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Review

EORTC–GCG process quality indicators for ovarian cancer surgery

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ABSTRACT

Introduction: Surgery is the mainstay of staging and treatment of ovarian cancer. Optimal quality of ovarian cancer surgery implies complete staging and removal of all macroscopic tumour with minimal harm to the patient in order to ensure best patient outcome. However, variation in the quality of ovarian cancer surgery is apparent. In order to assess and improve the quality of care, quality indicators can be used.
Methods: To identify candidate quality indicators, a literature search was performed using relevant MESH terms. These were assessed for validity, feasibility and measurability.
Results: Five quality indicators for staging of presumed early-stage ovarian cancer and six for primary debulking surgery for advanced disease are proposed.
Conclusion: The defined quality indicators can be used to monitor and improve the quality of surgery for ovarian cancer.

1. Introduction

In Europe, the annual incidence of cancer is estimated at between 338 and 447 per 100,000 individuals.[1] Ovarian cancer represents 4% of all cancers in women, and is ranked sixth most frequent for mortality.[2] The keystone of ovarian cancer treatment is surgery. Staging of ovarian cancer according to the International Federation of Gynaecology and Obstetrics (FIGO) is based on findings during explorative laparotomy and histopathology (Table 1). When the disease has spread throughout the peritoneal cavity, cytoreductive surgery with the removal of all macroscopic disease is related to better progression-free and overall survival.[3]

EUROCARE studies reviewed survival figures for common and rare malignancies in more detail, and demonstrated a wide variation in survival between the participating European countries. These variations can be explained by a number of factors, including differences in population, screening programmes, facilities for radiotherapy, access to new cancer drugs and also differences in the quality of delivered care.[1,4]

Quality of care has been defined by the Institute of Medicine as 'the degree to which health services for individuals and populations increase the likelihood of desired health outcomes and are consistent with current professional knowledge'.[5] Good quality means providing patients with appropriate

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Table 1 – ovarian cancer staging according to FIGO.[27]

Stage I	*Tumour limited to the ovaries*
IA	Tumour limited to one ovary; capsule intact, no tumour on ovarian surface; no malignant cells in ascites or peritoneal washings
IB	Tumour limited to both ovaries; capsule intact, no tumour on ovarian surface; no malignant cells in ascites or peritoneal washings
IC	Tumour limited to one or both ovaries with any of the following: capsule ruptured, tumour on ovarian surface, malignant cells in ascites or peritoneal washings
Stage II	*Tumour involves one or both ovaries with pelvic extension*
IIA	Extension and/or implants on uterus and/or tube(s); no malignant cells in ascites or peritoneal washings
IIB	Extension to other pelvic tissues; no malignant cells in ascites or peritoneal washings
IIC	Pelvic extension (IIA or IIB) with malignant cells in ascites or peritoneal washings
Stage III	*Tumour involves one or both ovaries with microscopically confirmed peritoneal metastasis outside the pelvis and/or regional lymph node metastasis*
IIIA	Microscopic peritoneal metastasis beyond pelvis
IIIB	Macroscopic peritoneal metastasis beyond pelvis 2 cm or less in greatest dimension
IIIC	Peritoneal metastasis beyond pelvis more than 2 cm in greatest dimension and/or regional lymph node metastasis
Stage IV	*Distant metastasis (excludes peritoneal metastasis)*

services in a technically competent manner, with good communication, shared decision making and cultural sensitivity.[5] Quality assurance can be defined as all those planned and systematic actions necessary to provide adequate confidence that a product or service will satisfy given requirements for quality.[6]

From the perspective of the gynaecological surgeon, this would mean that in the case of ovarian cancer, all visible tumour can be removed without complications, no harm is done to the patients and an optimal survival rate is achieved. In reality, however, restrictions to the extent of surgery are often to be made, due to tumour or patient-related factors such as invasion in vital organs or co-morbidities, but also due to the technical skills of the surgeon.

Quality of care can be assessed and optimised by the use of structural, process and outcome quality indicators.[5,7] Structural indicators refer to resources, e.g. access to specific technologies, the number of staff and proportion of specialists to other doctors. Process indicators refer to what providers do and how well they do it, both technically and interpersonally. Technical process refers to whether the right choices are made in diagnosing and treating the patient and to whether care is provided in an effective and skilful manner. Whether care is effective can be judged according to the evidence from good studies that show a link between a particular process and better outcomes. Outcomes are defined as states of health or events that follow care and that may be affected by health care.[5,7]

The need for strict quality control procedures in cancer care and more specifically in surgical oncology has been repeatedly emphasised, as much in daily practice as in clinical trials.[5,8,9]

Indeed, structural factors such as being operated on by a gynaecological oncologist and in a specialised hospital have been associated with a better survival for ovarian cancer patients.[10] Hence, centralising surgery for gynaecological oncology has been proposed as a way to improve the quality of surgical care by several authors.[11–13]

A risk-adjusted model for studying outcomes in gynaecological surgery has been developed and found useful in identifying areas ready for quality improvement with the aim of subsequently reducing peri-operative morbidity and mortality.[14,15]

The identification of process quality indicators for surgery is a challenging task due to the lack of quantifiable parameters.[16] However, process quality indicators have the advantage that they are more easily measurable in a timely fashion, that no risk-adjustment is necessary and that they give 'actionable' feedback for quality improvement initiatives.[17–19] Process quality indicators are especially useful for physicians and departments who want to audit and improve their practice. Technical process indicators are often preferred by different stakeholders.[20]

The aim of this paper is to develop a list of process quality indicators for ovarian cancer surgery that can be used by gynaecological oncology surgeons and gynaecological oncology units to audit and improve their practice in an easy and practical way. We focus on two routinely performed operations for ovarian cancer: staging laparotomy for ovarian cancer macroscopically confined to the pelvis and debulking laparotomy for advanced-stage (FIGO stage IIIB-IV) ovarian cancer. Although the success of surgery depends on multiple peri-operative factors, e.g. correct and timely diagnosis and the anaesthetic and post-operative care, in this paper, we limited the list of indicators to process quality indicators related to the surgery itself.

2. Methods

To develop the process indicators, the methodology as described by Rubin and colleagues was followed.[17]

First, we identified candidate quality indicators for ovarian cancer surgery in the literature from existing guidelines and expert opinion by searching the PUBMED online bibliographic database. The terms used for the literature search were as follows: quality, quality assurance, quality control, technique, variability, guidelines, delay, timing, prognosis, outcome and survival combined with surgery, operation, ovarian cancer, staging and debulking. The bibliography of each article was reviewed for other potentially relevant papers.

As a next step, the available scientific evidence that a potential process quality indicator positively affects outcome

was reviewed. Priority was given to systematic reviews, meta-analyses and randomised controlled trials. If such level of evidence was not available, then lower levels of evidence were evaluated. Guidelines and standards of care formulated by international societies were also reviewed, as an acceptance of a quality indicator by the gynaecological oncology community will add to its validity.

Candidate process quality indicators were selected if they were supported by sufficient high level scientific evidence or were generally accepted by international gynaecological oncology societies, if improvement of the process was under the direct control of the surgeon and if the necessary data for the evaluation were considered easily accessible in the medical notes and surgical report.[17,19]

3. Results

The proposed process quality indicators for staging laparotomy of presumed early-stage ovarian carcinoma proposed by the Gynecologic Oncology Group and the European Organisation for Research and Treatment of Cancer (EORTC–GCG) are summarised in Table 2. The proposed process quality indicators for cytoreductive surgery for advanced-stage ovarian cancer are summarised in Table 3. We further discuss the supporting evidence of the quality indicators below, first for early-stage ovarian cancer, then for advanced-stage ovarian cancer.

3.1. *Quality indicators for staging laparotomy for ovarian cancer macroscopically confined to the pelvis*

3.1.1. *Timing of staging laparotomy*

Theoretically, treatment of patients with a suspicious ovarian mass should not be delayed after the first symptoms or signs appear, to avoid further tumour growth and stage progression. Furthermore, delaying treatment after cancer diagnosis is very distressing for patients.[21]

No randomised trials, systematic review or meta-analysis have investigated the effect of delay of treatment after diagnosis on the survival outcome of patients with early-stage ovarian cancer. The influence of waiting time before treatment on the outcome of ovarian cancer patients has only been investigated in two small studies. Kirwan and colleagues investigated the effect of delays in primary care referral on the survival of ovarian cancer patients in a retrospective audit of 135 patients. No evidence was found that treatment delay adversely affected survival at 18 months, but only a very small number of patients had a significant delay before they were treated.[22] Lehner and colleagues found that timing of laparotomy after laparoscopy for an ovarian mass, later found to be malignant, was a factor predictive of the stage of the disease.[23]

Indirect support for the importance of timely treatment of ovarian cancer can be found in the studies investigating treatment delays in other cancers. A systematic review of the influence of waiting time for radiotherapy in different types of cancer showed an increased risk of local recurrence with increasing waiting time.[24] A retrospective analysis of 4399 melanoma patients showed a survival benefit for patients, who were treated in a rapid access clinic with reduced waiting times.[25]

In spite of the scarcity of evidence, avoiding treatment delay is considered a very important aspect of cancer treatment by the community. Different governments have set up targets to ensure timely treatment of cancer patients.[4,24] Gagliardi and colleagues developed ovarian cancer surgery quality indicators using a modified Delphi approach, in which a team of experts comes to a consensus list based on the available evidence and discussion. The expert panel selected the 'proportion of patients who undergo definitive surgery or treatment within two weeks of decision to treat' as one of the prioritised quality indicators.[11]

To specify the quality measure for timely treatment; the United Kingdom (UK) National Cancer Plan can serve as an example. It states that all patients should start cancer treatment within one month after urgent referral, except for good clinical reasons or their personal choice. The reasons for a potential delay should be documented.[26]

3.1.2. *Type of abdominal incision*

There is a general consensus that staging laparotomy for ovarian cancer grossly confined to the pelvis should be performed through a vertical incision. A vertical incision is considered necessary to ensure good access to the whole abdomen, including the posterior side of the abdominal cavity, diaphragms and the retroperitoneal space.

Guidelines of international organisations like FIGO, the Gynecologic Oncology Group (GOG) and the European Organisation for Research and Treatment of Cancer (EORTC) concur with this, all stipulating that a laparotomy to stage ovarian cancer should be performed through a midline incision.[27–29]

Table 2 – Proposed EORTC–GCG quality indicators for staging laparotomy in ovarian cancer grossly confined to the pelvis.

Quality indicator	Accepted standard (%)
1. % of patients with a suspicious ovarian mass undergoing staging laparotomy within 1 month after decision to treat or documented clinical or patient-related reason for delay	⩾95
2. % of performed staging laparotomies for an ovarian mass suspected to be malignant performed through a vertical incision	⩾95
3. % of performed staging laparotomies in which all of the following procedures are included: total hysterectomy, bilateral salpingo-oophorectomy, cytology of the peritoneal cavity, infracolic omentectomy, random peritoneal biopsies and systematic pelvic and para-aortic lymphadenectomy if medium or high risk features	⩾95
4. % of surgery reports with documented presence or absence of cyst rupture before or during surgery	⩾95
5. % of surgery reports with documented presence or absence of dense adhesions, % of dense adhesions biopsied	⩾95

Table 3 – Proposed EORTC–GCG quality indicators for primary debulking surgery in stage III–IV epithelial ovarian cancer.

Quality indicator	Accepted standard (%)
1. % of patients with advanced-stage ovarian cancer undergoing debulking laparotomy within 31 days after decision to treat or documented clinical or patient-related reason for delay	⩾95
2. % of patients undergoing debulking surgery with the spread of disease fully assessed for operability at the start of surgery and initial findings documented in the operation notes	⩾95
3. % of debulking operations including a hysterectomy, bilateral salpingo-oophorectomy and infracolic omentectomy when the surgeon considers optimal debulking feasible	⩾95
4. % of debulking operations for advanced ovarian cancer at the end of which complete cytoreduction, defined as no macroscopic residual disease at the end of the operation, was achieved	⩾50
5. % of debulking operations including a pelvic and para-aortic lymphadenectomy when otherwise complete debulking has been achieved	⩾90
6. % of debulking operations for which the size and location of residual disease at the end of the operation is documented in the operation notes	⩾95

This consensus is supported by a small retrospective study. McGowan found that 71% of ovarian cancer patients who were operated via a transverse incision had an incomplete intra-operative evaluation of the extent of disease compared with only 42% of the group operated via a vertical incision.[30]

As this requirement is generally accepted by all international organisations concerned, we expect a vertical incision to be used in 100% of the patients undergoing laparotomy for an ovarian mass suspected to be malignant.

3.1.3. *Staging procedures for ovarian cancer macroscopically confined to the pelvis*

In daily practice, when performing surgery for an ovarian mass without visible metastases, the decision to perform a full staging procedure will depend on the assessment of the nature of the mass. The use of intra-operative frozen section analysis is a valuable tool to differentiate malignant from benign ovarian masses, with acceptable sensitivity and specificity.[31,32]

If an ovarian mass is identified as being an invasive malignancy, further procedures should be completed to allow correct FIGO staging. To fulfil all FIGO staging requirements (Table 1), the following procedures need to be carried out:[27]

- Any ascites or peritoneal fluid should be sent for cytological evaluation.
- Full exploration of entire pelvic and abdominal contents, with biopsies of suspicious areas.
- When no obvious extra-ovarian spread is noted, random peritoneal biopsies from the peritoneal reflection of the bladder, posterior cul-de-sac, both paracolic gutters, subdiaphragmatic surfaces and pelvic sidewall should be taken.
- Hysterectomy and bilateral salpingo-oophorectomy is recommended.
- the infracolic omentum should be removed, even if clinically uninvolved.
- A pelvic and para-aortic lymphadenectomy should be performed.

Pelvic and para-aortic lymphadenectomy theoretically can be omitted in well differentiated and stage IA ovarian tumours, as lymph node metastases are extremely rare in these cases. However, information on histology and staging is usually not available during surgery. Re-staging procedures for lymphadenectomy can be omitted in this patient group.[33]

It is of utmost importance to carefully explore all the above-mentioned areas during the staging procedure. The sample technique and exact numbers of biopsies needed appear to be less important. One study investigated the quality of diaphragmatic scrape and wash specimens in 46 ovarian cancer patients. Although wash specimens had a better quality when scored by a pathologist, there was a perfect agreement between washes and scrapes.[34]

Although no randomised controlled trials or meta-analyses support the benefit of complete staging, it is absolutely necessary for tailoring of adjuvant chemotherapy. Only if fully staged, patients with a well differentiated early-stage ovarian cancer (FIGO stage Ia–IIa, grade 1) can be spared chemotherapy.[35–37] Without complete staging, a significant number of higher staged cancers are missed. Both Young and Soper showed that approximately 30% of patients with assumed early-stage ovarian cancer were upstaged, when an initial inadequate staging procedure was completed during a second procedure.[38,39] Lin and colleagues found 37% positive staging biopsies in patients with serous borderline tumours.[40]

Staging is not only important in clinical decision making, the accuracy of staging has also been demonstrated to be a prognostic factor in stage I ovarian carcinoma. In the EORTC ACTION trial, investigating the benefit of adjuvant chemotherapy for early ovarian cancer, detailed staging guidelines were given in the protocol. Staging adequacy, categorised according to completeness as shown in Table 4, was a statistically significant prognostic factor for overall and recurrence-free survival in the univariate and multivariate analysis.[36] Furthermore, three retrospective studies in 351, 138 and 125 patients have shown a survival benefit for comprehensively staged patients, independent of the use of adjuvant chemotherapy.[41–43]

These staging guidelines have been widely adopted by international organisations, and are included in many local guidelines with only small adaptations, e.g. regarding the number of biopsies and washings to be taken.[28,29,35,41,42,44–54] The expert panel developing ovarian cancer quality indicators using a modified Delphi approach considered adequate staging according to FIGO an important quality indicator.[11]

Table 4 – Staging guidelines of the EORTC ACTION trial.[36]

Surgical staging category	Staging guidelines following bilateral salpingo-oophorectomy and total abdominal hysterectomy
Optimal	Inspection and palpation of all peritoneal surfaces; biopsies of any suspect lesion for metastases; peritoneal washings; infracolic omentectomy; (blind) biopsies of right hemi diaphragm, of right and left paracolic gutter, of pelvic sidewalls, of ovarian fossa, of bladder peritoneum and of cul-de-sac; sampling of iliac and peri-aortic lymph nodes
Modified	Everything between optimal and minimal staging
Minimal	Inspection and palpation of all peritoneal surfaces and retroperitoneal area; biopsies of any suspect lesion for metastases; peritoneal washing; infracolic omentectomy
Inadequate	Less than minimal staging but at least careful inspection and palpation of all peritoneal surfaces and the retroperitoneal area; biopsies of any suspect lesion for metastases

Some studies have given special attention to the value of lymphadenectomy in the staging of presumed early ovarian cancer. A randomised study compared systematic pelvic and para-aortic lymphadenectomy with lymph node sampling only. The authors concluded that systematic lymphadenectomy detects a higher proportion of patients with metastatic lymph nodes, but the trial was underpowered to make conclusions on the effect of systematic lymphadenectomy on progression free and overall survival.[45] However, a beneficial effect of systematic lymphadenectomy on survival is suggested by a retrospective study in 6686 women with clinical stage I ovarian cancer. In patients with stage I non-clear cell epithelial carcinoma, the extent of the node resection was associated with improved 5-year disease-specific survival.[55]

In spite of the absence of randomised trials supporting the need for comprehensive staging, the need for adequate staging is demonstrated by the high number of patients that are upstaged by comprehensive staging on the one hand and the subgroup of patients that possibly can be spared from chemotherapy after comprehensive staging on the other hand. Given the overwhelming international consensus on adequate staging for early-stage ovarian cancer, all patients suffering from ovarian cancer macroscopically confined to the pelvis should undergo optimal staging laparotomy.

3.1.4. *Cyst rupture and dense adhesions*

The largest study evaluating prognostic factors in invasive stage I ovarian cancer demonstrated that cyst rupture before or during surgery, together with the degree of differentiation, is one of the most important prognostic factors.[56] Cyst rupture during surgery changes FIGO stage IA or IB to FIGO stage IC, which is associated with a worse progression-free and overall survival.[56,57] Hence, all efforts should be made to avoid cyst rupture during surgery and cyst rupture or intact removal of the cyst also should be clearly reported in the surgery report to enable correct staging.

Dembo and colleagues studied two cohorts of more than 200 patients with FIGO stage I–II ovarian cancer. They found the presence of dense adhesions to be the second most important prognostic factor, after the degree of differentiation of the tumour. Adhesions were considered dense if so described by the surgeon, if sharp dissection was required, if a raw or oozing area was left in the location of the adherence or if cyst rupture resulted from dissecting the adhesions.[58] Although the prognostic value of dense adhesions has not been confirmed in the multivariate analyses of the larger study by Vergote and colleagues,[56] histologically proven involvement of adjacent pelvic tissues defines FIGO stage II.[27] Hence, adhesions of an ovarian tumour should be biopsied, and the presence or absence of dense adhesions should be described in the surgery report.

3.2. *Cytoreduction for advanced-stage ovarian cancer*

Primary debulking surgery with the removal of as much tumour as possible followed by combination chemotherapy is currently the standard treatment for advanced-stage ovarian cancer.[27,54]

In 1975, Griffith was the first to demonstrate that surgery improved survival if no tumour nodules bigger then 1.5 cm were left at the end of the operation.[59] The rationale behind the concept is multiple: removal of poorly vascularised tumour, higher growth fraction and better sensitivity to chemotherapy after surgery, the need for fewer chemotherapy cycles to treat smaller tumour nodules, removal of chemotherapy-resistant clonogenic cells and enhancement of the host immuno-competence.[60–62] Debulking surgery has also been linked with a better quality of life.[63]

3.2.1. *Timing*

As for staging laparotomy, cytoreduction for advanced-stage ovarian cancer should be carried out without delay after diagnosis based on the assumption of avoiding further tumour growth and patient distress.[63] The chances of complete debulking surgery and its associated better survival decrease with higher pre-operative tumour load and worse performance status.[64]

Although also for advanced-stage ovarian cancer, a direct relationship between treatment delay and adverse survival outcome has never been proven, we propose to include a quality indicator for timely surgical management of advanced ovarian cancer, based on the same arguments as for early-stage ovarian cancer.

3.2.2. *Procedure*

Although all debulking operations have the common goal to remove as much tumour as possible, there is no standard debulking procedure due to the nature of the disease.

The uterus, both tubes and both ovaries as well as the omentum must always be removed. Other procedures performed differ from patient to patient, depending on where the tumour has spread. Bowel resections,[65–71] extensive peri-

toneal implant elimination,[72] stripping or resection of the diaphragm,[73–76] splenectomy ± distal pancreatectomy [77–83] and partial hepatectomy[84] have all been found feasible in small case series, and can be performed with acceptable morbidity.

Primary debulking surgery has never been proven to result in better overall survival in a randomised trial but since the publication of Griffith, a volume of literature indicating its clinical usefulness has accumulated. Analysis of the patients included in GOG protocol 97 showed that residual tumour nodules at the end of the operation should be smaller than 2 cm in diameter for the patient to benefit from the operation.[85] Numerous retrospective studies and analyses of large clinical trials have shown an improved survival with decreasing size of residual nodes at the end of an operation, with the best survival outcome if all disease was debulked to no macroscopic disease at the end of the operation.[64,86–92] This led to an international consensus that the goal of cytoreductive surgery should be 'no visible disease at the end of the operation', also called complete cytoreduction.[35,54] There is some debate as to whether this better survival after complete cytoreduction reflects a true therapeutic effect of surgery or rather a selection of less aggressive tumours. In the latter case, ultra-radical surgery with its associated morbidity and mortality would not be advisable. However, although pre-operative disease characteristics like ascites, largest diameter of the tumour and tumour volume are proven negative prognostic factors and influence the resectability of the tumour, extensive surgery by skilled surgeons has been shown to be able to significantly reverse these negative prognostic factors.[89,93–95]

The strongest evidence in support of cytoreductive surgery of advanced ovarian cancer is provided by a meta-analysis showing a 5.5% increase in median survival for every extra 10% in maximal debulking.[96]

Unfortunately, not all debulking operations for advanced-stage disease are successful. Optimal debulking rates of up to 70–90% have been reported in expert centres, but success rates can be low as 10%.[62,93,95,97–101,101,102] Complete debulking should be achieved in at least 50% of patients with advanced ovarian cancer who are operated on.[97] As initial findings at laparotomy and residual disease at the end of the operation are important prognostic factors for women with advanced-stage ovarian cancer, size and location of disease at the start and end of the operation should be clearly documented in the operation notes.[11]

Another frequently discussed issue is the value of systematic pelvic and para-aortic lymphadenectomy in patients with advanced ovarian cancer. Since the 1980s, it has been known that up to 80% of stage III ovarian cancer patients have positive lymph nodes in the pelvic or para-aortic area, and it was supposed that the survival of these patients improved if they underwent a systematic lymphadenectomy.[103–106] Furthermore, pathological findings after chemotherapy suggested that retroperitoneal lymph nodes were not efficiently treated by chemotherapy.[107–111] A large retrospective study with 13,918 advanced ovarian cancer patients indeed suggests an improved survival if a more extended lymphadenectomy is performed.[112] However, a randomised controlled trial comparing systematic pelvic and para-aortic lymphadenectomy with the selective removal of enlarged nodes only showed a benefit in progression-free survival but not in overall survival in women with optimally debulked advanced ovarian cancer.[113] Unfortunately, the study was probably underpowered to detect a possible survival benefit due to the low number of events.[3,113] There is no unanimity on how the results of this study should be interpreted. Two important discussion points remain. First, do we accept a higher morbidity rate to improve the progression-free survival but not overall survival of patients with optimally debulked advanced ovarian cancer and second, does systematic pelvic and para-aortic lymphadenectomy prolong survival if the disease is otherwise completely debulked.[114,115] The answer to the first question is a matter of clinical judgement. The issue of lymphadenectomy in otherwise completely debulked advanced ovarian cancer has never been addressed in a randomised controlled trial. Theoretically, the removal of tumour containing lymph nodes smaller than one centimetre is of most benefit if it renders optimal debulking in complete debulking, thus if all intraperitoneal disease could be removed.[33] Eisenkop demonstrated that macroscopically positive lymph nodes often only became apparent during lymphadenectomy, hence the removal of palpable enlarged lymph nodes only would be insufficient to achieve complete debulking in the retroperitoneal space.[116]

In a comparative non-randomised study, Scarabelli and colleagues found a survival benefit for patients with no residual intraperitoneal disease who underwent systematic lymphadenectomy.[117] Analysis of the surgical data from 889 patients included in the SCOTROC-1 trial, investigating first-line chemotherapy in advanced ovarian cancer (docetaxel-carboplatin versus paclitaxel-carboplatin), also suggests that lymphadenectomy is beneficial if all intraperitoneal disease is removed. It shows a strikingly inferior progression free survival for patients with no macroscopic disease at the end of the operation if they were operated on in the UK. This inferior outcome of UK patients can be explained by the fact that pelvic and para-aortic lymphadenectomy is not performed in the UK in patients with advanced-stage ovarian cancer or because the intraperitoneal surgery is performed less radically than in the other countries that accrued in the SCOTROC trial.[118] Du Bois and colleagues evaluated the role of systematic lymphadenectomy when macroscopically complete intraperitoneal resection is achieved, in 1095 patients included in three first-line protocols. The 5-year survival rate of patients who underwent systematic lymphadenectomy appeared to be significantly improved.[119]

We conclude that pelvic and para-aortic lymphadenectomy, defined as exploration of the retroperitoneal space with the removal of at least all suspicious lymph nodes, in advanced ovarian cancer patients is indicated only if all intraperitoneal disease is completely debulked. The benefit of systematic lymphadenectomy in intraperitoneal completely debulked ovarian cancer will be investigated in a randomised controlled trial (AGO-LION).[119]

4. Discussion

The aim of this paper was to propose process-based quality indicators for ovarian cancer surgery, focussing on staging laparotomy for ovarian cancer macroscopically confined to the pelvis and debulking laparotomy for advanced-stage ovarian cancer.

Poor quality of care, lack of adherence to local guidelines and associated inferior outcome has been seen in several countries.[43,100,120–126] This poor quality of care cannot be accepted, and the first initiatives have been taken to improve the quality of ovarian cancer care.[11,14]

The first step in quality assurance is the development of quality indicators to measure the quality of care and identify areas for improvement. Process-based quality indicators are under the control of care providers, and indicate precisely what a surgeon should do to obtain a high likelihood of a favourable outcome.[17,127] As such, the proposed quality indicator list offers a well designed tool for gynaecologists to audit their surgical practice, identify areas for improvement and eventually optimise the surgical care for all their patients.

Of course, the proposed quality indicators will need to be evaluated for their feasibility, reliability and validity. The feasibility of quality assessment depends on the availability of the data in the operation reports, which may not always reflect the quality of the actual performed surgery. Ideally, process quality indicators are based on well conducted randomised clinical trials establishing the positive relationship between process and outcome. Unfortunately, in surgical practice only a few randomised clinical trials are available to support the benefit of an operation or certain aspects of it. However, analyses of the surgical data of local databases and data collected in clinical trials offer insight into the importance of surgical processes. Also guidelines by international expert organisations are available to set standards in surgical practice.

To achieve optimal quality of care for ovarian cancer patients, attention also needs to be given to factors not included in the proposed list of quality indicators, such as correct and complete pre-operative assessment, anaesthetic and post-operative care, appropriate post-operative chemotherapy and communication with the patients and their family. However, the role of state-of-the-art surgery cannot be overestimated. Hence, the optimisation of its quality is an important step in improving outcome for ovarian cancer patients.

5. Conclusion

The quality of staging procedures and debulking laparotomy has been shown to be important in the care of patients with epithelial ovarian cancer. However, data have shown major variances in current surgical care for ovarian cancer patients. Process-based quality indicators are easily measurable in a timely fashion, and are 'actionable' to improve clinical practice. Based on the available evidence and international expert agreement, we identified process-based quality indicators for staging laparotomy for early-stage ovarian cancer and debulking laparotomy for high-stage ovarian cancer. These quality indicators can be used as a tool to audit current practice and advance attempts to improve the quality of ovarian cancer surgery.

Conflict of interest

None declared.

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REFERENCES

1. Verdecchia A, Francisci S, Brenner H, et al. Recent cancer survival in Europe: a 2000–02 period analysis of EUROCARE-4 data. *Lancet Oncol*. 2007;**8**:784–96.
2. Bray F, Loos AH, Tognazzo S, La VC. Ovarian cancer in Europe: cross-sectional trends in incidence and mortality in 28 countries, 1953–2000. *Int J Cancer* 2005;**113**:977–90.
3. du Bois A, Harter P. The role of surgery in advanced and recurrent ovarian cancer. *Ann Oncol* 2006;**17** (Suppl. 10):x235–40.
4. Fentiman IS. Two week wait for suspected cancer: milestone or millstone? *Int J Clin Pract* 2005;**59**:1251–2.
5. National Cancer Research Board. Institute of Medicine and Commission on Life Sciences NRC. Ensuring quality cancer care. Washington, DC: National Academy Press; 1999.
6. Hoyle D. *ISO9000 quality systems handbook*. Oxford: Butterworth-Heinemann; 1994.
7. Mainz J. Defining and classifying clinical indicators for quality improvement. *Int J Qual Health Care* 2003;**15**:523–30.
8. Landheer ML, Therasse P, Van de Velde CJ. The importance of quality assurance in surgical oncology. *Eur J Surg Oncol* 2002;**28**:571–602.
9. European Union of Medical Specialists. Charter on quality assurance in medical specialist practice in the European Union. <http://admin.uems.net/uploadedfiles/174.pdf>; 1996 [accessed 14.8.08].
10. Vernooij F, Heintz P, Witteveen E, Van der Graaf Y. The outcomes of ovarian cancer treatment are better when provided by gynecologic oncologists and in specialized hospitals: a systematic review. *Gynecol Oncol* 2007;**105**:801–12.
11. Gagliardi AR, Fung MF, Langer B, Stern H, Brown AD. Development of ovarian cancer surgery quality indicators using a modified Delphi approach. *Gynecol Oncol* 2005;**97**:446–56.
12. Munstedt K, von Georgi R, Misselwitz B, Zygmunt M, Stillger R, Kunzel W. Centralizing surgery for gynecologic oncology – a strategy assuring better quality treatment? *Gynecol Oncol* 2003;**89**:4–8.
13. Bristow RE, Berek JS. Surgery for ovarian cancer: how to improve survival. *Lancet* 2006;**367**:1558–60.
14. Aletti GD, Santillan A, Eisenhauer EL, et al. A new frontier for quality of care in gynecologic oncology surgery: multi-institutional assessment of short-term outcomes for ovarian cancer using a risk-adjusted model. *Gynecol Oncol* 2007;**107**:99–106.
15. Podratz KC. Quality improvement in gynecologic surgery: the new frontier. *Am J Obstet Gynecol* 2006;**195**:891–5.
16. Ottevanger PB, Therasse P, van de Velde C, et al. Quality assurance in clinical trials. *Crit Rev Oncol Hematol* 2003;**47**:213–35.
17. Rubin HR, Pronovost P, Diette GB. From a process of care to a measure: the development and testing of a quality indicator. *Int J Qual Health Care* 2001;**13**:489–96.
18. Shekelle PG, MacLean CH, Morton SC, Wenger NS. Assessing care of vulnerable elders: methods for developing quality indicators. *Ann Int Med* 2001;**135**:647–52.
19. Mainz J. Developing evidence-based clinical indicators: a state of the art methods primer. *Int J Qual Health Care* 2003;**15**(Suppl. 1):i5–11.

20. Gagliardi A, Lemieux-Charles L, Brown A, Sullivan T, Goel V. Stakeholder preferences for cancer care performance indicators. *Int J Health Care Qual Assur* 2008;**21**:175–89.
21. Visser MR, van Lanschot JJ, van der Velden J, Kloek JJ, Gouma DJ, Sprangers MA. Quality of life in newly diagnosed cancer patients waiting for surgery is seriously impaired. *J Surg Oncol* 2006;**93**:571–7.
22. Kirwan JM, Tincello DG, Herod JJ, Frost O, Kingston RE. Effect of delays in primary care referral on survival of women with epithelial ovarian cancer: retrospective audit. *BMJ* 2002;**324**:148–51.
23. Lehner R, Wenzl R, Heinzl H, Husslein P, Sevelda P. Influence of delayed staging laparotomy after laparoscopic removal of ovarian masses later found malignant. *Obstet Gynecol* 1998;**92**:967–71.
24. Chen Z, King W, Pearcey R, Kerba M, Mackillop WJ. The relationship between waiting time for radiotherapy and clinical outcomes: a systematic review of the literature. *Radiother Oncol* 2008;**87**:3–16.
25. Pacifico MD, Pearl RA, Grover R. The UK Government two-week rule and its impact on melanoma prognosis: an evidence-based study. *Ann R Coll Surg Engl* 2007;**89**:609–15.
26. Department of Health. The NHS cancer plan. A plan for investment. A plan for reform. London. http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_4009609; 2000 [accessed 29.8.08].
27. Benedet JL, Bender H, Jones III H, Ngan HY, Pecorelli S. FIGO staging classifications and clinical practice guidelines in the management of gynecologic cancers. FIGO Committee on Gynecologic Oncology. *Int J Gynaecol Obstet* 2000;**70**:209–62.
28. Hoskins WJ. Epithelial ovarian carcinoma: principles of primary surgery. *Gynecol Oncol* 1994;**55**:S91–6.
29. Vergote I, Trimbos BJ. Treatment of patients with early epithelial ovarian cancer. *Curr Opin Oncol* 2003;**15**:452–5.
30. McGowan L. Abdominal incisions and staging in ovarian cancer. *Arch Surg* 1986;**121**:800–2.
31. Medeiros LR, Rosa DD, Edelweiss MI, et al. Accuracy of frozen-section analysis in the diagnosis of ovarian tumors: a systematic quantitative review. *Int J Gynecol Cancer* 2005;**15**:192–202.
32. Geomini P, Bremer G, Kruitwagen R, Mol BW. Diagnostic accuracy of frozen section diagnosis of the adnexal mass: a metaanalysis. *Gynecol Oncol* 2005;**96**:1–9.
33. Harter P, Gnauert K, Hils R, et al. Pattern and clinical predictors of lymph node metastases in epithelial ovarian cancer. *Int J Gynecol Cancer* 2007;**17**:1238–44.
34. Eltabbakh GH, Mount SL. Comparison of diaphragmatic wash and scrape specimens in staging of women with ovarian cancer. *Gynecol Oncol* 2001;**81**:461–5.
35. Trimbos JB, Schueler JA, van der Burg M, et al. Watch and wait after careful surgical treatment and staging in well-differentiated early ovarian cancer. *Cancer* 1991;**67**:597–602.
36. Trimbos JB, Vergote I, Bolis G, et al. Impact of adjuvant chemotherapy and surgical staging in early-stage ovarian carcinoma: European Organisation for Research and Treatment of Cancer-Adjuvant ChemoTherapy in Ovarian Neoplasm trial. *J Natl Cancer Inst* 2003;**95**:113–25.
37. Winter-Roach B, Hooper L, Kitchener H. Systematic review of adjuvant therapy for early stage (epithelial) ovarian cancer. *Int J Gynecol Cancer* 2003;**13**:395–404.
38. Young RC, Decker DG, Wharton JT, et al. Staging laparotomy in early ovarian cancer. *JAMA* 1983;**250**:3072–6.
39. Soper JT, Johnson P, Johnson V, Berchuck A, Clarke-Pearson DL. Comprehensive restaging laparotomy in women with apparent early ovarian carcinoma. *Obstet Gynecol* 1992;**80**:949–53.
40. Lin PS, Gershenson DM, Bevers MW, Lucas KR, Burke TW, Silva EG. The current status of surgical staging of ovarian serous borderline tumors. *Cancer* 1999;**85**:905–11.
41. Zanetta G, Rota S, Chiari S, et al. The accuracy of staging: an important prognostic determinator in stage I ovarian carcinoma. A multivariate analysis. *Ann Oncol* 1998;**9**:1097–101.
42. Le T, Adolph A, Krepart GV, Lotocki R, Heywood MS. The benefits of comprehensive surgical staging in the management of early-stage epithelial ovarian carcinoma. *Gynecol Oncol* 2002;**85**:351–5.
43. Sijmons EA, van Lankveld MA, Witteveen PO, Peeters PH, Koot VC, van Leeuwen JS. Compliance to clinical guidelines for early-stage epithelial ovarian cancer in relation to patient outcome. *Eur J Obstet Gynecol Reprod Biol* 2007;**131**:203–8.
44. Bristow RE. Surgical standards in the management of ovarian cancer. *Curr Opin Oncol* 2000;**12**:474–80.
45. Maggioni A, Benedetti-Panici P, Dell'Anna T, et al. Randomised study of systematic lymphadenectomy in patients with epithelial ovarian cancer macroscopically confined to the pelvis. *Brit J Cancer* 2006;**95**:699–704.
46. Greer BE, Rutledge FN, Gallager HS. Staging or restaging laparotomy in early-stage epithelial cancer of the ovary. *Clin Obstet Gynecol* 1980;**23**:293–303.
47. ESMO minimum clinical recommendations for diagnosis, treatment and follow-up of ovarian cancer. *Ann Oncol* 2001;**12**:1205–7.
48. Bell J, Brady MF, Young RC, et al. Randomized phase III trial of three versus six cycles of adjuvant carboplatin and paclitaxel in early stage epithelial ovarian carcinoma: a Gynecologic Oncology Group study. *Gynecol Oncol* 2006;**102**:432–9.
49. Sevin BU. Intraoperative staging in ovarian cancer. Baillieres. *Clin Obstet Gynaecol*. 1989;**3**:13–21.
50. Mayer AR, Chambers SK, Graves E, et al. Ovarian cancer staging: does it require a gynecologic oncologist? *Gynecol Oncol* 1992;**47**:223–7.
51. Raymond E, Drolet Y, Marpeau L, et al. Long-term follow-up after adjuvant chemotherapy in completely resected early stage ovarian carcinoma. *Eur J Obstet Gynecol Reprod Biol* 1997;**72**:181–90.
52. Gibbs DD, Gore ME. Pursuit of optimum outcomes in ovarian cancer: methodological approaches to therapy. *Drugs* 2001;**61**:1103–20.
53. Trope C, Kaern J. Adjuvant chemotherapy for early-stage ovarian cancer: review of the literature. *J Clin Oncol* 2007;**25**:2909–20.
54. du Bois A, Quinn M, Thigpen T et al. In: 2004 consensus statements on the management of ovarian cancer: final document of the 3rd International Gynecologic Cancer Intergroup Ovarian Cancer Consensus Conference (GCIG OCCC 2004). *Ann Oncol 2005*;**16** (Suppl 8):viii7–12.
55. Chan JK, Munro EG, Cheung MK, et al. Association of lymphadenectomy and survival in stage I ovarian cancer patients. *Obstet Gynecol* 2007;**109**:12–9.
56. Vergote I, De Brabanter J, Fyles A, et al. Prognostic importance of degree of differentiation and cyst rupture in stage I invasive epithelial ovarian carcinoma. *Lancet* 2001;**357**:176–82.
57. Chan JK, Tian C, Monk BJ, et al. Prognostic factors for high-risk early-stage epithelial ovarian cancer: a Gynecologic Oncology Group study. *Cancer* 2008;**112**:2202–10.
58. Dembo AJ, Davy M, Stenwig AE, Berle EJ, Bush RS, Kjorstad K. Prognostic factors in patients with stage I epithelial ovarian cancer. *Obstet Gynecol* 1990;**75**:263–73.
59. Griffiths CT. Surgical resection of tumor bulk in the primary treatment of ovarian carcinoma. *Natl Cancer Inst Monogr* 1975;**42**:101–4.

60. Covens AL. A critique of surgical cytoreduction in advanced ovarian cancer. *Gynecol Oncol* 2000;**78**:269–74.
61. Munstedt K, Franke FE. Role of primary surgery in advanced ovarian cancer. *World J Surg Oncol* 2004;**2**:32.
62. Peter A, Heintz M. Surgery in ovarian cancer: the concept of cytoreductive surgery. *Curr Opin Obstet Gynecol* 1996;**8**:8–11.
63. Blythe JG, Wahl TP. Debulking surgery: does it increase the quality of survival? *Gynecol Oncol* 1982;**14**:396–408.
64. Wimberger P, Lehmann N, Kimmig R, Burges A, Meier W, du Bois A. Prognostic factors for complete debulking in advanced ovarian cancer and its impact on survival. An exploratory analysis of a prospectively randomized phase III study of the Arbeitsgemeinschaft Gynaekologische Onkologie Ovarian Cancer Study Group (AGO-OVAR). *Gynecol Oncol* 2007;**106**:69–74.
65. Salani R, Zahurak ML, Santillan A, Giuntoli RL, Bristow RE. Survival impact of multiple bowel resections in patients undergoing primary cytoreductive surgery for advanced ovarian cancer: a case-control study. *Gynecol Oncol* 2007;**107**:495–9.
66. Wu PC, Lang JH, Huang RL, Liu J, Tang MY, Lian LJ. Intestinal metastasis and operation in ovarian cancer: a report on 62 cases. Baillieres. *Clin Obstet Gynaecol* 1989;**3**:95–108.
67. Buttarelli M, Houvenaeghel G, Lelievre L, Jacquemier J, Guiramand J, Delpero JR. Pelvic posterior exenteration with immediate colo-rectal anastomosis: is it justified and feasible in advanced stage ovarian carcinoma? *Ann Chir* 2006;**131**:431–6.
68. Bidzinski M, Derlatka P, Kubik P, et al. The evaluation of intra- and postoperative complications related to debulking surgery with bowel resection in patients with FIGO stage III–IV ovarian cancer. *Int J Gynecol Cancer* 2007;**17**:993–7.
69. Estes JM, Leath CA, Straughn JM, et al. Bowel resection at the time of primary debulking for epithelial ovarian carcinoma: outcomes in patients treated with platinum and taxane-based chemotherapy. *J Am Coll Surg* 2006;**203**:527–32.
70. Cai HB, Zhou YF, Chen HZ, Hou HY. The role of bowel surgery with cytoreduction for epithelial ovarian cancer. *Clin Oncol (R Coll Radiol)* 2007;**19**:757–62.
71. Hertel H, Diebolder H, Herrmann J, et al. Is the decision for colorectal resection justified by histopathologic findings: a prospective study of 100 patients with advanced ovarian cancer. *Gynecol Oncol* 2001;**83**:481–4.
72. Eisenkop SM, Nalick RH, Wang HJ, Teng NN. Peritoneal implant elimination during cytoreductive surgery for ovarian cancer: impact on survival. *Gynecol Oncol* 1993;**51**:224–9.
73. Silver DF. Full-thickness diaphragmatic resection with simple and secure closure to accomplish complete cytoreductive surgery for patients with ovarian cancer. *Gynecol Oncol* 2004;**95**:384–7.
74. Montz FJ, Schlaerth JB, Berek JS. Resection of diaphragmatic peritoneum and muscle: role in cytoreductive surgery for ovarian cancer. *Gynecol Oncol* 1989;**35**:338–40.
75. Cliby W, Dowdy S, Feitoza SS, Gostout BS, Podratz KC. Diaphragm resection for ovarian cancer: technique and short-term complications. *Gynecol Oncol* 2004;**94**:655–60.
76. Devolder K, Amant F, Neven P, van Gorp T, Leunen K, Vergote I. Role of diaphragmatic surgery in 69 patients with ovarian carcinoma. *Int J Gynecol Cancer* 2008;**18**:363–8.
77. Chen LM, Leuchter RS, Lagasse LD, Karlan BY. Splenectomy and surgical cytoreduction for ovarian cancer. *Gynecol Oncol* 2000;**77**:362–8.
78. Nicklin JL, Copeland LJ, O'Toole RV, Lewandowski GS, Vaccarello L, Havenar LP. Splenectomy as part of cytoreductive surgery for ovarian carcinoma. *Gynecol Oncol* 1995;**58**:244–7.
79. Ayhan A, Al RA, Baykal C, Demirtas E, Ayhan A, Yuce K. The influence of splenic metastases on survival in FIGO stage IIIC epithelial ovarian cancer. *Int J Gynecol Cancer* 2004;**14**:51–6.
80. Eisenkop SM, Spirtos NM, Lin WC. Splenectomy in the context of primary cytoreductive operations for advanced epithelial ovarian cancer. *Gynecol Oncol* 2006;**100**:344–8.
81. Magtibay PM, Adams PB, Silverman MB, Cha SS, Podratz KC. Splenectomy as part of cytoreductive surgery in ovarian cancer. *Gynecol Oncol* 2006;**102**:369–74.
82. Hoffman MS, Tebes SJ, Sayer RA, Lockhart J. Extended cytoreduction of intraabdominal metastatic ovarian cancer in the left upper quadrant utilizing en bloc resection. *Am J Obstet Gynecol* 2007;**197**:204–9.
83. Yildirim Y, Sanci M. The feasibility and morbidity of distal pancreatectomy in extensive cytoreductive surgery for advanced epithelial ovarian cancer. *Arch Gynecol Obstet* 2005;**272**:31–4.
84. Merideth MA, Cliby WA, Keeney GL, Lesnick TG, Nagorney DM, Podratz KC. Hepatic resection for metachronous metastases from ovarian carcinoma. *Gynecol Oncol* 2003;**89**:16–21.
85. Hoskins WJ, McGuire WP, Brady MF, et al. The effect of diameter of largest residual disease on survival after primary cytoreductive surgery in patients with suboptimal residual epithelial ovarian carcinoma. *Am J Obstet Gynecol* 1994;**170**:974–9.
86. Vergote IB, De Wever I, Tjalma W, Van Gramberen M, Decloedt J, van Dam P. Neoadjuvant chemotherapy or primary debulking surgery in advanced ovarian carcinoma: a retrospective analysis of 285 patients. *Gynecol Oncol* 1998;**71**:431–6.
87. Aletti GD, Dowdy SC, Gostout BS, Jones MB, Stanhope CR, Wilson TO, et al. Aggressive surgical effort and improved survival in advanced-stage ovarian cancer. *Obstet Gynecol* 2006;**107**:77–85.
88. von Georgi R, Franke FE, Munstedt K. Influence of surgery and postoperative therapy and tumor characteristics on patient prognosis in advanced ovarian carcinomas. *Eur J Obstet Gynecol Reprod Biol* 2003;**111**:189–96.
89. Eisenkop SM, Spirtos NM, Friedman RL, Lin WC, Pisani AL, Perticucci S. Relative influences of tumor volume before surgery and the cytoreductive outcome on survival for patients with advanced ovarian cancer: a prospective study. *Gynecol Oncol* 2003;**90**:390–6.
90. Chi DS, Eisenhauer EL, Lang J, et al. What is the optimal goal of primary cytoreductive surgery for bulky stage IIIC epithelial ovarian carcinoma (EOC)? *Gynecol Oncol* 2006;**103**:559–64.
91. Eisenhauer EL, bu-Rustum NR, Sonoda Y, Aghajanian C, Barakat RR, Chi DS. The effect of maximal surgical cytoreduction on sensitivity to platinum-taxane chemotherapy and subsequent survival in patients with advanced ovarian cancer. *Gynecol Oncol* 2008;**108**:276–81.
92. Engel J, Eckel R, Schubert-Fritschle G, et al. Moderate progress for ovarian cancer in the last 20 years: prolongation of survival, but no improvement in the cure rate. *Eur J Cancer* 2002;**38**:2435–45.
93. Aletti GD, Gostout BS, Podratz KC, Cliby WA. Ovarian cancer surgical resectability: relative impact of disease, patient status, and surgeon. *Gynecol Oncol* 2006;**100**:33–7.
94. Todo Y, Sakuragi N, Oikawa M, et al. Cytoreductive surgery combined with organ resection for advanced ovarian carcinoma. *Int J Clin Oncol* 2003;**8**:90–6.
95. Eisenhauer EL, bu-Rustum NR, Sonoda Y, et al. The addition of extensive upper abdominal surgery to achieve optimal cytoreduction improves survival in patients with stages IIIC–IV epithelial ovarian cancer. *Gynecol Oncol* 2006;**103**:1083–90.

96. Bristow RE, Tomacruz RS, Armstrong DK, Trimble EL, Montz FJ. Survival effect of maximal cytoreductive surgery for advanced ovarian carcinoma during the platinum era: a meta-analysis. *J Clin Oncol* 2002;**20**:1248–59.
97. Weide R, Arndt M, Pandorf A, Heymanns J, Thomalla J, Koppler H. Ovarian cancer treatment reality in northern Rheinland-Pfalz (Germany). Suboptimal surgical treatment as a possible cause for inferior survival. *Onkologie* 2007;**30**:611–7.
98. Bristow RE, Tomacruz RS, Armstrong DK, Trimble EL, Montz FJ. Survival effect of maximal cytoreductive surgery for advanced ovarian carcinoma during the platinum era: a meta-analysis. *J Clin Oncol* 2002;**20**:1248–59.
99. Engelen MJ, Kos HE, Willemse PH, et al. Surgery by consultant gynecologic oncologists improves survival in patients with ovarian carcinoma. *Cancer* 2006;**106**:589–98.
100. du Bois A, Rochon J, Lamparter C, Pfisterer J. Pattern of care and impact of participation in clinical studies on the outcome in ovarian cancer. *Int J Gynecol Cancer* 2005;**15**:183–91.
101. Soegaard AE, Knudsen A, Svarrer T, et al. The results of treatment of epithelial ovarian cancer after centralisation of primary surgery. Results from North Jutland, Denmark. *Gynecol Oncol* 2005;**99**:552–6.
102. Giede KC, Kieser K, Dodge J, Rosen B. Who should operate on patients with ovarian cancer? An evidence-based review. *Gynecol Oncol* 2005;**99**:447–61.
103. Pereira A, Magrina JF, Rey V, Cortes M, Magtibay PM. Pelvic and aortic lymph node metastasis in epithelial ovarian cancer. *Gynecol Oncol* 2007;**105**:604–8.
104. Burghardt E, Girardi F, Lahousen M, Tamussino K, Stettner H. Patterns of pelvic and paraaortic lymph node involvement in ovarian cancer. *Gynecol Oncol* 1991;**40**:103–6.
105. Fukasawa H, Kikkawa F, Tamakoshi K, Kawai M, Arii Y, Tomoda Y. Lymphadenectomy in stage-III serous cystadenocarcinoma of the ovary. *Int J Gynaecol Obstet* 1995;**51**:239–45.
106. Spirtos NM, Gross GM, Freddo JL, Ballon SC. Cytoreductive surgery in advanced epithelial cancer of the ovary: the impact of aortic and pelvic lymphadenectomy. *Gynecol Oncol* 1995;**56**:345–52.
107. Burghardt E, Lahousen M, Stettner H. The significance of pelvic and para-aortic lymphadenectomy in the operative treatment of ovarian cancer. *Baillieres Clin Obstet Gynaecol* 1989;**3**:157–65.
108. Di Re F, Fontanelli R, Raspagliesi F, Di Re E. Pelvic and para-aortic lymphadenectomy in cancer of the ovary. *Baillieres Clin Obstet Gynaecol* 1989;**3**:131–42.
109. Kimball RE, Schlaerth JB, Kute TE, et al. Flow cytometric analysis of lymph node metastases in advanced ovarian cancer: clinical and biologic significance. *Am J Obstet Gynecol* 1997;**176**:1319–26.
110. Joulie F, Morice P, Rey A, et al. Are nodal metastases in ovarian cancer chemoresistant lesions? Comparative study of initial lymphadenectomy or after chemotherapy. *Gynecol Obstet Fertil* 2004;**32**:502–7.
111. Isonishi S, Niimi S, Sasaki H, Ochiai K, Yasuda M, Tanaka T. Drug sensitivity-related benefit of systematic lymphadenectomy during cytoreductive surgery in optimally debulked stages IIIc and IV ovarian cancer. *Gynecol Oncol* 2004;**93**:647–52.
112. Chan JK, Urban R, Hu JM, et al. The potential therapeutic role of lymph node resection in epithelial ovarian cancer: a study of 13918 patients. *Brit J Cancer* 2007;**96**:1817–22.
113. Benedetti-Panici P, Maggioni A, Hacker N, et al. Systematic aortic and pelvic lymphadenectomy versus resection of bulky nodes only in optimally debulked advanced ovarian cancer: a randomized clinical trial. *J Natl Cancer Inst* 2005;**97**:560–6.
114. Morice P, Pautier P, Lhomme C, Castaigne D. Re: Systematic aortic and pelvic lymphadenectomy versus resection of bulky nodes in optimally debulked advanced ovarian cancer: a randomized clinical trial. *J Natl Cancer Inst* 2005;**97**:1620–1.
115. Querleu D, Ferron G. Re: Systematic aortic and pelvic lymphadenectomy versus resection of bulky nodes in optimally debulked advanced ovarian cancer: a randomized clinical trial. *J Natl Cancer Inst* 2005;**97**:1621–3.
116. Eisenkop SM, Spirtos NM. The clinical significance of occult macroscopically positive retroperitoneal nodes in patients with epithelial ovarian cancer. *Gynecol Oncol* 2001;**82**:143–9.
117. Scarabelli C, Gallo A, Visentin MC, Canzonieri V, Carbone A, Zarrelli A. Systematic pelvic and para-aortic lymphadenectomy in advanced ovarian cancer patients with no residual intraperitoneal disease. *Int J Gynecol Cancer* 1997;**7**:18–26.
118. Crawford SC, Vasey PA, Paul J, Hay A, Davis JA, Kaye SB. Does aggressive surgery only benefit patients with less advanced ovarian cancer? Results from an international comparison within the SCOTROC-1 Trial. *J Clin Oncol* 2005;**23**:8802–11.
119. du Bois A, Reuss A, Harter P, et al. The role of lymphadenectomy in advanced epithelial ovarian cancer (AOC) in patients with macroscopically complete resection of intraperitoneal disease. *Int J Gynecol Cancer* 2006;**16**(Suppl. 3): 599–615. Abstract 008.
120. Grilli R, Alexanian A, Apolone G, et al. The impact of cancer treatment guidelines on actual practice in Italian general hospitals: the case of ovarian cancer. *Ann Oncol* 1990;**1**:112–8.
121. Munstedt K, von Georgi R, Zygmunt M, Misselwitz B, Stillger R, Kunzel W. Shortcomings and deficits in surgical treatment of gynecological cancers: a German problem only? *Gynecol Oncol* 2002;**86**:337–43.
122. Wolfe CD, Tilling K, Raju KS. Management and survival of ovarian cancer patients in south east England. *Eur J Cancer* 1997;**33**:1835–40.
123. Chan JK, Zhang M, Hu JM, Shin JY, Osann K, Kapp DS. Racial disparities in surgical treatment and survival of epithelial ovarian cancer in United States. *J Surg Oncol* 2008;**97**:103–7.
124. Sengupta PS, Jayson GC, Slade RJ, Eardley A, Radford JA. An audit of primary surgical treatment for women with ovarian cancer referred to a cancer centre. *Brit J Cancer* 1999;**80**:444–7.
125. Marx C, Bendixen A, Hogdall C, Ottosen C, Kehlet H, Ottesen B. Organisation and quality of primary surgical intervention for ovarian cancer in Denmark. *Acta Obstet Gynecol Scand* 2007;**86**:1496–502.
126. Akeson M, Zetterqvist BM, Holmberg E, Horvath G. Improved survival with clinical guidelines? Evaluation of a quality register linked to clinical guidelines for ovarian cancer in the western health care region in Sweden between 1 September 1993 and 1 June 1998. *Acta Obstet Gynecol Scand* 2005;**84**:1113–8.
127. Rubin HR, Pronovost P, Diette GB. The advantages and disadvantages of process-based measures of health care quality. *Int J Qual Health Care* 2001;**13**:469–74.