should be deep enough to secure adequate cervical stroma preventing slippage but not deep enough to enter the endocervical canal (15, 16). After the suture is tightened, anterior knots are placed and tails left long enough for ease of later removal, usually 2–3 cm (15). The Shirodkar approach differs from the McDonald approach as it requires additional incisions and dissection of the paracervical area in order to reflect the bladder anteriorly and the rectum posteriorly, with the goal of placing the suture at the level of the internal os (8, 18). The choice of vaginal cerclage technique is dependent on provider preference and experience, although many prefer the McDonald approach due to ease of placement and removal and theoretical decreased risk of complication with insertion and removal. There is minimal high-quality evidence that one technique is superior to the other, and most comparative studies show similar efficacy (14).

Transabdominal Cerclage: Transabdominal cerclage was first introduced by Benson and Durfee in 1965 (9). As classically described, the suture is placed at the cervicoisthmic junction, which is where the isthmus of the uterus, "the constricted part of the uterus between the body and the cervix" (19), abuts the internal os. Therefore, the suture is placed just superior to the internal os, rather than inferior as would be the case with most transvaginal cerclage procedures, where the vaginal fornices limit a more superior (cephalad) placement. Twenty-five years after its inception, its utility was summarized by Novy, stating, "the transabdominal route is beneficial in treating patients with cervices that are either extremely short, congenitally deformed, deeply lacerated or markedly scarred because of previously failed transvaginal cerclage procedures" (20).

DOI: 10.1201/9781003312109-53

A nearly 90% success rate was noted in a review of the world's literature at that time that comprised 130 pregnancies (20). Although historically the transabdominal cerclage approach via open laparotomy has clearly been a more morbid procedure, the literature has supported this technique as a safe and effective intervention for reducing the risk of pregnancy loss in specific patient populations with cervical insufficiency.

Since its introduction more than 50 years ago, abdominal cerclage has been predominantly performed by perinatologists with the traditional laparotomy approach. A shift towards a less invasive technique aiming at decreasing morbidity and improving maternal outcomes has led to a more multidisciplinary team approach where the maternal fetal medicine specialists identify patients at risk and minimally invasive surgery specialists perform the procedure preconceptually or in early pregnancy. Many modifications of the original technique by Benson (9) have been described, including laparoscopic and robotic approaches (10–13).

53.3 Laparoscopic/Robotic Transabdominal Cerclage

Surgical Technique: Minimally invasive transabdominal cerclage can be performed laparoscopically. The use of conventional laparoscopy or robot laparoscopy is based on the surgeon's preference, experience, and comfort level; however, the surgical technique is the same for both approaches. The patient is placed on a padded table in a dorsal lithotomy position using Allen stirrups. The arms are tucked at the patient's side. A uterine manipulator is used only in nonpregnant patients. Port placement varies depending on anatomy and size of the uterus; however, with most procedures a traditional four-port approach is sufficient. Three 8 mm robotic ports and one 12 mm disposable port is used. The pneumoperitoneum is maintained at 10–12 mmHg throughout the procedure. The table is then positioned in a Trendelenburg position to allow for mobilization of the bowel from the pelvis and to allow for full access to the posterior cul-de-sac. This is critically important especially in a pregnant patient where uterine manipulation is limited.

At this point, identification of all anatomical and surgical landmarks is performed to include the round ligaments, vesicouterine peritoneal reflection, cervicoisthmic junction anteriorly and posteriorly, and bilateral uterine vasculature complexes. The da Vinci surgical system (Intuitive Surgical, Sunnyvale, California) is utilized with three or four arms depending on need. After docking all arms, monopolar scissors are placed in arm 1 and Maryland bipolar graspers are used in arm number 2. When performing this procedure in a pregnant patient, the 12 mm accessory port is used to introduce an EndoPaddle Retract TM (Covidean), or equivalent such as laparoscopic snake retractor, to deflect the gravid uterus anteriorly or posteriorly (Figure 53.1). The anterior leaflet of the broad ligament is entered sharply with the scissors. The incision is initiated medial to the round ligament and extended to the contralateral side. This step allows for mobilization of the bladder away from the operative site. Delicate and meticulous dissection is essential to avoid capillary bleeding that may significantly hinder visualization of surgical planes. Once the uterine artery complex is identified bilaterally in the anterior compartment, attention is turned to the posterior side. The isthmic portion is identified and the posterior leaflet of the broad ligament is developed allowing access to the vasculature bilaterally. A blunt dissection technique is utilized to access the avascular space just medial to the uterine artery and lateral

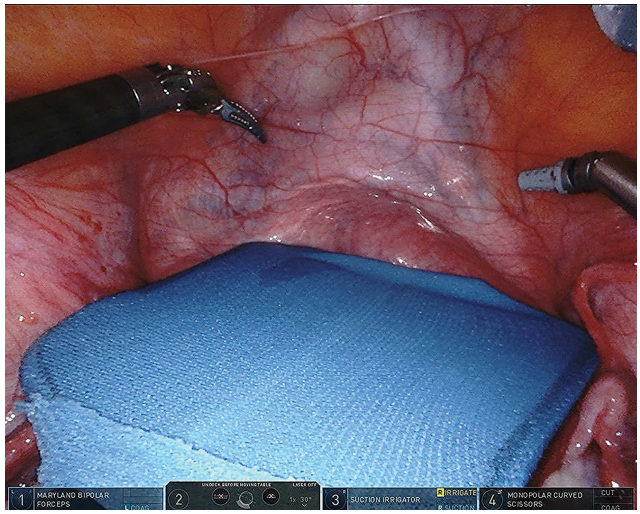


FIGURE 53.1 Laparoscopic retraction device viewing anterior cul-de-sac with gentle posterior uterine deflection.

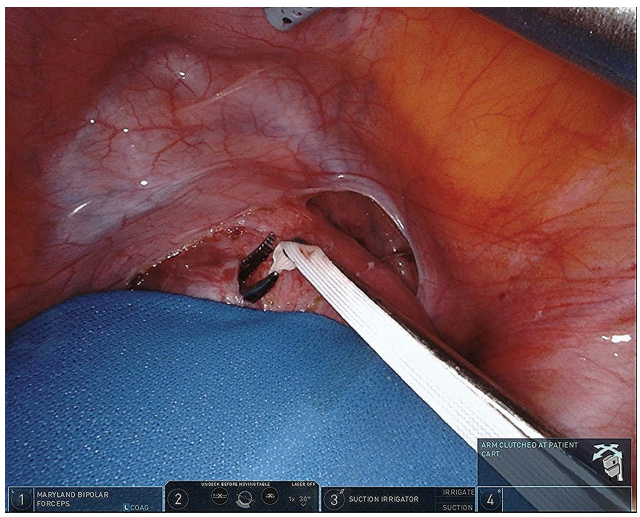


FIGURE 53.2 Avascular tunnel created at the cervicouterine isthmus medial to the uterine arteries.

to the cervicoisthmic portion. This is carried out with robotic Debakey forceps utilizing the basic principles of minimally invasive surgical techniques of "push and spread" and "gentle whipping" to allow for the tip of the forceps to traverse from anterior to posterior without disrupting the vasculature. Once the avascular tunnels are created bilaterally a 5 mm Mersilene tape is introduced via the accessory laparoscopic port without any needles attached. The tape is passed through the previously created avascular tunnel from anterior to posterior (Figure 53.2). The tape is checked to ensure it lies flat, without twists, before securing in place (Figure 53.3).

An alternative approach is to create a small window in the broad ligament bilaterally. Using a Mersilene tape suture with a blunt needle BP-1 (Ethicon Endo Surgery, Raritan, New Jersey), the needle is passed from top down in the avascular plane between the cervix and uterine vessels on patient's left side and then passed out through the broad ligament window. The needle and the tape are then pulled back through the left window toward the posterior cul-de-sac and around the cervix.

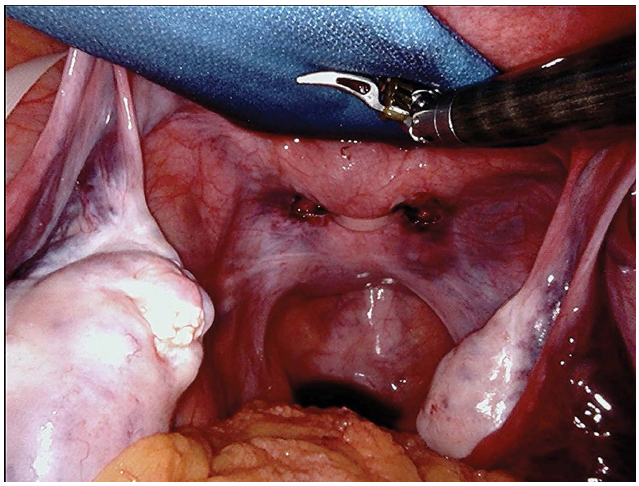


FIGURE 53.3 Mersilene tape without twists – posterior view.

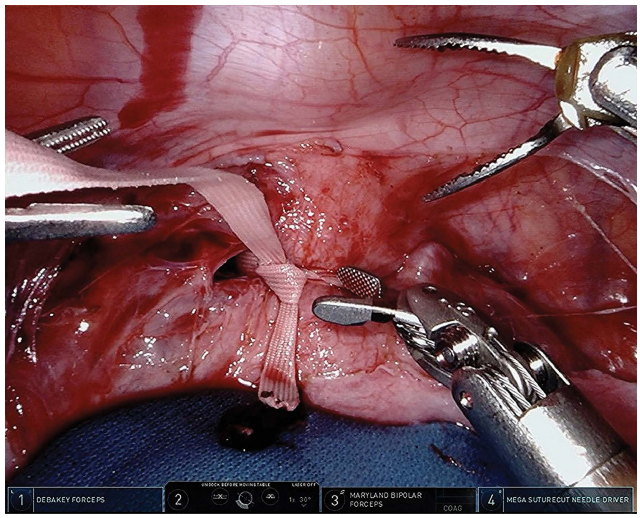


FIGURE 53.5 Knot secured anteriorly.

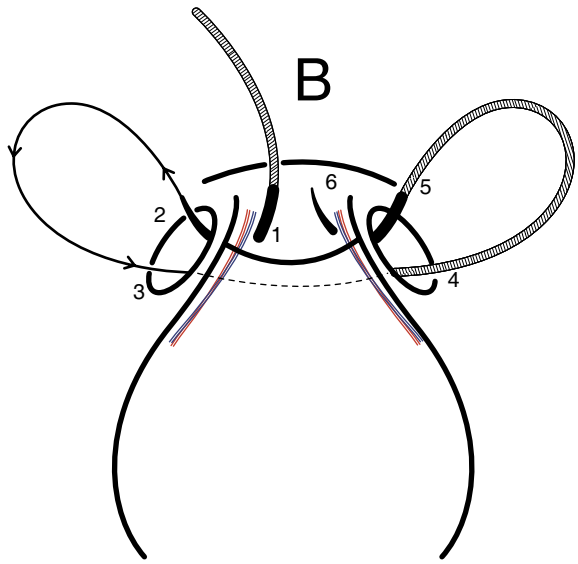


FIGURE 53.4 Schematic drawing of the needle pathway with Mersilene tape: (B) bladder; (1) insertion point of needle (medial to the blood vessels); (2) needle exit point; (3) needle is placed back through the created window and pushed behind the cervix toward the window on the right side; (4) needle and tape are pulled out through the created window on the right side; (5) entry point of needle on the right side (medial to the blood vessels); (6), exit point of the needle (medial to the blood vessels).

The suture is then pulled through the right peritoneal window. Next, the needle is regrasped and placed from back to front in the avascular plane between the uterine vessels and the cervix on patient's right side (Figure 53.4). The needle is cut off and the knot is tied anteriorly (Figure 53.5). Six knots are placed securely, and the tape is trimmed to remove access. The tape and knot can be reperitonealized to decrease likelihood of adhesions. This is accomplished with a 3.0 Monocryl suture on an SH needle in a running fashion. Fetal heart tones are evaluated pre- and postoperatively.

Transvaginal ultrasound can be utilized to visualize the cerclage tape at the cervicoisthmic junction (Figure 53.6).

Surgical Timing: As no randomized trials have been conducted, there is a lack of consensus regarding a recommendation for preconception versus postconception abdominal cerclage placement. Preconception placement has been associated with similar outcomes as postconception and has the additional benefits of a lack of risk of injury to an existing pregnancy and improved surgical exposure (21). An important consideration, however, with respect to preconception placement is the fact that up to 26% of such patients may not go on to have a pregnancy subsequent to the procedure (22). Additional studies have been performed looking at preconception versus postconception cerclage placement and have shown either similar live birth rates (23) or reduction in preterm birth prior to 34 weeks and reduced operative complications with preconception placement (24), although these studies were from time periods of open laparotomy for abdominal cerclage placement.

With respect to transabdominal cerclage placement during pregnancy, the procedure is ideally performed in the late first trimester through early second trimester. This allows for most early spontaneous abortions to occur prior to surgical intervention and also provides sufficient time for some degree of fetal aneuploidy evaluation as desired and anatomical assessment via ultrasound. As the uterus enlarges with advancing gestation, risks increase as visualization becomes further compromised, leading to a more technically challenging surgery.

Preoperative Care: Preoperative prenatal care should ensure, with the greatest certainty possible, that the fetus is anatomically and genetically normal, within the limitations of early ultrasound and through screening or diagnostic genetic testing (as per patient preference). Preoperative transabdominal and transvaginal ultrasound should be utilized to verify gestational age and assess the anatomic integrity of the fetus. As early as the late first and early midtrimester, ultrasound can be critical to evaluate for congenital malformations which would likely preclude cerclage intervention, including anencephaly, cystic hygroma, cesarean scar ectopic, urinary tract obstructions, cardiac malformations and abdominal wall defects, and others (25, 26). Nevertheless, despite these precautions, clinical

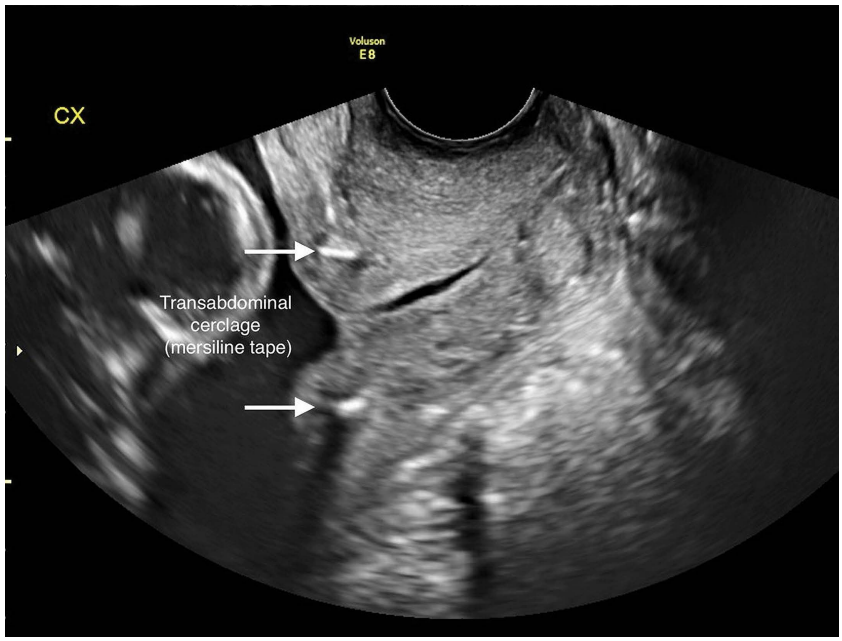


FIGURE 53.6 Transabdominal cerclage tape visualized on transvaginal ultrasound at 17 weeks' gestation. Note placement at the level of the internal os.

circumstances may arise with respect to miscarriage and fetal demise which will need to be addressed. Management of these complications is necessarily unique given the presence of a suture at the cervicoisthmic junction.

Fetal Monitoring: Transabdominal cerclages placed postconception are performed during the previable stage of fetal development, typically in the late first and early second trimesters. Fetal heart rate monitoring by Doppler or bedside ultrasound is performed before and after the procedure. The American College of Obstetricians and Gynecologists states, "no currently used anesthetic agents have been shown to have any teratogenic effects in humans when using standard concentrations at any gestational age" (27). As traditional laparotomy approach is utilized less and less, transabdominal cerclage placement by minimally invasive techniques is primarily an outpatient procedure and does not require additional postoperative fetal monitoring.

Perioperative/Perinatal Complications: Once a cerclage is placed, whether preconceptionally or prophylactically in early pregnancy, guiding principles of management are ongoing patient support and clinical surveillance. Cerclage is a surgical procedure and as such, although considered relatively safe, has inherent risk for complications. Intraamniotic infection, bleeding, PPROM, and suture "migration" are relatively rare, but patient complaints consistent with these potential adverse events must be considered and assessed as indicated. First trimester pregnancy loss does not in and of itself require suture removal to safely perform sufficient cervical dilation and uterine evacuation to operatively complete an incomplete or missed abortion. In the early midtrimester and certainly later, although some have reported the ability to perform a dilation and evacuation with abdominal cerclage in situ (28), management of pregnancy loss may require removal of the cerclage. Ideally, this would be accomplished via minimally invasive approach (laparoscopy). Cerclage removal in these circumstances allows for less risk of cervicoisthmic trauma, which may occur with mechanical dilation and instrumentation of the cervix and uterus, and would also allow for the option of misoprostol administration and the medical evacuation of the intrauterine contents. Efforts should be directed at removing the products of conception transvaginally, rather than through hysterotomy which would increase risks in future pregnancy. In the third trimester, when fetal demise is diagnosed, laparoscopic cerclage removal, when possible, followed by labor induction would be appropriate. At times, however, a laparotomy may be required for abdominal cerclage removal. Again, in most circumstances, a hysterotomy for delivery is avoided when feasible. In the setting of prior cesarean section(s), particularly a prior vertical cesarean incision, history of myomectomy, a plan for permanent sterilization, or patient request, hysterotomy may be considered on an individualized basis.

Delivery Considerations: With respect to delivery timing, there are no randomized clinical trials by which to provide evidence-based recommendations. Our general approach is to discuss with the patient the well-established potential risks of late-preterm and early term delivery (29, 30) and then generally recommend delivery at 37 weeks by scheduled cesarean section. Patients who prefer to await further advancement in gestational age are counseled as to the potential risks of labor in the setting of abdominal cerclage including the potential for tearing of the suture, cervicouterine trauma, bleeding, uterine rupture, and need for emergency cesarean section. Strict instructions and precautions are provided, and we recommend that the pregnancy be delivered no later than 39 weeks. Patients are counseled to present urgently to labor and delivery for assessment should they experience regular uterine activity at any time. At the time of cesarean delivery, we typically leave the abdominal cerclage in situ given its generally accepted utility in future pregnancy, although literature in this regard is lacking. In those patients for whom the cerclage is no longer desired, it can be removed at the time of cesarean section. If

cerclage removal is anticipated to be complicated and/or the patient is a poor surgical candidate, it may be reasonable to leave the cerclage in-situ; however, long-term adverse events have been reported (31). When delivery is contemplated prior to 36 6/7 weeks, we counsel patients as to the benefits of late antenatal corticosteroids in accordance with guidance from the Society of Maternal-Fetal Medicine (32).

53.4 Transabdominal Cerclage Outcomes

The goal for intervention with a cervical cerclage, both transvaginal and transabdominal, is prevention of a preterm birth. Given the historically noted increased morbidity with a laparotomic approach to cervical cerclage placement, a systematic review sought to determine if improved perinatal outcome would be noted when comparing traditional open abdominal cerclage placement to vaginal cerclage in women who had a prior failed vaginally placed cerclage (33). The study demonstrated that women who were treated with an abdominal cerclage following a prior failed nonemergent vaginally placed cerclage in a prior pregnancy (via open laparotomy in the studies evaluated) were significantly less likely to experience the outcome of perinatal death or delivery at < 24 weeks than women who underwent a subsequent vaginally placed cerclage (6% vs 12.5%) (33). These perinatal benefits, however, must be weighed against the noted 3.4% occurrence of operative morbidity including need for blood transfusion, injury to bowel or bladder, uterine artery injury, and anesthesia complications; none of which occurred in the vaginally placed cerclage group. Another study looking similarly at abdominal cerclage placement in 75 women with past histories of unsuccessful transvaginal cerclage procedures found a fetal salvage rate of 96% and a median gestational age of delivery of 36 weeks with 72 of the 75 women delivering beyond 24 weeks' gestation (34). Additional efficacy of the abdominal cerclage procedure was reported in an observational cohort study evaluating pregnancy outcomes after transabdominal cervicoisthmic cerclage via laparotomy in 101 women with a classic history of cervical insufficiency and severe cervical defects precluding transvaginal cerclage placement (35). It was noted using the patient's prior pregnancies as historical controls that neonatal survival in this group prior to abdominal cerclage placement was 27.5%; significantly less than the 93.5% rate seen in subsequent pregnancies treated with abdominal cerclage. Following abdominal cerclage, only 7% of deliveries were noted prior to 32 weeks, compared to 76% in past pregnancies. While median blood loss was 50 mL, intraoperative hemorrhage of 800 mL, 850 mL, and 1500 mL, respectively, occurred in three patients. These significant improvements in outcomes is likely related to suture placement above the internal os, which anatomically would provide greater structural support than a suture placed significantly more distally, when lack of cervical anatomical integrity exists.

Most available data on transabdominal cerclage are comparison studies of open laparotomy technique versus minimally invasive techniques, mostly conventional laparoscopy. Most data report similar obstetric outcomes for conventional laparoscopic transabdominal cerclage compared to the laparotomy approach (23, 36–38). In 2017, Moawad et al. reported a systematic review comparing 26 studies with 1116 patients who underwent transabdominal cerclage by laparotomy approach to 15 studies with 728 patients who underwent transabdominal cerclage by conventional laparoscopy (22). The authors reported similar neonatal survival and higher rates of > 34-week delivery compared to laparotomy, when first trimester losses were excluded (22). This systematic review did not include robotic-assisted cerclage given the paucity of studies at the time of the review. Recently, there has been a surge of literature on robotic cerclage placement, although high-quality studies on robotic cerclage are lacking, with most literature consisting of case reports and case series. Gonzales et al. reported a case series of 11 patients who underwent robotic transabdominal cerclage in pregnancy with 81.8% delivering a viable neonate and 72.7% delivering at > 34 weeks' gestational age (39). According to a small review article on robotic cerclage by Iavazzo et al., no clear advantage over conventional laparoscopy could be determined given the absence of high-quality studies (40). A multicenter, retrospective cohort study on robotic transabdominal cerclage showed a 4.0 and 3.6 times greater odds of delivering after 34 and 37 weeks' gestational age, respectively, when comparing women prerobotic cerclage to postrobotic cerclage (41). When compared to prior pregnancy outcomes, the odds of neonatal survival were 12.6 times greater after robotic-assisted transabdominal cerclage (41). In summary, a minimally invasive approach offers the same advantages and efficacy when compared to traditional placement via laparotomy, without the expected morbidity associated with open procedures.

53.5 Conclusion

Preterm delivery remains the leading cause of maternal morbidity and mortality not only in the United States but around the world (3, 4). Cervical insufficiency plays a significant role leading to preterm delivery and its associated complications. This poses an unparalleled emotional, physical, and financial burden on families and society. Our responsibility remains to identify mothers at risk, evaluate for possible etiologies, and offer them the most evidence-based therapeutic options. There is growing evidence that a transabdominal cerclage offers better obstetrical outcomes for this patient population, approaching nearly 90% success rate, with a 10% incidence of preterm birth at < 33 weeks in the transabdominal group (42).

Therefore, when after careful patient evaluation a determination is made that the best course of action for the prevention of preterm parturition is the placement of a transabdominal cerclage, the benefits of a minimally invasive technique should be strongly considered and the patient cared for in a center with the requisite expertise required.

References

1. ACOG. Practice bulletin 142: cerclage for the management of cervical insufficiency. *Obstet Gynecol*. 2014;123(2):372–379.
2. Ludmir J. Sonographic detection of cervical incompetence. *Clin Obs Gynecol*. 1988;31:101–109.
3. Matthews TJ et al. Infant mortality statistics from the 2013 period linked birth/infant death data set. *Natl Vital Stat Rep*. 2015;64:1–30.
4. Watkins WJ et al. All-cause mortality of low birthweight infants in infancy, childhood, and adolescence: population study of England and wales. *PLOS Med*. 2016;13(5):e1002018.
5. Rumack CM et al., eds. *Diagnostic Ultrasound*, 4th edn. Philadelphia: Elsevier; 2011.
6. Harger JH. Cerclage and cervical insufficiency: an evidence-based analysis. *Obstet Gynecol*. 2002;100(6):1313–1327.
7. Shirodkar V. A new method of operative treatment for habitual abortions in the second trimester of pregnancy. *Antiseptic*. 1955;52:299–300.

8. Mcdonald I. Suture of the cervix for inevitable miscarriage. *J Obs Gynaecol Br Emp*. 1957;64:346–350.
9. Benson RC et al. Transabdominal cervicouterine cerclage during pregnancy for treatment of cervical incompetence. *Obstet Gynecol*. 1965;25:145–155.
10. Lesser KB et al. Transabdominal cerclage: a laparoscopic approach. *Obstet Gynecol*. 1998;91(5):855–856.
11. Mourad J et al. Needleless robotic-assisted abdominal cerclage in pregnant and nonpregnant patients. *J Minim Invasive Gynecol*. 2016;23(3):298–299.
12. Moore ES et al. Robotic-assisted transabdominal cerclage (RoboTAC) in the non-pregnant patient. *J Obstet Gynaecol*. 2012;32(7):643–647.
13. Wolfe L et al. Robotic-assisted laparoscopic placement of transabdominal cerclage during pregnancy. *Am J Perinatol*. 2008;25(10):653–655.
14. Wood SL et al. Cerclage: Shirodkar, McDonald, and modifications. *Clin Obstet Gynecol*. 2016;59(2):302–310.
15. Berghella V et al. Cervical insufficiency. In: Creasy RK et al., eds. *Maternal-Fetal Medicine Principles and Practice*, 7th edn. Elsevier; 2014:654–662.
16. Suhag A et al. Cervical cerclage. *Clin Obs Gynecol*. 2014;57(3):557–567.
17. Berghella V et al. Operative procedures on the cervix. In: Apuzzio J et al., eds. *Operative Obstetrics*, 3rd edn. Taylor and Francis; 2006.
18. Frieden F et al. The Shirodkar operation: a reappraisal. *Am J Obstet Gynecol*. 1990;163(3):830–833.
19. Wendell-Smith CP. The lower uterine segment. *BJOG*. 1954;61(1):87–93.
20. Novy MJ. Transabdominal cervicoisthmic cerclage: a reappraisal 25 years after its introduction. *Am J Obstet Gynecol*. 1991;164:1635–1642.
21. Burger NB et al. Preconceptional laparoscopic abdominal cerclage: a multicenter cohort study. *Am J Obstet Gynecol*. 2012;207(4):273.e1–273.e12.
22. Moawad GN et al. Systematic review of transabdominal cerclage placed via laparoscopy for the prevention of preterm birth. *J Minim Invasive Gynecol*. 2018;25(2):277–286.
23. Tulandi T et al. Pre and post-conceptional abdominal cerclage by laparoscopy or laparotomy. *J Minim Invasive Gynecol*. 2014;21(6):987–993.
24. Dawood F et al. Transabdominal cerclage: preconceptual versus first trimester insertion. *Eur J Obstet Gynecol Reprod Biol*. 2016;199:27–31.
25. Karim JN et al. Systematic review of first-trimester ultrasound screening for detection of fetal structural anomalies and factors that affect screening performance. *Ultrasound Obstet Gynecol*. 2017;50(4):429–441.
26. Kenkhuis MJA et al. Effectiveness of 12–13-week scan for early diagnosis of fetal congenital anomalies in the cell-free DNA era. *Ultrasound Obstet Gynecol*. 2018;51(4):463–469.
27. ACOG. Nonobstetric surgery during pregnancy. Committee opinion 696. *Obstet Gynecol*. 2017;129:777–778.
28. Martin A et al. Controversies in family planning: management of second-trimester losses in the setting of an abdominal cerclage. *Contraception*. 2013;87(6):728–731.
29. Tita ATN et al. Timing of elective repeat Cesarean delivery at term and neonatal outcomes. *N Engl J Med*. 2009;360(2):111–120.
30. Clark SL et al. Neonatal and maternal outcomes associated with elective term delivery. *Am J Obstet Gynecol*. 2009;200(2):156.e1–156.e4.
31. Hawkins E et al. Vaginal erosion of an abdominal cerclage 7 years after laparoscopic placement. *Obstet Gynecol*. 2014;123(2).
32. SMFM Publications Committee. Implementation of the use of antenatal corticosteroids in the late preterm birth period; women at risk for preterm delivery. *Am J Obstet Gynecol*. 2016;215(2):B13– B15.
33. Zaveri V et al. Abdominal versus vaginal cerclage after a failed transvaginal cerclage: a systematic review. *Am J Obstet Gynecol*. 2002;187(4):868–872.
34. Debbs RH et al. Transabdominal cerclage after comprehensive evaluation of women with previous unsuccessful transvaginal cerclage. *Am J Obstet Gynecol*. 2007;197(3):317.e1–317.e4.
35. Lotgering F et al. Outcome after transabdominal cervicoisthmic cerclage. *Obstet Gynecol*. 2006;107(4):779–784.
36. Carter JF et al. Abdominal cerclage for the treatment of recurrent cervical insufficiency: laparoscopy or laparotomy? *Am J Obstet Gynecol*. 2009;201(1):1–4.
37. Ades A et al. Transabdominal cervical cerclage: laparoscopy versus laparotomy. *J Minim Invasive Gynecol*. 2015;22(6):968–973.
38. Burger NB et al. Effectiveness of abdominal cerclage placed via laparotomy or laparoscopy: systematic review. *J Minim Invasive Gynecol*. 2011;18(6):696–704.
39. Gonzales SK et al. Robotic-assisted laparoscopic abdominal cerclage placement during pregnancy. *J Minim Invasive Gynecol*. 2018;25(5):832–835.
40. Iavazzo C et al. Robotic assisted laparoscopic cerclage: a systematic review. *Int J Med Robot Comput Assist Surg*. 2018;e1966.
41. Tyan P et al. Robot-assisted transabdominal cerclage for the prevention of preterm birth: a multicenter experience. *Eur J Obstet Gynecol Reprod Biol*. 2019;232:70–74.
42. Davis G et al. Patients with a prior failed transvaginal cerclage: a comparison of obstetric outcomes with either transabdominal or transvaginal cerclage. *Am J Obstet Gynecol*. 2000;183(4):836–839.
43. Iams JD et al. The length of the cervix and the risk of spontaneous premature delivery. *N Engl J Med*. 1996;334(9):567–573.

54 PRINCIPLES OF FETAL SURGERY

Eyal Krispin and Alireza A. Shamshirsaz

54.1 Introduction

Fetal surgery introduced over four decades ago is an evolving field of medicine. Diagnostics, management options, and surgical techniques have progressed significantly, but the principles have remained unchanged. A correct and precise prenatal diagnosis is needed to clearly identify the anomaly and roll out associated genetic or structural deviations. A thorough knowledge of the disease is needed and thus specialized centers with multidisciplinary partnership of specialized personnel should lead the care. Interventions should be considered when a high perinatal morbidity or mortality is expected and no effective post-natal treatment is available. Treatment should be based on animal models and favorable evidence in literature. While fetal surgery involves adverse maternal outcomes, it should not compromise the reproductive future of the patient nor should it increase maternal mortality. Full transparency of potential maternal adverse outcomes should be discussed and considered thoroughly.

The leading imaging modality for prenatal diagnosis of fetal anomalies is ultrasound. In recent years, the use of magnetic resonance imaging (MRI) has grown and shown to be beneficial. Genetic evaluation is required. Fetal medicine options vary significantly, and each approach requires different specialized instrumentations.

As the field of fetal medicine evolves, ethical issues arise. The accepted ethical framework should balance the risks to the mother against the expected advantages to the fetus. Efficacy and adverse outcomes should be fully transparent to the parents, and a true understanding and informed consent must be obtained.

54.1.1 Preoperative Planning

Rigorous criteria govern the inclusion of patients in fetal surgery due to potential risks to both mother and fetus, necessitating thorough evaluation. Understanding the pathology, assessing the benefits, and discussing risks are essential. Patients must comprehend the prolonged treatment process and have adequate support systems.

Fetal surgeries pose technical challenges, including limited space and visualization, with each procedure being unique. Meticulous planning and consideration of real-time alternatives are crucial. Uterine entry location is carefully chosen to avoid harm to maternal organs, vessels, and the placenta, while ensuring an effective approach to the target.

Tocolytic treatment is routinely recommended to maintain uterine quiescence during procedures. Patients with frequent contractions may be ineligible for fetal intervention due to the risk of preterm labor or placental abruption.

Standardized uterine entry criteria are vital, with limited attempts to minimize complications. Surgical instruments must be prepared and alternative options available, with the entire surgical team briefed on the procedure, potential complications, and expected outcomes.

Anesthesia type varies based on the surgical approach, ranging from local anesthesia to general anesthesia. Coordination with a neonatal intensive care unit (NICU) providers ensures preparedness for potential urgent cesarean deliveries.

54.2 Ultrasound-Guided Needle-Based Procedures

54.2.1 Intrauterine Transfusion (IUT)

Intrauterine transfusion of red blood cells is the standard therapy for severe fetal anemia from a number of different etiologies: alloimmunization, congenital infection (e.g., parvovirus B19), fetomaternal hemorrhage, and other rare causes of fetal anemia such as Fanconi anemia.

The diagnosis is done by Doppler ultrasound when the fetal middle cerebral artery is at peak systolic velocity. A middle cerebral artery peak systolic velocity (MCA-PSV) greater than or equal to 1.5 multiples of the median (MoM) is considered indicative of severe fetal anemia and is usually used as the cut-off for considering transfusion (1).

Both intravascular and intraperitoneal routes have been described for the intrauterine transfusion of red blood cells. While intravascular transfusion (IVT) has become the generally accepted and preferred method, intraperitoneal transfusion (IPT) remains an option in cases where the vascular access is challenging. Some clinicians advocate for a combined approach (IVT and IPT) in an attempt to prolong transfusion intervals. These techniques have not been compared in a randomized control trial.

Obtaining vascular access may differ according to placental location. In anterior placenta, the umbilical insertion site would be the preferred location for transfusion. When the placenta is posterior, accessing the cord insertion may be challenging due to the distance and having the fetus obstructing the vision and the path. The intrahepatic portion of the umbilical vein provides an alternative site in these cases.

The transfused blood should contain packed red blood cells, O RhD negative, Kell negative, irradiated, washed, cytomegalovirus negative, leucocyte depleted, fresh with higher hematocrit (HCT) levels (70%–80%).

Transfusion amounts should be calculated in real time according to HCT levels sampled prior to initiating the transfusion and estimated fetal weight.

54.2.2 Vesicoamniotic and Thoracoamniotic Shunts

Fetal lower urinary tract obstruction (LUTO) and fetal pleural effusions are serious conditions requiring specialized prenatal interventions.

LUTO: Characterized by urethral obstruction, LUTO can lead to significant fetal morbidity and mortality. Vesicoamniotic shunt (VAS) is a surgical option to divert urine from the bladder into the amniotic cavity, aiding in preserving pulmonary development in severe cases like posterior urethral valves or urethral atresia (2). Precise patient selection and prenatal diagnosis are critical for successful outcomes (3).

Fetal pleural effusions: Accumulation of fluid around the fetal lungs, this condition can impair cardiac function and

DOI: 10.1201/9781003312109-54

lung development. Thoracoamniotic shunt (TAS) is a surgical intervention to drain fluid from the thoracic cavity into the amniotic space, potentially improving cardiac and pulmonary function (4). Detailed prenatal diagnosis and management are essential for optimizing outcomes.

Both TAS and VAS involve percutaneous ultrasound-guided shunt insertion, with careful consideration of shunt placement and assessment of shunt effectiveness through prenatal and postnatal monitoring. Complications include shunt misplacement, maternal or fetal organ injury, and postoperative issues like shunt dislodgment or obstruction (5).

Intrauterine procedures like bladder/chest tap serve as preliminary steps to shunt placement, aiding in fluid analysis and monitoring (3, 4). Close follow-up and timely intervention are crucial to manage potential complications and optimize outcomes for both mother and fetus.

54.2.3 Selective Fetal Reduction

This section addresses selective reduction in cases involving a monochorionic placenta. Selective fetal reduction is a medical procedure performed during a multiple pregnancy to decrease the number of fetuses, aiming to enhance the chances of a healthy outcome for both the mother and the remaining fetuses. Indications for selective reduction in monochorionic twins include structural or genetic fetal anomalies, selective fetal growth restriction, twin–twin transfusion syndrome, and twin anemia polycythemia. It can also be considered as a treatment for twin reversed arterial perfusion syndrome (TRAP) to reduce the acardiac twin and improve the outcome of the pump twin. When multiples share a placenta, reducing a single fetus necessitates specific methods to avoid harming the remaining fetus, typically involving halting the blood supply to the reduced fetus through various energy-transforming procedures. Radiofrequency ablation (RFA) is a minimally invasive procedure that uses thermal energy from radiofrequency waves to deactivate targeted fetal tissue, reducing the number of fetuses in a pregnancy. Guided by ultrasound, a needle electrode is inserted into the targeted fetus and connected to a generator emitting heat to ablate tissue, often targeting the umbilical cord or vital structures. RFA offers advantages such as its minimally invasive nature, specific targeting, and early application in higher-order pregnancies, potentially reducing associated risks.

Bipolar cord coagulation is another technique for selective fetal reduction. Under ultrasound guidance, bipolar forceps are used to coagulate and occlude blood vessels in the umbilical cord, halting blood flow and resulting in fetal demise. While technically more challenging than RFA, it can prevent intertwin cord entanglement in monoamniotic pregnancies.

Both RFA and bipolar coagulation carry potential complications, including maternal risks of infection, bleeding, and injury to adjacent structures, as well as fetal complications like injury or premature labor. Open discussions with healthcare providers are crucial to understanding these risks and making informed decisions about care.

54.3 Cardiac Intervention

Various intrauterine cardiac interventions can address specific cardiac abnormalities, contingent upon the medical team's expertise. These interventions encompass:

- *Balloon Atrial Septoplasty*: Involves inserting a balloon catheter into the fetal heart to widen a narrow or restrictive atrial septum, enhancing blood flow between the atria.
- *Atrial Shunt Placement*: Suitable for fetuses with pulmonary atresia and intact ventricular septum with evolving hypoplastic right heart syndrome, allowing blood flow between the atria to bypass the underdeveloped left side of the heart.

These procedures, guided by advanced imaging like ultrasound and fetal echocardiography, are performed by a multidisciplinary team comprising fetal medicine specialists, pediatric cardiologists, and interventional radiologists. However, they entail risks such as procedure-related complications, preterm labor, premature membrane rupture, and fetal harm. Hence, meticulous patient selection, comprehensive counseling, and risk–benefit assessment are imperative before proceeding (6).

54.4 Chorioangiomas

Chorioangiomas are benign vascular tumors in the placenta during pregnancy, associated with complications like fetal anemia, hydrops fetalis, and preterm labor. Coagulation procedures aim to reduce their size by disrupting blood flow. Methods include:

- *Laser Coagulation*: Direct delivery of laser energy into chorionic vessels via a fiber optic cable inserted into the tumor or by fetoscopic intervention.
- *Radiofrequency Ablation*: Thermal energy generated by radiofrequency waves heats and shrinks the tumor tissue.
- *Embolization*: Injection of substances like microspheres into blood vessels feeding the chorioangioma, blocking blood flow and inducing tumor coagulation (7) (Figure 54.1).

54.4.1 Fetoscopic Procedures

54.4.1.1 Fetoscopic Laser Photocoagulation of Placental Anastomosis

This procedure is offered for complicated monochorionic pregnancies. The most common indication is advanced twin–twin transfusion syndrome (TTTS) (8). Other indications can be selective fetal growth restriction (sFGR) and twin anemia polycythemia (TAPS).

Fetoscopic laser photocoagulation of placental anastomoses (FLPC) is a specialized procedure used to treat certain complications that can arise in pregnancies with monochorionic twins. Monochorionic twins share a single placenta, and in some cases, abnormal blood vessel connections called anastomoses can form between their circulatory systems. These anastomoses can lead to imbalanced blood flow, resulting in conditions such as TTTS, sFGR, and TAPS (Figure 54.2).

During the procedure, a fetoscope, which is a thin, flexible instrument with a camera and light source, is inserted into the uterus through a small incision in the mother's abdomen. The fetoscope allows the surgeon to visualize the placenta and identify the abnormal blood vessel connections. Diode or Yag laser energy is then used to selectively coagulate or seal these vessels, thereby redirecting blood flow and restoring a more balanced circulation between the twins (Figures 54.3 and 54.4).

The goal of fetoscopic laser photocoagulation is to address the underlying cause of complications such as TTTS, sFGR, and TAPS and improve the outcomes for both twins. By interrupting the abnormal blood flow, this procedure aims to mitigate the risks associated with imbalanced circulation, such as fluid imbalance, growth abnormalities, organ damage, and intrauterine fetal demise.

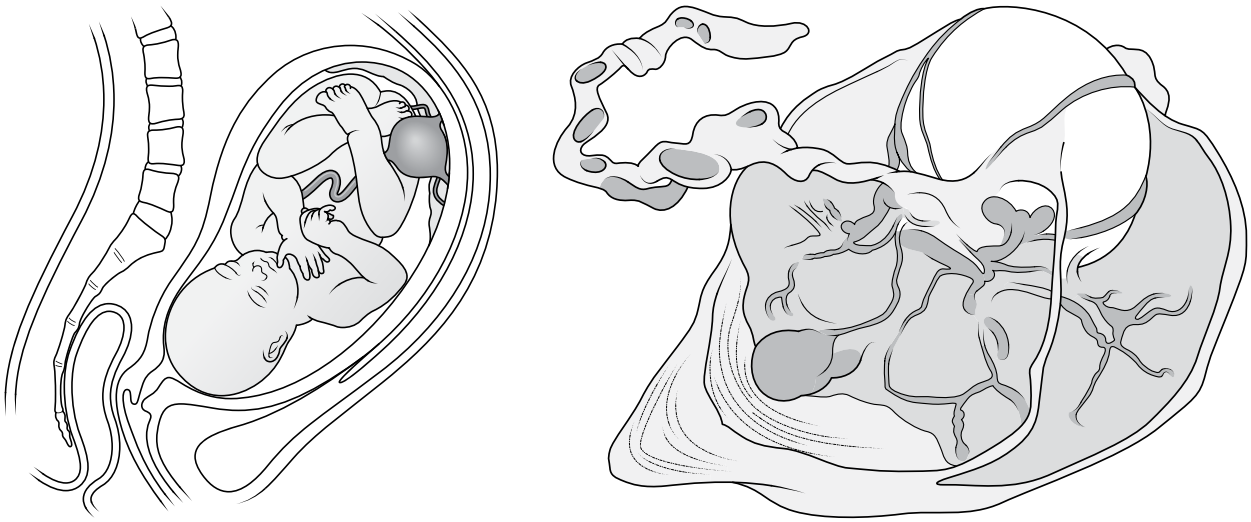


FIGURE 54.1 (a) Singleton gestation complicated by large chorioangioma; (b) magnification of the chorionic plate demonstrating normal placenta umbilical cord chorioangioma and feeding chorionic vessels.

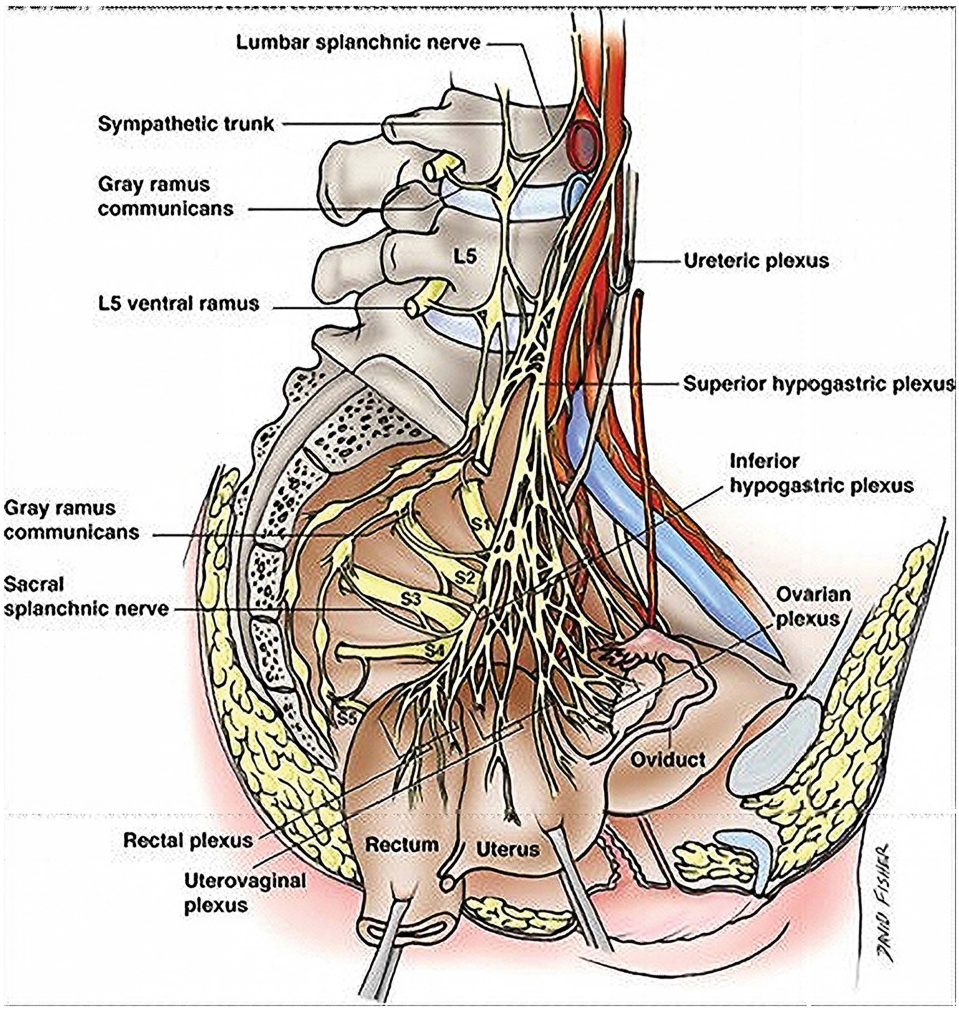


FIGURE 54.2 Chorionic vessel anastomoses.

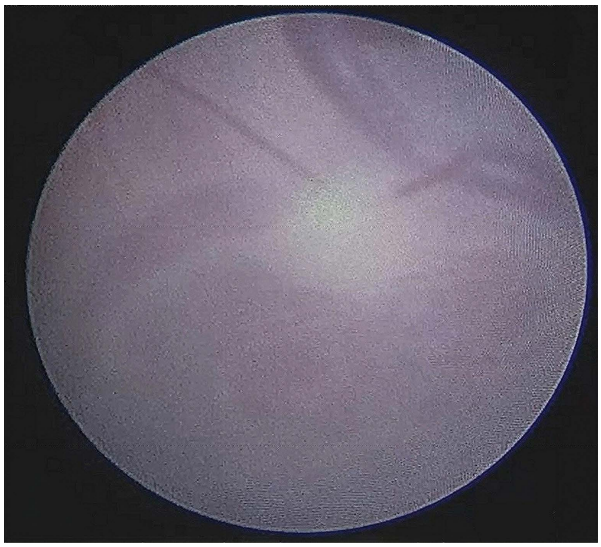


FIGURE 54.3 Chorionic vessel anastomoses being coagulated by laser.

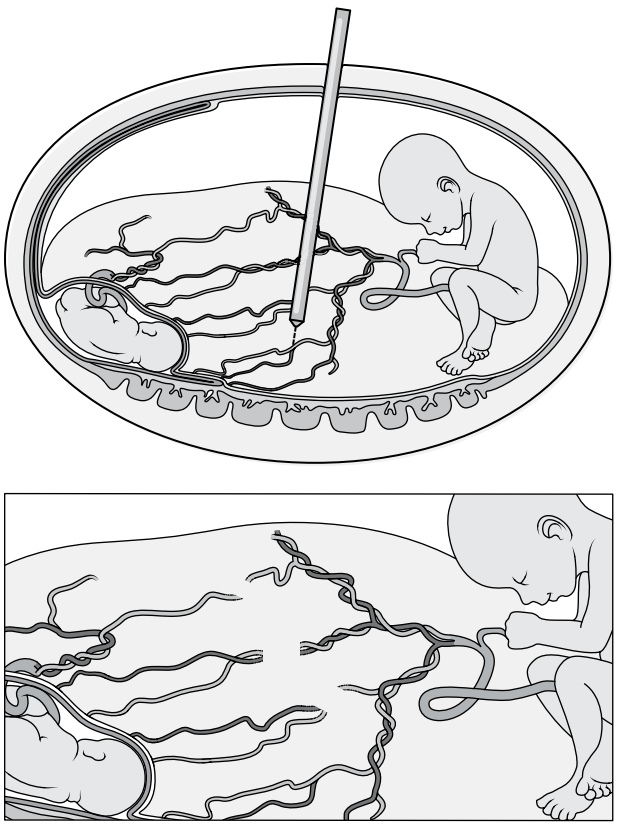


FIGURE 54.4 (a) Fetoscopic view of twin–twin transfusion syndrome; (b) chorionic vessel anastomoses being coagulated by laser.

Following the intervention, close monitoring of the pregnancy continues aiming to diagnose potential complications associated with the procedure (9). Additional interventions or treatments may be required based on the individual circumstances of each case. The success of fetoscopic laser photocoagulation depends on various factors, including the stage of pregnancy, the severity of the complications, and the overall health of the twins (10).

54.4.2 Fetoscopic Endoluminal Tracheal Occlusion (FETO)

Fetoscopic endoluminal tracheal occlusion (FETO) is a procedure offered for pregnancies complicated by severe congenital diaphragmatic hernia (CDH) (11).

CDH involves a defect in the diaphragm, allowing abdominal organs to enter the chest cavity, impacting lung development. Severe cases lead to pulmonary hypoplasia, pulmonary hypertension, and cardiac compression. FETO aims to enhance lung growth for CDH infants.

During FETO, a fetoscope guides a balloon catheter into the fetal trachea, inflating it to stimulate lung expansion by limiting fluid flow. Balloon removal typically occurs after 6 weeks, via ultrasound-guided needle puncture or fetoscopic retrieval. If labor occurs, an ex utero intrapartum treatment (EXIT) procedure may be necessary before term. Postnatal care is crucial for optimal outcomes (Figure 54.5).

54.5 Vasa Previa

Vasa previa is a rare obstetric complication where fetal blood vessels, unprotected by the umbilical cord or placenta, traverse the cervix and are at risk of rupture during labor or delivery. While vasa previa itself does not typically require fetal surgery, its diagnosis during pregnancy may prompt certain interventions to mitigate the associated risks (12).

Vasa previa is classified into three types: type I involves low velamentous cord insertion near the cervix; type II includes vessels bridging between placental lobes; and type III entails vessels originating from and traveling to the placenta. Diagnosis involves detailed prenatal ultrasound with Doppler flows, including both transabdominal and transvaginal approaches. Documentation should include vasa previa type and distance from the cervix. Fetal surgery has been previously proposed to type II vasa previa with the aim to avoid prolonged hospitalization to monitor the fetus and allow vaginal delivery (13). The decision to pursue fetal surgery for vasa previa is highly individualized and depends on several factors, including the gestational age, the type and location of the vasa previa, and the overall health of the mother and fetus and the patient's will. It requires close collaboration between obstetricians, maternal–fetal medicine specialists, and other relevant healthcare providers.

54.6 Amniotic Band Release

Amniotic band syndrome occurs when strands of the amniotic sac entangle parts of the fetus, leading to constriction and various complications (Figures 54.6–54.8). Its cause is unknown, and severity varies, with the most serious being when bands constrict vital areas like the umbilical cord, potentially causing fetal death.

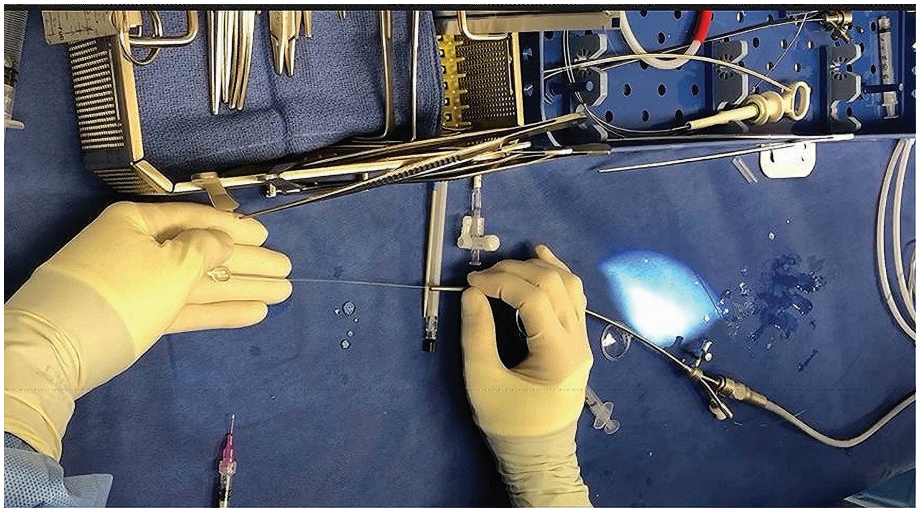


FIGURE 54.5 Preparation of fetoscope and FETO balloon.

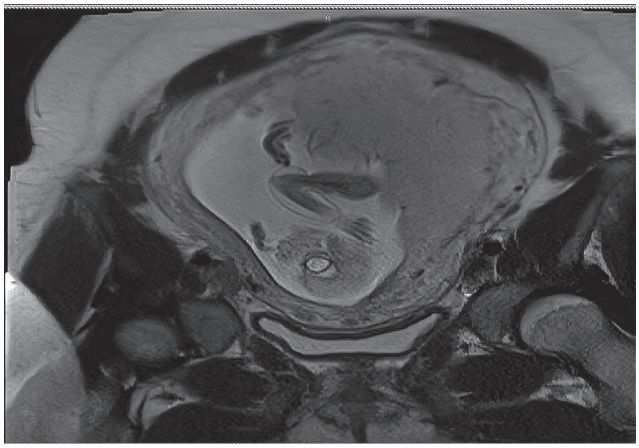


FIGURE 54.6 MRI image demonstrating amniotic band constricting the arm above the elbow, causing severe edema distally to the constriction.

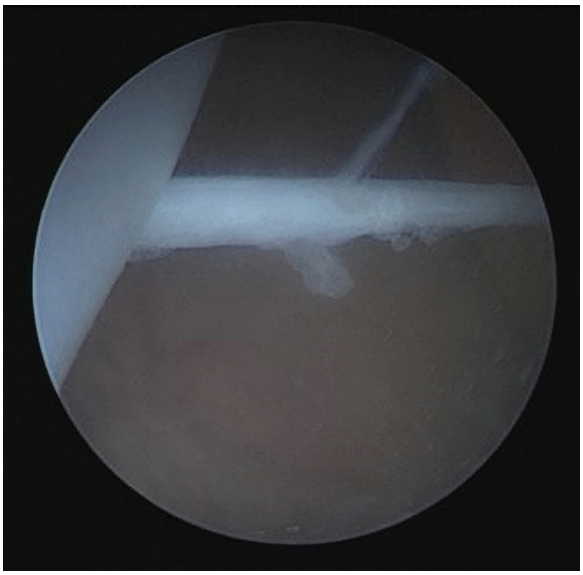


FIGURE 54.7 Amniotic band demonstrated fetoscopically.

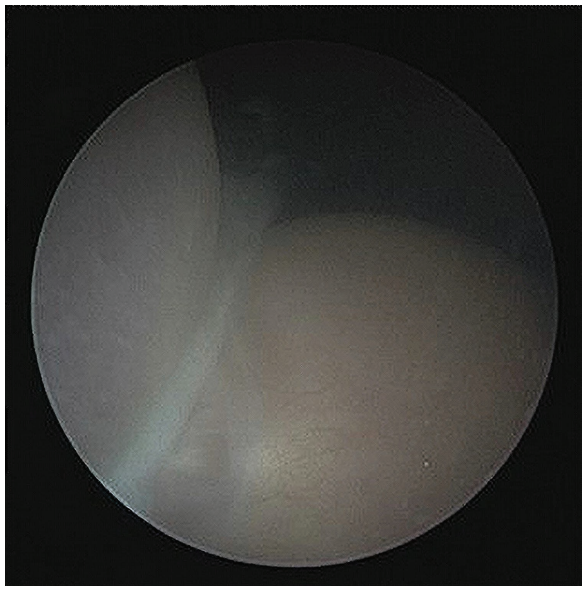


FIGURE 54.8 Amniotic band constricting the arm, demonstrated fetoscopically.

Fetoscopic release is a surgical option for cases where bands threaten the fetus's life or limb. It aims to release constriction and prevent further damage (14). Using scissors or a laser fiber via fetoscope, this procedure has shown promising results, potentially averting limb amputation and fetal demise if the umbilical cord is affected.

54.6.1 Fetoscopic Repair of Spina Bifida

Spina bifida, an open neural tube defect, presents complex challenges in fetal surgery. Traditional open fetal surgery techniques have shown efficacy in repairing spina bifida and advantages compared to postnatal repair (15). However, treatment is associated with maternal risks and prolonged recovery.

In recent years, percutaneous and laparotomy-assisted fetoscopic repair techniques have emerged as a promising alternative (16, 17).

By combining minimally invasive fetoscopic techniques, these innovative procedures aim to mitigate maternal complications while providing effective treatment for the fetus.

54.7 Percutaneous Approach

The percutaneous fetoscopic spina bifida is a minimally invasive surgery, during which specialized instruments are inserted to the uterine cavity to visualize and repair the defect. During this procedure three to four ports are inserted through the maternal abdominal wall into the uterus. The procedure aims to close the defect and minimize fetal trauma, thereby reducing the risk of complications associated with spina bifida.

It is a minimally invasive procedure, resulting in reduced maternal morbidity, shorter hospital stays, and faster recovery times. However, percutaneous fetoscopic repair has its challenges and limitations. It is associated with relatively higher rates of premature preterm rupture of membranes as well as preterm birth. Long-term studies are needed to evaluate the durability of the repair, neurodevelopmental outcomes, and the impact on the natural history of spina bifida.

54.8 Laparotomy-Assisted Approach

The laparotomy-assisted fetoscopic repair technique offers several advantages when compared to traditional open fetal surgery options. The preliminary step done by laparotomy allows exteriorization of the uterus as needed. This enables two important things that cannot be achieved by the percutaneous approach: (1) plication of the membranes prior to trocar entry, which presumably reduces the rates of chorioamniotic separation (Figure 54.9) and premature preterm rupture of membranes (PPROM); (2) optimal selection of trocar placement location according to placental and lesion location.

By incorporating fetoscopic visualization and avoiding hysterectomy, it minimizes maternal morbidity and shortens the recovery period. The procedure allows for precise repair of the spina bifida defect while ensuring adequate fetal oxygenation and minimizing fetal trauma. It has been demonstrated that in comparison to the open hysterotomy repair, this approach is associated with less uterine thinning and dehiscence and significantly higher rates of vaginal delivery in the index pregnancy and future pregnancies (18).

FIGURE 54.9 MRI image demonstrating chorioamniotic separation.

54.9 Open Hysterotomy Surgeries

Open hysterotomy spina bifida repair is a significant surgery for both mother and fetus, conducted under general anesthesia for maternal comfort and to prevent uterine contractions. The procedure begins with a carefully executed laparotomy to access the uterus, ensuring controlled entry. The size and location of the hysterotomy vary based on the spina bifida defect's characteristics, ranging from 4 to 8 cm.

Once the uterus is open, the surgeon directly visualizes the spina bifida defect and exposed spinal cord, proceeding with delicate repair techniques. This involves dissection to align the spinal cord with surrounding tissues and closure of the defect using sutures or patches, aiming for a secure and watertight seal to protect the spinal cord and promote normal development.

Following repair, meticulous closure of the uterus and abdominal layers is performed. Postoperative care includes monitoring for complications, pain management, and wound care. Prenatal repair has shown improved outcomes, reduced need for ventriculoamniotic shunts, and better short-term motor function. However, the decision to proceed is based on careful evaluation of the specific case, considering factors such as defect complexity, gestational age, and potential maternal morbidities associated with this major surgery (15).

Open hysterotomy fetal surgeries can be effective in addressing certain fetal conditions other than open spina bifida including congenital pulmonary airway malformation (CPAM), sacrococcygeal teratoma (SCT), and pericardial teratoma (19).

54.9.1 Ex Utero Intrapartum Treatment (EXIT)

EXIT is a surgical technique performed during childbirth to provide immediate medical intervention under placental support, for certain fetal conditions that may require intervention before the baby's complete transition to independent breathing outside the womb.

During the EXIT procedure, the mother undergoes general anesthesia. A cesarean section is initiated, and oftentimes a larger low segment or classical uterine incision is required. Instead of delivering the baby entirely, the procedure involves partially delivering the baby while keeping the umbilical cord and placenta attached. This allows the baby to continue receiving oxygenated blood from the placenta while medical interventions are performed.

With the baby's head and shoulders delivered, the surgical team establishes an airway for the baby by placing an endotracheal tube or performing a tracheostomy if needed. This ensures a secure airway and facilitates breathing for the baby. Other necessary interventions can also be carried out during this time, such as repairing certain birth defects, removing obstructions, or stabilizing the baby's condition.

Once the necessary interventions are completed, the baby is fully delivered and transitioned to independent breathing. The umbilical cord is then clamped and cut, and the baby receives standard neonatal care.

The EXIT procedure is primarily performed in cases where the fetus has conditions that may compromise their ability to breathe or require immediate surgical intervention upon delivery. These may include large airway obstructions such as cervical lymphatic malformation or teratoma, congenital high airway obstruction syndrome (CHAOS), or large lung CPAM (20).

The decision to perform an EXIT procedure is made on a case-by-case basis, considering various factors such as the

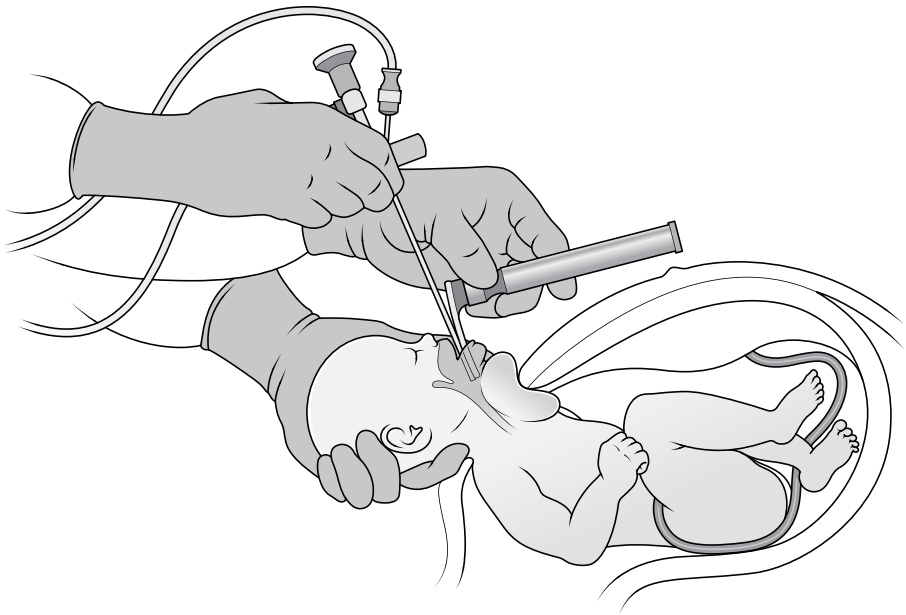


FIGURE 54.10 EXIT procedure aiming to secure an airway due to large cervical teratoma.

specific fetal condition, gestational age, overall health of the mother and fetus, and the potential risks and benefits of the procedure such as blood transfusion of pregnant person up to 10% (20). It is a highly specialized technique that aims to optimize outcomes for babies with critical conditions requiring immediate attention at the time of birth (Figure 54.10).

References

1. Mari G et al. Noninvasive diagnosis by Doppler ultrasonography of fetal anemia due to maternal red-cell alloimmunization. Collaborative group for Doppler assessment of the blood velocity in anemic fetuses. *N Engl J Med*. 2000;342:9.
2. Morris RK et al. Percutaneous vesicoamniotic shunting versus conservative management for fetal lower urinary tract obstruction (PLUTO): a randomised trial. *Lancet*. 2013;382(9903):1496–1506.
3. Nassr AA et al. Novel scoring system for determining fetal candidacy for prenatal intervention for severe congenital lower urinary tract obstruction. *Eur J Obstet Gynecol Reprod Biol*. 2021;262:118–123.
4. Shamshirsaz AA et al. Primary fetal pleural effusion: characteristics, outcomes, and the role of intervention. *Prenat Diagn*. 2019;39(6):484–488.
5. Nassr AA et al. Successful in utero percutaneous fetoscopic release of a wrapped pleuro-amniotic shunt around the fetal arm: case report and review of the literature. *Fetal Diagn Ther*. 2018;43(2):156–160.
6. Schidlow DN et al. Fetal interventions for structural heart disease. *Echocardiography*. 2017;34(12):1834–1841.
7. Sanz Cortes M et al. Innovation in fetal surgery: use of vascular plugs in placental chorioangioma with fetal hydrops. *Prenat Diagn*. 2022;42(11):1471–1474.
8. Senat MV et al. Endoscopic laser surgery versus serial amnioreduction for severe twin-to-twin transfusion syndrome. *N Engl J Med*. 2004;351:136–144.
9. Krispin E et al. Iatrogenic chorioamniotic separation and septostomy following fetoscopic laser photocoagulation for twin–twin transfusion syndrome. *Ultrasound Obstet Gynecol*. 2022;59(4):506–512.
10. Krispin E et al. Prediction of dual survival following fetoscopic laser photocoagulation for twin–twin transfusion syndrome. *Ultrasound Obstet Gynecol*. 2023;61(4):511–517.
11. Deprest JA et al. TOTAL trial for severe hypoplasia investigators. Randomized trial of fetal surgery for severe left diaphragmatic hernia. *N Engl J Med*. 2021;385(2):107–118.
12. Oyelese Y. Vasa previa: time to make a difference. *Am J Obstet Gynecol*. 2019;221(6):539–541.
13. Chmait RH et al. Fetoscopic laser ablation therapy for type II vasa previa. *Fetal Diagn Ther*. 2020;47(9):682–688.
14. Belfort MA et al. Fetoscopic amniotic band release in a case of chorioamniotic separation: an innovative new technique. *AJP Rep*. 2016;6(2):e222–e225.
15. Adzick NS et al. MOMS investigators. A randomized trial of prenatal versus postnatal repair of myelomeningocele. *N Engl J Med*. 2011;364(11):993–1004.
16. Pedreira DA et al. Fetoscopic single-layer repair of open spina bifida using a cellulose patch: preliminary clinical experience. *J Matern Fetal Neonatal Med*. 2014;27(16):1613–1619.
17. Belfort MA et al. Fetoscopic open neural tube defect repair: development and refinement of a two-port, carbon dioxide insufflation technique. *Obstet Gynecol*. 2017;129(4):734–743.
18. Krispin E et al. Systematic classification and comparison of maternal and obstetrical complications following 2 different methods of fetal surgery for the repair of open neural tube defects. *Am J Obstet Gynecol*. 2023;229(1):53.e1–53.e8.
19. Nassr AA et al. Prenatal management of fetal intrapericardial teratoma: a systematic review. *Prenat Diagn*. 2017;37(9):849–863.
20. Shamshirsaz AA et al. Perinatal characteristics and early childhood follow up after ex-utero intrapartum treatment for head and neck teratomas by prenatal diagnosis. *Prenat Diagn*. 2021;41(4):497–504.

55 OBESITY AND MINIMALLY INVASIVE GYNECOLOGY

Jordann-Mishael Duncan, Gina Ranieri, and Michelle Louie

55.1 Introduction

The minimally invasive gynecologic surgeon must be prepared to manage patients with obesity, defined by the World Health Organization (WHO) as a body mass index (BMI) of 30 kg/m^2 or more (1). Obesity, including severe obesity, defined as a BMI of 40 kg/m^2 or more, is common and has been increasing with half the US population projected to be obese by 2030 (1). While many obese patients will require and desire surgical intervention, obesity poses unique challenges and risks due to physiologic changes in the cardiovascular, respiratory, gastrointestinal, renal, and immune systems (2, 3).

The benefits of minimally invasive surgery (MIS) for obese patients include less postoperative pain; less blood loss; fewer surgical site complications, episodes of venous thromboembolism (VTE), sepsis, and ileus; shorter convalescence; improved quality of life; shorter hospitalization with no increase in readmission or reoperation rates; and reduced mortality compared with laparotomy (2, 4, 5). Patients with severe obesity are particularly vulnerable to surgical and postoperative complications (6), so a multifaceted approach is recommended to maintain a less invasive surgical approach resulting in improved outcomes and decreased morbidity.

55.2 Preoperative Considerations

55.2.1 Surgical Approach

Like nonobese patients, vaginal hysterectomy has been recommended as the preferred route of hysterectomy when technically feasible (7). Either laparoscopic or robotic surgery should be considered over vaginal hysterectomy for obese patients with significant soft tissue preventing vaginal access or relative contraindications such as malignancy or other extrauterine disease such as adhesions, adnexal pathology, and severe endometriosis. For severely obese patients, robotic-assisted surgery may have an advantage over conventional laparoscopy in reducing physical strain for the surgeon and assistants. All minimally invasive routes have fewer complications than laparotomy in obese and severely obese patients, so providers should consider referral to experienced minimally invasive surgeons when necessary.

55.2.2 Preoperative Evaluation

If gynecologic office examination is limited due to increased vulvar and abdominal adiposity, surgeons can consider examination under anesthesia in the operating room. At this time, surgeons can also determine how the patient will tolerate steep Trendelenburg and perform cervical cancer screening and endometrial biopsy for patients with abnormal uterine bleeding (8).

In cases of severe obesity, even exam under anesthesia may be limited, so surgeons may rely on imaging to assist in surgical planning. If pelvic ultrasound images are inadequate or technically infeasible, magnetic resonance imaging (MRI) is well suited for obese patients because the radiofrequency waves can penetrate subcutaneous tissue (9), but referral to a specialty center with a bariatric MRI may be necessary.

55.2.3 Preoperative Testing and Optimization

Lifestyle changes are the first step to decreasing perioperative risk by improving comorbid health conditions, which is more impactful than decreasing BMI alone for perioperative risk adjustment. Risk factors for coronary artery disease (CAD) include atherosclerotic cardiovascular disease, heart failure, systemic hypertension, pulmonary hypertension related to sleep apnea, obesity hypoventilation, cardiac arrhythmias, and previous VTE (10). Patients with poor exercise tolerance and/or at least one risk factor should obtain a 12-lead electrocardiogram prior to surgery (10). Patients with three or more CAD risk factors or diagnosed coronary heart disease (CHD) may require additional noninvasive testing such as exercise stress testing and transesophageal dobutamine stress test echocardiography (10) in addition to cardiology referral.

Chronic antihypertensives are generally continued up until surgery. Beta-blockers are cardioprotective and should be continued. Diuretics are usually held the night before surgery. If angiotensin-converting enzyme (ACE) inhibitors or angiotensin II receptor blockers (ARBs) are prescribed for heart failure or poorly controlled hypertension, they should be continued. In other cases, ACE inhibitors and ARBs are held the day of surgery.

Routine screening of asymptomatic, low-risk obese patients for diabetes before surgery is not necessary prior to gynecologic surgery (5). Patients with known diabetes should undergo preoperative EKG and evaluation of serum creatinine, blood glucose, and hA1C (11). Non-urgent surgery should be delayed for patients with an A1C ≥8.5% (12) to allow for optimization. Oral medications such as metformin are held the day of surgery, while patients on insulin should administer half of their intermediate-acting insulin or 60%–80% of long-acting or pump basal insulin on the day of surgery (13).

A preoperative chest radiograph may be considered for severely obese patients, as baseline imaging could assist in evaluating postoperative respiratory difficulties (14). Because obese patients are at high risk for obstructive sleep apnea (OSA), the STOP-Bang questionnaire (15) should be administered preoperatively, and intermediate- and high-risk patients should be referred for polysomnogram. For patients with uncontrolled OSA undergoing a high-risk procedure with need for postoperative opioid use, non-urgent surgery should be delayed for preoperative optimization. Patients should bring their continuous positive airway pressure (CPAP) device or oral appliances to continue their therapy postoperatively. Those with suspected or known OSA, CAD, difficult airway, or poorly controlled hypertension should have preoperative consultation with anesthesiology (5).

55.3 Intraoperative Considerations

55.3.1 Prophylaxis

Obesity is associated with a two- to threefold increased risk of VTE, and the risk associated with severe obesity is even higher. The Caprini scoring system is recommended to assess VTE risk during gynecologic surgery (16). Caprini scores > 5

DOI: 10.1201/9781003312109-55

have a 1.8% higher risk of VTE compared to Caprini scores of 3–4 (17), so chemoprophylaxis in addition to mechanical prophylaxis should be considered.

As obesity is a risk factor for postoperative surgical site infection due to tissue hypoxia, chronic inflammation, and altered antibiotic pharmacokinetics, it is recommended that 3 g, rather than 2 g, of cefazolin be administered within 60 minutes of incision for patients weighing > 120 kg^2. Chlorhexidine has been shown to be superior to iodine for abdominal prepping (18). Surgeons should refer to the chlorhexidine product labeling to understand the maximum covered surface area. For example, the 26 mL 2% chlorhexidine gluconate/70% isopropyl alcohol applicator is only approved to cover a 13.2 × 13.2-inch area, so obese patients will generally require two applicators.

55.3.2 Patient Positioning

Obese patients are at higher risk of nerve injury and pressure sores, particularly if surgery is longer than 6–8 hours (2). A bariatric bed is ideal, but bed extenders could be used to avoid compression of the brachial plexus or median nerve (3). For laparoscopic or robotic-assisted surgery, the arms should be tucked at the patient's sides in the anatomic position with padding of wrist, hands, and elbows to reduce risk of nerve injury (2). Low lithotomy position with padded stirrups and additional padding along the ankles, knees, and hips will help to avoid compression injury. The sacrum should be well supported by the table while soft tissue may extend below the end of the bed (3) (Figure 55.1). Anti-slide padding such as egg crate foam, gel pad, or bean bag should be used (2) (Figure 55.1). Some experts recommend the use of a chest strap to prevent sliding, while others avoid this due to the risk of chest compression and interference with ventilation (19).

If needed, breast tissue may be secured to the strap or torso to prevent airway compression or interference with the endotracheal tube. The panniculus may be taped caudally to the patient's thighs with cloth tape or an iodine-impregnated adhesive to prevent excessive tension on trocars (2) (Figure 55.1). The panniculus can also be retracted caudally using towel clamps or a Foley catheter; however, these techniques are known to cause more tissue trauma and postoperative pain compared to adhesives (3). Prior to sterile preparation and draping, a tilt test should be performed to ensure that the patient does not slide significantly during steep Trendelenburg and that the patient can tolerate the physiologic changes. Setting a timer and assigning a circulating nurse to periodically check patient positioning can help prevent compression or pinch points as the surgery progresses and shifting may occur.

When performing vaginal hysterectomy, the patient should be positioned with the introitus in alignment with the edge of the bed. Steep Trendelenburg is not beneficial in vaginal hysterectomy as this can interfere with placement of the posterior vaginal retractor (20).

55.3.3 Abdominal Entry

Bony landmarks such as the anterior superior iliac spine, costal margin, and xyphoid should be used to guide trocar placement as these are more reliable than soft tissue landmarks like the umbilicus (3, 19). The umbilicus is usually displaced caudally but still represents the thinnest point of entry. Some surgeons recommend initial trocar placement through the umbilicus, with subsequent camera port placement supraumbilically for better triangulation (19). With the umbilicus displaced caudally, it is below the bifurcation of the abdominal aorta (3), and a Veress needle or optical trocar should be placed at 90 degrees, perpendicular to the abdominal wall, to avoid vascular injury and decrease the distance traversed (in contrast to the 45-degree placement angle that is recommended for nonobese patients) (19).

Other authors recommend initial entry either supraumbilically or in the left upper quadrant to optimize triangulation and decrease misdirection by the umbilicus if significantly displaced (2). Proper orogastric tube placement should be performed due to risk of stomach perforation, as obese patients have larger gastric volumes and decreased stomach emptying. Obese patients also have a higher incidence of fatty liver and hepatomegaly, so care should be taken to avoid liver injury with left upper quadrant and supraumbilical port placement. Longer trocars and Veress needles (150 mm) may be used to transverse a thicker abdominal wall. With the Veress needle, there is higher risk of failure and intraperitoneal insufflation (3), but performing open entry in obese patients can be technically challenging in nonumbilical entry sites. Many experts

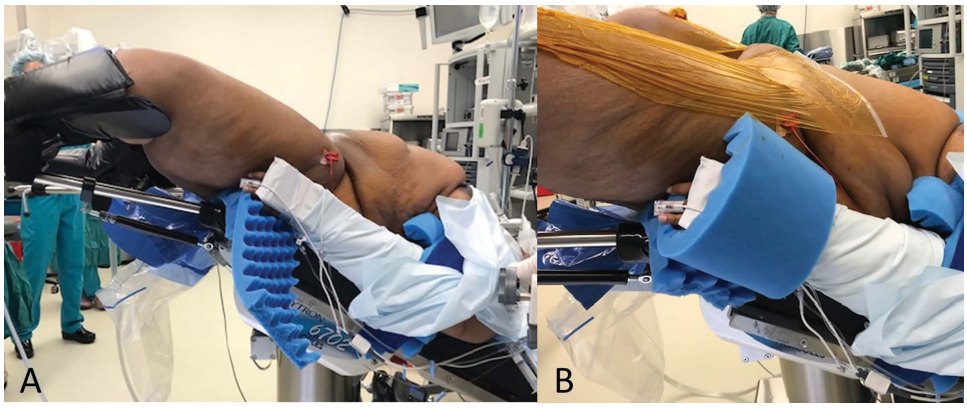


FIGURE 55.1 Patient positioning. (A) "Tilt test" in a patient with severe obesity (BMI > 40 kg/m^2), showing cephalad displacement of panniculus. Also note use of appropriately sized Allen stirrups, bed extenders, protective foam, anti-slip pad, and chest strap to avoid nerve injury. (B) Same patient in Trendelenburg position after using iodinated adhesive to secure panniculus prior to port placement, which helps improve ergonomics and visualization.

prefer to use advanced fixation or "balloon" trocars, which avoid trocar displacement in the thick abdominal wall during surgery.

55.3.4 Ventilation

Due to the cardiovascular and pulmonary changes that occur in obese patients, insufflation pressure between 12 and 15 mmHg in combination with 30 to 50 degrees of Trendelenburg decreases airway compliance and ventilation. Thus, the surgeon must communicate frequently with anesthesia colleagues to ensure that oxygenation and ventilation is adequate. Temporarily decreasing insufflation pressure to 9–12 mmHg, decreasing the degree of Trendelenburg, or reserving steep Trendelenburg for the most critical portions of the case (e.g., colpotomy) can allow minimally invasive surgery to proceed without compromising patient safety.

Increased abdominal pressure secondary to abdominal adiposity can falsely elevate central venous pressure, giving the false impression of volume depletion. An indwelling Foley should be present during all cases, and fluids should be given to maintain a urine output of 30 cc/hr (2).

55.3.5 Visualization

Visualization may be impaired by excess visceral fat, limited insufflation, or Trendelenburg capability. Although it may be challenging to place due to redundant vaginal tissue, a uterine manipulator can afford improved exposure and safety. A 30- or 45-degree laparoscope can also improve visualization. Redundant large bowel can be retracted from the pelvis with laparoscopic bowel retractors based through an additional port or a puppet stitch placed through the bowel epiploica and tensioned cranially (2) (Figure 55.2). Temporary oophoropexy to suspend the ovaries to the abdominal wall or round ligament can be performed to improve visualization of the posterior cul-de-sac and ovarian fossae during procedures like excision of endometriosis (Figure 55.3).

Retroperitoneal dissection is usually necessary to identify and lateralize the ureter because visceral fat obscures transperitoneal visualization. However, visceral fat also makes retroperitoneal dissection more challenging due to capillary bleeding and masking of avascular planes. It is helpful to keep reliable anatomic landmarks in view such as the external iliac artery and medial umbilical ligament to avoid disorientation and injury to vital structures. It is important to identify and use natural cleavage planes in the adipose tissue during blunt dissection to maintain hemostasis and avoid staining.

During vaginal surgery in obese patients, long vaginal retractors with a handle and blade that follow the same axis can aid in deeper sidewall retraction (20). Vessel sealing devices may improve speed and ease during surgery in the obese patient (20, 21).

55.3.6 Morcellation and Closure

In a study comparing contained power morcellation, abdominal morcellation through a minilaparotomy, and vaginal morcellation, no significant differences were found in perioperative complications between techniques (22). Vaginal morcellation avoids extension of an abdominal incision and thus decreases hernia risk and potentially decreases soft tissue complications like infection or seroma. However, visualization and adequate space may be limited due to redundant soft tissue.

Abdominal morcellation is performed by extending a trocar incision. Some experts advocate for using a suprapubic rather than umbilical site for morcellation since obese patients are at increased risk for umbilical hernia (2). Self-retaining retractors can improve visualization during both vaginal and abdominal morcellation.

Consideration can be made for fascial closure for all trocar sites 8 mm or greater as herniation can occur (23), especially in obese patients. The use of fascial closure devices will aid in closure when exposure of the fascia is challenging due to increased adiposity.

55.4 Postoperative Management

55.4.1 Prophylaxis

In obese patients, atelectasis can continue for up to 48 hours and in severely obese patients up to 5 days. The risk of atelectasis can be decreased by cessation of smoking at least 4 weeks before surgery (24), early mobilization, adequate postoperative analgesia without oversedation, incentive spirometer use, and deep breathing exercises (25).

A Caprini score > 8 is associated with an 11% increase in VTE, so these patients may be candidates for extended chemical prophylaxis postoperatively (17). There is evidence to support higher and prolonged doses of pharmacologic prophylaxis in the obese population (26, 27). Studies performed in the bariatric surgery population suggest an increase in dosage of

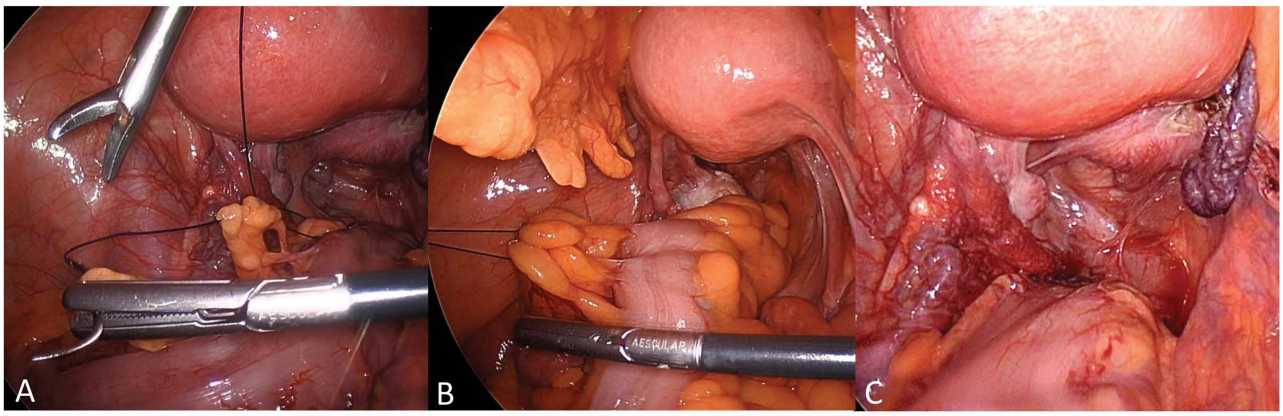


FIGURE 55.2 "Puppet stitch" of the colon. (a) Monofilament suture is passed through the bowel epiploica. (b) The suture is tensioned through the trocar or anterior abdominal wall. (c) Improved posterior cul-de-sac visualization after puppet stitch.

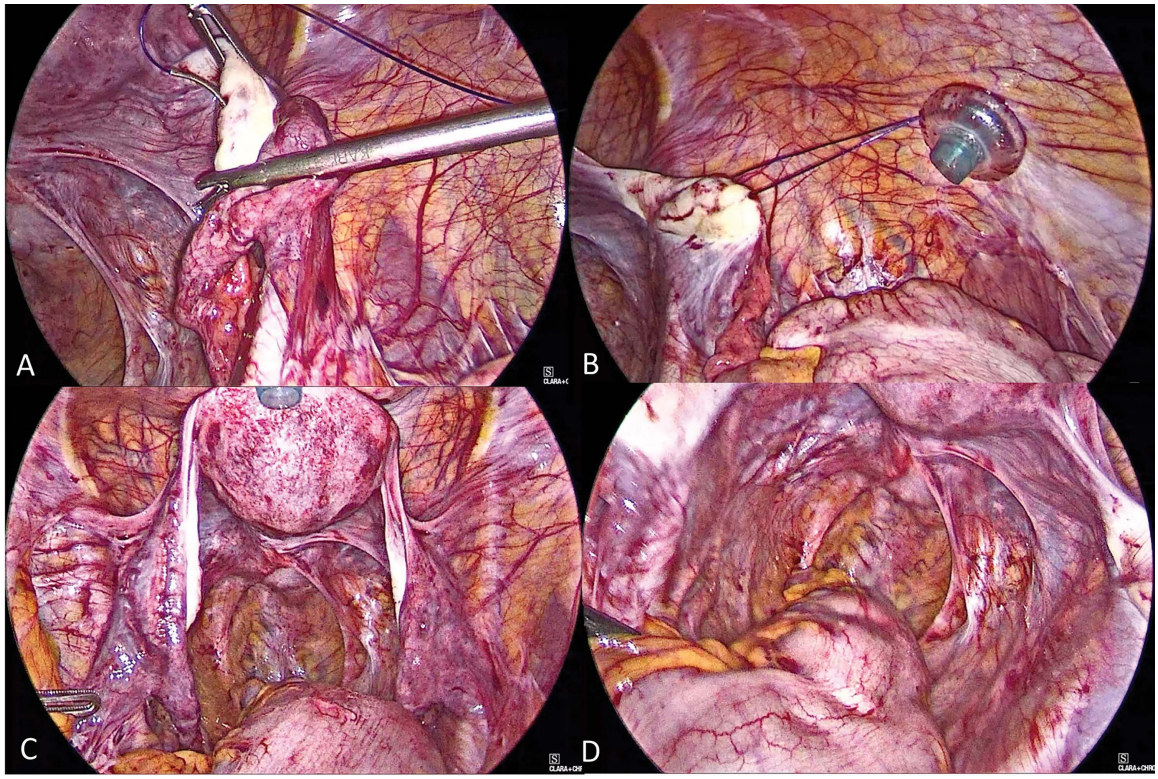


FIGURE 55.3 Oophoropexy. (a) Monofilament suture is passed through the ovary. (b) The suture is tensioned through the trocar or anterior abdominal wall. (c) Visualization prior to oophoropexy. (d) Improved visualization of bilateral ovarian fossae following oophoropexy.

enoxaparin to 40 mg twice daily for a BMI of > 40 kg/m^2 and 60 mg twice daily for a BMI > 50 kg/m^2 (26, 27).

55.4.2 Enhanced Recovery After Surgery (ERAS)

ERAS protocols have been widely adopted by most institutions in the United States and have benefits regardless of obesity (28). Obesity alone should not serve as a contraindication to same-day discharge (29). ERAS protocols call for preoperative and postoperative multimodal pain management including nonnarcotic medications such as NSAIDs, cyclooxygenase-2 (COX-2) inhibitors, gabapentin, and acetaminophen, which decrease the total narcotic requirement and help to avoid respiratory depression (30).

Patients with previous bariatric surgery including Roux-en-Y gastric bypass, sleeve gastrectomy, and adjustable gastric banding should not be given NSAIDs due to the increased risk of gastritis, ulceration, and perforation (31). Obese patients with cirrhosis should not exceed 2 g/day of acetaminophen, and NSAIDs should be avoided due to the risk of acute renal failure (32).

55.4.3 Management of Comorbidities

Ambulatory surgical patients with diabetes who are stable and tolerating oral intake can be discharged on their existing antihyperglycemic regimen (33). Blood glucose should be titrated to 80–180 mg/dL and monitored every 4–6 hours if without oral intake or before meals and at bedtime in patients with a regular diet (13).

Patients with chronic hypertension should resume their usual medications postoperatively. If patients without preexisting hypertension require antihypertensive therapy during their hospitalization, they should continue medications until their blood pressure < 140/80 for 24 hours. Once discharged, these patients should check their blood pressures twice daily for at least 5 days and follow up with their primary care clinician (34).

Patients with known or suspected OSA should be placed in an upright, semi-upright, or lateral position to improve apnea–hypopnea index and oxyhemoglobin saturation. Fluid restriction, lower salt content fluids, and upright positioning can help ameliorate the rostral fluid shift phenomenon where redistribution of fluid from the legs into the neck can worsen upper airway collapse (35). CPAP should begin in post-anesthesia care unit (PACU) and continued postoperatively. Patients without a diagnosis of OSA or noncompliance with CPAP should use CPAP if hypoxemia, airway obstruction, apnea, or hypoventilation occurs. Oxygenation and ventilation should be monitored while hospitalized and adequate oxygenation while awake and asleep should be confirmed prior to discharge.

55.5 Conclusion

Obesity is common in the gynecologic population and causes physiologic derangements that affect patient outcomes after minimally invasive surgery. However, understanding the pathologic changes associated with obesity and anticipating potential surgical barriers help to eliminate obesity as a contraindication to minimally invasive surgery. With thoughtful application of preoperative screening and risk assessments, intraoperative techniques and modifications, and appropriate postoperative care, minimally invasive surgery is not only safe and feasible but preferred, due to less morbidity, fewer complications, and decreased time to full recovery.

References

1. Obesity: preventing and managing the global epidemic. Report of a WHO consultation. *World Health Organ Tech Rep Ser*. 2000; 894:1–253.
2. Scheib SA et al. Laparoscopy in the morbidly obese: physiologic considerations and surgical techniques to optimize success. *J Minim Invasive Gynecol*. 2014;21(2):182–195.
3. Louie M et al. Considerations for minimally invasive gynecologic surgery in obese patients. *Curr Opin Obstet Gynecol*. 2016;28(4):283–289.
4. Blikkendaal MD et al. Hysterectomy in very obese and morbidly obese patients: a systematic review with cumulative analysis of comparative studies. *Arch Gynecol Obstet*. 2015;292(4):723–738.
5. ACOG. Committee opinion 619: gynecologic surgery in the obese woman. *Obstet Gynecol*. 2015;125(1):274–278.
6. Siedhoff MT et al. Effect of extreme obesity on outcomes in laparoscopic hysterectomy. *J Minim Invasive Gynecol*. 2012;19(6):701–707.
7. ACOG. Committee Opinion 701. Choosing the route of hysterectomy for benign disease. *Obstet Gynecol*. 2017;129(6):e155–e159.
8. ACOG. Committee opinion 557: management of acute abnormal uterine bleeding in nonpregnant reproductive-aged women. *Obstet Gynecol*. 2013;121(4):891–896.
9. Rothschild PA et al. MR imaging of excessively obese patients: the use of an open permanent magnet *Magn Reson Imaging*. 1991;9:151–154.
10. Poirier P et al. Cardiovascular evaluation and management of severely obese patients undergoing surgery: a science advisory from the American Heart Association. *Circulation*. 2009;120(1):86–95.
11. Khan N et al. Perioperative management of blood glucose in adults with diabetes mellitus [Internet]. *UpToDate*, 2022. Availble at: www.uptodate.com/contents/perioperative-management-of-blood-glucose-in-adults-with-diabetes-mellitus?search=diabetes%20perioperative&source=search_result&selectedTitle=1~150&usage_type=default&display_rank=1.
12. AAGBI. Peri-operative management of the surgical patient with diabetes 2015. *Anaesthesia*. 2015;70(12):1427–1440.
13. ADA. Diabetes care in the hospital: standards of medical care in diabetes 2018. *Diabetes Care*. 2018;41(Suppl 1):S144–S151.
14. Smetana G. Evaluation of perioperative pulmonary risk [Internet]. *UpToDate*, 2022. Accessed at: www.uptodate.com/contents/evaluation-of-perioperative-pulmonary-risk.
15. Pivetta B et al. Use and performance of the STOP-bang questionnaire for obstructive sleep apnea screening across geographic regions: a systematic review and meta-analysis. *JAMA Netw Open*. 2021;4(3):e211009.
16. ACOG. Prevention of venous thromboembolism in gynecologic surgery. ACOG practice bulletin 232. *Obstet Gynecol*. 2021;138(1):e1–e15.
17. Pannucci CJ et al. Individualized venous thromboembolism risk stratification using the 2005 caprini score to identify the benefits and harms of chemoprophylaxis in surgical patients: a meta-analysis. *Ann Surg*. 2017;265(6):1094–1103.
18. Hibbard J. Analyses comparing the antimicrobial activity and safety of current antiseptic agents: a review. *J Infusion Nursing*. 2005;28(3):197–207.
19. Menderes G. Challenges of robotic gynecologic surgery in morbidly obese patients and how to optimize success. *Curr Pain Headache Rep*. 2019;23(7):51.
20. Matthews KJ et al. Hysterectomy in obese patients: special considerations. *Clin Obstet Gynecol*. 2014;57(1).
21. Kroft J et al. Energy-based vessel sealing in vaginal hysterectomy: a systematic review and meta-analysis. *Obstet Gynecol*. 2011;118(5):1127–1136.
22. Meurs E et al. Comparison of morcellation techniques at the time of laparoscopic hysterectomy and myomectomy. *J Minim Invasive Gynecol*. 2017;24(5):843–849.
23. Burke WM et al. Robotic surgery in the obese gynecologic patient. *Clin Obstet Gynecol*. 2011;54(3):420–430.
24. Sorensen LT. Wound healing and infection in surgery: the pathophysiological impact of smoking, smoking cessation, and nicotine replacement therapy: a systematic review. *Ann Surg*. 2012;255(6):1069–1079.
25. Grott K et al. *Atelectasis* [Internet]. StatPearls Publishing; 2022.
26. Sebaaly J et al. Enoxaparin dosing at extremes of weight: literature review and dosing recommendations. *Ann Pharmacother*. 2018;52(9):898–909.
27. Borkgren-Okonek MJ et al. Enoxaparin thromboprophylaxis in gastric bypass patients: extended duration, dose stratification, and antifactor Xa activity. *Surg Obes Relat Dis*. 2008;4(5):625–631.
28. Shin HD et al. Does ERAS benefit higher BMI patients? A single institutional review. *J Plast Reconstr Aesthet Surg*. 2021;74(3):475–479.
29. Haight PJ et al. Safety and feasibility of same-day discharge following minimally invasive hysterectomy in the morbidly obese patient population. *Gynecol Oncol*. 2023;170:203–209.
30. Steinberg AC et al. Preemptive analgesia for postoperative hysterectomy pain control: systematic review and clinical practice guidelines. *Am J Obstet Gynecol*. 2017;217(3):303–313 e306.
31. Yska JP et al. NSAID use after bariatric surgery: a randomized controlled intervention study. *Obes Surg*. 2016;26(12):2880–2885.
32. Rakoski M et al. Pain management in patients with cirrhosis. *Clin Liver Dis*. 2018;11(6):135–140.
33. Dogra P et al. *Diabetic Perioperative Management* [Internet]. StatPearls Publishing; 2022.
34. Bisognano J. Perioperative management of hypertension [Internet]. *UpToDate*, 2022. Accessed at: www.uptodate.com/contents/perioperative-management-of-hypertension.
35. Lam T et al. Is Perioperative fluid and salt balance a contributing factor in postoperative worsening of obstructive sleep apnea? *Anesth Analg*. 2016;122(5):1335–1339.

56 INNOVATIONS AND MEDICAL DEVICES

S. Abbas Shobeiri

56.1 Introduction

Innovation within the medical device industry does not necessarily entail inventing something entirely new. From an entrepreneurial perspective, it can involve the application of existing ideas or products in new settings or innovative ways. In such a context, the successful launch of medical devices and services relies on five key pillars:

1. Swift release of new medical devices and services, supported by
2. Scientific endorsement from key opinion leaders, followed by
3. Comprehensive clinical education for practitioners in the field. Additionally,
4. Clear communication of problems and flaws to the designers while
5. Building and protecting brand equity and value.

From the patient's standpoint, they desire safe and effective procedures that enable a quick return to normal activities. Surgeons and operators, on the other hand, seek devices that are safe and efficient and ensure fair compensation for their time and effort. Society looks for medical devices that reduce costs by simplifying existing procedures or providing innovative solutions to previously unsolvable problems. Thus, innovation in the medical device industry is greatly influenced by stakeholders such as patients, care providers, doctors, payers, policymaking groups, and manufacturers or suppliers, all contributing to real-world healthcare decision making.

Once a device is ready for market release, companies must navigate country-specific regulatory requirements to safeguard patient safety and ensure market efficiency. This regulatory aspect poses a significant bottleneck regarding time and costs for any medical device or biomaterial-based therapy (1). This chapter will focus on the driving forces behind medical innovation, disruptive innovation methods, the patenting process, marketing and economic considerations, and general regulatory factors, particularly in the device sector.

56.2 Success or Failure of Medical Devices

The customer discovery process is the most important factor in determining a medical device's success in the market. Often, the concept of a medical device is driven by technological innovation. The innovator adopts a vision of how the innovation will change lives. However, the dilemma is that the target population does not need the innovation and does not adopt it. Customer discovery involves interviewing hundreds of customers to understand the customers' lives and needs before wasting time and precious resources.

In their paper on navigating the challenges from concept to certified product, Wieringa et al. emphasize that innovation in medical technology is a complex process to improve patient and staff experiences while generating profit for the innovators. However, many innovative ideas fail to succeed in practice (2). This often occurs due to the absence of certain crucial elements, such as the lack of a customer discovery process (3) and the factors noted here:

- *Relevance*: Does the product fulfill a need in the market?
- *Validity*: Is the device based on sound technical principles?
- *Reliability*: Does the device function as intended?
- *Ease of use*: Is the device designed to maximize user accessibility?
- *Robustness*: Is the device designed to withstand real-world usage conditions?
- *Compatibility*: Can the device withstand local factors such as temperature, dust, fluids, and other devices?
- *Foolproof*: Has the device been analyzed to prevent improper handling and ensure use according to its intended purposes?
- *Compliance*: Has the device been designed following local regulatory requirements, pricing policies, and reimbursement criteria of health insurance organizations?

Once a device manufacturer successfully bridges the gap between an idea and a certified product, the clinical introduction stage determines how the innovation performs in real-world use within the challenging clinical environment. Understanding human factors becomes paramount when developing medical devices, often surpassing technological expertise.

56.3 The Forces behind Disruptive Device Innovation

Medical device innovations hold significant social relevance, and various market factors drive disruptive innovations within the industry (4). These factors include:

- *Increasing demand for healthcare services*: Demographic shifts, such as population aging, immigration, and fluctuations in birth rates, alter the overall healthcare needs and drive the demand for innovative solutions.
- *Increasing demand for higher efficiency*: With a rising number of procedures and patients, while the number of physicians remains relatively constant, there is a need for higher efficiency in healthcare delivery. Primary care physicians and surgeons must see more patients and perform more procedures within the same time frame.
- *Increasing patient empowerment*: Healthcare consumers are becoming more educated and have easy access to information through smartphones. Patients often conduct their research, consult online sources, and arrive at healthcare providers with specific requests or suggested solutions.
- *Increasing influence of market forces*: The healthcare landscape constantly changes with evolving regulations, payment models, and delivery systems. Device choices are influenced by quality, safety, and the innovative utilization of available resources.

DOI: 10.1201/9781003312109-56

Established companies with strong market positions may focus on improving existing products rather than pursuing disruptive innovations that may disrupt their markets and challenge their established positions. This approach helps them safeguard production facilities and maintain dominance within specific categories (3). Market-driven research often perceives industry-funded, curiosity-driven innovation as riskier. However, such a mindset can leave room for competitors to create new markets (seeking the "blue ocean" [5]) for their products. Alternatively, dominant companies may acquire emerging technologies to maintain their status quo.

A balanced portfolio for a company is achieved by blending curiosity-driven and market-driven inventions. Medical innovation thrives at the intersection of clinical expertise (physicians and nurses) and academic contributions (scientists, engineers, and human factors experts). Curiosity-driven, high-risk products are often developed with support from government grants or angel investors who are willing to sustain the associated risks.

56.4 Innovations That Disrupt the Market

Christensen et al. argue that disruptive innovations are often simpler products that fulfill customers' essential needs (6). For instance, the Toyota Corolla, initially unable to climb hills, appealed to a large population segment and gradually improved over time, creating a niche market. Another example is the introduction of Apple computers, which overcame the complexities of DOS computers and provided a user-friendly alternative. Disruptive innovations are typically simpler, more convenient, and initially target the low end of the market. Figure 56.1 illustrates how a disruptive technology (red line) emerges from an existing technology (green line), starting in the neglected part of the market and eventually capturing higher market segments. Established technologies, bound by their entrenched infrastructure, often need help to adapt and eventually face obsolescence. This phenomenon includes Kodak film technology succumbing to digital technology and the competition between Apple and DOS computers in the 1980s.

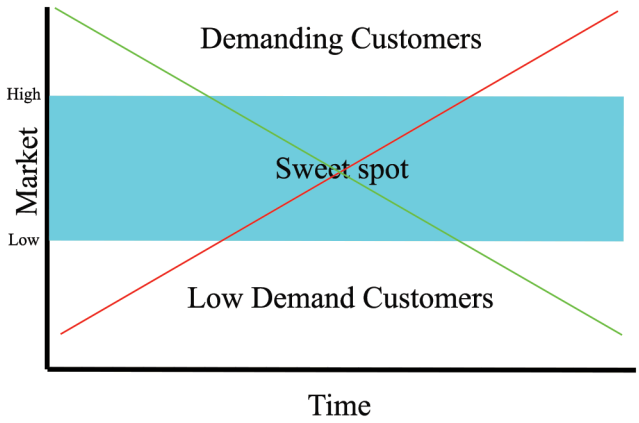


FIGURE 56.1 The progress of disruptive innovation. When graphing low vs high performance in the time it takes to enter the market, a medical device's performance (red line) can appeal to different segments. If a company is reaching for the most demanding customers, this takes much time and leaves the market open for the least demanding customers. The sweet spot for most of the customers is in the blue zone where a device can be made and introduced into the market quickly enough to meet the demand of the majority of the customers (From ref 20 with permission).

The performance of a physician can be seen as a time-dependent product. General surgeons, for example, require approximately 13 years of higher education to reach board eligibility, and experience often correlates with higher performance. However, new technologies can boost the performance of younger surgeons. For instance, invasive cardiologists gained a significant portion of the cardiothoracic surgery market by utilizing technologically advanced stents as an alternative to major surgeries.

Within each industry, various technologies occupy different niches within the market and profit from them. A successful medical device may be simplified to cross multiple levels and cater to various levels of specialization. This allows the medical device industry to serve a larger population, providing less skilled individuals with a more convenient and cost-effective way to perform tasks previously carried out by more expensive specialists in centralized and inconvenient locations (6). The industry actively seeks "blue ocean" opportunities, offering solutions ranging from self-care and telemedicine to highly specialized care only available at major hospitals. Physicians can introduce new innovative, disruptive technologies by simplifying procedures for office-based settings and making them more convenient and cost-effective (Figure 56.2).

The innovation of medical devices, despite their social necessity, is primarily driven by economic considerations. However, the industry's history has witnessed various medicolegal controversies and instances where seemingly reputable studies promoting the value of certain products were later discredited. As a result, seasoned physicians understandably exhibit caution and are not early adopters of new technologies entrepreneurs introduce. In contrast, younger and less experienced physicians may be more inclined to embrace these innovations to gain market share and leverage them as marketing tools. Unfortunately, this eagerness to adopt untested products can lead to entanglement in lawsuits and further contribute to a sense of hesitation among physicians over time.

To address these challenges, medical schools are increasingly emphasizing the importance of evidence-based medicine, which improves patient care and enhances marketing and the bottom line of medical practices. Additionally, there is a growing focus on educating students about the process of patenting and bringing a product to market, enabling them to understand better the complexities and considerations involved in the commercialization of medical innovations.

56.5 The Patenting Process

Patents grant the patent owner the exclusive right to prevent others from commercially exploiting the patented invention. This includes making, distributing, importing, using, and selling the invention without the patent owner's consent. The patenting process typically occurs early in an invention's concept and design stage (7). It is important to note that patent rights are territorial, meaning they are applicable only within the region or country where the patent has been granted and filed following the respective laws (8).

The rationale for patents is rooted in exchanging the public disclosure of how an invention works for a limited monopoly

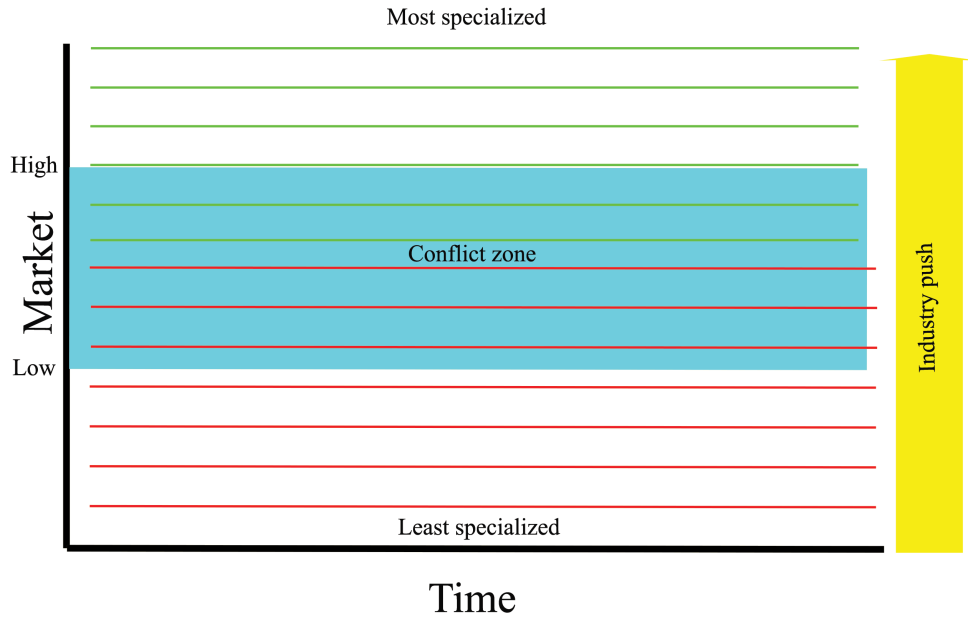


FIGURE 56.2 The medical device industry strives to enable lower-skilled, less specialized healthcare providers to accomplish more complex tasks by providing simple-to-use solutions. When graphing where the skills overlap, there is conflict, but the market is opened for doctors with the introduction of new medical devices to care for more demanding patients (From ref 20 with permission).

over its commercial exploitation. New patents often build upon prior patents, fostering technological innovation and advancement. To be eligible for patent protection, an invention must meet certain requirements:

- *Novelty*: The invention must be new, not publicly known or published.
- *Inventive Step*: The invention must involve an inventive step that is not obvious to someone skilled in the field.
- *Utility*: The invention must be useful and practical for any applicable use.

Typically, patent rights last for 20 years from the filing date. During this period, the patent owner can sell, license, and transfer their rights. In the United States, the Bayh–Dole Act (1980) allows universities and hospitals to commercialize inventions derived from federal funds. However, it mandates sharing royalties with the inventor and grants the government "march-in" rights under certain circumstances (7).

56.6 The Economic Perspective

Hospitals continuously seek ways to reduce medical expenditures, with labor being the primary expense, followed by supply chain management. The trend has been to simplify tasks traditionally performed by specialists, allowing generalists to handle them, and tasks previously undertaken by physicians are now being delegated to nurses and other healthcare professionals. However, despite these efforts to streamline and downsize, healthcare spending in the United States has remained the same, as reflected in the gross domestic product (GDP) expenditure. The savings resulting from equipment and personnel innovations have yet to necessarily translate into improved patient care. Instead, there has been a shift towards top-heavy hospital management, increased value in instrument manufacturer stocks, and stagnant physician salaries without a corresponding decrease in overall healthcare expenditure.

56.6.1 The Valley of Death for Medical Device Development

The research and development (R&D) process involves a critical phase known as the "valley of death" that lies between government-funded fundamental research and industry-driven commercialization of profitable products (9, 10). This phase represents a gap in private investment markets, where financing for research supporting "platform" technologies tends to be inadequate. Generic technologies are often expensive or risky, making it challenging for the industry to develop products independently. Paradoxically, these platform technologies are the foundation for new devices, products, and even entire market categories (10, 11).

Before a medical device can be introduced to the market, it must meet specific standards and regulatory requirements based on its classification. Medical devices are classified into Class I, II, or III, depending on their level of risk and the necessary level of control to ensure safety and efficacy (12).

Devices with low risk are categorized as Class I and are subject to general controls. On the other hand, most implants fall into the high-risk Class III category, requiring the most comprehensive and stringent standards. Such devices are granted a preliminary investigational device exemption (IDE) for clinical trials regulated by the United States Food and Drug Administration (FDA). These trials aim to gather the necessary safety and efficacy data to support the safe introduction of the device to the market (Figure 56.3) (1).

56.6.2 Investigation of R&D from the Biomaterials Laboratory to the Preclinical Facilities

Numerous organizations adhere to specific standards and frameworks to ensure that R&D studies are meticulously

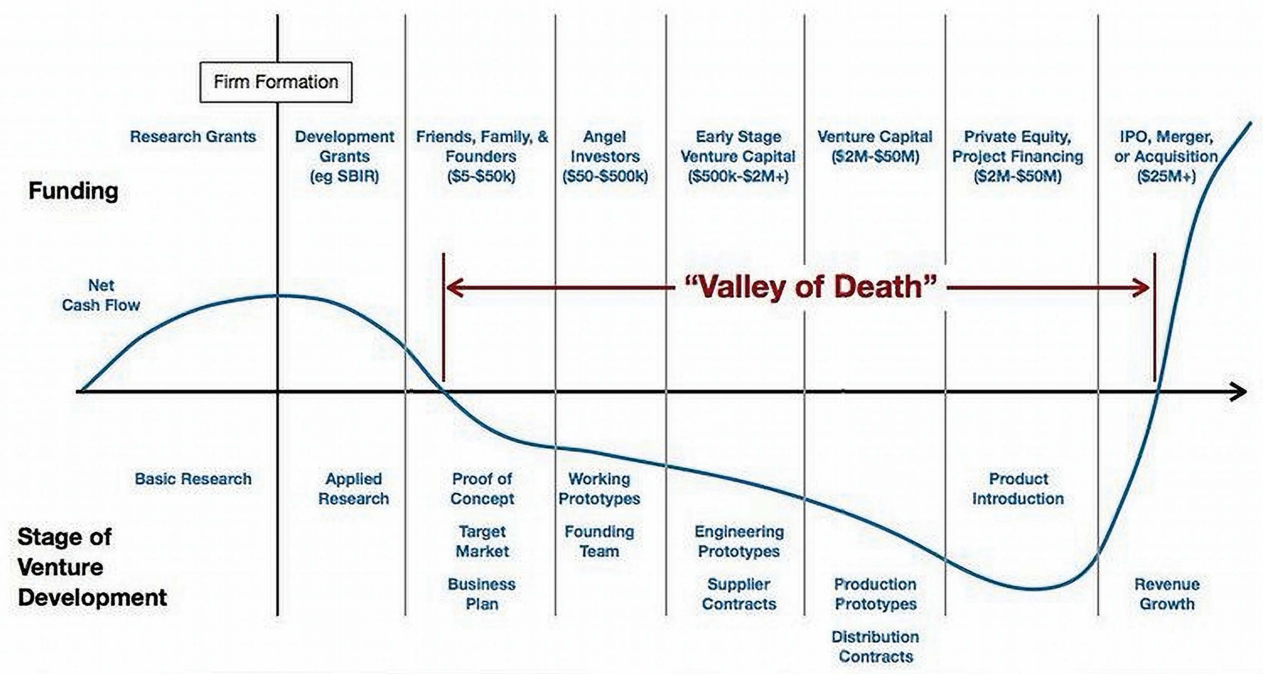


FIGURE 56.3 The cash flow "Valley of Death" as a function of the development stage (time) with typical funding sources at various stages; SBIR: small business innovative research (From ref 21 with permission).

planned, executed, monitored, recorded, reported, and archived. The International Organization for Standardization (ISO), Good Laboratory Practice (GLP), and the Association for Assessment and Accreditation of Laboratory Animal Care International (AAALAC) are among the organizations that accredit R&D processes and facilities when the required standards are met. AAALAC, a private nonprofit organization, promotes the humane treatment of animals in scientific research through voluntary accreditation and assessment programs.

During the R&D process, a group comprising academic and development-oriented members is assembled to investigate crucial aspects before significant investments are made. These members assess:

- The novelty of the medical device
- The international patent landscape related to the device
- Existing competing devices in the market
- Similarities with patented or closely related devices
- Regulatory challenges associated with device development and marketing
- The anticipated costs of device development and marketing

Based on this assessment, the R&D expenses associated with preclinical work can be estimated, enabling an objective decision on whether further investment is warranted (1).

Developers often face a challenge when academic requirements necessitate the publication of their findings, potentially exposing their ideas to others for development. It is crucial to differentiate between marketable ideas and academic work and to obtain a patent as soon as possible. An alternative approach is initially securing a patent in one country, providing one year of protection. Since 2013, the first-to-file system has replaced the first-to-invent system, allowing inventors time to evaluate their ideas further before deciding whether to pursue international patent protection (1).

56.7 Innovation Clusters

The commercial success of a medical device goes beyond its technological capabilities. It involves offering cost-effective solutions, ensuring user-friendliness for customers (such as doctors), establishing robust clinical evidence, adhering to regulatory requirements, and implementing effective marketing strategies (1). However, the process of commercializing a medical device can be highly expensive. As larger companies may be reluctant to invest in newer technologies, an emerging trend is the establishment of small- and medium-sized enterprise incubators within major clinical settings and universities. These incubators foster collaborative agreements that involve investments and joint ventures with larger companies. Universities create incubators where companies operate on campus, providing a conducive environment for innovation.

Once an innovative idea is identified, addressing patent and intellectual property concerns and executing business agreements (such as nondisclosure, collaborative research, and material transfer) are essential steps to gain a realistic understanding of costs and revenue expectations (1). Like the approach adopted by the global design company IDEO (Palo Alto, California, USA), a collaborative environment that brings inventors, investors, hospitals, universities, and companies is vital to foster innovation at the right place and time. The timing of innovation plays a crucial role in its successful launch.

56.7.1 The Importance of Clear, Concise, and Closed-Loop Communication about Medical Device Adverse Events

There needs to be more education of users, poor implementation, and the absence of a feedback loop are common pitfalls in the successful evolution of medical innovations. However, it is crucial to separate inventors and investors from the assessment mechanism to ensure objectivity (3).

In the United States, there is a general perception among physicians and patients that medical devices are proven safe before they are marketed. Unfortunately, this perception has led to a cycle of rushed products entering the market and only being withdrawn after complications become evident, often due to a lack of effective feedback mechanisms.

It is important to recognize that innovations in medical devices only sometimes translate into advances in medical practice (13). Achieving a positive impact on healthcare requires human factor engineering to enhance healthcare teams' skills rather than relying solely on technology (14). In this regard, nursing plays a crucial role in the acceptance, application, and routine use of medical devices (3).

Medical devices have the potential to make physicians and their teams more efficient. Like continuous improvement in the automotive industry, medical devices require multiple iterations and technological advancements, which can only be achieved through an effective feedback loop. The input of the entire healthcare team is vital for driving these improvements. Ideally, medical sales representatives in the operating room should serve as a bridge between developers and users, but the current incentive mechanisms often prioritize sales over facilitating feedback and improvement (3).

During this phase of innovation, many companies, under economic pressure, need to establish effective communication loops. They focus on widespread marketing to many inexperienced users to demonstrate profitability. Unfortunately, this approach does not lead to improved product design despite significant problems that arose in the field.

While it is important to emphasize the significance of good communication between physicians and industry, it is crucial to acknowledge that traditional methods used by industry representatives, such as wining and dining physicians, influence their reporting, creating biases and conflicts of interest. To address this issue and increase transparency, the Physician Payments Sunshine Act was enacted to shed light on the financial relationships between physicians, teaching hospitals, and device manufacturers (15).

56.7.2 Examples of Unethical Medical Device Development and Failure

Experimentation and chronic failure were part of a surgeon's life in the not-too-distant past. As Earle H. Clinical lecture on vesico-vaginal fistula (London Med Gazette 1829;5:198–202) stated, "in one [fistula] case . . . I performed upwards of thirty operations before success crowned my efforts." Devising ways to perform the surgeries more efficiently was part of a surgeon's life. Thomas Percival (1740–1804) stated in Percival T. Medical Ethics (Italian translation by Goracci Giada. 11–30. In: Patuzzo Sara., editor. Milano: Mimesis; 2015), "Whenever cases occur, attended with circumstances not theretofore observed, or in which the ordinary modes of practice have been attempted without success, it is for the public good . . . that new remedies and new methods of chirurgical (surgical) treatment should be devised." Yet, part of this preoccupation with surgical success in the absence of antibiotics and anesthesia resulted in patients' suffering. Experimentation was largely performed on African American slaves in days when their mere humanity was denied. Just as we perform experimentation in the animal laboratory these days, African American slaves were given to surgeons by their owners to make them "sound" for them to return to their duties. In days that it was unthinkable to have a woman undressed to examine them, Jay Marion Sims had black women slaves given to him, all nude, on all fours, held by strange men, without anesthesia as he tested Sims' speculum to look inside the vaginas. The thought process was that African Americans did not feel pain and that because of their promiscuity, it did not bother them to be nude. Sims' experimental subjects were many African American slaves, three of whom were Betsey, Lucy, and Anarcha, who were "given" to Sims by their owners to find a cure for vesicovaginal fistula (Sims, JM, *New York Medical Gazette* and *Journal of Health*, 1854 (Volume 5, pages 1–7)). Anarcha's injuries were inflicted by Sims himself when he used forceps to deliver her baby. Sims was glorified, and his statues were erected nationwide to celebrate an innovator and an American hero. Sims was part of a systemic discrimination that started in society and trickled into medical schools and our higher-level institutions.

The experimentation with medical equipment is like that of surgeons 200 years ago. While the motivation of the surgeons was fame and recognition, the motivation of the modern corporation is a fiduciary responsibility to the shareholders. The experimentations continue despite many advances over the past 200 years. Very recently, Havasupai Indian' blood was used without their consent to study genetic markers of depression when they were told the blood was collected to investigate the rising incidence of diabetes in the tribe.

In modern days, a meticulous and comprehensive monitoring system by medical device manufacturers can help detect safety concerns, but these concerns are often overlooked. To avoid duplicating efforts and gathering more meaningful data, utilizing the available data or collecting high-quality data can enhance the detection rate of safety events. An example highlighting the importance of data examination involves the monitoring of medical devices (16).

The case of the laparoscopic gastric band, used to treat morbid obesity, illustrates how earlier examination of existing data could have influenced practice. The FDA approved the gastric band device in 2001, and its usage peaked in 2008 (16). However, over time, reports surfaced describing complications such as band erosion, slippage, and variable effectiveness leading to inadequate weight loss, necessitating reoperation to revise, replace, or remove the device. A recent Medicare claim study revealed that $223 million (47%) of the $470 million spent on gastric band devices was for reoperations (16). The consensus is that the gastric band device should be significantly restricted (17). The question arises as to why the medical device monitoring system did not identify these concerns earlier.

Another example involves power morcellators, laparoscopic surgical devices for minimally invasive hysterectomy and myomectomy. These devices gained popularity in gynecology due to the advantages of laparoscopic procedures. However, in 2013, concerns emerged about the potential spread of undiagnosed cancerous tissue during power morcellation. The FDA investigated the issue and 2014 issued a safety communication discouraging the use of power morcellators for fibroid removal due to the risk of spreading unsuspected uterine sarcoma (18). Following the FDA's actions, the use of power morcellators rapidly declined. The largest manufacturer withdrew its device from the market, hospitals restricted their use, and insurance carriers denied reimbursement for surgeries involving these devices. A debate ensued about whether the FDA had adequately protected patients or whether their actions had interfered inappropriately with patient care (19).

These examples demonstrate the significance of thorough monitoring, analysis of existing data, and prompt regulatory actions to address safety concerns associated with medical devices.

56.8 Conclusion

Advancements in medical device innovations often stem from clinical expertise and the need to provide more efficient clinical care. While incremental improvements to existing solutions have their place, transformative paradigm shifts may be necessary when existing solutions are flawed. Disruptive innovations can drive real shifts in clinical outcomes, population health, patient satisfaction, surgical efficiency, and economic resource utilization. Successful innovation and marketing in the medical device industry require collaboration between customers (patients and surgeons) and technology providers (academia, SMEs, and large companies), with a focus on identifying and translating the needs of patients and surgeons into commercially viable solutions (1).

Introducing a medical device into the market or producing a device should involve comprehensive studies that address technological, societal, economic, and administrative challenges from the design phase onwards. A medical device is not passive; it affects the immediate team, social contexts, and supporting mechanisms within organizations. A value analysis to assess specific milestones at certain times is crucial financially. The adoption of medical devices by insurance providers and the establishment of appropriate reimbursement are significant milestones before mass production. Systematic methods exist for performing these tasks. However, a crisis in the medical instrument industry necessitates "responsible innovation" for a medical device to succeed in the market (6). The term "responsible" implies that manufacturers are responsible for adequately educating and providing continuous quality control feedback mechanisms in the field once a product is released. Providing proper training to healthcare professionals before they use medical devices is essential.

The complexity of what a "responsible" innovation is may point to the recent rise of robotic technologies, which have positively and negatively impacted healthcare. The successful implementation of robotic systems relied on cautious introduction, intensive training, and close follow-up by highly skilled professionals. The economic analysis of robots may be mixed, but patient outcomes have improved, resulting in more repeatable surgeries and shorter hospital stays. However, the belief that less highly compensated individuals can perform tasks more efficiently in expedient settings did not hold in this case. The success of robotic technology is attributed to a methodical approach to training and implementation.

To prevent litigation and ensure patient safety, the healthcare instrument industry, venture capital, entrepreneurial energy, and technology development must effectively interface with regulators, insurers, physicians, hospitals, and medical schools. While the FDA protects patients, responsibility is shared among the clinical community, manufacturers, and payers. Currently, there is a significant divide in the accessibility of information to evaluate the value, safety, efficacy, and quality of medical devices (16). To address this, device identifiers in insurance claims forms can provide valuable data for monitoring device malfunctions and failures, like prescription drug safety, which is monitored using insurance claims databases. Organizations such as X12 have recommended the integration of unique device identifiers (UDIs) in medical devices to enhance patient safety and improve tracking.

Ensuring patient safety and driving innovation in the medical device industry requires collaboration, responsible innovation, comprehensive training, and integrating standards and identifiers to avoid litigation (Figure 56.4). Balancing regulation and innovation to safeguard patients without stifling progress

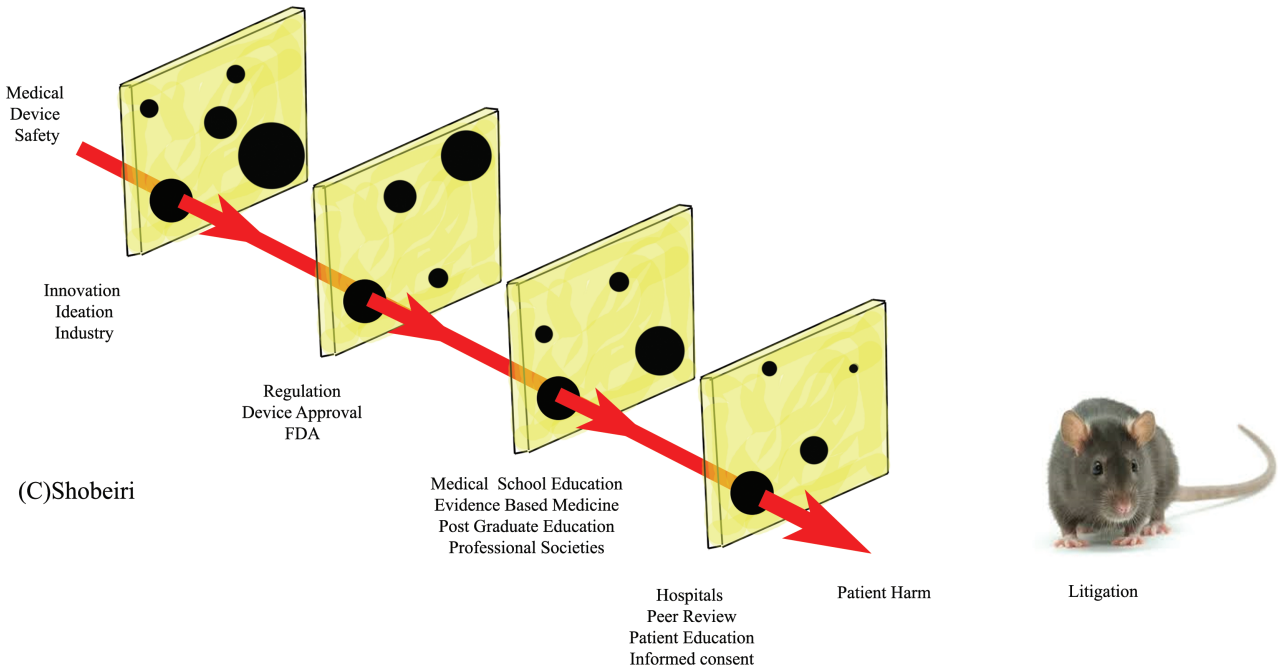


FIGURE 56.4 The layered human processes meant to create security are like cheese slices with holes. When the holes in each process align perfectly, a medical device hazard passes through all defenses and causes patient harm. Ideally, weaknesses in one process are stopped by additional layers of security, and patient harm does not materialize (From ref 20 with permission).

is important. Education and training should be prioritized, and industry standards for adequate training and certification should be established to ensure the competent use of medical devices.

References

1. Bayon Y et al. Innovating in the medical device industry – challenges & opportunities ESB 2015 translational research symposium. *J Mater Sci Mater Med*. 2016;27(9):144.
2. Abenstein J. Technology assessment for the anesthesiologist. *Anesthesiol Clin*. 2006;24(4):677–696.
3. Wieringa FP et al. Avoiding pitfalls in the road from the idea to certified product (and the harsh clinical environment thereafter) when innovating medical devices. *TNO Industrie en Techniek Proceedings of the IEEE Benelux EMBS Symposium/ Belgian Day on Biomedical Engineering*, 2007.
4. Dumay AC. Innovating eHealth in the Netherlands. Stud Health Technol Inform. 2007;127:157–65. PMID: 17901609.
5. Kim WC et al. *Blue Ocean Strategy, Expanded Edition: How to Create Uncontested Market Space and Make the Competition Irrelevant*. Harvard Business Rev Press; 2014.
6. Christensen CM et al. Will disruptive innovations cure health care? *Harv Bus Rev*. 2000;78(5):102–112;199.
7. FDA. *Overview of device regulation* [Internet]. 2024. Available at: www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/overview-device-regulation.
8. World Intellectual Property Organization. *Patents* [Internet]. 2023. Available at: www.wipo.int/patents/en/.
9. Li TW et al. Assurance of medical device quality with quality management system: an analysis of good manufacturing practice implementation in Taiwan. *BioMed Res Int*. 2015; 670420.
10. MedTech Europe. *The European medical industry in figures* [Internet]. 2023. Available at: www.medtecheurope.org/wp-content/uploads/2023/10/the-european-medical-technology-industry-in-figures_2023.pdf.
11. Roberts EB. Technological innovation and medical devices. In: *Symposium on New Medical Devices: Factors Influencing Invention, Development, and Use*. National Academy of Engineering/Institute of Medicine; 1987.
12. Sharma A et al. Health care policy and regulatory implications on medical device innovations: a cardiac rhythm medical device industry perspective. *J Intervent Card Electrophysiol*. 2013;36(2):107–117.
13. Bohn R. Measuring and managing technical knowledge. *Sloan Management Review*. 1994;36(1):61–73.
14. Koppenheffer M. Want to please patients? Maybe you should start a specialty hospital [Internet]. 2015. Available at: www.linkedin.com/pulse/want-please-patients-maybe-you-should-start-specialty-eiman?trk=public_profile_article_view.
15. Ibrahim AM et al. Monitoring medical devices: missed warning signs within existing data. *JAMA*. 2017;318(4):327–328.
16. FDA. *Medical device recall report FY2003 to FY2012* [Internet]. 2013. Available at: www.fdanews.com/ext/resources/files/03/03-31-14-Recalls.pdf.
17. Stein KM. The long and winding road after FDA approval: a medical device industry perspective. *Circulation*. 2017; 135(20):1877–1878.
18. Redberg RF et al. Power morcellators, postmarketing surveillance, and the us food and drug administration. *JAMA*. 2017;318(4):325–326.
19. Levitz J et al. How morcellators simplified the hysterectomy but posed a hidden cancer risk, *Wall Street J*. April 11, 2014 10:33 pm ET, https://www.wsj.com/articles/how-morcellators-simplified-the-hysterectomy-but-posed-a-hidden-cancer-risk-1397269145?gaa_at=eafs&gaa_n=AWEtsqddmmKyKjxv_MOa-EW5wegCKxgyVR-rDQHwd-gPJXFKPkSHp9SvxlvIM3QL3aM%3D&gaa_ts=6973feae&gaa_sig=FW0ofuzkUof1oPNnQcut3OuM7VrWC_UwZ2BAYs0VGdKHKnZSawnkurIPSpH1uQ-I3TB1qUs6MQKX33znFs55sw%3D%3D Accessed 1/23/2026.
20. Shobeiri SA, ed. *Innovation and Evolution of Medical Devices*. Springer; 2018.
21. Hargedon A. *Into the valley of death* [Internet]. 2020. Available at: www.greentechmedia.com/articles/print/into-the-valley-of-death.

57 INFORMED CONSENT IN MINIMALLY INVASIVE GYNECOLOGIC SURGERY

Isabelle C. Band and Louise P. King

57.1 Background

Informed consent (IC) is a central tenet in the ethical practice of medicine and surgery. Although frequently we refer to "signing consent" with reference to a legal document, the key to truly informed consent is a process during which physicians and patients exchange information regarding a patient's condition and treatment options. The process culminates in the patient's decision to undergo (or forgo) a specific treatment or procedure (1). IC allows providers to respect patient autonomy, dignity, and self-determination. This in turn builds trust, strengthens the patient–physician relationship, and allows for shared decision making (2).

National organizations including the American College of Obstetricians and Gynecologists, American Medical Association, and American College of Surgeons all provide guidance on IC (1, 3, 4). From an ethical perspective, according to Beauchamp and Childress, there are two preconditions to the IC process (5). The first is that the patient must exhibit competence to understand their condition and treatment options and to decide which to pursue (5). Competence is a legal term, but several medical tests (e.g., the Mini-Mental Status Examination) are utilized to evaluate decision-making capacity (6). Adults are presumed to have competence, unless formally determined otherwise, while minors are not; those with psychiatric and mental/developmental disabilities are not automatically presumed to lack competence (6). Patients must also show voluntariness (i.e., freedom from coercion or pressure) to provide IC (7). If the preconditions are met, healthcare professionals in turn disclose material information, ensure understanding, and recommend a plan. Several US Supreme Court cases have addressed what constitutes material information. From a legal perspective, courts generally require that disclosure include the nature of proposed treatment/procedure, anticipated results, alternative treatments, risks and benefits of the treatment/procedure and of alternative approaches including nontreatment (*Canterbury v. Spence*, *Truman v. Thomas*), the physician's personal or economic interests (*Gates v. Jenson*), diagnostic tests that may rule out a possible condition (*Jandre v. Physicians Insurance Co of Wisconsin*), and any other information that a reasonable person would want to know (*Nixdorf v. Hicken*) (8). The final step of IC is for the patient to share their decision and specifically authorize a plan (represented physically by signing a form) (5).

There are a variety of models to guide physicians in how they disclose information in the process of informed consent (2). While we strive to avoid paternalism – or substituting our own judgment for that of any patient – experts note in some instances the patient may request or desire more specific guidance. Emanuel et al. describe a continuum between purely informative discussions, supportive discussions, and providing strong potentially paternalistic recommendations depending on the circumstances that present (2). That said, in most scenarios, the ideal model will typically be one that is deliberative: one in which the physician is engaged with the patient in an exploration of options congruent with the patient's values.*

Regardless of the model used, when working with patients seeking benign gynecologic surgical procedures, several key issues may arise. This chapter will highlight the key ethical questions related to IC in minimally invasive gynecologic surgery (MIGS). We will explore several topics: conflicts of interest, disclosures regarding experience, performance level and shift length, and special considerations for vulnerable patient populations. To guide these discussions, relevant ethical principles and frameworks will be utilized, including beneficence, non-maleficence, distributive justice, reproductive justice, autonomy, human dignity, self-determination, and utilitarianism.

57.2 Conflicts of Interest

Avoiding conflicts of interest (COI) is a critical element of IC for all healthcare professionals (HCPs). HCPs should avoid the risk that the primary interest of patient health is unduly influenced by a secondary interest (e.g., a personal or financial relationship with an individual or organization) (9). Secondary interests must always be disclosed as they may be a COI without the surgeon believing it influences their attitude. Research shows that unconscious bias, arising from innocuous interactions and gifts, instills feelings of reciprocity in the beneficiary and may be more widespread and harmful than conscious bias (10). COIs exist in all aspects of medical care including surgery and, specifically, MIGS. Consider the following example: a surgeon helped generate and collect evidence for a novel surgical device, from which they now profit. The tool shows promise to improve outcomes in MIGS and there is a growing body of research supporting its use. Is this a conflict of interest? In this case, the surgeon has both financial and nonfinancial (e.g., the potential to break new ground in research) COIs. Therefore, this should be disclosed to the patient during the IC process. Similarly, significant support from a particular industry or representative of same would create a COI. One option to resolve COI is to create a review committee, whose members all lack relevant conflicts and who could review the case and develop a policy on the acceptability of relevant activities (10). Alternative actions to aid in resolving conflicts include encouraging second opinions and the use of patient advocates to combat potential bias (10). Resolving conflicts in favor of the interests of the patient is the ethical response – disclosure alone is not always sufficient.

* Author's note: for further reading on models for the informed consent process, see Emanuel's *Four Models of the Physician–Patient Relationship.*

DOI: 10.1201/9781003312109-57

57.3 Physician Disclosure of Experience and Performance Rate

Are physicians obligated to disclose their volume of experience and performance rate with a particular surgery? What are the benefits of requiring this disclosure and do they offset potential risks? From a legal perspective, this question has been disputed in the courts with contradictory decisions. In *Duttry v. Patterson*, the Pennsylvania Supreme Court considered a physician's experience and qualifications irrelevant to IC, regardless of whether the patient requests the information (11). In contrast, in *Johnson v. Kokemoor*, the Wisconsin Supreme Court found that physicians are required to disclose their level of experience when a "reasonable person" would expect to be told this information (8). This decision also stated that a physician's risk statistics as compared to other physicians falls under the purview of IC (11). From an ethics perspective, transparency and disclosure would be favored. Ethicists Clarke and Oakley have argued that a surgeon's skill level is a required disclosure because experience and skill impact surgical risk (12). Research revealing lower mortality rates associated with surgeries performed by surgeons with a high versus low annual volume may support this (13). It has also been proposed that physicians are most skilled after residency given the intensity of the training (14, 15). Finally, studies have shown that female physicians achieve statistically lower morbidity and mortality for their patients, perhaps because they are more likely to practice patient-centered care, taking more time talking with their patients, and displaying more empathy (16, 17). These hypotheses must be balanced with an effort to avoid stereotypes, gender bias, and ageism.

Truth-telling by physicians is an important principle in medical ethics (18). Patients are entitled to information about their diagnosis and treatment, but physicians are also obligated to avoid harm (18). In some cases, sharing information (e.g., an incidental genetic testing finding suggesting high risk of a nonpreventable and incurable disease) could cause great harm and distress with little benefit. Given the rise of the digital age, patients feel more entitled to information about their doctors and empowered to obtain it themselves online. Upon a patient's request for pertinent information about their condition or treatment options, including about the surgeon's level of experience with the surgery, the surgeon should provide the information accurately.

But is a surgeon ethically bound to disclose their volume and performance rate without prompting? Potential benefits of disclosure are twofold. First, it would allow patients to make more informed decisions about how to balance their own priorities when choosing where to receive care. Some patients may still prioritize a lower volume surgeon with whom they already have a relationship; some may not. Second, it may incentivize providers to increase volume, improve technique, and minimize complications (11). Both benefits would help minimize harm to patients; however, research has yet to demonstrate that either of these benefits are directly incentivized by requiring disclosure (11). Performance rates are difficult to interpret and are often inaccurate when reported at the level of an individual practitioner. Many factors outside of physician expertise influence surgical outcomes, including quality of postsurgical care, patient comorbidities, race, social determinants of health, and type of insurance (11, 19). To control for these confounders, surgeon performance rates would need to be calculated at an institutional level using risk-adjustment and stratification (11). The performance rate would also need to be contextualized with an institutional or regional average. Assuming that a performance rate is accurate and risk-adjusted, would a patient want this information? Schwartz at al. surveyed Medicare patients about how they decided where to have surgery and found that the main factor was surgeon reputation (20). With respect to performance data, they wanted to learn about it through a referring provider, indicating that the data is most valuable when interpreted by a trusted and unbiased healthcare professional (11, 20). Notably, obstetrics and gynecology is one of the few surgical disciplines in which referrals are internally controlled (21). In most other disciplines, patients are referred to surgery by another provider; however, in obstetrics and gynecology, frequently patients receive a diagnosis in need of surgery from their OB/GYN and that surgeon then decides whether to refer out or not (21). This in some cases represents a conflict of interest that should be resolved in favor of disclosure and possible referral to another surgeon, given lack of a neutral referral from another clinician such as a primary care physician.

Required disclosure of volume and performance may present several risks. Lower volume early in surgical careers may deter patients from seeking care from younger, less experienced surgeons. From a utilitarian perspective, we need surgeons to continue to enter the workforce and develop their skills post residency and fellowship. Appropriate early cases allow surgeons to build the skill set and reputation required to effectively treat many more patients in the future. Even so, patients are entitled to accurate information about the skill level and experience of their surgeon. In the setting of academic medicine, the relative inexperience of resident and fellow surgeons is compensated for by the experience of attending surgeons. A patient may still refuse to be operated on by a trainee (resident or fellow). In these situations, the surgeon should inform the patient that the trainee is supervised and a critical part of the surgical team. Attending surgeons must disclose which portions of the procedure will be completed by them and which by trainees, to the best of their ability. If the patient persists in refusing care that involves trainees, the physician should refer the patient to another qualified provider outside the academic center if possible. In an emergent situation, the beneficence afforded by the academic surgical team potentially outweighs a patient's autonomous request not to involve trainees. Even so, if a patient with capacity refuses surgical intervention, legally the team cannot proceed.

Requiring disclosure of experience level may bring justice concerns to light. Patients with more resources have access to the most experienced and skilled surgeons and with required disclosure may become more selective. Due to financial and insurance barriers, patients with lower socioeconomic status (SES) will not have the privilege to be as selective. This will inevitably exacerbate the healthcare disparities that already exist in the US, including the fact that those with the lowest income and education level have the poorest health (22). Physicians may also be discouraged from taking on higher risk patients – including patients of color who more frequently face surgical complications due to systemic racism and societal inequities rather than biological factors – as they will be incentivized to optimize their performance rate (11, 19).

All this said, the risks and practical concerns associated with requiring disclosure of volume and performance rate are likely outweighed by the benefits. Physicians should be supported in disclosing performance rates that are risk-adjusted and contextualized with institutional or regional averages (11).

57.4 Physician Disclosure of Shift Length

Is a physician obligated to disclose their daily or weekly volume of procedures and/or call? Does a patient have the right to know that their surgeon has been awake for 24 continuous hours? Standards of IC demand that physicians disclose factors that could compromise the treatment or procedure (23). Lack of sleep negatively impacts neurobehavioral performance, and physician exhaustion is a documented cause of medical error (23, 24). Research shows that a majority of patients would request a different surgeon if they knew their surgeon was at the end of a 24-hour shift (25). So, who should bear the responsibility of determining when a surgeon's sleep deprivation presents a material risk to the patient? Given the shift in the patient–surgeon relationship from paternalism to patient-centered care, physician disclosure and discussion would help build trust and enhance informed decision making (26). However, this information may not be useful or interpretable by patients. Individual surgeons differ in the effects they experience from lack of sleep. It may be reasonable to defer to individual physician judgment, guided by principles of professionalism (26). Requiring such a disclosure may confuse and frighten patients and exacerbate existing justice issues as discussed in the previous section (23). Rather than placing the onus on patients to judge how shift length might impact a surgeon's abilities, individual institutions should develop evidence-based policies that limit working hours (both shift lengths and total hours per week) to minimize harm to patients and prevent physician burnout. Institutions should make efforts to identify at-risk surgeons to support them and prevent safety issues (27).

57.5 Vulnerable Populations

The 1974 Belmont Report introduced the concept of vulnerable populations in medicine and research, which include racial minorities, minors, refugees, and those who are cognitively or intellectually impaired, are incarcerated, are socioeconomically disadvantaged, have low literacy, and cannot speak English (28, 29). As mentioned in the "Background" section, voluntariness is a precondition of IC (5). In situations of extreme vulnerability, true IC can be illusory given a lack of resources and access.

To understand the importance of IC in MIGS and obstetrics and gynecology more broadly, it is useful to reflect on the history of medicine in the United States. Several notable historical moments illustrate how neglect for IC can result in violations of human dignity and autonomy. One example involves Dr. J. Marion Sims, the first surgeon to successfully perform vesicovaginal fistula surgery (30). To practice his surgical technique, Dr. Sims operated repeatedly on three enslaved black women, Lucy, Anarcha, and Betsey, without anesthesia (30). His experiments on slaves – along with the more well-known histories of the Tuskegee experiments and Henrietta Lacks – demonstrate the ways in which the medical system has exploited black bodies (30). This gruesome history has present-day reverberations. A 2020 poll revealed that 70% of black Americans have been treated unfairly by the healthcare system and 55% distrust it (31). To help reestablish trust in the system, racism and bias trainings should be required at the institutional level and resources should be allocated towards increasing surgeon diversity (32). A licensed medical interpreter should always be used to communicate with patients who do not speak the surgeon's primary language. For patients who cannot read, the IC process should be conducted orally rather than with written information. Information should also be provided at a level fitting to the patient's health literacy level (4, 33). While accounting for vulnerabilities and power dynamics, surgeons should remain respectful to patient autonomy and empower patients to engage in a shared decision-making process (28). Research has revealed that decision-making capacity assessments are disproportionately requested for black and Hispanic patients (34). The risk versus benefit of capacity assessments should be carefully considered in certain populations as they may undermine trust between the patient and physician (34).

The 1927 Supreme Court case *Buck v. Bell* was another historical moment in which IC and reproductive autonomy were disregarded with sweeping repercussions. The case centered on Carrie Buck, who was forcibly sterilized for being "feebleminded" after being raped and impregnated by her foster parents' nephew (35, 36). The Supreme Court ultimately upheld a state's right to forcibly sterilize those considered "unfit to procreate" (35). As a result of the decision, 70,000 Americans were forcibly sterilized and robbed of their reproductive autonomy during the 20th century. State-mandated sterilization targeted poor, "mentally deficient," blind, deaf, diseased, and "promiscuous" people (35). This history of forced sterilization and eugenics should serve as a reminder to respect reproductive autonomy. Select gynecologic surgeries compromise fertility, sometimes irreversibly. For patients of reproductive age, this should always be explicitly addressed in the IC process. Physicians may be tempted to judge a patient's fitness to parent or family planning goals based on their intellectual capabilities, gender identity, comorbidities, or age. But IC centers on partnering with a patient to make a decision that respects their values rather than imposing your own.

In an effort to protect the more vulnerable, Medicaid patients are subjected to a 30-day hold prior to undergoing sterilization procedure after providing IC (37). Individuals with commercial insurance experience no such hold. Recent research found that women with Medicaid have similar decision-making processes around sterilization as those with commercial insurance (28). Despite the protective intent behind this mandate, it creates a hierarchical system of access that restricts reproductive autonomy to those of higher socioeconomic status (37). It also hinders reproductive justice, which is the right "to maintain personal bodily autonomy, have children, not have children, and parent the children we have in safe and sustainable communities," regardless of race, socioeconomic status, or gender identity (38). After *Dobbs v. Jackson Women's Health Organization* overruled *Roe v. Wade* in 2022, thereby delegating to states the right to regulate abortion and creating uncertainty around abortion access, many more individuals are seeking out sterilization procedures (39). Physicians should advocate against policies that restrict access to contraception – or any other reproductive health intervention – based solely on socioeconomic status and insurance type (40).

57.6 Conclusion

Informed consent ensures that surgeons respect patient autonomy, dignity, and self-determination. Components of the IC process include resolving COIs in favor of the patient's interest, disclosing foreseeable risks associated with a procedure, counseling on fertility preservation where applicable, and making efforts to protect vulnerable patients. Not only is informed consent legally and ethically mandated, but it is also highly valued by both patients and surgeons. In a survey of 150 urogynecology patients, Hallock et al. found that knowledge

and understanding of their surgery was a critical component of patient satisfaction (41). Propst et al. surveyed obstetrics and gynecology residents and found that 90% have obtained IC for a procedure for which they were unsure of all risks and about 60% desired more training in IC (42). Therefore, increased education about the IC process is warranted and would enhance both patient well-being and physician confidence.

References

1. ACS. *Informed consent*. Available at: www.facs.org/for-medical-professionals/education/for-your-patients/prepare-your-patients-well/informed-consent/ (Accessed Jul 2023).
2. Emanuel EJ et al. Four models of the physician–patient relationship. *JAMA*. 1992;267(16):2221–2226.
3. AMA. *Informed consent*. Available at: https://code-medical-ethics.ama-assn.org/ethics-opinions/informed-consent (Accessed Jul 2023).
4. ACOG. *Informed consent and shared decision making in obstetrics and gynecology, committee opinion* [Internet]. Available at: www.acog.org/clinical/clinical-guidance/committee-opinion/articles/2021/02/informed-consent-and-shared-decision-making-in-obstetrics-and-gynecology (Accessed Jul 2023).
5. Beauchamp TL et al. *Principles of Biomedical Ethics*, 8th edn. Oxford University Press; 2019.
6. Stewart C. Competence: definition, rights & responsibilities [Internet]. *Britannica*. Available at: www.britannica.com/topic/competence-health-law (Accessed Jul 2023).
7. Knifed E et al. Patients' perception of the informed consent process for neurooncology clinical trials. *Neuro Oncol*. 2008;10(3):348–354.
8. Murray B. Informed consent: what must a physician disclose to a patient? *AMA J Ethics*. 2012;14(7):563–566.
9. Emanuel EJ et al. *The concept of conflicts of interest* [Internet]. 2008. eweb:312076. Available at: https://repository.library.georgetown.edu/handle/10822/960637 (Accessed Jul 2023).
10. Johnson J et al. Joint issues – conflicts of interest, the ASR hip and suggestions for managing surgical conflicts of interest. *BMC Medical Ethics*. 2014;15(1):63.
11. Burger I et al. Disclosure of individual surgeon's performance rates during informed consent. *Ann Surg*. 2007;245(4):507–513.
12. Clarke S et al. Informed consent and surgeons' performance. *J Med Philos*. 2004;29(1):11–35.
13. Birkmeyer JD et al. Surgeon volume and operative mortality in the United States. *N Engl J Med*. 2003;349(22):2117–2127.
14. Choudhry NK et al. Systematic review: the relationship between clinical experience and quality of health care. *Ann Intern Med*. 2005;142(4):260–273.
15. Tsugawa Y et al. Physician age and outcomes in elderly patients in hospital in the US: observational study. *BMJ*. 2017;357:j1797.
16. Tsugawa Y et al. Comparison of hospital mortality and readmission rates for medicare patients treated by male vs female physicians. *JAMA Intern Med*. 2017;177(2):206–213.
17. Basky G. Gender may not be the biggest factor in women doctors' lower patient mortality rates. *CMAJ*. 2021;193(33):E1308–E1309.
18. Sullivan RJ et al. Truth-telling and patient diagnoses. *J Med Ethics*. 2001;27(3):192–197.
19. Lucas FL et al. Race and surgical mortality in the United States. *Ann Surg*. 2006;243(2):281–286.
20. Schwartz LM et al. How do elderly patients decide where to go for major surgery? Telephone interview survey. *BMJ*. 2005;331(7520):821.
21. Zetka JR. The making of the "women's physician" in American obstetrics and gynecology: re-forging an occupational identity and a division of labor. *J Health Soc Behav*. 2008;49(3):335–351.
22. Kim Y et al. Socioeconomic disparities in health outcomes in the United States in the late 2010s: results from four national population-based studies. *Arch Public Health*. 2023;81(1):15.
23. Czeisler CA et al. Should sleep-deprived surgeons be prohibited from operating without patients' consent? *Ann Thorac Surg*. 2013;95(2):757–766.
24. Rothschild JM et al. Risks of complications by attending physicians after performing nighttime procedures. *JAMA*. 2009;302(14):1565–1572.
25. Blum AB et al. US public opinion regarding proposed limits on resident physician work hours. *BMC Med*. 2010;8(1):33.
26. Ginwalla RF et al. Exploring the limits of surgeon disclosure: where are the boundaries? *Bulletin Am Coll Surgeons*. 2016. Available at: https://bulletin.facs.org/2016/08/exploring-the-limits-of-surgeon-disclosure-where-are-the-boundaries/ (Accessed Jul 2023).
27. McAlister C. Breaking the silence of the switch – increasing transparency about trainee participation in surgery. *N Engl J Med*. 2015;372(26):2477–2479.
28. Overcarsh P et al. Informed consent in gynecologic surgery. *Curr Opin Obstet Gynecol*. 2019;31(4):240.
29. US Department of Health and Human Services, Office for Human Research Protection. *Read the Belmont report*. 2018. Available at: www.hhs.gov/ohrp/regulations-and-policy/belmont-report/read-the-belmont-report/index.html (Accessed Jul 2023).
30. Zhang S. The surgeon who experimented on slaves. *The Atlantic*, 2018. Available at: www.theatlantic.com/health/archive/2018/04/j-marion-sims/558248/ (Accessed Jul 2023).
31. Hostetter M et al. Understanding and ameliorating medical mistrust among Black Americans. *The Commonweath Fund, New York*, 2021. Available at: www.commonwealthfund.org/publications/newsletter-article/2021/jan/medical-mistrust-among-black-americans (Accessed Aug 2023).
32. Williams-Karnesky RL et al. Shoring up the pipeline: increasing diversity in surgery by enhancing equity and inclusion in the surgical learning environment. *Bulletin Am Coll Surgeons*, 2021. Available at: https://bulletin.facs.org/2021/01/shoring-up-the-pipeline-increasing-diversity-in-surgery-by-enhancing-equity-and-inclusion-in-the-surgical-learning-environment/ (Accessed Jul 2023).
33. Natavio MF et al. The use of a low-literacy version of the Medicaid sterilization consent form to assess sterilization-related knowledge in Spanish-speaking women: results from a randomized controlled trial. *Contraception*. 2018;97(6):546–551.
34. Garrett WS et al. Racial disparities in psychiatric decisional capacity consultations. *PS*. 2023;74(1):10–16.
35. Health News. The supreme court ruling that led to 70,000 forced sterilizations. *NPR*, 2016. Available at: www.npr.org/sections/health-shots/2016/03/07/469478098/the-supreme-court-ruling-that-led-to-70-000-forced-sterilizations (Accessed Jul 2023).
36. Smith JD. *Carrie Buck (1906–1983). Encyclopedia Virginia*. Available at: https://encyclopediavirginia.org/entries/buck-carrie-1906-1983/ (Accessed Jul 2023).
37. Maykin MM et al. Discriminatory regulations on postpartum sterilization for Medicaid recipients propagate health inequities. *Lancet Reg Health Am*. 2022;6.
38. Sister Song. *Reproductive justice* [Internet]. Available at: www.sistersong.net/reproductive-justice (Accessed Jul 2022).
39. Bolton A et al. More people are opting to get sterilized – and some are being turned away. *NPR*, 2022. Available at: www.npr.org/sections/health-shots/2022/07/29/1113573995/more-people-are-opting-to-get-sterilized-and-some-are-being-turned-away (Accessed Jul 2023).
40. ACOG Committee on Health Care for Underserved Women. *Access to contraception, committee opinion 615*, 2015. Available at: www.acog.org/clinical/clinical-guidance/committee-opinion/articles/2015/01/access-to-contraception#:~:text=The%20American%20College%20of%20Obstetricians,availability%20of%20affordable%20and%20accessible (Accessed Oct 2023).
41. Hallock JL et al. Patient satisfaction and informed consent for surgery. *Am J Obstet Gynecol*. 2017;217(2):181.e1–181.e7.
42. Propst K et al. Informed consent education in obstetrics and gynecology: a survey study. *J Surg Educ*. 2019;76(4):1146–1152.

Taylor & Francis
Taylor & Francis Group
http://taylorandfrancis.com

INDEX

Note: Page numbers in *italics* indicate a figure and page numbers in **bold** indicate a table on the corresponding page.

3D sonography, 253
3D ultrasound, 67, 243, *243*

A

abdominal pregnancies, 88
abnormal pregnancies, *see* gestational trophoblastic disease (GTD)
abnormal uterine bleeding (AUB), 94, 232
  acute nongestational uterine bleeding, 101
  classification of causes, **232**
  coagulopathy, ovulatory dysfunction, endometrial, iatrogenic, not yet classified (COEIN)
    coagulopathy (AUB-C), 238
    endometrial (AUB-E), 238
    iatrogenic (AUB-I), 238–239
    not yet classified (AUB-N), 239
    ovulatory dysfunction (AUB-O), 238
  FIGO system, 95, *95*, **96**, *98*, *105*
  nonpregnant patient, 232
  PALM-COEIN, 94, *95*
  pathogenesis of chronic
    adenomyosis (AUB-A), 97–98
    coagulopathies (AUB-C), 99
    endometrial disorders (AUB-E), 99–100
    HyPO-P, 99–100, *100*
    iatrogenic bleeding (AUB-I), 100–101
    malignancy/hyperplasia (AUB-M), 99
    not otherwise classified (AUB-N), 101
    ovulatory disorders (AUB-O), 99
    polyps (AUB-P), 96–97
  pathophysiology, 269
  patient with CSD, 269
  polyps, adenomyosis, leiomyomas, malignancy/hyperplasia (PALM)
    adenomyosis (AUB-A), 233–234, *234*
    endometrial and cervical polyps (AUB-P), 233, *233*, *234*
    leiomyomas (AUB-L), 234–236, *235*
    malignancy and hyperplasia (AUB-M), 236–238, *237*
  women with chronic
    elastography, 104
    hysteroscopy, 104
    imaging, 103
    laboratory assessment, 103
    magnetic resonance imaging, 104
    notation, 104
    physical examination, 103
    sonohysterography, 104
    structured history, 101–103, *102*
    TVUS, 103
absolute risk reduction (ARR), 26–27
Acessa ProVu® system, 150, *150*
acquired uterine arteriovenous malformation, 254
activated partial thromboplastin time (APTT), 101, 103
adenomyosis
  adenoma nodule, *118*
  altered uterine contractility, 122, *122*
  anatomical alterations, 122
  atrophic endometrium, *119*
  bleeding, *121*, 121–122
  elastic nodule, *117*
  fibrotic nodule, *117*
  glandular tissue, *119*
  hard nodule, *118*
  hysteroscopic image, *234*, *235*
  imaging, 122, *122*
  infertility/reduced fertility, 122
  internal endometriosis, *119*
  MRI, 125–129, *126*, *127*, *128*, *129*
  Müllerian ducts, 117
  myometrium, *118*
  non-neoplastic endometrial glands, *118*
  pain, 121
  PALM, 233–234
  PALM-COEIN classification, *121*
  pathophysiology, 118–121
  radiological image, *120*
  stroma, *119*
  suppression before IVF, 219
  symptomatology, 121
  transvaginal ultrasound image, *120*
  TUS *vs.* MRI, 129–130, *130*
  ultrasound, 122–125, *123*, *124*, *125*
adnexal masses
  characterization of, 68, 70
  differential diagnosis, **314**
  intraoperative technique
    abdominal entry, 316
    frozen section, 317
    oophorectomy, 316
    ovarian cystectomy, 316
    in pregnancy, 318
    specimen removal, 316–317
    tubo-ovarian abscess, 317–318
  preoperative assessment
    imaging, 314–315
    imaging modality, 315
    initial patient evaluation, 314
    ovarian torsion, 315
    surgical planning, 315–316
    surveillance, 315
    tumor markers, 315, **315**
Alexis Contained Extraction System, *45*
allografts, 76
ALLY Uterine Positioning System™, 37, *37*
alpha fetoprotein (AFP), 88
American Association of Gynecologic Laparoscopists (AAGL), 3
American College of Urethral Diverticulaians and Gynecologists (ACOG), 94, 139, 415, 439, 464
American Society for Reproductive Medicine (ASRM), 81, 216
amniografts, 263
anesthesia, *see* general anesthesia (GA); local anesthesia
angular pregnancy, 85
anti-Müllerian hormone (AMH), 16, 153, 189, 219, 311
artificial reproductive techniques (ART), 133
Asherman syndrome (AS), *see* intrauterine adhesions (IUAs)
assisted reproductive technologies (ART), 219, 280
autografts, 76
axonotmesis, 169

B

band-aid surgeries, 3
bias, 27
bilateral salpingo-oophorectomy (BSO), 163, 190, 311, 336
bipolar cautery device, 2
bladder endometriosis, 211–212, *212*, *215*
bleeding, *see* abnormal uterine bleeding (AUB)

C

cannabinoids, 162
categorical (nominal) data, 25
cellular vaporization, 59, *60*
censoring, 26
Centers for Disease Control and Prevention (CDC), 79, 161
cervical cancer, *see also* gynecologic cancer; uterine cancer
  gynecologic aspects
    epidemiology, 342
    etiology, 342
    screening, 342–343, **343**
    vaccination, 343, **344**
  surgical aspects
    adjuvant hysterectomy, 351
    adjuvant therapy, 349
    carcinoma of cervical stump, 351
    decreasing radicality, 349–351, *350*
    evaluation, 343–344
    follow-up after treatment, **351**, 351–352
    lymphadenectomy, 346
    lymph node evaluation, 344–345
    minimally invasive, 346–348, *347*
    neoadjuvant chemotherapy, 348–349
    ovarian transposition, 351
    preoperative evaluation, 344
    radical hysterectomy, 345–346, *346*, **348**, **349**
    radical parametrectomy, 351
    radical trachelectomy, 351
    staging, 344, **345**
    surgical treatment of recurrent disease, 352
cervical pregnancies, 87
cervical ripening, 225
cesarean scar defects (CSDs)
  assessment, 269–270, **270**
    hysteroscopy, 271–272
    laparoscopy, 272
    magnetic imaging resonance, 271
    ultrasound, *270*, 270–271
    vaginal reconstruction, 272
  epidemiology, 268–269
  risk factors, 268–269
  symptoms, 269–270, **270**
  treatment

medical, 271
surgical, 271
cesarean scar pregnancies (CSP), 86–87, *87*
chocolate cysts, *see* endometriomas
choriocarcinoma, 254, 357
chromic surgical gut, 72
chronic pelvic pain (CPP)
acetaminophen, 161
analgesics, 161
bladder instillation, 163
bladder symptom management, 162
cannabinoids, 162
chronic pain conditions, 157, **157**
diagnostic testing, 159
evaluation, 158
gastrointestinal symptom management, 162–163
goal setting, 159
injections, 163
neuromodulation, 163
nonpharmacologic treatments
diet, 160
lifestyle modifications, 159–160
pathophysiology, 156–157, *157*
pharmacological treatments
acetaminophen, 161
analgesics, 161
anticonvulsant, 162
antidepressants, 161–162
hormonal therapy, 161
opioids, 161
SMR, 162
physical activity and exercise
acupuncture, 161
pain psychology, 160
PFPT, 160
sexual therapy, 160
sleep, 160
psychological assessment, 159
surgery
adhesiolysis, 164
hysterectomy, 163–164
system-based etiology, **156**
trauma-informed care, 157
treatment, 159
C-incision tissue extraction technique (ExCITE), 45, 145
coelioscopy, 1
cognitive behavioral therapy (CBT), 29, 160
color Doppler ultrasound, 66
color Doppler ultrasound transvaginal sonography, 253, *253*
colostomy, laparoscopic
choice of stoma, 360
complications, 361
extraperitoneal rectal injury, 359
indications, 359
large bowel obstruction, 359
preoperative considerations, 359
procedure, 359–360, *360*
rectovaginal fistula, 359
complete blood count (CBC), 81, 89, 103, 315, 425
computed tomography (CT), 68, 133, 397, 421
conflicts of interest (COI), 464
confounder bias, 27
conscious sedation, 152, 225, 246
consent-based studies, 22
constipation
algorithm for, *388*
anorectal manometry, 388
barium and MRI defecography, 388–389
biofeedback, 389
colonoscopy, 388
colon transit, 389
definition, 387
evaluation, 387–388
laboratory testing, 388
medications, 389
sacral neuromodulation, 389
subgroups, 387
continuous (ordinal) data, 24–25, *25*
continuous positive airway pressure (CPAP), 452
contraception, 79, 100, 185, 274, 285, 302
contrast-enhanced ultrasound (CEUS), 67
cornuotomy, 85
corticotropin releasing hormone (CRH), 16
cosmetic gynecology
clitoris and clitoral prepuce, 416
genital depigmentation, 418
labia majora, 417, *418*
labia minora, **416**, 416–417, *417*
mons pubis, 418, **419**
preoperative counseling, 415
sexual function procedures, 419
terminology, 415, **415**
vagina, 417–418, *418*
Cox proportional hazards regression, 26
cystoscopy/vaginoscopy
complications of stents, 412
female urethrocystoscopy, 409, *409*, *410*
iatrogenic ureteral injury, 410
important stent considerations, 411
intraoperative localization, 410
obstruction, 410
postoperative management, 412
procedure steps, 411
types of ureteral injury, 409–410
ureteral injury, 410
ureteral stenting, 410–411, *411*
ureteral stents for gynecologic surgery, 409

D

data types
count, 25
distribution, 24–25, *25*
effect measures, 26–27
nominal, 25
ordinal, 24–25, *25*
standard deviation (SD), 24–25, *25*
TTE data, 25–26
deep endometriosis (DE), 67, 176, *177*, 204, 217
deep vein thrombosis (DVT), 69, 306, 422
devices, *see also* medical devices
anti-slip, 41–42, *42*
compression, 29
electrosurgical unit (ESU), 35, *36*
energy, 37
insufflator, 35
suction, 37
diagnostic imaging
communication in MIGS, 70
computed tomography (CT), 68
digital subtraction angiography (DSA), 69–70
interventional radiology in MIGS, 69–70
magnetic resonance (MR), 67–68
ultrasound, 66–67
X-ray, 122
diaphragmatic endometriosis, 192–195, *193*, *194*
disease-free survival (DFS), 316, 324, 346
disseminated intravascular coagulation (DIC), 89
dorsal nerve of the clitoris (DNC), 169
Duplojet spray system, 431, *431*

E

early endoscopy, 1
early pregnancy loss (EPL), 80, *see also* retained products of conception (RPOC)
congenital uterine anomalies, 257
definition, 252
ectopic pregnancy (EP), 79
abdominal pregnancies, 88
β-hCG, 80
cervical, 87
CSP, 86–87, *87*
emergencies, 89
endocrine markers, 80
etiology, 79
fallopian tube, 79–80
heterotopic pregnancies, 88–89
incidence, 79
interstitial ectopic pregnancy, 84–85, *85*, *86*
laboratory testing, 80
management of, 81
medical management, 81
methotrexate protocols efficiency
adverse reactions, 82
combination protocols, 82
expectant management of tubal, 83
follow-up, 82–83
multiple-dose, 82
protocol comparison, 82
single dose, 81–82
subsequent fertility, 83
treatment protocols, **82**
two dose, 82
ovarian pregnancies, 88
PUL, 80–81
risk factors, 79
salpingectomy *vs*. salpingostomy, 84
surgical management, 83–84
transabdominal ultrasound, 80
elastography, 104, 114
electrodesiccation, 64–65
electromechanical morcellation (EMM), 45
electronically controlled fluid management system, 228
electronic medical record (EMR), 22
electrosurgery
analogy of electric current, *55*
bipolar, *56*, 56–57
bipolar instruments, 62–64, *63*, *64*
electrodesiccation, 64–65
current, 56, *56*
cutting/coagulation, 58, *58*
dispersive electrode, 57–58, *58*
effects on tissue, 55–56, **56**
coagulation, 59–60, *60*
cutting (electrosection), 59, *59*
desiccation, 59–60, *60*
fulguration, 60–61, *61*
electromotive force, *55*
harmonic scalpel, 65

monopolar, 56–57, *57*
monopolar systems
capacitive coupling, 62, *62*
direct coupling, 61–62, *62*
insulation failure, 61, *61*
power density, *56*, 56–57
waveforms, 57, *57*
electrosurgical unit (ESU), 35, *36*
endometrial cancer, *see* uterine cancer
endometrial echo complex (EEC), 103
endometriomas
cyst drainage, 189
diode laser treatment, 190, *190*
medical management, 179
ovarian, 188, *189*
surgical excision, *189*
endometriosis, *see also* fertility considerations, endometriosis; gastrointestinal endometriosis; genitourinary endometriosis
in adolescent populations, 183
clinical symptoms, 176
consent process, 204
forms, 175
histology, 175–176, *176*
hormonal therapy, 180–181
aromatase inhibitors, 182–183
combined hormonal contraceptives, 181
danazol, 183
GnRH agonists, 182
GnRH antagonists, 182
progesterone-only medications, 181
SPRM, 181–182
imaging tests, 176–177
and infertility, 183
laboratory diagnosis, 177–178, *178*
lesion phenotypes, 175–176, *176*
medical management
first line, 179, **180**
nonhormonal therapies, 180
second-line, 179, **180**
medical therapy, 179–180
multidisciplinary involvement, 205
neuromodulators, 180
NSAIDs, 180
pathophysiology
environmental factors, 175
genetic factors, 175
immune factors, 175
Metaplasia theory, 175
precursor cell theory, 175
Sampson's theory, 175
peri-and post-menopause, 184
perioperative period
postoperative medical management options, 184–185
preoperative medical management options, 184
and pregnancy, 183–184
surgical management
confirmed/suspected endometriosis, 187
menstrual bleeding, 190
ovarian endometriomas, 188–190, 189
superficial endometriosis, 187–188, 187, 188
suspected/confirmed, 187
visual detection of superficial, 187–188
endometriosis fertility index (EFI), 216–217, *217*
endometriosis interna, 119
endometriotic cysts, *see* endometriomas
enhanced recovery after surgery (ERAS), 28, 435, 455
carbohydrate loading, 28
early feeding, 29
invasive gynecologic surgery, **30**
MIS procedures, 30–31
modern fasting, 28
opioid sparing analgesia, 29
premedications, 28–29
prophylaxis, 28–29
urinary catheter removal, 29
epithelial ovarian cancer (EOC), 321
advanced-stage
cytoreductive surgery, 323–324
diagnostic laparoscopy, 322–323
development, 308
early stage, 321–322
risk, 310
secondary cytoreductive surgery, 324–325
ergonomics, 34, *34*, 36, 38, 48
Essure system, 278
estradiol, 18, 94, 108, 304
estrogen, 18, 19, 100, 109, 120, 181, 184, 236, 304
selective estrogen receptor modulators, 306, **306**
urinary incontinence, 382–383
vaginal, 295, 300, 306, **306**, 362, 405
expanded polytetrafluoroethylene (ePTFE), 76, **76**
extracorporeal C-incision tissue extraction (ExCITE) technique, 45, 145
extrapelvic endometriosis, 175, 192
abdominal peritoneal cavity
caudal hepatic displacement, 196–197, *197*
fibrous pericardium, 198
pericardial endometriosis, 198, *199*
right diaphragm lesions, 195, *196*
right hepatic lobe, 195–196, *197*
supramesocolic compartment, 192–195
surgical technique, 198
suturing of the right diaphragm, 197–198, *198*
trocar placement, 195, *195*
abdominal wall endometriosis (AWE)
abdominal scars, 200–201
external inguinal ring (superficial), 202
inguinal canal, *201*, 201–202
internal inguinal ring, 201–202
umbilical endometriosis (UE), 201
fibrous pericardium, 198
infiltrating, left diaphragm
anterior thoracic wall, 199–200, *200*
Glisson's capsule and parenchyma, 199, *199*
inframesocolic compartment, 200
paracolic gutters, 200
left diaphragm (mediastinal portion), 198
perineal scar endometriosis, 202
ex utero intrapartum treatment (EXIT), 450–451, *451*

F

fecal incontinence, *384*
colonoscopy, 386
colostomy/ileostomy, 387
dietary interventions, 386
evaluation, 385–386
nonsurgical management, 386
physical examination, 386
sacral neuromodulation, 386
sphincteropasty, 386
ultrasound, 386
Fellowship in Minimally Invasive Gynecologic Surgery (FMIGS), 4
female reproductive anomalies
bicornuate uterus, *300*, 300–301, *301*
complete uterovaginal aplasia, *293*, 293–295, *294*, *295*
intrauterine septum, 301–302, *302*
unicornuate uterus, 297–298, *298*
uterus duplex/didelphys, 298, *299*, 300
vaginal aplasia with functioning uterus, *296*, 296–297
vaginal/cervical aplasia with single functioning uterus, 297, *297*
female reproductive system, *see also* pelvic anatomy
hypothalamus, 16, **16**, **18**
hypothalamus-pituitary-ovarian axis, 17–18
menstrual cycle, 17, *17*, *20*
ovarian cycle, 18–19, *19*
ovarian surface, 16
pituitary gland, 16, **16**, **18**
uterine cycle, 19–20
uterine physiology, 16–17
femoral nerve, 40, 168, *171*, 331
fenestrations, 192
fertility considerations, endometriosis
endometriosis classification systems, 216–218, *217*
history, 216
mechanisms of infertility, 218
preservation
oocyte/embryo cryopreservation, 219–220
OTC, 220
treatments for infertility
conventional medical therapies, 218
surgical excision, 219
in vitro fertilization, 218–219
fetal surgery
amniotic band syndrome, 448–449, *449*
cardiac intervention, 446
chorioangiomas
FETO, 448, *449*
fetoscopic procedures, 446–447, *447*, *448*
laparotomy-assisted approach, 450, *450*
open hysterotomy surgeries
EXIT, 450–451, *451*
percutaneous approach, 450
preoperative planning, 445
spina bifida, 449–450
ultrasound-guided needle-based procedures
intrauterine transfusion (IUT), 445
selective fetal reduction, 446
vesicoamniotic and thoracoamniotic shunts, 445–446
vasa previa, 448
fetoscopic endoluminal tracheal occlusion (FETO), 448, *449*
fistulas, *see* obstetric lacerations; nonobstetric urogenital fistulas (NOF); ureterouterine fistula
Fitz-Hugh–Curtis syndrome, 280–281, *281*
Floseal, 430, *430*
follicle stimulating hormone (FSH), 16, 153

G

gastrointestinal endometriosis
bowel shaving technique, *208*, 208–209

discoid resection technique, 209, *209*
history, 205
imaging, *206*, 206–207, *207*
physical exam, *205*, 205–206
segmental resection technique, 210
surgical technique, *207*, 207–208
general anesthesia (GA)
complications, 437
ERAS, 435
fluid management, 435
gynecological procedures, 436, *436*
intraoperative considerations, 435
patient positioning, 435
physiologic changes during laparoscopy, **434**
cardiovascular system, 434
renal system, 435
respiratory system, 435
postoperative concerns, 437
preoperative considerations, 433–434
regional anesthesia, 436–437
genetic testing, 308
and counseling, 308–310
criteria for, 309
hormone replacement therapy, 311–312
pathogenic mutations, 310, **310**
risk-reducing surgery, **311**, 312
genitofemoral nerve, 168
genitourinary endometriosis
bladder endometriosis, 211–212, *212*, *215*
history, 210
imaging, 211, *211*
physical exam, 210–211
preoperative workup, 210
ureteral endometriosis, 212–214, *214*
genitourinary syndrome of menopause (GSM)
anatomy, 304
clinical manifestation, 305
energy-based devices (EBDs), 306–307
evaluation, 305
low dose vaginal estrogen, 306
lubricants/moisturizers, 306
physiology, 304
selective estrogen receptor modulators, 306, **306**
systemic treatments, 304–305
therapeutic management, 305, **305**
vasomotor symptoms, 304–305
genome-wide association studies (GWAS), 110
gestational trophoblastic disease (GTD), 81, 253, 355–357
gestational trophoblastic neoplasia (GTN), 355
chemotherapy-resistant, 357
hysterectomy, 356–357
postsurgical surveillance, 355
role of second curettage, 356
uterus removed, *356*
gonadotropin-releasing hormone (GnRH), 16, 161, 179
grafts, 75–76
biologic grafts
allografts, 76
autografts, 76
xenografts, 76–77
host tissue response, 76
ideal properties, 77
synthetic mesh, 76, **76**
growth hormone releasing hormone (GHRH), 16
gynecologic cancer, 25, 69, *see also* cervical cancer; epithelial ovarian cancer (EOC); uterine cancer
CT, 68
hormone replacement therapy timing, 311–312
MR, 68
pathogenic mutations, 310, **310**
risk-reducing surgery, 311–312, **311**
screening, 310–311

H

HARMONIC ACE™, *38*
Hasson technique, 43, 140–141
health-related quality-of-life (HRQoL), 153
heavy menstrual bleeding (HMB), 70, 94, 102, 118, 183, 238
hemostasis, 84
local endometrial, 238
mechanism, 429
meticulous, 202
normal endometrial, *97*
THAs
biologic agents, 430
fibrin sealants, 430–431
flowable agents, 430
mechanical agents, 429
microfibrillar collagen (MFC), 430
microporous polysaccharide, 430, *430*
oxidized regenerated cellulose (ORC), 429, *429*
TISSEEL, 431, *431*
VISTASEAL, 431, *431*
hereditary breast and ovarian cancer (HBOC) syndrome, 308
hereditary malignancies, *see* genetic testing; gynecologic cancer
heterotopic pregnancies, 88–89
high-intensity focused ultrasound (HIFU), 70, 152
hormone replacement therapy (HRT), 142, 184, 311–312
Human Chorionic Gonadotropin (hCG), 18, 253, 355
hyaluronic acid (HA) gel, 163, *247*, 264, 304, 419
hydatidiform mole, 355, 356, *356*
hysterectomy, laparoscopic and robot-assisted
abnormal menstrual bleeding, 190
adnexa, 142
broad ligament, 142–143, *143*
colpotomy cup, 143–145, *144*
complications
vaginal cuff dehiscence (VCD), 147
wound/SSI, 147
cuff closure, 143–145, *144*
endometriosis-associated pain, 190
extraction, 145, *145*
laparoscopic equipment setup, 140
morcellation, 145, *145*
peritoneal access, 140–141
postoperative follow-up, 147
preoperative preparation
antibiotic prophylaxis, **139**, 139–140
patient selection, 139
robotic equipment setup, 140
supracervical hysterectomy, 145–146
trachelectomy, 146
trocar placement and instrumentation, 141–142
uterine manipulators, 140
uterine vessels, 143, *144*
hysterosalpingocontrast sonography (HyCoSy), 67
hysterosalpingo-foam sonography (HyFoSy), 67
hysterosalpingography (HSG), 67, 122, 243, 281, 397
hysteroscopic myomectomy, *see* myomectomy, hysteroscopic
hysteroscopy, 85, 104, 114, 261, 271, 301, *see also* abnormal uterine bleeding (AUB); Müllerian anomalies; office hysteroscopy

I

iliohypogastric nerve, 39, 167, 373
ilioinguinal nerve, 168, 201
imaging systems, 133, 159, 176–177, 206–207, 211, 344, 403, 404
adenomyosis, 122
camera head functions, 34–35
capturing, 34–35
computed tomography (CT), 68–69, 421
elastography, 104
light sources, 35
magnetic resonance (MR), 67–68, 104, 244, 271, 421
modality, 315, 445
sonohysterography, 104, 244
transvaginal ultrasound (TVUS), 103
ultrasound, 66–67
video monitors, 34
inferior hypogastric plexus (IHP), 13, 169, 172, *173*
infiltrative lesions, 175, 193
informed consent (IC), 47, 204
conflicts of interest (COI), 464
experience and performance rate, 465
shift length, 466
vulnerable populations, 466
intermenstrual bleeding (IMB), 100, 232, 269
International Federation of Gynecology and Obstetrics (FIGO's), 94
International Ovarian Tumor Analysis (IOTA), 66
International Society for Gynecologic Endoscopy (ISGE), 236
intrauterine systems (IUS), 101
intracorporeal endoscopic knot tying, 2
intrauterine adhesions (IUAs)
adhesion detection, 260–261, *262*
classification systems, 261
etiology, 260, *261*
fertility and AS, 264–265
live birth rates, 265, **265**
postoperative management
hormonal therapy, 264
mechanical barriers, 263–264
stem cell therapy, 264
postoperative outcome, 264
pregnancies after adhesiolysis, 265
pregnancy rates, 265, **265**
prevalence, 260
symptomatology, 260
treatment, 261, *263*
intrauterine growth restriction (IUGR), 254, 265

intrauterine transfusion (IUT), 445
investigator-sponsored research (ISR), 22
in vitro fertilization (IVF), 2, 79, 179, 218
in vitro maturation (IVM), 220
iron deficiency anemia (IDA), 94
isthmocele, *see* cesarean scar defects (CSDs)

K

Kaplan–Meier method, 25
Kegel exercises, 381

L

laparoscopes, 35, *35*
Laparoscopic Approach to Cervical Cancer (LACC), 321, 346
laparoscopic coagulating shears (LCS), 65
laparoscopic complications
  direct application
    bowel injury, 426, *426*
    capacitive coupling, 425
    direct coupling, 425, *425*
    genitourinary complications, 426–427, *427*
    insulation failure, 425
    vascular injuries, 425, *426*
  intraoperative considerations
    abdominal entry, 422–424, *423*, *424*
    electrosurgery complications, 424–425
    patient positioning, 422, *423*
    pneumoperitoneum, 424
  postoperative considerations
    hernia prevention, 427
    VTE, 427
    wound infections, 427
  preoperative considerations
    history and physical, 421
    imaging, 421–422
    informed consent, 422 (*see also* informed consent)
    patient selection, 421
    prior surgeries, 421, **421**
    surgical clearance, 422
laparoscopic hysterectomy, *see* hysterectomy, laparoscopic and robot-assisted
laparoscopic myomectomy, *see* myomectomy, laparoscopic and robot-assisted
laparoscopic radiofrequency ablation (lap-RFA), 150, *150*, 152
laparoscopic supracervical hysterectomy (LSH), 145–146
laparoscopy, 1, 84, 247, 276, 288, 322, 422
  abdominal entry/trocar placement, 42–43
    direct trocar placement, 43
    direct visual entry, 43
    indirect/closed entry, 43, *43*
    open entry, 43, *44*
  endometriosis procedures, 5
  energy systems, 55–56 (*see also* electrosurgery)
  fellowship, 4
  gynecologic, 35
  imaging, 34–35
  instruments, *36*, 36–38, *37*, *38*
  late 20th century, 3–4
  MIS advancements, 4–5
  operative, 1
  operating room setup
    ergonomics, 34
    patient safety culture, 34
    surgical team, 34
  in 1970s, 2
  timeline, *1*
  tissue retrieval, 44–46, *45*
  video technology, 2–3
  vNOTES, 4
lateral cutaneous femoral nerve, 168
LeFort colpocleisis, 369
leiomyoma, *see also* uterine leiomyoma
  diagnosis/imaging, 133
  fertility, 133
  FIGO classification, 133
  HRQoL, 153–154
  management, 133
  menstrual bleeding, 154
  MRgFUS, 152–153
  myomectomy (*see* myomectomy, hysteroscopic; myomectomy, laparoscopic and robot-assisted)
  patient presentation, 133
  patient selection
    MRgFUS, 153
    RFA, 153
    UAE, 153
  preprocedural evaluation, 153
  prevalence, 133
  radiofrequency ablation (RFA), *150*, 150–152, *151*
  reducing blood loss
    adhesion prevention, 136
    intraoperative management, 135–136
    myoma enucleation, 136
    preoperative management, 135
    suture, 136
    tissue extraction, 136–137
  reintervention rates, 154, **154**
  SSS, 153–154
  UAE, 152, *152*
  volume reduction, 154, **154**
Lichtleiter, 1
local anesthesia, 224–225, 436
log-rank test, 25
low dose vaginal estrogen, *see* vaginal estrogen
lower urinary tract obstruction (LUTO), 445
luteal out-of-phase (LOOP), 99

M

magnetic resonance-guided focused ultrasound surgery (MRgFUS), 152–153
magnetic resonance imaging (MRI), 85, 104, 114, 133, 244, 386, 421, 452
Magrina–Bookwalter retractor, *49*
manual morcellation, 45, 137
Mayer–Rokitansky–Küster-Hauser (MRKH) syndrome, 121, 290–291
May–Thurner syndrome (MTS), 69
medical cannabinoid therapy, 162
medical devices
  customer discovery process, 457
  disruptive innovations, 458, *458*, *459*
  economic perspective, 459–460
  innovation clusters, 460–461
  layered human processes, *462*
  manufacturers, 461
  market factors, 457–458
  patents, 458–459
  pillars, 457
  preclinical facilities, 459–460
  research and development (R&D) process, 459, *460*
menopause, 109, 133, 184, 190, 232, 304
  genitourinary symptom, 405, 417
  premature, 310, 311
  therapeutic management, **305**
menstrual physiology, 94–96
methotrexate (MTX)
  adverse reactions, 82
  combination protocols, 82
  ectopic pregnancies, 83
  fertility, 83
  local injection, 85
  multiple dose, 82
  protocol comparison, 82
  single dose, 81–82
  treatment, 82–83
  two dose, 82
microfibrillar collagen (MFC), 430
microlaparoscopes, 35
minimally invasive surgery (MIS), 28, 321, 452
  intraoperative considerations
    abdominal entry, 453–454
    morcellation and closure, 454
    patient positioning, 453, *453*
    prophylaxis, 452–453
    ventilation, 454
    visualization, 454, *454*, *455*
  postoperative management
    ERAS, 455
    management of comorbidities, 455
    prophylaxis, 454–455
  preoperative considerations
    preoperative evaluation, 452
    surgical approach, 452
    testing and optimization, 452
mini-resectoscope, 233
missed abortion, 257–258, *258*
modern laparoscopy, 2
Morphological Uterus Sonographic Assessment (MUSA), 70
Müllerian anomalies
  cervical anomalies, 249
  classification, 242
  clinical implications
    uterine anomalies, 242–243
    uterine cervix, 243
    vaginal anomalies, 243
  complex, 250, *250*
  diagnosis
    hysterosalpingography (HSG), 243
    hysteroscopic, 244, *244*
    magnetic resonance imaging (MRI), 244
    sonohysterography (SHG), 244
    transvaginal sonography (TVS), *243*, 243–244
  treatment, 244–245, *245*
  uterine anomalies, 245
    dysmorphic uterus, 245–246, *246*
    miniaturized instruments, 247–249, *248*, *249*
    resectoscopic, 247
    septate uterus, 246–247, *247*
  vaginal anomalies
    bicorporeal uterus, 250
    longitudinal septum, 249–250, *250*
multimodal imaging, 421–422
muscular (partial-thickness infiltration, nodule), 193
myomectomy, hysteroscopic, 113, 235, 236

myomectomy, laparoscopic and robot-assisted, 133–134, *see also* myomectomy, hysteroscopic; uterine leiomyoma
instrumentation, 135
laparoscopic port placement (LSC), 134, *134*
reducing blood loss
adhesion prevention, 136
intraoperative management, 135–136
myoma enucleation, 136
preoperative management, 135
suture, 136
tissue extraction, 136–137
robotic trocar placement, *134*, 134–135
trocar placement, 134
uterine manipulator, 134

N

National Institute for Health and Care Excellence (NICE), 83
natural conception, 133
natural orifice transluminal endoscopic surgery (NOTES), 4, *see also* vaginal natural orifice transluminal endoscopic surgery (vNOTES)
near-infrared range (NIR) imaging, 333
nerve injuries
anti-slip devices, 41–42, *42*
gynecologic surgery, 168–169, **170**
lithotomy position, 41, *41*
lower limb, 39–40, **40**
obese patients, 41
patient positioning, 38–42
upper limb, **40**, 40–41
nerve-sparing endometriosis surgery, 172
nerve-sparing radical hysterectomy, 172
neuromuscular electrical stimulation (NMES), 171
neuropelveology
bladder hypersensitivity, 169
diagnosis, 166
extremity dermatomes, 169, *171*
gynecologic surgery, 168–169, **170**
hypogastric plexus, 169
incidence, 166
lumbar plexus, 167–168, *168*, *169*
novel treatments
LION procedure, 171, *171*
nerve-preserving surgeries, 172–173, *173*
pudendal nerve stimulation, 171–172, *172*
pelvic innervation, 166–167
pelvic somatic nerves, 169, 170, **170**
sacral plexus, 166–167, *167*, *171*
sympathetic innervation, 167
treatment, 166, 170
neuropraxia, 169
neurotmesis, 169
nonobstetric rectovaginal fistula
causes, **401**
colovaginal fistula, 401
diagnosis and classification, 401
enterovaginal fistula, 401
rectovaginal fistula, 401
surgical repair, 401–402
nonobstetric urogenital fistulas (NOF)
classification, 397, **397**, *397*
diagnosis, 396–397
flaps and sealants, 401
management, 398–399, *399*
operative and patient risk factors, **396**
postoperative care, 401
prevention, 397–398, *398*
surgical techniques, 399
timing of repair, 397–398, **399**
urethrovaginal fistula, 399, *400*
vesicouterine and vesicocervical, 400–401
VVF
abdominal approach, 399–400
vaginal approach, 399
nonsteroidal anti-inflammatory drugs (NSAIDs), 29, 161, 179, 180, 218, 224, 455
number needed to treat (NNT), 27, 219

O

obesity, 41, 108, 140, 336, 455
definition, 452
tilt test, **453**
observational studies
case-control study, 23, *23*
case report, 22
cohort study, 22–23, *23*
levels of evidence, *23*, 23–24
null hypothesis, 24
statistical power, 24
systematic reviews, 23
obstetrical uterine lacerations
prevention, 396
ureterouterine fistula, 395–396
vesicouterine fistula, 395
obstetric anal sphincter injuries (OASIS), 392
obstetric lacerations, *see also* nonobstetric urogenital fistulas (NOF); ureterouterine fistula
anatomy, 392, *393*
classification, 392, **392**
diagnosis, 392–393
repair instruments and supplies, 393–395, *394*, *395*
obturator nerve, 168
office hysteroscopy, *see also* hysteroscopy
economic benefits, 229, 230
gynecologic aspects
efficacy, 222–223
indications, 222
see-and-treat approach, 223
surgical aspects
distention media, 227
distention media delivery systems, 227–228, *228*
equipment, 225–227, *226*, *227*
hysteroscopy equipment maintenance, 228
office hysteroscopy setup, 223
pain management, 223–225
vaginoscopy, 229, *230*
opioids, 29, 161, 224
oral antispasmodics, 224
Ovarian-Adnexal Reporting & Data System (O-RADS™), 66
ovarian endometrioma, 176, *177*
ovarian pregnancies, 88
ovarian tissue cryopreservation (OTC), 220
oxidized regenerated cellulose (ORC), 429, *429*

P

PALM, *see* polyps, adenomyosis, leiomyomas, malignancy/hyperplasia (PALM)
PALM-COEIN, *see* polyps, adenomyosis, leiomyomas, malignancy/hyperplasia-coagulopathy, ovulatory disorders, endometrial dysfunction, iatrogenic, and not otherwise classified (PALM-COEIN)
patient positioning, 38–39, 195, 201, 337–338, *423*, 435, 453, *453*
pediatric and adolescent gynecology (PAG)
adolescent endometriosis, 291
laparoscopic considerations, 287–289, *288*
nonobstructive Müllerian and hymenal anomalies, 290, *290*
obstructive Müllerian and hymenal anomalies, 289, *289*
postoperative care
preoperative assessment and care, 287
pelvic anatomy, 392
anterior abdominal wall, 7, *7*, *8*
blood supply, 13, *13*
brim, 11, *11*
broad ligament, 11–12
extraperitoneal surgical spaces, 12–13
innervation, 13, *14*
neuroanatomy, *14*
pararectal space, 12
paravesical space, 12
presacral space, *9*, 9–11
rectovaginal space, 12–13
retropubic space, 12
sidewall, 11
superficial peritoneal anatomy, 7–8, *8*
surgical, 7
surgical dissection, 14
vesicocervical space, 12
pelvic autonomic nerves (PANs), 172–173, *173*
pelvic congestion syndrome (PCS), 69, 159
pelvic floor distress inventory (PFDI), 362, 380
pelvic floor dysfunction, 66, *see also* constipation; fecal incontinence; urinary incontinence
pelvic floor impact questionnaire (PFIQ), 362
pelvic floor physical therapy (PFPT), 160, 162, 362, 381
pelvic organ prolapse (POP), 51
colpocleisis, *368*, 369
evaluation, 362
graft POP surgery for level I, 365–366
level I/apical, **365**
native tissue POP surgery, 366–367, *367*
native tissue vaginal procedures, 367, *368*, 369
nonsurgical treatment, 362
outcome measures, **364**
surgical treatment, 362–365, *365*
Pelvic Organ Prolapse Quantification (POP-Q), 362, *363*
pelvic splanchnic nerves (PSN), 167, 172, *173*
percutaneous tibial nerve stimulation (PTNS), 163
pericardial endometriosis, 192–193, 198, *199*
perimenopause, 99, 118, 232, 311
perineal scar endometriosis, 202
peritoneal (superficial implant), 193
Pink Pad® Trendelenburg Patient Positioning System, 41, *42*
placenta accreta spectrum (PAS), 86, 257, 265, 272
placental site trophoblastic tumor (PSTT), 253, 257
plain surgical gut, 72

point of care ultrasound (POCUS), 89
poliglecaprone 26 (MONOCRYL), 72, 75
polycystic ovarian syndrome (PCOS), 16, 99
polypropylene (PROLENE), 75
polyps, adenomyosis, leiomyomas, malignancy/hyperplasia (PALM)
  adenomyosis (AUB-A), 233–234, *234*
  endometrial and cervical polyps (AUB-P), 233, *233*, *234*
  leiomyomas (AUB-L), 234–236, *235*
  malignancy and hyperplasia (AUB-M), 236–238, *237*
polyps, adenomyosis, leiomyomas, malignancy/hyperplasia-coagulopathy, ovulatory disorders, endometrial dysfunction, iatrogenic, and not otherwise classified (PALM-COEIN) 94, *95*, 104, *121*, 232
positron emission tomography (PET), 68, 344
postoperative nausea and vomiting (PONV), 29, 437
pregnancy of unknown location (PUL), 80
progesterone 18–19, *97*
  contraceptives, 181
  endometriosis, 181–182, 218
  ectopic pregnancies, 82, 89
  selective progesterone receptor modulators (SPRM), 181–182
  serum, in intrauterine viable pregnancy, 80
  uterine leiomyoma, 108, 109, 110
progesterone-associated endometrial changes (PAECs), 181
progression-free survival (PFS), 321, 344
prolactin releasing hormone (PRH), 16
pudendal nerve, 13, 40, 166–167, 380
pudendal nerve stimulation (PNS), 163, 171–172, *172*

R

randomized clinical trials (RCTs), 28, 84, 180
recurrent pregnancy loss (RPL), 98, 133, 222, 260
retained products of conception (RPOC), 252
  classification systems, 253, *254*
  clinical manifestations, 252, *252*
  diagnosis, 252–253
  differential diagnosis, 253–254
  early consequences, 254
  Gutenberg classification, 253, *254*
  management strategies
    nonsurgical, 254
    surgical, 255
  role of hysteroscopy, *252*, *255*
    complications, 257
    congenital uterine anomalies, 257
    efficacy and outcomes, 256–257, *257*
    intrauterine adhesions, 257
    miniaturized instruments, 256
    pathology confirmation, 257
    reproductive outcomes, 257
    resection rate, 257
    resectoscopic removal technique, 256, *256*
    tissue removal systems, 256
retrograde menstruation, 175
return electrode monitoring systems (REM), 58
Risk of Ovarian Malignancy Algorithm (ROMA), 315
robotic technology, 4
  hysterectomy (*see* hysterectomy, laparoscopic and robot-assisted)
  myomectomy (*see* myomectomy, laparoscopic and robot-assisted)
  surgeon console, 38, *39*
  vision cart, 38
Robotic *versus* Open Hysterectomy in Cervical Cancer (ROCC), 347
RUMI® II System, *36–37*

S

sacral neuromodulation (SNM), 163, 383
sacrocolpopexy/sacrohysteropexy, *366*, 366–367
sacrospinous ligament fixation (SSLF), 366
saline infusion sonohysterography (SIS), 67
same-day discharge (SDD), 29–30
selective progesterone receptor modulators (SPRM), 181–182
self-modulation behavior therapy, 160
sentinel lymph node (SLN) biopsy, 332
short tau inversion recovery (STIR), 67–68
silk suture, 75
skeletal muscle relaxants (SMRs), 162
Society of American Gastrointestinal Endoscopic Surgeons (SAGES), 3
Society of Reproductive Surgeons (SRS), 4
Sonata® system, *151*
sonohysterography (SHG), 104, 222, 244, 273
Spectral Doppler, 66
spinal cord stimulation (SCS), 163
squeeze bag system, 228
stress urinary incontinence (SUI)
  Burch procedure, *373*
  evaluation, 368, 372
  nonsurgical treatment, 372
  outcome measures, **369**
  surgical management, *370*
  surgical treatments, **371**, 372–373
subendometrial myometrium, 117
superficial endometriotic lesion, 175–176, *176*
superior gluteal nerve, 166
superior hypogastric plexus (SHP), 172
suprapubic cystostomy
  Bonanno cystostomy, 412, *412*
  complications, 413
  cystostomy tube placement, 412, *413*
  metal suprapubic trocars, *412*
  procedural steps, 413
  Stamey Malecot cystostomy, 412, *413*
  Supra-Foley cystostomy, 412, *413*
surgical site infections (SSI), 139
SURGIFLO, 430
suture
  characteristics and properties, **73–74**
  coated multifilament, 72
  leiomyoma, 136
  material properties
    absorbable natural suture, 72
    absorbable synthetic suture, 72, 75
    chromic surgical gut, 72
    nonabsorbable natural suture, 75
    nonabsorbable synthetic suture, 75
    plain surgical gut, 72
    polypropylene (PROLENE), 75
  poliglecaprone 26 (MONOCRYL), 72, 75
  selection, 75
  silk, 75
symptom severity scores (SSS), 153
synechiae, *see* intrauterine adhesions (IUAs)
synthetic mesh, 76, **76**, 77, **77**

T

testosterone, 305
thoracic endometriosis syndrome (TES), 192
thyroid stimulating hormone (TSH), 16
thyrotropin releasing hormone (TRH), 16, 99
time-to-event (TTE) data, 25–26
topical hemostatic agents (THAs), 316, 429
tranexamic acid (TXA), 20, 89, 135
transabdominal cerclage
  laparoscopic/robotic, *440*, 440–443, *441*, *442*
  surgical management strategies, 439–440
transcervical adhesiolysis (TCA), 263, *264*
transcervical evacuation, 85
transcervical radiofrequency ablation (T-RFA), 150, *150*, 152
transcutaneous electrical nerve stimulation (TENS), 163, 224
transvaginal sonography (TVS), 243, 253
transvaginal ultrasound (TVUS), 67, 80–81, 86, 103, *120*, *124*, *125*, 130, 217, 233, 315, *442*
TrenGuard™ Trendelenburg Patient Restraint, 42, *42*
tricyclic antidepressants (TCA), 39, 99, 162, 238
tubal sterilization
  abdominal access
    laparoscopy, 276
    mechanical devices, *277*, 277
    minilaparotomy, 276
    modified Pomeroy, 276
    salpingectomy, 276
    surgical electrocautery, 276–277
  fallopian tube anatomy, 274, *274*
  general considerations, 274–275
  history, 274
  normal pelvic anatomy, 274, *274*
  opportunistic salpingectomy, 275, *275*
  transcervical techniques, 277–278
tuboplasty, 280
  distal tubal occlusion, 282–284
  embryologic abnormalities, 285–286
  endometriosis of the fallopian tube, 284, *284*, *285*
  gynecologic aspects, 280–281
  proximal tubal occlusion, 282, *283*
  surgical aspects, 281–282
  tubal anastomosis, 285
twin–twin transfusion syndrome (TTTS), 446, *448*
two cell theory, 18

U

ultrasonography, 113, 159, 421
upper paracolpium, 12
urethral masses
  Skene's gland cysts
    diagnosis and imaging, 404
    incidence and etiology, 404, *404*
    management, 404
    presentation, 404
  urethral caruncle
    diagnosis and imaging, 405
    incidence and etiology, 404–405, *405*
    management, 405
    presentation, 405
    urethral prolapse, *405*, 405–406

urethral diverticula, *see also* vaginal masses
diagnosis and imaging, 403, *404*
incidence and etiology, 403
management, 403–404
presentation, 403, *403*
ureteral stents, 397, 409, 410–411, 427
urethrovaginal fistula (UVF), 399, *400*
urinary incontinence
antimuscarinic medications, 381–382
Beta-3 adrenergic, 382
bladder diary, 379
bladder retraining, 381
Bristol Stool Form Scale, *385*
diagnosis and treatment, *382*
estrogen, 382–383
evaluation, 379
Kegel exercise, 381
neurogenic bladder, 385
nonoperative (conservative) management, 381
onabotulinum toxin A, 383
pelvic floor muscle, 381
pharmacologic (medical) management, 381
physical examination, 380–381
posterior tibial nerve stimulation, 383
questionnaires, 379–380
refractory overactive bladder, 383
SNM, 383
types, 379
urinary retention, 383, 385
urodynamics, 381
uterine artery embolization (UAE), 68, 87, 113, 152, *152*
uterine cancer, *see also* cervical cancer; gynecologic cancer
classification, 327
epidemiology, 327
fertility sparing surgery, 339
genetics, 328
histologic subcategorizations, 327
hysteroscopic resection, 339
lymphadenectomy
accuracy of SLN biopsy, **335**, 335–336
choice of injection site, 333
choice of tracer, 332–333
intraoperative complications, 331
patterns of lymphatic drainage, 333
postoperative complications, 331–332
selective staging algorithms, 332
sentinel lymph node (SLN) biopsy, 332–336
ovarian preservation, 339
pathophysiology, 327–328
progestin-releasing IUDs, 339
risk factors, 327–328
surgery for advanced, 338–339
surgical modalities
complete lymphadenectomy, 336
laparoscopic *vs.* robotic-assisted laparoscopy, 337
patient access, 336
patient positioning, 337–338
uterine manipulation, *329*, *330*, *331*, 337
surgical staging, 328–329, **328**
elements, 329–330
importance, 330
uterine fibroid embolization (UFE), 69, 152, *see also* uterine artery embolization (UAE)
uterine leiomyoma, *see also* myomectomy, hysteroscopic; myomectomy, laparoscopic and robot-assisted
cervical, *109*
evaluation, 112–114
histological studies, fibroid tissues, 110–111
intramural, *108*
menstrual bleeding, 154
MRgFUS, 152–153
pathogeneses, 108–110
patient selection, 153
preprocedural evaluation, 153
procedure outcomes, 153–154, **154**
radiofrequency ablation (RFA), 150–152, *150*, *151*
reintervention rates, 154
symptomatology, *111*, 111–112, *112*
uterine fibroid embolization, 152
volume reduction, 154
uterosacral ligament suspension (USLS), 51, 362, 366, *367*

V

vaginal cuff dehiscence (VCD), 147
vaginal estrogen, 295, 300, 306, **306**, 362, 405
vaginal masses
Bartholin's gland cysts
diagnosis and imaging, 407
incidence and etiology, 406
management, 406
presentation, *406*, 406–407
epidermal inclusion cysts, 407
Gartner duct cysts
diagnosis and imaging, 406
incidence and etiology, 406
management, 406
presentation, 406
vaginal maturation index (VHI), 306
vaginal natural orifice transluminal endoscopic surgery (vNOTES), 4, 44, 47, 139
laparoscopic access, *52*, *53*
potential advantages, 53
room set up, *52*
vaginal surgery, 47
adnexal surgery, *50*, 51
anterior cul-de-sac, *50*, 51
apical suspension, 51
cystoscopy, 51
incision, 49, *50*
Lone Star retractor, *49*
morcellation techniques, 51
perioperative complications, 51–52
positioning, 48, *48*
posterior cul-de-sac, 49, *50*
preoperative considerations
draping, 48–49
positioning, 48
prepping, 48–49
rectal examination, 51
retractors, *49*
round ligaments, *50*, 51
self-retractors, *49*
uterine vessels, *50*, 51
utero-ovarian, *50*, 51
uterosacral ligaments, *50*, 51
ValleyLab™ F10 Energy Platform, 35, *36*
variants of uncertain significance (VUS), 309
venous thromboembolism (VTE), 427, 452
vesicovaginal fistula (VVF) repair, 399, **401**, 412
VICRYL RAPIDE, 75
videolaparoscopy, 2
virtual reality, 225
volume acquisition, 67

W

Walking Index for Spinal Cord Injury (WISCI-II), 171

X

xenografts, 76–77