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European trials with Total Mesorectal Excision

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INTRODUCTION

Until a few years ago, results after curative surgery for rectal cancer were not optimal, reflected in high local failure rates.¹⁻³ The basic conventional procedure involving blunt dissection, has been shown to result in an incomplete removal of mesorectal tissue, with a high risk for local failure and damage to the autonomous pelvic nerve plexus, resulting in a high incidence of sexual^{4,5} and bladder dysfunction.⁶ Lack of improvement in the surgical results of rectal cancer has prompted many investigators to seek different adjuvant therapy approaches in conjunction with surgery.

In several studies, the benefit of radiotherapy (RT) in the treatment of rectal cancer has been suggested. In a large prospective Swedish trial it was shown that preoperative hypofractionated radiotherapy results in better local control than postoperative radiotherapy.¹³ The role of chemoradiotherapy or chemotherapy (CT) as sole treatment still has to be determined. The Netherlands Adjuvant Colorectal Cancer Project (NACCP) did not show an effect of chemotherapy in rectal cancer.¹⁴ In the United States the opinion is that all patients with a Dukes' B or C lesion should have postoperative chemoradiotherapy.¹⁵ Chemo(radio)therapy is not routine in Europe and is still considered investigational therapy in rectal cancer.

Improvement in survival with radiotherapy alone was not demonstrated until the Swedish Rectal Cancer Trial (SRCT).⁷ This was the first randomised study to demonstrate a significant survival benefit in patients receiving preoperative radiation (compared with surgery alone). In recent years, local control and survival have been further improved by the introduction of total mesorectal excision (TME) surgery, as first described by Heald.⁸⁻¹⁰ With this technique, less morbidity^{4,11,12} and a reduction in abdominoperineal resections have also been reported.¹⁰

A major problem of published studies on adjuvant therapy in the treatment of primary rectal cancer is that surgery has not been standardised in these studies. Moreover, the surgeon remains an important factor in the accomplishment of tumour control and reduction of morbidity.¹⁶⁻¹⁸ Therefore, the effect of adjuvant therapy can only be studied when strict standardised and quality-controlled surgery is performed.

Optimal quality control of the surgical procedure must also include a standardised examination by pathologists.¹⁹⁻²⁰ Detection of mesorectal spread requires systematic examination of the specimen, by serial sectioning of the whole tumour and the surrounding mesorectum in the transverse plane. This method can be used to monitor differences in operative technique. Furthermore, standardised surgery can be documented photographically, due to reproducible gross specimen features.²¹

In Europe, TME has become the preferred standard of operative management for rectal cancers.²² Current clinical trials examining the role of adjuvant therapy in patients who are undergoing standardised operations are now setting the standard of surgical care in several European countries. We studied European trials in which TME-surgery is intentionally performed. Trials were classified in neoadjuvant and adjuvant trials. Furthermore a subdivision was made according to short- and long-term radiotherapy. Most of these trials are still in progress and have short follow-ups, so definitive results cannot be presented yet, apart from feasibility and interim analyses.

NEOADJUVANT TRIALS, SHORT-TERM PREOPERATIVE RADIOTHERAPY TME-trial, Dutch ColoRectal Cancer Group (DCRCG)

In this trial, patients with resectable rectal cancer underwent standardised TME surgery alone, or patients received preoperative radiotherapy (5x5 Gy) followed within 10 days after the start of radiotherapy by TME.²³ Table 1 shows the characteristics of this trial and the other trials described.

TME was performed according to strict and controllable quality demands. An extensive structure of workshops, symposia, and instruction videos helped to accomplish this goal. In addition, a monitoring committee of specially trained instructor-surgeons was formed for on-site instructions to optimise quality. R.J. Heald, W.E. Enker and Y. Moriya were involved as operating surgeons in different hospitals in The Netherlands and as instructors at several workshops about the trial. Pathological examination was done according to the protocol of Quirke.^{19,20} Special training courses were given to pathologists. A pathology review panel and a trained quality manager guaranteed quality control.

Taking into account an ineligibility rate and an R1-resection percentage of 25%, it was calculated that 1400 Dutch patients had to be randomised in order to detect a difference of 5% in local recurrence rate (LR) between the R0-patients in the TME alone group (LR 10%) and R0-patients in the RT-group (LR 5%).

From January 1996 until January 2000, 1861 patients were randomised; 1530 patients from 84 Dutch hospitals and 331 patients from 24 hospitals in other countries (mainly Sweden). The European Organisation for Research and Treatment of Cancer (EORTC) participated in the TME-trial under trialnumber 40971, in order to assure quality control of surgery for the EORTC-GastroIntestinal (GI) group.

Of the patients randomised to receive preoperative radiotherapy, 87% received it at the correct dose and were operated within 10 days after its inception. In total, 37% of the operations were attended by instructor-surgeons; in the first quarter, most operations (89%) were supervised by instructor-surgeons. Later on, this percentage decreased to 19% in the last quarter of the trial. Only perioperative blood loss was significantly higher in irradiated patients, and the perineal wound dehiscence rate was higher in irradiated abdominoperineal resection (APR)-patients.²⁴ The clinical leak rate was 12% in the low anterior resection (LAR)-group, with no difference between the randomisation groups. In the LAR-group, temporary stomas were constructed in 57% of the patients. The percentages for side-end anastomosis and pouch construction were 60% and 28%, respectively. From this trial it can be concluded that performing a large, multicentre trial with quality control of surgery is feasible. The accrual of the trial has been very good, and short-term preoperative radiotherapy was also demonstrated to be safe in combination with TME-surgery.

In a recent study by Nagtegaal et al.,²⁵ it was shown that pathology data need to be based on pathology reports and controlled by trained quality managers. A retrospective comparison of pathology data case record forms with hospital pathology reports was performed using the data from 300 patients from the TME-trial. Successive rounds of quality control appeared to be required for accuracy and completeness of pathology data.

The overall local recurrence rate up to 1 July 2000 (median follow-up 20 months, range 0.3-48.5 months) was low: 7% in the operated-upon with curative intent group (R0+R1) and 5% in the R0-group. The role of preoperative radiotherapy in combination with standardised TME-surgery is not known yet, because follow-up has not been completed.

Medical Research Council (MRC) CR07 trial

The aim of this trial is to address the following question in operable rectal cancer: Are local recurrence-free rates and quality of life optimised by giving all patients short-course preoperative radiotherapy, or is it preferable to give postoperative chemoradiotherapy only to those at high risk of recurrence (i.e. with involved margins following surgery)?

Randomisation is done for preoperative radiotherapy of 5x5 Gy and selective postoperative radiotherapy of 25x1.8 Gy; if randomised for this arm patients with involved circumferential margins receive chemoradiotherapy. Adjuvant chemotherapy can be given as per local policy to these patients, but also to other randomised patients.

Although the aim of the operation is to achieve complete local excision of the tumour, the performance of a formal total mesorectal excision is left to the surgeon's discretion. All specimens are assessed by the local pathologist using the procedure of Quirke and Dixon¹⁹ and Quirke et al.²⁰ Pathologists had to attend a training day, and a network of regional pathologists (including P. Quirke) has been established to handle any queries, and to provide further pathology training if required. A system of quality assurance was implemented to ensure uniformity of pathological reporting.

The trial is designed to show that there is less than a 5% difference in local recurrence rates at 2 years. This will require the randomisation of approximately 1800 patients.

The trial started in March 1998, and up to July 2000, 375 patients have been randomised from 46 centres in the UK, including South Africa and New Zealand. From an interim-analysis, it appeared that anastomotic leak rate is 10% in the LAR-group. Of the patients randomised to receive preoperative radiotherapy, 88% received it at the correct dose. Over 80% of patients in the postoperative arm with involvement of the circumferential margin received postoperative radiotherapy, 75% at the dose stated in the protocol.(newsletter MRC CR07, Spring 2000)

Stockholm IV trial

The aim of this study is to compare preoperative radiotherapy treatment with "conventional" fractionation (25x2 Gy) with treatment of 5x5 Gy, and to study a possible effect of different time intervals between the end of radiotherapy and surgery in operable rectal cancer. The main questions to be addressed are: A) Is preoperative radiotherapy given during 5 weeks with a conventional fractionation (25x2 Gy) followed by surgery after 4-8 weeks (arm 1) preferable to treatment with 5x5 Gy during one week followed by surgery within a week (arm 2) or after 4-8 weeks (arm 3)? B) Are there any clinically significant differences in the rate of local recurrence, survival time, postoperative morbidity and mortality, or late morbidity? C) Is the need of a permanent stoma less if the surgery is delayed?

Some centres and some patients will likely not accept the first randomisation arm, due to long treatment time. In these situations patients may be randomised only between the second and third arms.

Specimen-oriented surgery with total or partial mesorectal excision according to Heald is performed in the trial. In Sweden, introduction of TME was done on a general basis several years ago.^{10,26} In addition, the protocol of Quirke was introduced and taught to pathologists.¹⁰ In the Stockholm IV trial, the surgical specimen is judged according to this protocol.

Total accrual will be 840 patients. When 300 patients have been included and followed

for at least 2 years in the two-armed comparison, an interim analysis regarding cumulative local recurrence will be undertaken.

This study started in 1999 and up to 1 July 2000, 50 patients have been randomised.

NEOADJUVANT TRIALS, LONG-TERM PREOPERATIVE RADIOTHERAPY
Chirurgische Arbeitsgemeinschaft für Onkologie (CAO)/Arbeitsgemeinschaft
Radiologische Onkologie (ARO)/Arbeitsgemeinschaft Internistische Onkologie
(AIO), Rectal Cancer Study

In this trial, patients with advanced rectal cancer (uT3/4 or uN+ or Mason III/IV) are randomly assigned to pre- or postoperative radiochemotherapy: 50.4 Gy are applied to the pelvis. 5-fluorouracil (FU) is administered concomitantly as 120h-continuous infusion. Four cycles of 5-FU maintenance chemotherapy are applied. Radiochemotherapy is identical in both arms except for a small-volume boost of 5.40 Gy in the postoperative setting. The time interval between radiochemotherapy and surgery is 4-6 weeks in both arms.

Techniques of surgery are standardised and total mesorectal excision is mandatory for lesions in the lower and middle parts of the rectum. The pathology examination is done according to standardised procedures that were established by P. Hermanek.

A decrease in local recurrence rate is expected from 15% to 5-10% in the arm with preoperative radiochemotherapy vs. the arm with postoperative therapy. Furthermore a survival advantage of 5-10% is expected, with no difference in, or even lower toxicity. In total, 680 patients must be randomised in order to detect these differences.

Regular study meetings are held twice a year with review of patients charts including surgery and pathology reports and data of radiochemotherapy, to ensure quality control.

This trial started in the summer of 1994, and up to 1 July 2000, 597 patients have been recruited from 26 participating institutions. Accrual of the trial will probably close in December 2000, when more than 800 patients will have been randomised. From an interim-analysis it was concluded that accrual of the trial is going well and that neoadjuvant radiochemotherapy is tolerated excellently and bears no higher risk for peri- and postoperative morbidity.²⁷

EORTC 22921

This trial is conducted by the EORTC Radiotherapy Group and evaluates in a four-arm randomised study the effects of combining 5-FU/leucovorin (LV) with preoperative irradiation (45 Gy) vs. radiotherapy alone (45 Gy), and of postoperative 5-FU/LV vs. no adjuvant therapy in patients with resectable T3/4 adenocarcinoma of the rectum.

The surgical procedure should be performed as soon as possible 3-10 weeks after preoperative treatment in both arms. It is advised to perform a total dissection of the mesorectal fat in any case. In the trial pathological examination is not strictly performed according to Quirke. However, on the pathology form information is asked about the status and quality of the circumferential margin.

In a previous study of the EORTC-GI group using preoperative irradiation, the 5-year survival was 52% in clinically selected patients. The minimal clinically significant survival difference of interest is 10%. If it is assumed that 25% of the randomised patients will become potentially ineligible, a total of 992 patients have to be entered.

Quality control procedures take place by means of audits of the Radiation Physics Quality Assurance Committee of the cooperative group of Radiotherapy²⁸ and a Datamanagement

Study Group.

This trial started in April 1993 and up to 1 July 2000, the accrual was 759 patients.

ADJUVANT TRIALS

Study 92/157-004

Randomised phase III studies for a direct comparison of 5-FU/LV + monoclonal antibody (mAb) 17-1A vs. 5-FU/LV in colon cancer are completed, but not yet analysed for outcome. A comparable study for rectal cancer has not been conducted yet. Therefore, the 92/157-004 study was set up by the Austrian cooperative group. The objective of this study is to assess the efficacy of preoperative radiotherapy in combination with postoperative chemotherapy or postoperative immuno-chemotherapy.

At first all patients were treated with 10x2.5 Gy (5 days of 2x2.5 Gy) preoperative radiotherapy followed by surgery. The rationale for this scheme was the fear of side effects with the larger single dose of 5 Gy. After surgery, Dukes' B or C tumour patients were randomised between 5FU/LV vs. 5-FU/LV/mAb 17-1A. This trial has in the meantime been amended. Investigators are allowed to choose prolonged fractionation in order to permit inclusion in the study of patients whose tumours at presentation are felt to be unresectable (and those who have a bulky, but resectable tumours). Operable tumours at presentation may receive either short or prolonged fractionation radiotherapy according to individual practise.

In carcinoma of the middle or lower third of the rectum, the mesorectum should be removed completely, laterally as well as caudally, up to the visceral pelvic fascia of the pelvic floor. Pathological examination is done according to the protocol of Quirke.

The study is designed to detect a difference in 5 year survival from 70% for chemotherapy alone, as compared to 80% for chemotherapy plus mAb 17-1A. Total accrual is calculated to be 700 patients, with 350 patients per arm.

This trial started in July 1997 and accrual up to 1 July 2000 was 278 patients.

PROCTOR-trial, Dutch ColoRectal Cancer Group (DCRCG)

The successor to the TME-trial is the PROCTOR-trial (Preoperative Radiotherapy and/Or adjuvant Chemotherapy combined with Tme-surgery in Operable Rectal cancer). In this trial, the role of adjuvant chemotherapy (5FU/LV) is investigated in combination with standardised TME-surgery and pathology. Randomisation for preoperative short-term radiotherapy is continued in the PROCTOR-trial, but hospitals can also choose for an own policy of yes/no preoperative radiotherapy, until the outcome of the TME-trial is known. After surgery and pathological examination, TNM-stage II or III, R0 patients are randomised for chemotherapy with 5FU/LV or observation. The setup for this trial is the same as that for the TME-trial.

The overall survival in the arm treated without chemotherapy is expected to be approximately 60%. Assuming an improvement in overall survival from 60% to 70% in the arm with chemotherapy, 500 R0, TNM-stage II or III patients are needed per arm.

The PROCTOR-trial has been accruing patients since April 2000; up to 1 July 2000, eight patients have been randomised.

Table 1. Randomised phase III treatment trials in rectal cancer.

Trial	Year started	Year closed	Design	Inclusion-criteria	Stratification	No. of participating centres	Accrual	Target accrual	Main outcome parameter	Difference to be detected
Neoadjuvant, short-term radiotherapy TME-trial, DCRG 23,31	1996	2000	-TME -5x5 Gy RT + TME	Resectable adenocarcinoma within 15 cm of anal verge, without evidence of distant metastases, no upper age limit	Hospital, type of resection	108	1861	1400 (Dutch patients)	Local recurrence	5%
MRC CR07 trial	1998	Still open	-5x5 Gy + surgery -Surgery + selective 45 Gy	Resectable adenocarcinoma within 15 cm of anal verge, without evidence of distant metastases, upper age limit 75	A number of factors including surgeon	46	375	1800	Local recurrence	5% at 2 years of FUP
Stockholm IV	1999	Still open	-50 Gy + surgery -5x5 Gy + surgery within one week -5x5 Gy + surgery after 4-8 weeks	Operable adenocarcinoma, without evidence of distant metastases	Hospital	unknown	50	840	Postop morbidity and mortality, rate of sphincter preserving surgery, late morbidity, local recurrence, survival	When 300 patients have been included and followed for at least 2 years in the 2-arm comparison (2nd and 3rd arm), an interim-analysis regarding LR will be undertaken.
Neoadjuvant, long-term radiotherapy CAO/ARO/ AIO ²⁷	1994	Still open	-Surgery + 50.4 Gy+5.4 Gy boost/5-FU -50.4 Gy/5-FU + surgery	Advanced rectal cancer (dT3/T4 or uN ₁ or Mason CS III/IV) within 16 cm of anal verge, without evidence of distant metastases, upper age limit 75	Surgeon	26	597	680	Overall survival	10%
EORTC 22921	1993	Still open	-45 Gy + surgery -45 Gy/5FU-LV + surgery -45 Gy + surgery + 5FU-LV -45 Gy/5FU-LV + surgery + 5FU/LV	Resectable T3/T4 adenocarcinoma, within 15 cm of anal verge, without evidence of distant metastases, upper age limit 75	Institution, sex, tumour location (0-5, 5-10, 10-15 cm), stage (T3/T4)	40	759	992	Disease-free and overall survival	10% overall survival
Adjuvant Study 92/157-004	1997	Still open	-5x5 Gy or 10x2.5 Gy or 40-45 Gy + surgery + 5FU/LV -5x5 Gy or 10x2.5 Gy or 40-45 Gy + surgery + 5FU/LV/mAb17-1A	Dukes' B or C rectal tumour, within 16 cm of anal verge, R0 resection, at least 8 histologically investigated lymph nodes, upper age limit 80	Centre, preop RT-regimen, T-stage, N-stage	50	278	700	Overall survival	10%
PROCTOR trial, DCRG	2000	Still open	-no RT or 5x5 Gy + surgery -no RT or 5x5 Gy + surgery + 5FU/LV	TNM-stage II or III tumours, within 15 cm of anal verge, R0 resection	Centre, preoperative RT	6	8	1000	Overall survival	10%

DISCUSSION

The outcome after surgery for rectal cancer differs markedly between patients series, regarding both local recurrence rates and survival. A high incidence of local recurrence is associated with conventional, nonstandardised procedures.¹⁻³ To improve the results of surgery, various additional treatments, such as radiotherapy, chemotherapy, and immunotherapy, have been tested.

The Swedish Rectal Cancer Trial was the first trial to show that better local control achieved with preoperative radiotherapy resulted in improved survival.⁷ The results found in this trial confirmed the studies from P. Hermanek, which showed a clear correlation between survival and local recurrence rate.¹⁸ This can be explained by the fact that the disease recurs locally first and then disseminates to other organs in 20-30% of all patients with a recurrent rectal cancer.

In recent years local control and survival have been further improved by the introduction of the TME-technique, as first described by Heald.⁸⁻¹⁰ TME is accomplished by precise sharp dissection within the true pelvis around the integral mesentery under direct vision, enveloping the entire mid-rectum, with preservation of the hypogastric plexus.

The studies published so far on adjuvant therapy have been carried out without any adequate definition of the surgical procedure and without appropriate quality control. In none of the cases were explicit details given of the procedure applied, together with the criteria to be met with respect to safety margins, excision of mesorectum and lymph node dissection. Local recurrence rates in the “surgery alone” control groups of former trials were often high; 20% or more.^{7,29-33} Therefore, it is necessary to determine whether a further improvement can be obtained by adjuvant therapy, given the currently achievable global local recurrence rates of less than 10% by standardised TME-surgery alone. If optimal TME-surgery can be widely implemented, outcome improvement could, by the calculations of Hermanek, be four times as great as that achievable by adjuvant therapy, and at a fraction of the cost.

In this work an overview is given on European trials in which TME-surgery is intentionally performed. Most of these trials are still in progress and have too short a follow-up, so definitive results, apart from feasibility and interim-analyses, cannot be presented yet. In all trials described, TME-surgery is indicated, or at least advised, in low or middle rectal cancers. However, the extent of surgical quality control differs between the trials. In Sweden and The Netherlands, nation-wide projects have been conducted in which surgeons were trained to perform a proper TME in an attempt to improve their treatment results. The study of Martling et al.¹⁰ showed that local recurrence rate decreased by more than 50% as a result of a surgical teaching initiative in the county of Stockholm. The effect of the introduction of TME-surgery with quality control on outcome of rectal cancer was also investigated in The Netherlands. We compared results from Dutch patients in the TME-trial with results from a former randomised trial (CRAB-trial), in which conventional surgery was performed without quality control. It was found that the introduction of TME-surgery with quality control led to a substantial decrease in local recurrence rate and cancer death in The Netherlands.(paper submitted)

Besides better local control and survival, sharp TME-dissection has been associated with a higher incidence of sphincter preservation and pelvic autonomic and plexus preservation, avoiding both colostomy and impotence, as well as blood transfusions.^{4,11,12}

The proportion of abdominoperineal resections has come down from 35% or more^{1,34,35} to 30% or less in recent years.^{10,23} However, one adverse effect of the higher rate of sphincter-preserving procedures may be a higher rate of anastomotic leakage.³⁶ Higher leak rates with TME-surgery as compared to conventional surgery, have been reported.^{9,37} Several conventional surgery studies report overall anastomotic leak rates between 0% and 17.4%.^{35,38,39} The clinical leak rate of 12% in the Dutch TME-trial and 10% in the MRC CR07 trial are quite high, but within this range. Perhaps the construction of a high number of temporary colostomies and side to end anastomoses or pouches, have prevented increased clinical leak rates.⁴⁰⁻⁴²

Due to the extreme disability caused by local failure, a gain in local pelvic control per-se is generally accepted as a main objective of any adjuvant treatment.¹⁵ In terms of tumour biology, preoperative radiotherapy is preferred to postoperative radiotherapy because the tumour cells before the operation have a higher oxygen saturation and are therefore more sensitive to irradiation. Furthermore, preoperative radiotherapy devitalises tumour cells that may be dispersed in the course of the operation. Preoperative radiotherapy over several weeks results in “down-staging” in many cases, i.e. the size of the primary tumour is reduced, the possibility of lymph node metastases is reduced, and in isolated cases complete remission occurs.^{29,43} The timing dose and fractionation of preoperative radiotherapy in combination with TME-surgery are currently under investigation in the Stockholm IV trial.

One advantage of postoperative radiotherapy is that it allows the exclusion of patients with tumours in stages Dukes’ A or D. To be effective, postoperative radiotherapy should begin within 4-6 weeks of the operation to prevent tumour cell proliferation in the postoperative fibrous, hypoxic tissues. However, at this point many patients have not yet recovered from the operation and therefore, there is often a delay before they receive the adjuvant radiotherapy.^{13,44} In the MRC CR07 trial, the compliance of patients in the postoperative radiotherapy arm was lower than in the preoperative short-term radiotherapy arm. Therefore, higher compliance rates of the short-term preoperative radiotherapy regimen (compared to the postoperative radiotherapy plan), as shown in the Dutch TME and MRC CR07 trials, could explain the better results.

The probability of resistant cell lines may be smaller when irradiation is combined with chemotherapy and when these are given earlier in the disease, i.e. sooner in the treatment plan. Concurrent 5FU may have a sensitising effect on the radiotherapy. However, the role of chemoradiotherapy in the treatment of primary rectal cancer still has to be determined. In the United States the opinion is that all patients with a Dukes’ B or C lesion should have postoperative chemoradiotherapy.¹⁵ Chemoradiotherapy is not routine in Europe and is still considered investigational therapy in rectal cancer. The CAO/ARO/AIO and EORTC 22921 trials are ongoing to determine the role of chemoradiotherapy in combination with TME-surgery.

In the Dutch NACCP-study, chemotherapy as sole treatment showed no effect in combination with conventional surgery in the prevention of distant recurrences and improvement of survival.¹⁴ This may in part be explained by the high rate of local recurrence, which might have masked the beneficial effect of chemotherapy. The role of chemotherapy has never been tested in combination with standardised TME-surgery, but is now under investigation in the PROCTOR-trial. The efficacy of preoperative radiotherapy in combination with postoperative chemotherapy or postoperative immuno-chemotherapy is currently being

investigated in the Austrian 92/157-004 study.

For optimal quality control of the surgical procedure standardised examination by pathologists is important.^{19,20} In all trials, the circumferential margin was included for investigation. However, the protocol of Quirke was not used in all trials. In the Dutch, MRC CR07 and Swedish trials, this protocol has been used in combination with extensive pathological quality control.

The Dutch TME trial is one of the first trials in which the effect of adjuvant therapy in combination with TME surgery was evaluated. Standardisation of surgery, radiotherapy, and pathology were achieved. The accrual progressed swiftly and the trial was shown to be quite feasible. The design of the TME-trial has already resulted in a large reduction of the number of local recurrences. The first results on the role of preoperative radiotherapy in combination with standardised TME-surgery are presented at a large congress in April 2001 in The Netherlands (www.colorectal2001.com). Results of the other European TME-trials will take longer.

An effort will be made to achieve further standardisation and quality assurance of diagnostics in the PROCTOR-trial. Based on the data of the TME-trial, 20% of the cases with primary rectal cancer underwent an irradical resection either defined as an R1 (microscopic tumour left behind) or R2 (macroscopic tumour left behind) resection. Better selection of patients for preoperative radiotherapy in case of a locally advanced tumour or palliative procedures in patients with disseminated disease can be achieved by preoperative staging of rectal cancer with the routine use of a spiral computed tomography scan.

CONCLUSIONS

During the past decade, it has been clearly demonstrated that adjuvant treatment has the potential of improving not only prognosis in terms of local recurrence, but also in terms of overall survival. However, the question has yet to be answered as to whether in combination with TME-surgery, adjuvant therapy is capable of achieving any further improvement in outcome. In Europe, mesorectal excision, with its persistent decline in local recurrence rates, has become the new standard of operative management for rectal cancers, replacing conventional resection technique.²² Current clinical trials examining the role of adjuvant therapy in patients who are undergoing standardised operations, are now setting the standard of care in several European countries.

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