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Developments and quality assurance in rectal cancer surgery

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Abstract

One of the main problems in the treatment of rectal cancer is the development of local recurrences. In the last decades, major improvements have been realized in the surgical treatment of rectal cancer. The introduction of TME-surgery has led to a large reduction in local recurrence rates and improved survival. TME-based operations are now established as the standard of care for rectal cancer, and should form the basis for trials concerning the role of (neo)adjuvant therapy. However, training and quality control are prerequisites to obtain good results in all surgeons' hands. Furthermore, standardization in the description of operations and reporting of pathology specimens should be implemented as important features of quality control. In general, it is thought that high volume and specialist care produces superior results to low volume and non-specialist care, especially for those less frequent forms of cancer and in technically difficult operations, like those for rectal cancer. However, limiting the performance of rectal cancer surgery to highly specialized surgeons or to only those general surgeons who perform more than a certain volume is impractical in view of the prevalence of rectal cancer. This article reviews developments in the treatment of especially mobile rectal cancer and pays attention to variability in outcomes and quality assurance of surgery.

Keywords: Rectal cancer; Surgery; Developments; Quality assurance; Local control; Survival

1. Introduction

Colorectal cancer is the most common gastrointestinal cancer in the Western world. In 1995, 8000 new colorectal cancer patients were registered in The Netherlands, of whom approximately 25% had rectal carcinoma [1]. One of the main problems in the treatment of rectal cancer is the development of local recurrences; local recurrence rates vary widely with reported incidences from 5 to 45% [2,3]. These cause severe disabling symptoms, are difficult to treat, and usually kill the patient [4]. Recurrences of rectal cancer are often confined to the pelvis without distant metastases, and are considered locoregional failures [5,6]. Most of them become overt within 2 years of operation. In the last decades, major improvements have been realised in the surgical treatment of rectal cancer. This article reviews developments in the treatment of especially mobile rectal cancer and pays attention to variability in outcomes and quality assurance of surgery. Quality assurance has become an important topic in rectal cancer surgery and is of major importance for standardisation of treatment in (neo-)adjuvant therapy studies and improvement of outcomes.

2. Traditional surgical treatment

The surgical principles in the treatment of colorectal cancer were formulated by Lord Moynihan for the first time in 1908 [7]. Early in the beginning years of the 1900s, the local recurrence rate following surgery for rectal cancer was nearly 100%. Miles described a combined radical abdominal and perineal approach (APR) [8] to remove the pelvic mesocolon and the 'zone of upward spread' to solve this problem. For a long time, Miles' operation was the 'gold standard' for the treatment of rectal cancer, even for tumours above 15 cm from the anal verge. A frequently heard comment was indeed "One had not done a proper cancer operation if the man was not impotent thereafter". Since Miles described his abdominoperineal resection technique, various modifications have been proposed to improve patient prognosis and quality of life.

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Surgery related factors to which much attention has been paid are early vascular isolation and bowel ligation. Turnbull [9] described a technique in which lymphovascular isolation and ligation was performed prior to mobilisation of the segment of tumour-bearing colon. The idea behind this 'no-touch' isolation technique was to prevent early venous and lymphatic spread of tumour cells, based on the observation that tumour cells have the capacity to appear in the venous bloodstream at all times, especially after manipulation of any kind [10]. A prospective randomised multicentre study evaluating the effect of the 'no touch' concept, however, could not demonstrate a benefit with respect to overall survival. In subgroup analysis, the concept was shown to be of statistically significant benefit only when microscopic vascular invasion was present in the tumour [11].

En bloc resection of lymph nodes at the origin of the inferior mesenteric artery (IMA) from the aorta, often called 'high' ligation, was assumed in the 1960s to give a survival benefit compared with 'low' ligation, which allows selective preservation of the left colonic artery. Such benefit was demonstrated for cancer of both the left colon and rectum [12]. Two more recent comparative studies have failed, however, to show a survival benefit for 'high' or 'low' ligation [13,14]. It might be argued that once the tumour has spread to the 'high' nodes, the disease is generalised and surgery for cure cannot be achieved anymore.

Improvement in the quality of life after surgery was obtained due to the introduction of mechanical stapling devices [15] together with the observation that the safe distal margin is 2 cm from the primary tumour [16,17]. The combination of these two factors made lower resection with reconstruction possible, guaranteeing an anatomically and functionally intact anal sphincter, instead of the much more mutilating abdominoperineal resection with implicite definite colostomies. Developments of new approaches also included the coloanal anastomoses [18]. This technique has acceptable functional results and complication rates and therefore has become a viable alternative to the abdominoperineal resection in the treatment of low rectal cancer. In addition, significant functional improvement, particularly in the first 12–24 months after surgery, have been achieved with use of the colonic J-pouch [19].

Although controversy has existed [20,21], it is now clear that sphincter-saving surgery has no effect on cancer recurrence and mortality. In addition to the aforementioned surgical technicalities, the availability of blood transfusion and major improvements in anaesthesia, perioperative care management and control of infectious complications, have also enabled surgeons to resect the tumour and reconstruct the continuity of the bowel, rather than to only construct a colostomy and to leave the tumour *in situ* [22].

Nevertheless, despite the aforementioned developments, one of the problems in the treatment of rectal cancer surgery has been the inability of surgeons to optimise local tumour control. The basic conventional procedure involving blunt dissection, often resulted in incomplete removal of mesorectal tissue with high local recurrence rates [2,20,23]. Table 1 shows local recurrence after 'curative' surgery in conventional surgery; local recurrence from 12% up to 38% were reported. In addition, damage to the autonomous pelvic nerve plexus with the consequence of a high incidence of sexual [24] and bladder dysfunction [25] was very likely in conventional surgery with a great impact on the quality of life after surgery.

Table 1
Local recurrence after 'curative' conventional surgery

	Years studied	Patients investigated (*n*)	Local recurrence (*n*)	Local recurrence (%)	Remarks
Rao 1981 [107]	1967–1972	204	44	21.6	
Rich 1983 [108]	1968–1972	142	43	30.3	
Pahlman 1984 [109]	1974–1979	197	74	37.6	
Phillips 1984 [20]	1976–1980	848	124	14.6	
Philipsen 1984 [48]	1968–1976	382	105	27.5	27% received preop RT
McDermott 1985 [110]	1950–1983	934	193	20.7	
Pescatori 1987 [111]	1967–1980	162	19	11.7	
Athlin 1988 [112]	1971–1980	99	37	37.4	Undefined no. of pts received postop RT/CT
Rinnert-Gongora 1989 [113]	1973–1982	258	53	20.5	
Zirngibl 1990 [114]	1969–1985	1153	265	23.0	
Akyol 1991 [115]	1985–1989	294	49	16.7	
Stipa 1991 [116]	1970–1991	235	42	17.9	
Norstein 1993 [117]	1986–1988	275	81	29.5	
Adam 1994 [118]	1985–1990	141	32	22.7	6% received postop RT
Nymann 1995 [119]	1982–1990	175	37	21.1	
Damhuis 1997 [120]	1984–1991	902	162	18.0	8% received postop RT
Mollen 1997 [64]	1981–1986	232	42	18.1	27% received postop RT
Kapiteijn 1998 [23]	1988–1992	668	150	22.5	36% received postop RT

RT, radiotherapy; CT, chemotherapy; preop, preoperative; pts, patients.

3. Variability in outcomes

3.1. Hospital- and surgeon-related variability

There is evidence to suggest an association between higher-frequency and specialised institutions and surgeons, and improved outcome in oesophageal cancer, breast cancer, and periampullary/pancreatic neoplasms [26–28]. Inter-institution and intersurgeon variabilities in colorectal cancer surgery have also been shown in several studies. This applies to immediate results, such as surgical morbidity and mortality [29–33], as well as long-term results, such as local recurrence and survival [20,23,29,34–37]. An explanation of interinstitution and inter-surgeon variation in outcome is always difficult. The different patient and tumour-related factors have to be considered as well as the surgical technique itself; anaesthesia, pre- and postoperative care (including management of postsurgical complications and further follow-up), additional non-surgical treatment modalities, diagnosis and management of recurrences.

Table 2 shows a complete overview of published studies which have investigated the influence of hospital- and surgeon-related factors in colorectal cancer according to short- and long-term outcomes. With regard to short-term outcomes [20,23,30–33,36]. Fielding and colleagues drew attention to the differences in rates of clinically evident anastomotic leakage after resection for large bowel cancer [31]. A study by Hannan and colleagues [32] showed that hospitals with volumes of 40 or less procedures for colectomies had significantly higher standardised in-hospital mortality rates compared with hospitals with volumes higher than 40. Other studies found no correlation between hospital- and/or surgeon-related factors and short-term outcomes [31,38,39].

Several studies have investigated the effect of hospital volume on long-term outcomes. However, findings in literature are controversial [23,34–36], with also one report suggesting that, for example, hospital volume predicts clinical outcome for colorectal cancer, but not in the absolute magnitudes in comparison with the variation observed for higher-risk cancer surgeries [40–42]. Other studies investigated type of hospital, teaching status and localisation of hospitals. Hakama and colleagues [43] found university districts to have a better survival than non-university districts. Blomqvist and colleagues [44] found that 1-year relative survival was higher in large regional versus small local hospitals. We did not find an association between hospital volume and local recurrence rate in a population-based registry study in The West Netherlands [23].

The influence of individual surgeon volume and specialisation have also been investigated in several studies [20,29,36,37]. Hermanek suggests that, in order to maintain good quality of surgery, the minimum volume per surgeon should be approximately one or two radical resections per month [45]. In his study [36], however, there was one particular high-volume surgeon with a very poor outcome, which makes the conclusion about the role of volume controversial. In the study of Porter and colleagues, it was shown that outcome is improved both with colorectal surgical subspeciality training and a higher frequency of rectal cancer surgery [37]. Other studies, however, did not find associations between surgeon-related factors (e.g. consultants versus junior staff) and outcome [20,46,47], although sometimes wide variations between individual surgeons were reported [20,29].

When reviewing the data in the literature with respect to volume, it must be considered that the definitions of high volume are different with varying cut-off points. This makes comparison of the studies on hospital- and surgeon-related factors and outcome difficult, also since the data sources and statistical methods used are different. Cut-off points should be defined prospectively to avoid biases inherent in *post-hoc* analysis (in which the cut-off point can be selected to maximise volume-outcome associations).

In conclusion, it is evident from the data published that surgery is less than optimal as reflected in some hospitals or by some surgeons. It is therefore important to give surgeons the opportunity to undergo training and to adopt new and improved techniques. It is more difficult to find good arguments which support the hypothesis that treatment volume or specialisation in colorectal surgery *per se* are important factors. Rather, it could be that the relationship between treatment volume and results is more a consequence of bad organisation or badly trained surgeons than volume or specialisation itself.

3.2. Variability in definitions

Apart from variability in hospital and surgeon outcome, important factors responsible for the large range of local failure rates, are different definitions used for rectal cancer, curative resection, local recurrence and the methods used for detecting such a local failure. Tumour localisation is usually measured by endoscopy, but not all papers give accurate information on the assessment of tumour height [48,49]. The site of the tumour is important; lower tumours (i.e. below 10 cm) show higher local recurrence rates than higher tumours [48,50].

Furthermore, consensus is needed with regard to the definition of a curative resection and which group of patients is to be analysed for a certain outcome to make studies comparable. A study of Marsh and colleagues [51] showed that it is possible to define local recurrences in many different ways and by doing so widely different numerical values can be obtained. For the same series of patients, it was demonstrated that the local recurrence rate could be calculated as low as 4% or as high as 43% by exclusion or inclusion depending on the used definition. Marsh proposed in his paper that local recurrence

Table 2
Studies which have investigated the influence of hospital- and surgeon related factors in the outcome of colorectal cancer

Study	Study period	Patients (*n*)	Hospitals (*n*)	Surgeons (*n*)	Analysed factors	Analysed outcomes	Results
Short-term, hospital factors							
Luft and colleagues, 1979 [121]	1974–1975	73 427 colectomies (12 surgical procedures investigated)	1498		Hospital volume	In-hospital mortality	For colectomy, the actual death rate tends to flatten out at relatively low volumes; i.e. 10–50 procedures per yr
Flood and colleagues, 1984 [33]	1972	17 872 large bowel operations with cancer diagnoses (15 surgical categories investigated)	1040		Hospital volume	Death in hospital	• Evidence that high-volume is associated with better outcomes for surgical pts (including large bowel operations with cancer diagnoses) • Some evidence that low-volume hospitals are associated with the poorest outcome for low-risk surgical pts • Earlier publication 1982 [39]: mortality not related to volume
Kessler and colleagues, 1993 [30]	1984–1986	1115 rectal cancer pts	7		Individual hospitals	Operative/postoperative mortality	Institution was an independent factor for operative/ postoperative mortality
Begg and colleagues, 1998 [122]	1984–1993	3380 pelvic exenterations, pts $\geqslant$65 yrs (5 major cancer surgery procedures investigated)	26		Hospital volume	30-day mortality	Higher volume was linked with lower mortality for pelvic exenteration
Short-term, surgeon factors							
Reinbach, 1994 [123]	1992	116 colorectal cancer pts	2	10	Surgeon speciality interest	• Resection type	Surgeons without a speciality interest in colorectal cancer • removed less amount of colon/rectum • showed less lymph nodes in the mesenteric resection specimen • had less operative mortality
Lothian and Borders large bowel cancer project, 1995 [124]	1990–1992	750 colorectal cancer pts, 260 pts with rectal cancer		28 consultant surgeons	Variability between surgeons	• Resection type • Leak rate	The five consultants responsible for half of the rectal cancer pts had similar APR rates but lower leak rates in LAR pts compared with the others
Rosen and colleagues, 1996 [125]	1986–1994	1753 colorectal cancer pts	1	39	Colorectal versus. other institutional surgeons	In-hospital mortality	Mortality rate and length of stay was lower/shorter if a colorectal surgeon rather than a general surgeon had operated

Table 2 (*continued*)

Study	Study period	Patients (*n*)	Hospitals (*n*)	Surgeons (*n*)	Analysed factors	Analysed outcomes	Results
Khuri and colleagues, 1999 [38]	1991–1993	11 330 partial colectomies (eight procedures investigated)	125		Surgical volume	30-day mortality rate	No correlations found
Short-term, hospital + surgeon factors							
Fielding, 1980 [31]	1976–1980	1466 colorectal cancer pts	23	84	• Variation between surgeons • Comparison of teaching and district general hospitals	Leakage	• Variation in leakage: 5–30%. The surgeon was probably the most important single factor influencing leakage. • No difference between teaching and district general hospitals.
Kelly and colleagues, 1986 [126]	1977	2612 cancers of the colon or rectum (4 procedures investigated)	116	434	Hospital and physician factors: volume, board certification, teaching status, size and location	In-hospital mortality	• Higher volume and teaching hospitals had less in-hospital mortality • Pts were more likely to die in public hospitals compared with private, non-profit hospitals
Hannan and colleagues, 1989 [32]	1986	10 297 colectomies (5 procedures investigated)	250	1997	Hospital and physician volume	In-hospital mortality	Annual hospital thresholds appear to exist at 40 procedures for colectomies
Burns and colleagues, 1991 [127]	1988	3457 large bowel resections (11 medical conditions and five surgical conditions investigated)	47		Several hospital and physician characteristics (including volume)	• Length of stay • Patient mortality	• Volume of pts with the same condition treated by the hospital increases length of stay and mortality • Volume of pts treated by the physician decreases length of stay and mortality among those with surgical conditions • Medical school attended by the physician influences length of stay
Harmon and colleagues, 1999 [128]	1992–1996	9739 colorectal cancer pts	50	812	• Hospital volume • Surgeon volume	• In-hospital death • Total hospital charges • Length of stay	• Higher surgeon volume was associated with improvement of all three outcomes • Medium volume surgeons achieved results equivalent to high-volume surgeons when they operated in high- or medium-volume hospitals

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Table 2 (*continued*)

Study	Study period	Patients (*n*)	Hospitals (*n*)	Surgeons (*n*)	Analysed factors	Analysed outcomes	Results
Long-term, hospital/district factors							
Hakama and colleagues, 1989 [43]	1970–1981	7078 colon cancer pts	21 hospital districts		Type of hospital in district of residence	Actuarial relative survival	University did better than non-university districts
Mohner and Slisow, 1990 [129]	1976–1980	15 731 rectal cancer pts	334		Degree of centralised treatment in district	5-yr survival	Higher 5 yr relative survival in districts with a centralisation index of at least 60 (=at least 12 cases/yr)
Launoy 1992 [130]	1978–1984	1331 colorectal pts			Type of hospital	Actuarial survival	No association between hospital type and survival
Kapiteijn and colleagues, 1998 [23]	1988–1992	668 rectal cancer pts	12		Hospital volume	LR	No correlation between hospital volume and LR
Dahlberg 1998 [87]	1974–1995	423 rectal cancer pts	1		Concentration of surgery to a colorectal team	LR	Results of treatment can be improved by concentration of surgery to a colorectal team
Blomqvist and colleagues, 1999 [44]	1973–1992	30 811 rectal cancer pts	100		Hospital catchment area	Relative survival	1-yr relative survival was higher in large regional versus small local hospitals
Luna Perez 1999 [131]	1980–1995	82 pts with mid-rectal cancer			Cancer centre versus general hospitals • Hospital volume • Surgeon volume	• LR • OS • OS	Favourable prognostic factor for LR and OS was treatment at a cancer centre • No detectable caseload effect for surgeons • Survival of pts treated in hospitals with caseloads above 33 cases/yr was slightly worse than for those treated in hospitals with fewer caseloads
Kee *et al*. 1999 [132]	1990–1994	3217 colorectal cancer pts	19	71			
Kapiteijn and colleagues, 2001 (submitted), conventional surgery	1987–1990	269 rectal cancer pts	16		Hospital volume	• LR • DR • OS	Significant association between higher hospital volume and lower distant recurrence risk and higher survival
Kapiteijn and colleagues, 2001 (submitted), TME -surgery	1996–1999	661 rectal cancer pts	84		Hospital volume and specialisation	• LR • DR • OS	No associations found
Long-term, surgeon factors							
Phillips 1984 [20]	1976–1980	2336 colorectal cancer pts			Consultants versus junior staff	• LR	• No assocation between consultants versus junior staff and LR • Wide variation between consultant surgeons; significant for incidence of LR

Table 2 (*continued*)

Study	Study period	Patients (*n*)	Hospitals (*n*)	Surgeons (*n*)	Analysed factors	Analysed outcomes	Results
Porter and colleagues, 1998 [37]	1983–1990	683 rectal cancer pts	5	52	Surgeon • Volume • Specialisation	• LR • DSS	DSS correlated positively with surgeon specialisation and volume
Long-term, hospital and surgeon factors							
Norstein, 1998 [133]	1986–1988	1049 rectal cancer pts <75 yrs	64		Hospital • Volume • University/district/community • Specialism Surgeon • Specialists in GE/consultant/ in training	LR	• University hospitals had lower LR rates than district and community hospitals • Hospitals with a documented interest had lower LR rates than hospitals without • Pts operated on by surgeons in training had lower LR rates than pts operated on by a consultant or specialised surgeon
Parry and colleagues, 1999 [46]	1993	927 colorectal cancer pts			Hospital volume Surgeon • Consultant • Volume • Department • Surgeon volume	Survival • Cancer-related 5-yr survival	No assocations between hospital or surgeon volume and patient outcome • Surgical volume did not influence prognosis • Department was a significant factor in rectal carcinoma, whereas surgical quality group was only significant when department was excluded from the model.
Hermanek and colleagues, 1999 [47]	1984–1986	1539 colorectal cancer pts; 712 with rectal carcinoma	3 of 7 departments	43			Results from earlier publications: • Institution and surgeon are independent prognostic factors for LR and OS [36,134] • A minimum of 1 or 2 radical resections/month is necessary to obtain good quality of surgery [45]
Short + long -term							
Kingston *et al*. 1992 [135]	1981–1983	567 colorectal cancer pts	6	12 interested in colo-proctology	Type of hospital	• Operative mortality • 5 yr survival	Operative mortality and 5-yr survival were similar in teaching and district general hospitals

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Table 2 (*continued*)

Study	Study period	Patients (*n*)	Hospitals (*n*)	Surgeons (*n*)	Analysed factors	Analysed outcomes	Results
Simons and colleagues, 1997 [35]	1988–1992	2006 rectal cancer pts	125		• Type of hospital • Hospital volume	• Surgical procedure • Survival	• More SSP in teaching and high-volume hospitals • Improved survival in high-volume hospitals
Schrag and colleagues, 2000[34]	1991–1996	27 986 colon cancer pts aged 65 yrs	611		Hospital volume	• 30-day postoperative mortality • OS • Cancer-specific survival	• Difference in 30-day postoperative mortality between low versus high-volume hospitals • Association between higher hospital volume and longer survival
Simunovic and colleagues, 2000 [136]	1990	1072 rectal cancer pts			Hospital • Volume • Teaching status	• Treatment measures • Operative mortality • Long-term survival	No effect hospital volume and teaching status on treatment and outcome measures
McArdle and Hole, 1991 [29]	1974–1979	645 colorectal cancer pts	1	13 (specialised consultants)	Variation between surgeons	• Postoperative complications • Postoperative mortality • Survival	Significant variations between surgeons in: curative resections, leakage. postoperative mortality, LR, survival
Holm and colleagues, 1997 [137]	1980–1993	1399 rectal cancer pts	14	11	• Hospital volume, university versus non-university • Surgeon volume, experience	• Postoperative morbidity and mortality • LR • Death from rectal cancer	• Lower LR risk and death from rectal cancer in university hospitals • Lower LR risk and death from rectal cancer in more experienced surgeons

LAR, low anterior resection; APR, abdomino perineal resection; SSP, sphincter-saving procedure; LR, local recurrence; DR, distant recurrence; DSS, disease-specific survival; OS, overall survival; yr, year; pts, patients; TME, total mesorectal excision; GE, gastro-enterology.

after operation for rectal carcinoma should be defined as any detectable local disease at follow-up, occurring either alone or in conjunction with generalised recurrence, in all patients who have undergone resection.

Another confounding factor of analysis of local recurrence rates is the impact of the follow-up regimen on the eventually reported results. The methods for detecting local failure differ in accuracy [52], and the only reliable means to detect the true rate would be to do a routine autopsy [53] or second look operations [54]. However, this is not feasible and the most important recurrences are those which are clinically apparent and potentially harm the patient. In recent years, imaging diagnostics have improved (e.g. magnetic resonance imaging (MRI)), and potentially curable local recurrence patients can be more accurately identified.

In conclusion, investigators publishing about rectal cancer treatment should clearly state crucial definitions. It is obvious that the diversity in conducting and reporting surgical studies in rectal cancer does little to facilitate interstudy comparison or the evaluation of novel therapies.

4. Surgery in (neo-)adjuvant therapy studies

In order to improve local control and survival of conventional surgery, additional radiotherapy has been given. The results of studies using radiotherapy for rectal cancer, suggest that preoperative radiotherapy is more effective than postoperative irradiation in reducing local recurrence rates [55–57]. Swedish trials have shown improved local control and survival with the short-term 5×5 Gy preoperative radiotherapy scheme [55,56]. So far, chemotherapy alone for rectal cancer has shown little or no effect on disease-free and overall survival in combination with conventional surgery [58]. Combinations of radiotherapy and chemotherapy have also been given with improved outcomes, but sometimes at the expense of severe toxicity [59–61].

The studies so far published on adjuvant therapy have been carried out without any adequate definition of the surgical procedure and without appropriate quality control. In contrast with chemotherapy and radiotherapy, the quality of surgery appears to be difficult to examine. Nevertheless, standardisation and quality control of surgery are prerequisites to study the effect of (neo-)adjuvant therapy reliably, also since the surgeon can be an important factor in the accomplishment of tumour control (Table 2). In some trials, operation reports were reviewed by a surgical board [62], but otherwise no meaningful quality control on surgery was enhanced. Local recurrence rates in the 'surgery alone' control groups of these trials were often high; 20% or higher [359,60,63–65,83,78,111,693], representing non-standardised, conventional surgical techniques. Table 3 shows local recurrence rates after 'curative surgery' in surgery alone arms of randomised trials.

In addition, in none of the studies was explicit details given of safety margins, excision of mesorectum and lymph node dissection. Optimal quality control of the surgical procedure must also include a standardised examination by pathologists. Quirke and colleagues [66] described a method of detection of mesorectal spread

Table 3
Local recurrence after 'curative' surgery in surgery alone arms of randomised trials

	Years studied	Patients investigated (*n*)	Local recurrence (*n*)	Local recurrence (%)
Preoperative RT				
VASOG I 1975 [138]	1964–1969	87	32	36.8
EORTC 1988 [63]	1976–1981	175	49	28.0
Stockholm I 1990 [139]	1980–1987	425	120	28.2
Bergen 1990 [140]	1976–1985	131	31	23.7
North-West 1991 [141]	1982–1986	126	46	36.5
St. Marks 1994 [142]	1980–1984	210	51	24.3
MRC II 1996 [143][a]	1981–1989	140	65	46.4
SRCT 1997 [56]	1987–1990	557	131	23.5
Postoperative RT				
Odense 1986 [144]	1979–1985	250	57	22.8
Rotterdam 1991 [145]	1982–1989	84	28	33.3
MRC III 1996 [146]	1984–1989	235	79	33.6
EORTC 1997 [147]	1981–1986	88	30	34.1
Postoperative RT+CT				
GITSG (7175) 1985 [59]	1975–1980	58	14	24.1
NSABP R01 1988 [60]	1977–1986	184	45	24.5
Tveit, NARCPG 1997 [65]	1987–1991	70	21	30.0

RT, radiotherapy; CT, chemotherapy; EORTC, European Organization for Research and Treatment of Cancer; MRC, Medical Research Council; SRCT, Swedish Rectal Cancer Trial; NSABP, National Surgical Adjuvant Breast and Bowel Project.

[a] Only tethered tumours.

which required systematical examination of the specimen, by serial sectioning of the whole tumour and the surrounding mesorectum in the transverse plane. This method should be used to monitor differences in the operative technique. Furthermore, surgery can be documented photographically due to reproducible gross specimen features [67].

5. Lymph node dissection

In order to reduce local recurrence, and hence improve survival, more radical resections have been devised. Extended lymphadenectomy, involving dissection of pelvic and aortoiliac lymph nodes without resection of organs other than the rectum, was described as early as 1942 [68], but several subsequent papers in the late 1950s and early 1960s reported no statistically significant difference in survival after lateral pelvic node dissection [69,70] Stearns and Deddish [69] showed a greatly increased morbidity after the radical procedure, and noted that, in 51 patients with recurrence who came to autopsy, 23 (45%) had residual tumour in the pelvis.

Renewed interest in extended lymphadenectomy was reported by Koyama and colleagues in 1975 [71]. In 1989, Hojo and colleagues [72] reported the results of 437 patients, of which 192 had wide pelvic lymphadenectomy. The local recurrence rates for extended excision were significantly lower than those of conventional excision in patients with Dukes' B and C stages. Enker reported a large retrospective series consisting of 412 patients [73], of whom 192 had *en bloc* pelvic lymphadenectomy. The group of patients who seemed to benefit most from the extended dissection were those with mid-rectal Dukes' C cancers who underwent a sphincter-saving operation with a better cancer-specific 5-year survival in the extended lymphadenectomy group. However, a local recurrence rate of the 382 evaluable patients did not differ between the pelvic lymphadenectomy and conventional group. In a paper by Moriya and colleagues of 448 patients operated upon with curative intent, local recurrence rate was 9.3% of cases and disease-free 5-year survival was 70% [74]. Local recurrence rates in studies with extended lymphadenectomy are shown in Table 4.

Most studies on extended pelvic lymphadenectomy (EPL) have been retrospective with historical controls used as the control group. Only one prospective trial has been performed and this could not demonstrate an overall benefit, although in a subgroup analysis this benefit was present [75]. Partly because of the wide variety in lymph node yield and salvage methods and the differences in the definition of lymph node metastasis, there is still widespread controversy on the extent of LND that is recommended for primary cancer of the rectum.

Table 4
Local recurrence after 'curative' extended pelvic lymphadenectomy (versus conventional surgery in some studies)

	Years studied	Patients investigated (*n*)	Local recurrence (LR) (*n*)	Local recurrence (%)	Remarks[a]
Stearns 1959 [69]		122	22	18.0	
Glass 1985 [148]	1960–1981	75	10	13.3	
Hojo 1989 [72]	1969–1983				$P<0.05$ for Dukes B and C
• Extended excision		192	27	14.1	
• Conventional excision		245	47	19.2	
Michelassi 1988 [149]	1965–1981				$P=0.16$
• Wide pelvic lymphadenectomy		54	10	16.4	
• Conventional		73	7	9.4	
Moriya 1989 [150]	1974–1986				$P=$ NS
• Extended lat node dissection		43	5	11.6	Only 2 pts had postoperative RT
• Conventional lat node dissection		131	22	16.8	Dukes' B and C
Moriya 1995 [151]	1975–1992	133	11	8.2	
Enker 1986 [73]	1968–1976				$P=$ NS
• Pelvic lymphadenectomy		176	49	27.8	25% of extended and 20% of conventional pts received preoperative RT
• Conventional		206	59	28.6	
Moreira 1994 [152]	1981–1991				$P<0.05$
• Lateral lymph node dissection		95	7	7.4	
• No lateral lymph node dissection		83	13	15.7	
Hida 1997 [153]	1979–1988	144	18	12.5	
Moriya 1997 [74]	1980–1994		Overall LR	Overall LR	
• Lateral dissection		322	42	9.4	
• Without lateral dissection		126			
Saito 1999 [154]	1984–1995	177	14	7.9	

RT, radiotherapy; NS, Non-significant.
[a] $P=P$ value of the comparison of local recurrence rates between resection types.

Furthermore, extended lymph node dissection carries a higher postoperative morbidity which may be due to a longer time of operation and increased blood loss. Another strong argument against pelvic LND is the very high rate of bladder and sexual dysfunction [76] compared with the rates following conventional resections. The technique of nerve-sparing LND might decrease these complications [72], but it requires a meticulous surgical technique and accurate knowledge of the anatomy of the pelvic autonomic nervous system and prolongs the operation time even more [76].

For the aforementioned reasons, extended lymph node dissection has not become standard surgical practice in the Western world. In Japan, however, extended lymph node dissection has been the standard surgical procedure since the mid-1970s. This may be because postoperative morbidity and mortality are minimal in Japanese patients, possibly because of the low prevalence of obesity and atherosclerosis.

6. Total mesorectal excision (TME) surgery

The concept of TME was introduced by Heald at the North Hampshire Hospital in Basingstoke in 1979 [77]. By using a sharp dissection under direct vision a relatively bloodless plane is followed along the lipoma-like outer surface of the mesorectum. The sharp technique used in TME ensures a specimen with intact mesorectum with negative tumour margins in the majority of resectable (i.e. mobile) rectal cancers. Furthermore, the sharp technique allows for preservation of the pelvic autonomic nerves, reducing sexual and urinary dysfunction.

Heald's first series of 112 curative anterior resections showed a cumulative risk of local recurrence at 5 years of 2.7% and an overall corrected survival at 5 years of 87.5% with tumour-free survival of 81.7%. These results were, at the time, the best reported in rectal cancer treatment up to than [49]. However, many investigators doubted these findings and criticism focused on the patient case mix and analytical techniques [78], unclarified selection process [79] and incorrect use of definitions [51]. In Enker's series of 246 curable Dukes' B and C cases, only 18 tumours (7.3%) recurred locally, actuarial cancer-specific 5-year survival was 74.2% [80]. Aitken published a series of 64 curatively resected TME cases with at least 24 months follow-up: only 1 patient (1.6%) developed a local recurrence [81].

The acknowledgement of the important role of circumferential involvement in the occurrence of local recurrences [66,82–84] has led to the general introduction of TME surgery [85–87]. In The Netherlands, Sweden and Norway, nationwide projects have been conducted in which surgeons were trained to perform a proper TME in an attempt to improve their treatment results. Table 5 shows the local recurrence rates after TME in several studies.

In addition to better results in terms of recurrence, the introduction of TME surgery has been shown to result in a reduction of APRs [85,86]. However, higher leak rates with TME surgery compared with conventional surgery have been reported [88,89]. This increase can be partly explained by the removal of the pain-sensitive

Table 5
Local recurrence after 'curative' total mesorectal excision

	Years studied	Patients investigated (*n*)	Local recurrence (*n*)	Local recurrence (%)	Remarks
Heald 1986 [49]	1978–1986	112	3	2.7	
Colombo 1987 [155]	1977–1981	89	10	11.2	
Belli 1988 [156]	1981–1984	72	3	4.2	
Kirwan 1989 [157]	??–??	67	3	4.5	
Karanjia 1990 [158]	1978–1987	152	4	2.6	
Cawthorn 1990 [82]	1980–1987	122	9	7.4	
Dixon 1991 [159]	1978–1987	227	9	4.0	
Moran 1992 [160]	1983–1988	55	4	7.3	Only LAR
Tagliacozzo 1992 [161]	1984–1987	248	41	16.5	
Jatzko 1992 [162]	1984–1990	187	25	13.4	
MacFarlane 1993 [3]	1978–1991	135	7	5.2	
Enker 1995 [80]	1979–1993	246	18	7.3	70 patients had perioperative RT with or without CT
Aitken 1996 [81]	1989–1995	64	1	1.6	
Eu 1997 [163]	1989–1994	278	26	9.4	
Carvalho 1997 [164]	1994–1995	51	1	2.0	Adjuvant therapy was given in 33 patients
Hainsworth 1997 [165]	1989–1993	45	8	17.8	
Arenas 1998 [166]	1984–1997	64	4	6.3	42 patient received pre or postoperative RT
Maas 2000 [99]	1994–1995	42	3	7.1	
Martling and collegues 2000 [86]	1995–1996	381	21	5.5	54% of the pts received 5×5 Gy preoperative RT
Kapiteijn 2000 [167]	1996–1999	661	57	8.6	
Tocchi 2001 [168]	1990–1995	53	5	9.4	Only LAR

LAR, low anterior resection; CT, chemotherapy; RT, radiotherapy.

peritoneum, which prevents early detection of anastomotic failure [89,90]. Various other factors such as anastomotic technique [91–93], method of preparation of the bowel [94], use of a diverting colostomy [90], and the method of pelvic drainage [95] have been found to be related with leakage.

In higher rectal tumours (i.e. over 10 cm from the anal verge), a TME does not necessarily have to be performed. Studies on resected rectal specimens [96] suggest that metastatic spread in the mesorectum will rarely be found more than 3 cm distal to the macroscopic primary tumour. Thus, a distal mesorectal resection margin of less than 5 cm will most probably suffice [81] and although further studies are required, many advocates of TME now accept that a partial mesorectal excision (PME), which leaves the distal tail *in situ*, can be performed safely for tumours at 10–15 cm levels at a right angle to the bowel, and if the surgeons do not 'cone in' obliquely through the mesorectal fat during the resection.

The question has yet to be answered as to whether in combination with TME surgery with its low local recurrence rates and improved survival, adjuvant therapy is capable of achieving any further improvement in outcome. In most countries, mesorectal excision has become the new standard of operative management for rectal cancers, replacing the conventional resection technique. Current clinical trials examining the role of adjuvant therapy in patients who are undergoing standardised operations should now set the standard of surgical care in several countries.

7. Recent developments in The Netherlands

In The Netherlands, standards of care for rectal cancer surgery have been subject of interest for some years. The results of extended pelvic lymphadenectomy in Japan and the excellent results of TME by Heald and Enker were welcomed with interest, but also with scepticism; could these results be repeated in other surgeons' hands? Initially, attention was focused on the Japanese style extended lymphadenectomy. In his thesis, Steup concluded that the value of extended lymphadenectomy should be studied in a randomised controlled trial [97] and a trial was proposed to compare the D3 lymphadenectomy technique with TME. Many Dutch surgeons, however, feared a considerable morbidity with the Japanese D3 technique in Dutch patients. A second and third proposal was to compare conventional surgery with TME surgery or compare in a two-by-two factorial design yes/no short-term preoperative radiotherapy and conventional versus TME surgery. Both designs for trials, however, would allocate 25–30% of the patients to the inferior arm of conventional surgery without preoperative radiotherapy. The data from literature were so convincing with regard to the superiority of the TME technique [3,80,81], that a majority of the Dutch surgeons were of the opinion that it would be unethical to randomise patients in such a design. Furthermore, there are potential difficulties in a surgeon randomly applying different surgical techniques [98]. A final proposal was made for the TME trial: compare TME surgery with or without preoperative radiotherapy.

Moriya from the National Cancer Center Hospital in Tokyo visited The Netherlands in 1994–1995 to assess the feasibility of nerve preservation and pararectal resection comparable to the TME technique in a series of 47 Dutch patients. The nerve-preserving technique yielded good results in terms of morbidity and functional outcome. Of the 42 curatively operated patients, 3 (7.1%) developed a local recurrence. Sixty-seven percent were overall free of recurrence. From these results, it was concluded that preservation of the pelvic autonomous nerve system does not compromise radicality in mesorectal excision [99].

7.1. *The TME trial*

A large prospective randomised trial (TME trial) was started in 1996 under the auspices of the Dutch Colo-Rectal Cancer Group (DCRCG) to document local control when standardised TME is used and to answer the question of whether radiotherapy is still beneficial in TME-treated patients [85]. Eligibility criteria included histologically-confirmed primary adenocarcinoma of the rectum without evidence of distant metastases (M1).

An extensive structure of workshops (run together with Heald, Enker and Moriya), symposia, and instruction videos helped to accomplish that TME was performed according to strict quality demands. In addition, a monitoring committee of 21 specially trained instructor-surgeons was installed for on-site instructions. In each hospital, the first five TME procedures had to be supervised by an instructor-surgeon. Special training courses were given to pathologists for instruction of the protocol of Quirke [66]. The results of histopathological examination of the specimens were reviewed by a panel of supervising pathologists and a quality manager [100]. Treatment and follow-up details were checked by the study-coordinators. Local and distant recurrences were checked by a radiation oncologist.

The system of specially trained surgeons was validated in the previously conducted Dutch Gastric Cancer Trial (1989–1993) comparing Japanese style D2 lymph node dissection to routine dissection [101]. Surgical quality control turned out to be crucial in testing the hypothesis [102]. In addition, the role of the pathologist in quality control of surgery, was emphasised [103].

Patients were enrolled in the TME trial between January 1996 and December 1999. In total, 1861 patients were randomised; 1530 patients from 84 Dutch hospitals, 228 patients from 13 Swedish hospitals and 103 patients from 11 other European and Canadian centres. Short-term analysis showed that blood loss during the operation in irradiated patients was slightly increased (median 1100 ml in the RT+TME group and 1000 ml in the TME group, $P<0.001$) and irradiated APR patients showed more perineal complications (29 and 18% in the RT+TME and TME groups, respectively, $P=0.008$). In LAR patients, no significant difference was observed in clinical leakage (12% in the RT+TME group versus 11% in the TME group). The number of reinterventions (15 and 14% in the RT+TME and TME groups, respectively) and in-hospital deaths (4% in the RT+TME-group versus 3.3% in the TME group) in all eligible patients did not differ significantly (data not shown).

Before the start of the TME trial, there were doubts as to whether the excellent results obtained by specialised surgeons [3,80,81] could be repeated in a large multicentre trial. To investigate this, we compared the outcome in Dutch TME alone patients of the TME trial with results from a former randomised trial, the Cancer Recurrence And Blood transfusion (CRAB) trial) [104], in which conventional, non-standardised surgery was performed. This analysis (data not shown) showed that introduction of TME had led to a substantially lower local recurrence rate when analysing only the events that occurred within 2 years; 16.3% in the CRAB trial versus 8.6% in the TME trial. With this low local recurrence rate in the TME trial, we concluded that good results can be achieved in all surgeons' hands with thorough surgical instruction. These results are in concordance with the report of Martling and colleagues [86], who compared the Stockholm I and II randomised trials in which conventional surgery with or without preoperative radiotherapy was performed, with the TME project introducing the concept of TME to surgeons in Stockholm, and found that 2-year local recurrence rates had decreased from 14–15 to 6%.

We also investigated hospital volume in the CRAB versus TME trial. In the TME trial, the TME technique was taught to 1–3 surgeons per hospital surgical unit, of whom most had a special interest in oncology. The CRAB trial was performed during a period in which specialisation to oncology within a hospital surgical unit was not yet installed with every surgeon of the unit performing rectal cancer surgery. In the CRAB trial, higher hospital volume was associated with a lower distant recurrence ($P=0.006$) and higher overall survival ($P=0.011$). The association between higher hospital volume and lower local recurrence risk was of borderline significance ($P=0.07$). In the TME trial, hospital volume did not have an effect on any long-term outcome. The effect of surgeon volume was not analysed in the CRAB trial since no information was available on the individual surgeons and in the TME trial most operations were performed by two surgeons, the operating surgeon either with an instructor or non-instructor surgeon colleague, which makes individual surgeon volume analyses difficult to perform. We did analyse operations attended by instructor-surgeons (37% of the operations) versus those not attended by these surgeons. There was no effect of presence of instructor-surgeons on the outcomes, indicating that non-instructor surgeons were instructed well and have become familiar with the concept of TME surgery reaching equal outcomes to those achieved by instructor-surgeons. It is remarkable that the aforementioned improvements have been achieved in a relatively short time period (4 years), with a large number of surgeons participating in the trial ($n=213$).

The local recurrence analysis for all (Dutch+foreign) patients of the TME trial showed a 2-year local recurrence rate of 5.3%. The 2-year local recurrence rates were 8.2% in the TME group and 2.4% in the RT+TME group ($P<0.0001$). Preoperative radiotherapy reduced the local recurrence rate significantly for tumours with an inferior margin within 10 cm, but not for tumours 10–15 cm from the anal verge. For TNM II and III tumours, preoperative radiotherapy had a significant beneficial effect, but not for TNM I and IV tumours. The main conclusion of this analysis (data not shown) was that in a setting of standardised surgery, short-term preoperative radiotherapy still has beneficial effect on the local recurrence risk.

So far, chemotherapy has shown no effect on disease-free and overall survival, which may in part be explained by the high rates of local recurrence with conventional surgery. The role of adjuvant chemotherapy in combination with TME surgery is currently under investigation in the Preoperative Radiotherapy and/or Adjuvant Chemotherapy Combined with TME Surgery in Operable Rectal Cancer (PROCTOR) trial, the successor trial of the TME trial. In Europe, several other studies are investigating (neo-)adjuvant therapy in combination with optimal surgery [105].

8. Conclusions

In the last decades, major improvements have been made in the treatment of rectal cancer by the introduction of new surgical techniques and additional technicalities. This article reviewed developments in rectal cancer surgery and paid attention to variability in outcomes and quality control of surgery. Quality assurance has become an important topic and is of major importance for the standardisation of treatment in (neo-)adjuvant therapy studies and improvement of outcomes.

The introduction of TME surgery has led to a major improvement in local control and survival of rectal cancer patients. Now the question has to be answered as to whether other (neo-)adjuvant therapies other than short-term preoperative radiotherapy can improve the results after TME surgery even more. TME-based operations are now established as the standard of care for mobile rectal cancer and should form the basis for trials investigating the role of (neo-)adjuvant therapy.

In general, it is thought that high volume and specialist care produces superior results to low volume and non-specialist care, especially for those less frequent forms of cancer and in technically difficult operations, like those for rectal cancer. However, limiting the performance of rectal cancer surgery to highly specialised surgeons or to only those general surgeons who perform more than a certain volume is impractical in view of the prevalence of rectal cancer. The concentration process can also take place within one hospital surgical unit with 1–3 surgeons performing rectal cancer surgery. This has been demonstrated in the TME trial, in which training in TME surgery to surgeons who are dedicated to oncology, has led to an improved outcome without volume- or specialisation-related differences.

Quality assurance of the surgical technique requires besides training, adequate knowledge of the anatomy of the organs and nerves in the pelvis and other related structures. Furthermore, standardisation in the description of operations and reporting of pathology specimens should be implemented as important features of quality control. In addition, a multidisciplinary approach provides the best care for patients, because the benefits are primarily related to the access and use of standardised and up-to-date therapy. Similarly, patients participating in clinical trials generally experience a survival advantage over non-participating patients, which is probably partly due to the standardised treatment [106].

Within the TME trial structuralisation and audit of rectal cancer treatment has led to an improvement of treatment results and this infrastructure provides optimal conditions for conducting future rectal cancer trials. However, it is of utmost importance that outside the setting of trials, standardisation of treatment is also applied and sustained. Prospective audit is now essential to ensure that standards are maintained and optimum management is achieved. Population-based cancer registries, covering an increasing proportion of the world's population, are an invaluable source of data for these ultimate goals.

References

1. Visser O, Coebergh JWW, Schouten LJ, Van Dijck JAAM, eds. *Incidence of Cancer in The Netherlands, 1995*. Utrecht, Vereniging van Integrale Kankercentra, 1998.
2. Harnsberger JR, Vernava VM, Longo WE. Radical abdominopelvic lymphadenectomy: historic perspective and current role in the surgical management of rectal cancer. *Dis Colon Rectum* 1994, **37**, 73–87.
3. MacFarlane JK, Ryall RD, Heald RJ. Mesorectal excision for rectal cancer. *Lancet* 1993, **341**, 457–460.
4. Wiggers T, de Vries MR, Veeze Kuypers B. Surgery for local recurrence of rectal carcinoma. *Dis Colon Rectum* 1996, **39**, 323–328.
5. Abulafi AM, Williams NS. Local recurrence of colorectal cancer: the problem, mechanisms, management and adjuvant therapy. *Br J Surg* 1994, **81**, 7–19.
6. Holm T, Cedermark B, Rutqvist LE. Local recurrence of rectal adenocarcinoma after 'curative' surgery with and without preoperative radiotherapy. *Br J Surg* 1994, **81**, 452–455.
7. Moynihan BGA. The surgical treatment of cancer of the sigmoid flexure and rectum: with special attention to the principles observed. *Surg Gynecol Obstet* 1908, **6**, 463–466.
8. Miles WE. A method of performing abdomino-perineal resection for carcinoma of the rectum and of the terminal portion of the pelvic colon. *Lancet* 1908, **2**, 1812–1813.
9. Turnbull RBJ, Kyle K, Watson FR, *et al*. Cancer of the colon: the influence of the no-touch isolation technic on survival rates. *Ann Surg* 1967, **166**, 420–427.
10. Fisher ER, Turnbull RBJ. The cytologic demonstration and significance of tumour cells in the mesenteric venous blood in patients with colorectal carcinoma. *Surg Gynecol Obstet* 1987, **100**, 102–108.
11. Wiggers T, Jeekel J, Arends JW, *et al*. No-touch isolation technique in colon cancer: a controlled prospective trial. *Br J Surg* 1988, **75**, 409–415.
12. Bacon HE, Khubchandani IT. The rationale of aortoiliopelvic lymphadenectomy and high ligation of the inferior mesenteric artery for carcinoma of the left half of the colon and rectum. *Surg Gynecol Obstet* 1964, **119**, 503–508.
13. Surtees P, Ritchie JK, Phillips RK. High versus low ligation of the inferior mesenteric artery in rectal cancer. *Br J Surg* 1990, **77**, 618–621.
14. Pezim ME, Nicholls RJ. Survival after high or low ligation of the inferior mesenteric artery during curative surgery for rectal cancer. *Ann Surg* 1984, **200**, 729–733.
15. Kyzer S, Gordon PH. Experience with the use of the circular stapler in rectal surgery. *Dis Colon Rectum* 1992, **35**, 696–706.
16. Williams NS, Dixon MF, Johnston D. Reappraisal of the 5 centimetre rule of distal excision for carcinoma of the rectum: a study of distal intramural spread and of patients' survival. *Br J Surg* 1983, **70**, 150–154.
17. Pollett WG, Nicholls RJ. The relationship between the extent of distal clearance and survival and local recurrence rates after curative anterior resection for carcinoma of the rectum. *Ann Surg* 1983, **198**, 159–163.
18. Parks AG, Percy JP. Resection and sutured colo-anal anastomosis for rectal carcinoma. *Br J Surg* 1982, **69**, 301–304.
19. Parc R, Tiret E, Frileux P, *et al*. Resection and colo-anal anastomosis with colonic reservoir for rectal carcinoma. *Br J Surg* 1986, **73**, 139–141.
20. Phillips RK, Hittinger R, Blesovsky L, *et al*. Local recurrence following 'curative' surgery for large bowel cancer: I. The overall picture. *Br J Surg* 1984, **71**, 12–16.
21. Neville R, Fielding LP, Amendola C. Local tumor recurrence after curative resection for rectal cancer. A ten-hospital review. *Dis Colon Rectum* 1987, **30**, 12–17.
22. Norbury LEC. *Carcinoma of the Rectum. An Hunterian Lecture*. HK Lewis & Co. Ltd., 1941.
23. Kapiteijn E, Marijnen C, Klein Kranenbarg WM, *et al*. Local recurrence in patients with rectal cancer, diagnosed 1988–1992: a population-based study in the west Netherlands. *Eur J Surg Oncol* 1998, **24**, 528–535.
24. Havenga K, Enker WE, McDermott K, *et al*. Male and female sexual and urinary function after total mesorectal excision with autonomic nerve preservation for carcinoma of the rectum. *J Am Coll Surgeons* 1996, **182**, 495–502.
25. Petrelli NJ, Nagel S, Rodriguez Bigas M, *et al*. Morbidity and

mortality following abdominoperineal resection for rectal adenocarcinoma. *Am Surg* 1993, **59**, 400–404.
26. Matthews HR, Powell DJ, McConkey CC. Effect of surgical experience on the results of resection for oesophageal carcinoma. *Br J Surg* 1986, **73**, 621–623.
27. Yeo CJ, Cameron JL, Maher MM, *et al*. A prospective randomized trial of pancreaticogastrostomy versus pancreaticojejunostomy after pancreaticoduodenectomy. *Ann Surg* 1995, **222**, 580–588.
28. Sainsbury R, Haward B, Rider L, *et al*. Influence of clinician workload and patterns of treatment on survival from breast cancer. *Lancet* 1995, **345**, 1265–1270.
29. McArdle CS, Hole D. Impact of variability among surgeons on postoperative morbidity and mortality and ultimate survival. *Br Med J* 1991, **302**, 1501–1505.
30. Kessler H, Hermanek Jr P, Wiebelt H. Operative mortality in carcinoma of the rectum. Results of the German Multicentre Study. *Int J Colorectal Dis* 1993, **8**, 158–166.
31. Fielding LP, Stewart Brown S, Blesovsky L, *et al*. Anastomotic integrity after operations for large-bowel cancer: a multicentre study. *Br Med J* 1980, **281**, 411–414.
32. Hannan EL, O'Donnell JF, Kilburn Jr H, *et al*. Investigation of the relationship between volume and mortality for surgical procedures performed in New York State hospitals. *JAMA* 1989, **262**, 503–510.
33. Flood AB, Scott WR, Ewy W. Does practice make perfect? Part I: The relation between hospital volume and outcomes for selected diagnostic categories. *Med Care* 1984, **22**, 98–114.
34. Schrag D, Cramer LD, Bach PB, *et al*. Influence of hospital procedure volume on outcomes following surgery for colon cancer. *JAMA* 2000, **284**, 3028–3035.
35. Simons AJ, Ker R, Groshen S, *et al*. Variations in treatment of rectal cancer: the influence of hospital type and caseload. *Dis Colon Rectum* 1997, **40**, 641–646.
36. Hermanek P, Wiebelt H, Staimmer D, *et al*. Prognostic factors of rectum carcinoma-experience of the German Multicentre Study SGCRC. German Study Group Colo-Rectal Carcinoma. *Tumori* 1995, **81**, 60–64.
37. Porter GA, Soskolne CL, Yakimets WW, *et al*. Surgeon-related factors and outcome in rectal cancer. *Ann Surg* 1998, **227**, 157–167.
38. Khuri SF, Daley J, Henderson W, *et al*. Relation of surgical volume to outcome in eight common operations: results from the VA National Surgical Quality Improvement Program. *Ann Surg* 1999, **230**, 414–429.
39. Flood AB, Scott WR, Ewy W, *et al*. Effectiveness in professional organizations: the impact of surgeons and surgical staff organizations on the quality of care in hospitals. *Health Serv Res* 1982, **17**, 341–366.
40. Birkmeyer JD, Finlayson SR, Tosteson AN, *et al*. Effect of hospital volume on in-hospital mortality with pancreaticoduodenectomy. *Surgery* 1999, **125**, 250–256.
41. Glasgow RE, Showstack JA, Katz PP, *et al*. The relationship between hospital volume and outcomes of hepatic resection for hepatocellular carcinoma. *Arch Surg* 1999, **134**, 30–35.
42. Sosa JA, Bowman HM, Gordon TA, *et al*. Importance of hospital volume in the overall management of pancreatic cancer. *Ann Surg* 1998, **228**, 429–438.
43. Hakama M, Karjalainen S, Hakulinen T. Outcome-based equity in the treatment of colon cancer patients in Finland. *Int J Technol Assess Health Care* 1989, **5**, 619–630.
44. Blomqvist P, Ekbom A, Nyren O, *et al*. Survival after rectal cancer: differences between hospital catchment areas. A nationwide study in Sweden. *Gut* 1999, **45**, 39–44.
45. Hermanek P, Hohenberger W. The importance of volume in colorectal cancer surgery. *Eur J Surg Oncol* 1996, **22**, 213–215.
46. Parry JM, Collins S, Mathers J, *et al*. Influence of volume of work on the outcome of treatment for patients with colorectal cancer. *Br J Surg* 1999, **86**, 475–481.
47. Hermanek P, Mansmann U, Staimmer DS, *et al*. The German experience: the surgeon as a prognostic factor in colon and rectal cancer surgery. *Surg Oncol Clin N Am* 2000, **9**, 33–49.
48. Pilipshen SJ, Heilweil M, Quan SH, *et al*. Patterns of pelvic recurrence following definitive resections of rectal cancer. *Cancer* 1984, **53**, 1354–1362.
49. Heald RJ, Ryall RD. Recurrence and survival after total mesorectal excision for rectal cancer. *Lancet* 1986, **1**, 1479–1482.
50. Bentzen SM, Balslev I, Pedersen M, *et al*. Time to loco-regional recurrence after resection of Dukes' B and C colorectal cancer with or without adjuvant postoperative radiotherapy. A multivariate regression analysis. *Br J Cancer* 1992, **65**, 102–107.
51. Marsh PJ, James RD, Schofield PF. Definition of local recurrence after surgery for rectal carcinoma. *Br J Surg* 1999, **82**, 465–468.
52. Tornqvist A, Ekelund G, Leandoer L. The value of intensive follow-up after curative resection for colorectal carcinoma. *Br J Surg* 1982, **69**, 725–728.
53. Carlsson U, Lasson A, Ekelund G. Recurrence rates after curative surgery for rectal carcinoma, with special reference to their accuracy. *Dis Colon Rectum* 1987, **30**, 431–434.
54. Floyd CE, Corley RG. Local recurrence of carcinoma of the colon and rectum. *Am J Surg* 1695, **109**, 153–159.
55. Frykholm GJ, Glimelius B, Pahlman L. Preoperative or postoperative irradiation in adenocarcinoma of the rectum: final treatment results of a randomized trial and an evaluation of late secondary effects. *Dis Colon Rectum* 1993, **36**, 564–572.
56. Improved survival with preoperative radiotherapy in resectable rectal cancer. Swedish Rectal Cancer Trial. *N Engl J Med* 1997, **336**, 980–987.
57. Glimelius B, Isacson U, Jung B, *et al*. Radiotherapy in addition to radical surgery in rectal cancer: evidence for a dose-response effect favoring preoperative treatment. *Int J Radiat Oncol Biol Phys* 1997, **37**, 281–287.
58. Zoetmulder FAN, Taal BG, Van Tinteren H, on behalf of the NACCP. Adjuvant 5FU plus Levamisole improves survival in stage II and III colonic cancer, but not in rectal cancer. Interim analysis of the Netherlands Adjuvant Colorectal Cancer Project (NACCP). *ASCO Proc* 1999, **18**, 1021 (abstr).
59. Prolongation of the disease-free interval in surgically treated rectal carcinoma. Gastrointestinal Tumor Study Group. *N Engl J Med* 1985, **312**, 1465–1472.
60. Fisher B, Wolmark N, Rockette H, *et al*. Postoperative adjuvant chemotherapy or radiation therapy for rectal cancer: results from NSABP protocol R-01 (prior annotation incorrect). *J Natl Cancer Inst* 1988, **80**, 21–29.
61. O'Connell MJ, Martenson JA, Wieand HS, *et al*. Improving adjuvant therapy for rectal cancer by combining protracted-infusion fluorouracil with radiation therapy after curative surgery. *N Engl J Med* 1994, **331**, 502–507.
62. Krook JE, Moertel CG, Gunderson LL, *et al*. Effective surgical adjuvant therapy for high-risk rectal carcinoma. *N Engl J Med* 1991, **324**, 709–715.
63. Gerard A, Buyse M, Nordlinger B, *et al*. Preoperative radiotherapy as adjuvant treatment in rectal cancer. Final results of a randomized study of the European Organization for Research and Treatment of Cancer (EORTC). *Ann Surg* 1988, **208**, 606–614.
64. Mollen RMHG, Damhuis RAM, Coebergh JWW. Local recurrence and survival in patients with rectal cancer, diagnosed 1981–86: a community hospital-based study in the south-east Netherlands. *Eur Surg Oncol* 1997, **23**, 20–23.
65. Tveit KM, Guldvog I, Hagen S, *et al*. Randomized controlled trial of postoperative radiotherapy and short-term time-scheduled 5-fluorouracil against surgery alone in the treatment of

Dukes B and C rectal cancer. Norwegian Adjuvant Rectal Cancer Project Group. *Br J Surg* 1997, **84**, 1130–1135.
66. Quirke P, Durdey P, Dixon MF, *et al*. Local recurrence of rectal adenocarcinoma due to inadequate surgical resection. Histopathological study of lateral tumour spread and surgical excision. *Lancet* 1986, **2**, 996–999.
67. Quirke P. SN: The pathologist's role in the assessment of local recurrence in rectal carcinoma. *Surg Clin North Am* 1992, **1**, 1–17.
68. Kuru M. Rectal cancer. *Jpn J Surg* 1940, **41**, 832–877.
69. Stearns Jr. MW, Deddish MR. Five-year results of abdominopelvic lymph node dissection for carcinoma of the rectum. *Dis Colon Rectum* 1959, **2**, 169–172.
70. Deddish MR. Surgical procedures for carcinoma of the left colon and rectum, with five-year end-results following abdominopelvic dissection of lymph nodes. *Am J Surg* 1960, **99**, 188–191.
71. Koyama Y, Kodaira S, Hojo K, *et al*. Extended operation for rectal cancer. *Jpn J Cancer Clin* 1975, **21**, 1144.
72. Hojo K, Sawada T, Moriya Y. An analysis of survival and voiding, sexual function after wide iliopelvic lymphadenectomy in patients with carcinoma of the rectum, compared with conventional lymphadenectomy. *Dis Colon Rectum* 1989, **32**, 128–133.
73. Enker WE, Pilipshen SJ, Heilweil ML, *et al*. En bloc pelvic lymphadenectomy and sphincter preservation in the surgical management of rectal cancer. *Ann Surg* 1986, **203**, 426–433.
74. Moriya Y, Sugihara K, Akasu T, *et al*. Importance of extended lymphadenectomy with lateral node dissection for advanced lower rectal cancer. *World J Surg* 1997, **21**, 728–732.
75. Rouffet F, Hay JM, Vacher B, *et al*. Curative resection for left colonic carcinoma: hemicolectomy vs. segmental colectomy. A prospective, controlled, multicenter trial. French Association for Surgical Research. *Dis Colon Rectum* 1994, **37**, 651–659.
76. Hojo K, Vernava AM, Sugihara K, *et al*. Preservation of urine voiding and sexual function after rectal cancer surgery. *Dis Colon Rectum* 1991, **34**, 532–539.
77. Heald RJ. A new approach to rectal cancer. *Br J Hosp Med* 1979, **22**, 277–281.
78. Isbister WH. Basingstoke revisited. *Aust N Z J Surg* 1990, **60**, 243–246.
79. Nelson H, Beart RWJ. Surgical management: optimal procedures and overall results. Wanebo HJ, ed. *Colorectal Cancer*. Mostby-Year book, 1993, 199.
80. Enker WE, Thaler HT, Cranor ML, *et al*. Total mesorectal excision in the operative treatment of carcinoma of the rectum. *J Am Coll Surg* 1995, **181**, 335–346.
81. Aitken RJ. Mesorectal excision for rectal cancer. *Br J Surg* 1996, **83**, 214–216.
82. Cawthorn SJ, Parums DV, Gibbs NM, *et al*. Extent of mesorectal spread and involvement of lateral resection margin as prognostic factors after surgery for rectal cancer. *Lancet* 1990, **335**, 1055–1059.
83. Ng IO, Luk IS, Yuen ST, *et al*. Surgical lateral clearance in resected rectal carcinomas. A multivariate analysis of clinicopathologic features. *Cancer* 1993, **71**, 1972–1976.
84. de Haas Kock DF, Baeten CG, Jager JJ, *et al*. Prognostic significance of radial margins of clearance in rectal cancer. *Br J Surg* 1996, **83**, 781–785.
85. Kapiteijn E, Klein Kranenbarg WM, Steup WH, *et al*. Total Mesorectal excision (TME) with or without preoperative radiotherapy in the treatment of primary rectal cancer. *Eur J Surg* 1999, **165**, 410–420.
86. Martling AL, Holm T, Rutqvist LE, *et al*. Effect of a surgical training programme on outcome of rectal cancer in the County of Stockholm. Stockholm Colorectal Cancer Study Group, Basingstoke Bowel Cancer Research Project. *Lancet* 2000, **356**, 93–96.
87. Dahlberg M, Glimelius B, Pahlman L. Changing strategy for rectal cancer is associated with improved outcome. *Br J Surg* 1999, **86**, 379–384.
88. Carlsen E, Schlichting E, Guldvog I, *et al*. Effect of the introduction of total mesorectal excision for the treatment of rectal cancer. *Br J Surg* 1998, **85**, 526–529.
89. Heald RJ, Karanjia ND. Results of radical surgery for rectal cancer. *World J Surg* 1992, **16**, 848–857.
90. Karanjia ND, Corder AP, Holdsworth PJ, *et al*. Risk of peritonitis and fatal septicaemia and the need to defunction the low anastomosis. *Br J Surg* 1991, **78**, 196–198.
91. McGinn FP, Gartell PC, Clifford PC, *et al*. Staples or sutures for low colorectal anastomoses: a prospective randomized trial. *Br J Surg* 1985, **72**, 603–605.
92. Zollinger RM, Sheppard MH. Carcinoma of the rectum and the rectosigmoid. A review of 729 cases. *Arch Surg* 1971, **102**, 335–338.
93. Hallbook O, Pahlman L, Krog M, *et al*. Randomized comparison of straight and colonic J pouch anastomosis after low anterior resection. *Ann Surg* 1996, **224**, 58–65.
94. Goligher JC, Graham NG, De Dombal FT. Anastomotic dehiscence after anterior resection of rectum and sigmoid. *Br J Surg* 1970, **57**, 109–118.
95. Fazio VW. Sump suction and irrigation of the presacral space. *Dis Colon Rectum* 1978, **21**, 401–405.
96. Scott N, Jackson P, al Jaberi T, *et al*. Total mesorectal excision and local recurrence: a study of tumour spread in the mesorectum distal to rectal cancer. *Br J Surg* 1995, **82**, 1031–1033.
97. Steup WH. *Colorectal Cancer Surgery with Emphasis on Lymphadenectomy. An Analysis on Indication, Technique, Morbidity and Results*. PhD Thesis, University of Leiden, 1995.
98. Russell I. Evaluating new surgical procedures. *Br Med J* 1995, **311**, 1243–1244.
99. Maas CP, Moriya Y, Steup WH, *et al*. A prospective study on radical and nerve-preserving surgery for rectal cancer in The Netherlands. *Eur J Surg Oncol* 2000, **26**, 751–757.
100. Nagtegaal ID, Kranenbarg EK, Hermans J, *et al*. Pathology data in the central databases of multicenter randomized trials need to be based on pathology reports and controlled by trained quality managers. *J Clin Oncol* 2000, **18**, 1771–1779.
101. Bonenkamp JJ, Songun I, Hermans J, *et al*. Randomised comparison of morbidity after D1 and D2 dissection for gastric cancer in 996 Dutch patients. *Lancet* 1995, **345**, 745–748.
102. Sasako M, Maruyama K, Kinoshita T, *et al*. Quality control of surgical technique in a multicenter, prospective, randomized, controlled study on the surgical treatment of gastric cancer. *Jpn J Clin Oncol* 1992, **22**, 41–48.
103. Bunt AM, Hermans J, Smit VT, *et al*. Surgical/pathologic-stage migration confounds comparisons of gastric cancer survival rates between Japan and Western countries. *J Clin Oncol* 1995, **13**, 19–25.
104. Houbiers JG, Brand A, van de Watering LM, *et al*. Randomised controlled trial comparing transfusion of leucocyte-depleted or buffy-coat-depleted blood in surgery for colorectal cancer. *Lancet* 1994, **344**, 573–578.
105. Kapiteijn E, van de Velde CJ. European trials with total mesorectal excision. *Semin Surg Oncol* 2000, **19**, 350–357.
106. Stiller CA. Centralised treatment, entry to trials and survival. *Br J Cancer* 1994, **70**, 352–362.
107. Rao AR, Kagan AR, Chan PM, *et al*. Patterns of recurrence following curative resection alone for adenocarcinoma of the rectum and sigmoid colon. *Cancer* 1981, **48**, 1492–1495.
108. Rich T, Gunderson LL, Lew R, *et al*. Patterns of recurrence of rectal cancer after potentially curative surgery. *Cancer* 1983, **52**, 1317–1329.

109. Pahlman L, Glimelius B. Local recurrences after surgical treatment for rectal carcinoma. *Acta Chir Scand* 1984, **150**, 331–335.
110. McDermott FT, Hughes ES, Pihl E, *et al*. Local recurrence after potentially curative resection for rectal cancer in a series of 1008 patients. *Br J Surg* 1985, **72**, 34–37.
111. Pescatori M, Mattana C, Maria G, *et al*. Outcome of colorectal cancer. *Br J Surg* 1987, **74**, 370–372.
112. Athlin L, Bengtsson NO, Stenling R. Local recurrence and survival after radical resection of rectal carcinoma. *Acta Chir Scand* 1988, **154**, 225–229.
113. Rinnert GS, Tartter PI. Multivariate analysis of recurrence after anterior resection for colorectal carcinoma. *Am J Surg* 1998, **157**, 573–576.
114. Zirngibl H, Husemann B, Hermanek P. Intraoperative spillage of tumor cells in surgery for rectal cancer. *Dis Colon Rectum* 1990, **33**, 610–614.
115. Akyol AM, McGregor JR, Galloway DJ, *et al*. Recurrence of colorectal cancer after sutured and stapled large bowel anastomoses. *Br J Surg* 1991, **78**, 1297–1300.
116. Stipa S, Nicolanti V, Botti C, *et al*. Local recurrence after curative resection for colorectal cancer: frequency, risk factors and treatment. *J Surg Oncol Suppl* 1991, **2**, 155–160.
117. Norstein J, Bergman A, Langmark F. Risk factors for local recurrence after radical surgery for rectal carcinoma: a prospective multicentre study. *Br J Surg* 1993, **80**(Suppl.), S22.
118. Adam IJ, Mohamdee MO, Martin IG, *et al*. Role of circumferential margin involvement in the local recurrence of rectal cancer. *Lancet* 1994, **344**, 707–711.
119. Nymann T, Jess P, Christiansen J. Rate and treatment of pelvic recurrence after abdominoperineal resection and low anterior resection for rectal cancer. *Dis Colon Rectum* 1995, **38**, 799–802.
120. Damhuis RA, Wiggers T, Wereldsma JC. Association between age and local recurrence of rectal cancer: results from a retrospective study of 902 patients. *Int J Colorectal Dis* 1997, **12**, 235–239.
121. Luft HS, Bunker JP, Enthoven AC. Should operations be regionalized? The empirical relation between surgical volume and mortality. *N Engl J Med* 1979, **301**, 1364–1369.
122. Begg CB, Cramer LD, Hoskins WJ, *et al*. Impact of hospital volume on operative mortality for major cancer surgery. *JAMA* 1998, **280**, 1747–1751.
123. Reinbach DH, McGregor JR, Murray GD, *et al*. Effect of the surgeon's specialty interest on the type of resection performed for colorectal cancer. *Dis Colon Rectum* 1994, **37**, 1020–1023.
124. Lothian and Borders large bowel cancer project: immediate outcome after surgery. The consultant surgeons and pathologists of the Lothian and Borders Health Boards. *Br J Surg* 1995, **82**, 888–890.
125. Rosen L, Stasik JJ, Read JF, *et al*. Variations in colon and rectal surgical mortality. Comparison of specialties with state-legislated data base. *Dis Colon Rectum* 1996, **39**, 129–135.
126. Kelly JV, Hellinger FJ. Physician and hospital factors associated with mortality of surgical patients. *Med Care* 1986, **24**, 785–800.
127. Burns LR, Wholey DR. The effects of patient, hospital, and physician characteristics on length of stay and mortality. *Med Care* 1991, **29**, 251–271.
128. Harmon JW, Tang DG, Gordon TA, *et al*. Hospital volume can serve as a surrogate for surgeon volume for achieving excellent outcomes in colorectal resection. *Ann Surg* 1999, **230**, 404–411.
129. Mohner M, Slisow W. Effect of regional centralized treatment on chances of survival in rectal cancer in East Germany. *Zentralbl Chir* 1990, **115**, 801–812.
130. Launoy G, Le CX, Gignoux M, *et al*. Influence of rural environment on diagnosis, treatment, and prognosis of colorectal cancer. *J Epidemiol Community Health* 1992, **46**, 365–367.
131. Luna PP, Reyna HA, Labastida AS, *et al*. The surgeon as prognostic factor for local recurrence and survival in the anal sphincter preservation for mid-rectal cancer. *Rev Invest Clin* 1999, **51**, 205–213.
132. Kee F, Wilson RH, Harper C, *et al*. Influence of hospital and clinician workload on survival from colorectal cancer: cohort study. *Br Med J* 1999, **318**, 1381–1385.
133. Norstein J, Langmark F. Results of Rectal Cancer Treatment: A National Experience. In Soreide O, ed. *Rectal Cancer Surgery. Optimisation, Standardisation, Documentation*. Berlin, Springer-Verlag, 1997, 17–28.
134. Hermanek P. Impact of surgeon's technique on outcome after treatment of rectal carcinoma. *Dis Colon Rectum* 1999, **42**, 559–562.
135. Kingston RD, Walsh S, Jeacock J. Colorectal surgeons in district general hospitals produce similar survival outcomes to their teaching hospital colleagues: review of 5-year survivals in Manchester. *J R Coll Surg Edinburgh* 1992, **37**, 235–237.
136. Simunovic M, To T, Baxter N, *et al*. Hospital procedure volume and teaching status do not influence treatment and outcome measures of rectal cancer surgery in a large general population. *J Gastrointest Surg* 2000, **4**, 324–330.
137. Holm T, Johansson H, Cedermark B, *et al*. Influence of hospital and surgeon related factors on outcome after treatment of rectal cancer with or without preoperative radiotherapy. *Br J Surg* 1997, **84**, 657–663.
138. Roswit B, Higgins GA, Keehn RJ. Preoperative irradiation for carcinoma of the rectum and rectosigmoid colon: report of a National Veterans Administration randomized study. *Cancer* 1975, **35**, 1597–1602.
139. Cedermark B, Johansson H, Rutqvist LE, *et al*. The Stockholm I trial of preoperative short term radiotherapy in operable rectal carcinoma. A prospective randomized trial. Stockholm Colorectal Cancer Study Group. *Cancer* 1995, **75**, 2269–2275.
140. Horn A, Halvorsen JF, Dahl O. Preoperative radiotherapy in operable rectal cancer. *Dis Colon Rectum* 1990, **33**, 823–828.
141. James RD, Haboubi N, Schofield PF, *et al*. Prognostic factors in colorectal carcinoma treated by preoperative radiotherapy and immediate surgery. *Dis Colon Rectum* 1991, **34**, 546–551.
142. Goldberg PA, Nicholls RJ, Porter NH, *et al*. Long-term results of a randomised trial of short-course low-dose adjuvant preoperative radiotherapy for rectal cancer: reduction in local treatment failure. *Eur J Cancer* 1994, **30A**, 1602–1606.
143. Medical Research Council Rectal Cancer Working Party. Randomised trial of surgery alone versus radiotherapy followed by surgery for potentially operable locally advanced rectal cancer. *Lancet* 1996, **348**, 1605–1610.
144. Balslev I, Pedersen M, Teglbjaerg PS, *et al*. Postoperative radiotherapy in Dukes' B and C carcinoma of the rectum and rectosigmoid. A randomized multicenter study. *Cancer* 1986, **58**, 22–28.
145. Treurniet Donker AD, van Putten WL, Wereldsma JC, *et al*. Postoperative radiation therapy for rectal cancer. An interim analysis of a prospective, randomized multicenter trial in The Netherlands. *Cancer* 1991, **67**, 2042–2048.
146. Medical Research Council Rectal Cancer Working Party. Randomised trial of surgery alone versus surgery followed by radiotherapy for mobile cancer of the rectum. *Lancet* 1996, **348** 1610–1614.
147. Arnaud JP, Nordlinger B, Bosset JF, *et al*. Radical surgery and postoperative radiotherapy as combined treatment in rectal cancer: final results of a phase III study of the European Organization for Research and Treatment of Cancer. *Br J Surg* 1997, **84**, 352–357.
148. Glass RE, Ritchie JK, Thompson HR, *et al*. The results of surgical treatment of cancer of the rectum by radical resection and extended abdomino-iliac lymphadenectomy. *Br J Surg* 1985, **72**, 599–601.

149. Michelassi F, Block GE, Vannucci L, *et al*. A 5- to 21-year follow-up and analysis of 250 patients with rectal adenocarcinoma. *Ann Surg* 1988, **208**, 379–389.
150. Moriya Y, Hojo K, Sawada T, *et al*. Significance of lateral node dissection for advanced rectal carcinoma at or below the peritoneal reflection. *Dis Colon Rectum* 1989, **32**, 307–315.
151. Moriya Y, Sugihara K, Akasu T, *et al*. Nerve-sparing surgery with lateral node dissection for advanced lower rectal cancer. *Eur J Cancer* 1995, **31A**, 1229–1232.
152. Moreira LF, Hizuta A, Iwagaki H, *et al*. Lateral lymph node dissection for rectal carcinoma below the peritoneal reflection. *Br J Surg* 1994, **81**, 293–296.
153. Hida J, Yasutomi M, Fujimoto K, *et al*. Does lateral lymph node dissection improve survival in rectal carcinoma? Examination of node metastases by the clearing method. *J Am Coll Surg* 1997, **184**, 475–480.
154. Saito N, Koda K, Nobuhiro K, *et al*. Nerve-sparing surgery for advanced rectal cancer patients: special reference to Dukes C patients. *World J Surg* 1999, **23**, 1062–1068.
155. Colombo PL, Foglieni CL, Morone C. Analysis of recurrence following curative low anterior resection and stapled anastomoses for carcinoma of the middle third and lower rectum. *Dis Colon Rectum* 1987, **30**, 457–464.
156. Belli L, Beati CA, Frangi M, *et al*. Outcome of patients with rectal cancer treated by stapled anterior resection. *Br J Surg* 1988, **75**, 422–424.
157. Kirwan WO, O'Riordain MG, Waldron R. Declining indications for abdominoperineal resection. *Br J Surg* 1989, **76**, 1061–1063.
158. Karanjia ND, Schache DJ, North WR, *et al*. 'Close shave' in anterior resection. *Br J Surg* 1990, **77**, 510–512.
159. Dixon AR, Maxwell WA, Holmes JT. Carcinoma of the rectum: a 10-year experience. *Br J Surg* 1991, **78**, 308–311.
160. Moran BJ, Blenkinsop J, Finnis D. Local recurrence after anterior resection for rectal cancer using a double stapling technique. *Br J Surg* 1992, **79**, 836–838.
161. Tagliacozzo S, Accordino M. Pelvic recurrence after surgical treatment of rectal and sigmoid cancer. A prospective clinical trial on 274 patients. *Int J Colorectal Dis* 1992, **7**, 135–140.
162. Jatzko G, Lisborg P, Wette V. Improving survival rates for patients with colorectal cancer. *Br J Surg* 1992, **79**, 588–591.
163. Eu KW, Seow CF, Ho JM, *et al*. Local recurrence following rectal resection for cancer. *J R Coll Surg Edinburgh* 1998, **43**, 393–396.
164. Carvalho N, Farricha V, Giria J. Total mesorectal excision for rectal cancer. *Br J Surg* 1997, **84**(Suppl. 2), 27.
165. Hainsworth PJ, Egan MJ, Cunliffe WJ. Evaluation of a policy of total mesorectal excision for rectal and rectosigmoid cancers. *Br J Surg* 1997, **84**, 652–656.
166. Arenas RB, Fichera A, Mhoon D, *et al*. Total mesenteric excision in the surgical treatment of rectal cancer: a prospective study. *Arch Surg* 1998, **133**, 608–611.
167. Kapiteijn E, Putter H, van de Velde CJH. Impact of surgical training on recurrence and survival in rectal cancer.
168. Tocchi A, Mazzoni G, Lepre L, *et al*. Total mesorectal excision and low rectal anastomosis for the treatment of rectal cancer and prevention of pelvic recurrences. *Arch Surg* 2001, **136**, 216–220.