



The circumferential margin in rectal cancer: recommendations based on the Dutch Total Mesorectal Excision Study

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Abstract

A very low local recurrence rate in rectal cancer is possible with optimal staging, preoperative radiotherapy and the use of total mesorectal excision (TME). Data from a study where patients were randomised for preoperative radiotherapy (or not) and complete removal of the tumour and mesorectum were examined. A consensus meeting was held to discuss the data in which the following guidelines for implementation were made. Adequate imaging is necessary to increase the likelihood of a R0 resection. Advances cases (possible margin to the endopelvic fascia less than 2 mm) need a long course of preoperative radiotherapy. Primary resectable cases benefit from a short course of radiation directly followed by surgery. A continuous quality control of surgery is mandatory in order to maintain the skill for a TME. A complete pathology report is important for the quality control of the surgical treatment and to predict the outcome of treatment. All of the involved disciplines in the diagnosis and treatment of rectal cancer should focus on the circumferential margin to guide for optimal treatment. Multidisciplinary teams are important for the achievement of optimal treatment planning of rectal cancer patients and maintenance of the highest level of quality control. © 2002 Elsevier Science Ltd. All rights reserved.

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1. The crucial role of the surgeon

Survival after treatment of rectal cancer varies widely worldwide. In Europe, these variations are related to age, country and period of diagnosis. Inter-country and time differences are probably related to stage at diagnosis, variation in treatment and postoperative mortality [1]. Not only differences among countries, but also between hospitals within a given country [2] and even at an individual level of surgeons [3] have been reported. Until recently, most attention has been paid to survival only, but now it has been shown that local recurrence is important since differences in local control have an inverse relationship with survival [2,4]. The local recurrence rate after resection of a rectal carcinoma is directly related to the surgical technique, the radicality of the resection

and the optimal use of (preoperative) radiotherapy. This makes the surgeon the most important prognostic factor in the determination of the outcome since the technique of rectal excision has the biggest impact on the rate of local recurrence. Every attempt should be made by the surgeon to achieve a R0 resection, which means complete removal of the tumour including its lateral and caudal spread in the mesorectum.

2. Staging

There is a clear relationship between the distance of the primary tumour or metastatic lymph node to the endopelvic fascia and the rate of local recurrence. A distance less than 1 or 2 mm is considered as inadequate [5]. The classical way to examine the extent of a rectal tumour is by digital examination. Clinical terms such as fixed or tethered are often difficult to interpret and often do not reflect the exact relationship of the primary

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tumour to the endopelvic fascia. Most old studies of imaging techniques have focused on the accuracy rates for T and N staging, but not on the relationship of the tumour and its spread to the endopelvic fascia. As a consequence, the present staging system expressed in TNM or Dukes' does not discriminate between limited and extensive T3 tumours. Classification of T4 tumours is also not very accurate in the present TNM staging system. In order to plan the type of resection, extent of tumour growth has to be determined in all six directions: lateral left and right, ventral, dorsal, caudal and cranial. To overcome the subjective interpretation between mobile and fixed tumours, objective criteria have to be introduced in the staging of rectal cancer. Preoperative imaging with a spiral computed tomography (CT) scan or high resolution magnetic resonance imaging (MRI) [6] is important, since it can depict both the margin of the tumour in relation to the endopelvic fascia and the presence of systemic disease in an accurate way.

3. Radiotherapy

A reduction of local recurrences by a half or one-third as a result of either preoperative or postoperative radiotherapy is achieved in most series [7]. In the United States, based on the Gastrointestinal Tumor Study Group (GITSG) and North Central Cancer Treatment Group (NCCTG)-Mayo results, combined modality postoperative treatment with chemotherapy and high-dose pelvic irradiation (over 50 Gy) was recommended for patients with stages II and III rectal cancer [8]. An analysis of patients treated with postoperative chemotherapy and radiation therapy indicates that these patients may have more chronic bowel dysfunction compared with those who undergo surgical resection alone. Improved radiation planning and techniques can be used to minimise treatment-related complications. These techniques include the use of multiple pelvic fields, prone positioning, customised bowel immobilisation moulds (belly boards), bladder distension, visualisation of the small bowel through oral contrast, and the incorporation of three-dimensional or comparative treatment planning [9]. However, in a randomised controlled trial, preoperative irradiation was more effective than postoperative radiotherapy with a higher percentage of patients receiving radiotherapy and fewer complications due to the treatment. Substantial improvement in overall survival has been demonstrated with preoperative radiation therapy in the Swedish Rectal Cancer Trial [4]. A systematic overview of 22 trials looking at the effect of adjuvant radiotherapy for resectable rectal cancer involving 8507 patients confirmed the effectiveness of a 1-week course of preoperative radiotherapy compared with long treatment pre- or postoperatively [10].

4. Quality control and the relevance of previous studies

A major problem of published studies on adjuvant therapy in the treatment of primary rectal cancer is that surgery has not been standardised in any of the old studies. A control mechanism for quality control in standardised surgery is the supervising of the operation by trained instructor-surgeons and a standardised examination of the specimen by pathologists. The completeness of the removal of an intact mesorectum requires systematic examination of the specimen both by macroscopic examination and serial sectioning of the whole tumour and the surrounding mesorectum in the transverse plane for determination of the intactness of the mesorectal fascia and the completeness of the mesorectum.

The lowest reported rates of local recurrences are within the range of 4–8% following rectal resection with appropriate mesorectal excision (total mesorectal excision (TME) for low/middle rectal tumours and mesorectal excision at least 5 cm below the tumour for high rectal tumours) [11,12]. A significant effect of surgical training on outcome due to instruction and specialisation was observed in Sweden with a decrease of the 2-year local recurrence rate from 15 to 6% [13]. A similar observation was found in a previous study in The Netherlands with similar hospitals participating as in the trial (a reduction in local recurrences from 16 to 8%).

This low incidence of local relapses following meticulous mesorectal excision has led some investigators to question the routine use of adjuvant radiation therapy since the local recurrence rate in all radiotherapy studies was still higher than in series reporting on optimal surgery alone. Thus, after the introduction of standardised surgery and pathology the value of adjuvant treatments can now be completely redefined.

It was decided in The Netherlands to run a randomised trial of resectable rectal cancer with standardised TME surgery and pathology comparing no radiotherapy versus a short course of preoperative radiotherapy (5×5 Gray). Reduction of the local failure rate from 8.2% in the control arm to 2.4% in the arm with radiotherapy was achieved [14]. Based on these data, it was decided to implement the use of short-course preoperative radiotherapy in rectal cancer. Quality control was found to be of the utmost importance, mainly as result of individual specialisation, without a direct relationship between hospital volume and outcome.

With this low local recurrence rate following optimal surgery, chemotherapy is now also considered subject to investigation in stage II and III patients (PROCTOR study). It has been standardised treatment in the US 10 years ago (National Institute of Health (NIH) consensus) [8], but in a Dutch national study with a 7-years follow-up, no effect of postoperative chemotherapy in conjunction with radiotherapy was observed in rectal cancer [15]. However, all of these conclusions were made before the

standardisation of surgery and there was no quality control of the surgical treatment during the study period.

5. Development and implementation of guidelines

The production of guidelines is an extensive task starting with the collection of the available evidence from the literature. Preferably, this has to be conducted by means of a systematic review and meta-analysis of the data. Based on the outcome, recommendations can be made. There are distinct differences in guideline development in Europe that are usually on a national basis, as opposed to the whole of the United States where there are major differences in recommendations, as mentioned before. In The Netherlands, the Dutch Gastrointestinal Working party is responsible for the national guidelines on gastrointestinal malignancies. A mandated member represents all scientific associations both diagnostic and therapeutic with a relationship to the subject. Oncology nurses and general practitioners also participate in the working group. Representatives from the different specialities of the eight Comprehensive Centers are also members. After the formulation of critical statements, recommendations are made after a review of the literature and consultations of the regional gastrointestinal working parties. These regional gastrointestinal tumour groups from the Comprehensive Cancer Centers are requested to look after the implementation of the guidelines. Several projects are underway to evaluate the effect of this process. The Dutch Institute for Healthcare Improvement supports the collection of evidence and the available data from the Cochrane Colorectal Cancer Group and the Colorectal Cancer Collaboration are also used for this purpose.

Based on the evidence of the Dutch TME study and the existing guidelines. The following recommendations can be made:

1. It is essential to split (based on adequate imaging) the patients with rectal cancer into two groups. Firstly, in cases with a likelihood of a R0 resection (margin from the tumour to the circumferential margin more than 2 mm) and, secondly, in the more advanced cases. This is based on the observation of 15% of the cases in the TME study undergoing a R1 resection having a correspondingly high local recurrence rate.
2. Advanced cases need a long course of high-dose radiotherapy followed by a waiting period of 6 to allow for downstaging and downsizing. The role of concomitant chemotherapy is investigational.
3. Primary resectable cases need a short course of radiotherapy followed within 1 week by a resection. Although subgroup analysis suggests a limited effect for early and high tumours, it seems better

to include all cases since the adverse effects of the radiotherapy are limited.

4. A continuous quality control of the surgery is mandatory, since optimal surgery alone has an important effect on the local recurrence rate. Based on data of this study, there is a recommendation for specialisation in every hospital and not for a centralisation of rectal cancer care in a limited number of hospitals. To maintain the present high standard of surgery, it is wise to continue on a permanent basis the instruction of the TME technique through the use of videos, workshops and site visits to the hospitals that want to continue with the surgical treatment of rectal cancer.
5. Complete pathology reports about the macroscopic and microscopic analysis of the specimen following a strict protocol is essential for quality control. A report on every case about the completeness of the mesorectum has to be given to the surgeon since an incomplete specimen is related to a higher local recurrence independent of the tumour extension. On a microscopical level, the closest distance of the tumour or involved lymph node has to be mentioned in every report. Serial sectioning of the specimen in the transverse plane is the best way to report this distance. A revision of the TNM staging is necessary in which the distance from the tumour to the circumferential margin is included. In this way, T3 tumours have to be divided into two categories.
6. Every hospital where rectal cancer is treated needs a documented way of working in multidisciplinary teams to look after the quality control of all of the disciplines involved and to be a platform to discuss the treatment plan for the individual patient.

6. The circumferential margin for all disciplines

The staging of rectal tumours before the operation has always focused on measuring the extent of the tumour growth from the inside to the outside. Now we are aware of the importance of the outside of the specimen as a guidance for a R0 resection. Pathology also reports from inside to outside. Starting from the mucosa, the depth of infiltration was measured. In addition, radiology has focused until recently on accurate T staging. The now clearly established importance of the circumferential margin means that every discipline can focus on this factor. All the disciplines now work together, making the treatment of the individual patient and the formulating of new study proposals more in line with one another. Through the efforts of

multidisciplinary working teams, consisting of diagnostic and therapeutical specialities and the participation of nurses and psychosocial workers, the care of the patient with rectal cancer can be improved. Further improvements can be made by increased anatomical awareness of the autonomic nerves just outside the circumferential margin. Sparing of these nerves will result in less functional and sexual disturbances.

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