Articles

Randomised trial of surgery alone versus radiotherapy followed by surgery for potentially operable locally advanced rectal cancer

*Medical Research Council Rectal Cancer Working Party**

Summary

Background Survival rates after surgery for rectal cancer remain at about 40% at 5 years from diagnosis. The aim of this study was to find out whether local recurrence rate could be reduced and survival increased by a moderately high dose of preoperative radiotherapy in patients with locally advanced, but otherwise operable, carcinoma of the rectum.

Methods We carried out a prospective randomised trial of surgery alone (n=140) versus surgery preceded by 40 Gy radiotherapy (n=139) given in 20 fractions of 2 Gy over 4 weeks. The patients, from 20 regional centres throughout the UK, were enrolled between 1981 and 1989, and followed up for a minimum of 5 years or to death.

Findings 217 patients died, 114 of 140 allocated surgery alone and 103 of 139 allocated preoperative radiotherapy: median survival times were 24 months and 31 months, respectively. The hazard ratio for overall survival was 0·79 (95% CI 0·60–1·04, p=0·10). At 5 years' follow-up 65 patients allocated surgery alone and 50 who received preoperative radiotherapy had local recurrence (hazard ratio 0·68 [0·47–0·98], p=0·04); the corresponding numbers of patients with distant recurrence were 67 and 49 (hazard ratio 0·66 [0·46–0·95], p=0·02). There was a significant benefit of radiotherapy on disease-free survival (hazard ratio 0·76 [0·58–1·0], p=0·05). There was no increase in postoperative or late complications in the radiotherapy group.

Interpretation Our results provide further evidence that preoperative radiotherapy can reduce the rate of local recurrence of rectal cancer in patients with locally advanced disease. However, survival results are still equivocal, and so we must await the results of a meta-analysis of all radiotherapy trials from which precise and definitive results, particularly for survival, may be obtained.

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See Commentary page 1600

Introduction

Rectal cancer is one of the most common malignant diseases with 11 500 cases diagnosed in the UK in 1994 alone. Little change has been seen in survival rates, which remain at about 40% at 5 years from diagnosis. In an attempt to increase the rate of curative resection and hence survival, several trials have investigated the role of preoperative radiotherapy in treatment of rectal cancer. The first UK Medical Research Council (MRC) trial of preoperative radiotherapy for rectal cancer was a three-arm randomised trial with 824 patients comparing a control (surgery alone) group with a group treated with 20 Gy given in 10 equal fractions and another treated with a single exposure of 5 Gy.[1] These doses of radiation were chosen after trials by the Veterans Administration Surgical Adjuvant Group[2] and the Princess Margaret Hospital, Toronto,[3] suggested survival advantage with radiotherapy for patients with tumours of Dukes' stage C. Despite the suggestion of a real biological effect of the radiotherapy in the first MRC trial, with significant changes in tumour stage, no advantage was found for either radiotherapy group over the control group in terms of disease recurrence or survival. However, the trial did demonstrate the importance of fixity as a prognostic factor—80% of mobile tumours had apparently curative resections compared with 50% of partially fixed, and 30% of fixed tumours. The importance of fixity was reflected in the survival pattern; 5-year survival for fixed or partially fixed tumours was just 29% compared with 48% for mobile tumours.

In 1981, the MRC began this trial of a higher dose of preoperative radiotherapy in patients with fixed or partially fixed tumours of the rectum who were thought to be suitable for abdominoperineal excision or anterior restorative resection. The aim was to increase the number of patients in whom curative resection could be done, and so improve survival rates. The dose of radiation (40 Gy in 20 fractions over 4 weeks) was chosen as the highest that was deemed safe before anterior resection with the wide-field technique proposed. We present the results of this trial with a minimum follow-up time for surviving patients of 5 years.

Patients and methods

Eligible patients were men or women younger than 80 years who; had histologically proven adenocarcinoma of the rectum partially or totally fixed within the pelvis with the lower margin of the tumour within 15 cm of the anal verge; were deemed suitable and fit for the proposed treatment and available for regular follow-up; were free of disseminated disease (confirmed by clinical and radiological examination); and had had no previous malignant disease. We gained local ethics committee approval for the study and consent from the participants.

When an eligible patient was enrolled, the randomised treatment allocation was obtained by means of a telephone call to

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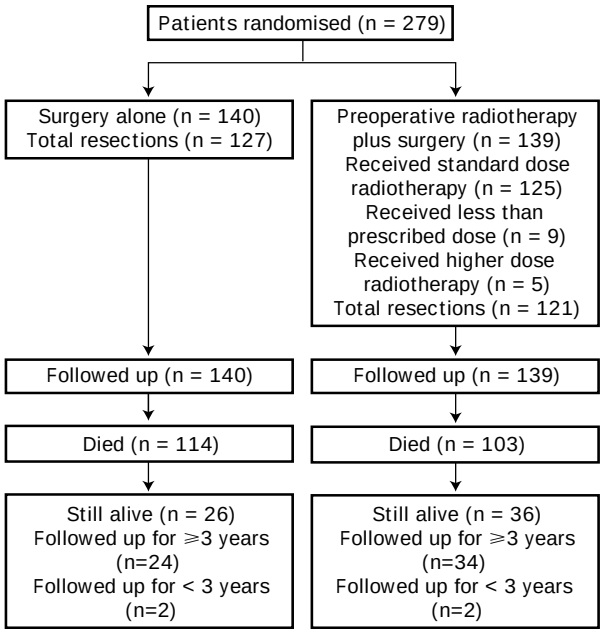


Figure 1: **Trial profile**

the MRC Cancer Trials Office in Cambridge. Eligibility was confirmed and treatment allocated by minimisation on three factors: treatment centre, extension of tumour (fixed or partially fixed), and intended operation (abdominoperineal excision or anterior restorative resection). Patients then proceeded to immediate surgery or to radiotherapy followed by surgery after a minimum of 4 weeks.

Megavoltage radiotherapy was started as soon as possible after randomisation. Two parallel opposed fields 18 cm by 15 cm were positioned to cover the tumour with an adequate proximal margin (normally 5 cm). 20 daily fractions of 2 Gy at the mid-plane central axis of the volume of the tumour were given over 4 weeks.

Patients were seen every 3 months for 1 year, then every 6 months for 4 years. Patients who completed 5 years follow-up and those who were lost to follow-up were flagged on the Office of Population Censuses and Surveys (OPCS) register so that we would be notified of date and cause of death. At each visit, the status of the abdominal and perineal wounds was assessed, late complications of treatment recorded, and evidence of local or distant recurrence noted. Criteria for suspicion of local recurrence were pain, increasing in severity and requiring medication, or disturbance of bladder function, induration in the perineum or pelvis on examination, or palpation of a mass in the pelvis or at the anastomosis. Biopsy samples were taken whenever possible, and pelvic radiography was done to look for evidence of bone destruction.

Event-free times were recorded from the date of randomisation. For the analyses the date of first local recurrence was taken as the date of the first new clinical or histological evidence of local recurrence; we included an assessment of clinical evidence of local recurrence at death. The date of first confirmed distant recurrence was also recorded. Disease-free survival time was measured from randomisation to the first event (local or distant recurrence, or death from any cause). For all these endpoints, event-free times were censored at 5 years from randomisation, because at this point a large proportion of surviving patients had been discharged from hospital follow-up, and accurate continuing data on disease recurrence were no longer available. Survival times were not censored at 5 years; all surviving patients have been flagged on the OPCS central register, and were presumed alive on Jan 1, 1995.

Statistical analysis

We intended to enrol 450 patients (with the anticipation of 251 deaths); this sample size would have provided 90% power to detect a 15% increase in the 3-year survival rate (from 35% to 50%), which was thought plausible at the time the trial was designed. Based on accrual to the previous MRC preoperative radiotherapy trial, we expected that this number would be accrued in 4 to 5 years.

Proportions were compared by the χ^2 test, and ordered categorical data by the Mann-Whitney test. Survival curves were calculated by the Kaplan-Meier method, and compared by the Mantel-Cox version of the log-rank test. Hazard ratios were calculated for all endpoints; a hazard ratio of less than 1 indicates benefit to the radiotherapy group. All analyses were carried out by intention to treat.

	Surgery only (n=140)	Radiotherapy plus surgery (n=139)
Age (years)		
<51	10 (7%)	13 (9%)
51–60	30 (21%)	30 (22%)
61–70	59 (42%)	55 (40%)
71–80	41 (29%)	41 (29%)
Sex		
Male	97 (69%)	95 (68%)
Female	43 (31%)	44 (32%)
Extension of tumour		
Partially fixed	69 (49%)	69 (50%)
Fixed	71 (51%)	70 (50%)
Type of surgery		
ARR	51 (36%)	45 (32%)
APE	89 (64%)	94 (68%)
Height of tumour (cm)		
0–4	28 (20%)	23 (17%)
5–8	70 (50%)	71 (53%)
9–15	42 (30%)	40 (29%)
>15	0	1 (1%)
Unknown	. .	4
Number of quadrants involved		
1	16 (12%)	21 (16%)
2	20 (14%)	19 (14%)
3	39 (28%)	37 (27%)
4	63 (46%)	58 (43%)
Unknown	2	4

ARR=anterior restorative resection; APE=abdominoperineal excision.

Table 1: **Pretreatment characteristics by allocated treatment**

Results

Recruitment into the trial started in November, 1981, and ended in November, 1989, when 279 patients had been enrolled; 140 patients were allocated surgery alone and 139 preoperative radiotherapy (figure 1). Recruitment, initially steady, declined after publication, and perhaps misinterpretation, of the disappointing results of the first MRC trial of low-dose radiotherapy. After 7 years of accrual, only slightly more than half the required number of patients had been entered. We decided to continue the trial only until the launch, in November, 1989, of the UK Coordinating Committee on Cancer Research (UKCCCR) adjuvant X-ray and fluorouracil infusion study (AXIS) for treatment of colorectal cancer. This ongoing trial includes randomisation with respect to preoperative radiotherapy for rectal tumours.

Of the 279 patients, 217 died. The surviving patients were followed-up for a minimum of 5 years with the exception of seven patients, lost to follow-up within 5 years of randomisation, who could not be traced through the OPCS and were censored at the date last known to be alive.

Pretreatment characteristics of the patients were well balanced (table 1). 69 (49%) of 140 patients allocated surgery only had partially fixed tumours and 71 (51%) had fixed tumours. Of the 139 patients who had radiotherapy and surgery 69 (50%) had fixed tumours and 70 (50%) had fixed tumours. Abdominoperineal excision was the intended operation for about two-thirds of patients in both groups.

	Surgery only (n=140)	Radiotherapy plus surgery (n=139)
Type of surgery		
APE	75 (54%)	70 (51%)
ARR with protective colostomy	18 (13%)	18 (13%)
ARR without protective colostomy	20 (14%)	20 (15%)
Hartmann's operation	14 (10%)	8 (6%)
Laparotomy with colostomy	10 (7%)	6 (4%)
Laparotomy without colostomy	. .	3 (2%)
Colectomy and ileostomy	. .	2 (1%)
No surgery	3 (2%)	9 (7%)
Not recorded	. .	3
Residual disease		
No residual disease	66 (48%)	73 (55%)
Pelvic disease only	33 (24%)	23 (17%)
Abdominal disease only	16 (12%)	14 (11%)
Pelvic and abdominal disease	19 (14%)	14 (11%)
No surgery	3 (2%)	9 (7%)
Unknown	3	6
Results of surgery		
Curative	56 (40%)	66 (47%)
Indeterminate	22 (16%)	15 (11%)
Palliative	59 (42%)	43 (31%)
No surgery/laparotomy only	3 (2%)	15 (11%)

ARR=anterior restorative resection; APE=abdominoperineal excision.

Table 2: **Type of surgery by allocated treatment**

125 (90%) patients received the planned dose of 40 Gy over 4 weeks. Nine patients received less than the prescribed dose of radiation: two received no radiotherapy because they were judged too ill, three failed to complete the full treatment because of their deteriorating condition, and treatment was stopped early in four patients (ischiorectal abscess and perineal breakdown, bowel obstruction, a prearranged time for surgery, and refusal to continue by the patient). A further five patients received slightly higher doses of radiation than planned to accommodate altered fractionation schedules.

Of patients who received radiotherapy, 61 (45%) of 137 reported no significant morbidity. 45 (33%) of all patients suffered diarrhoea and 30 (22%) had skin reactions. Only four (3%) patients complained of nausea and 3 (2%) of abdominal pain.

The median time from randomisation to surgery was 7 days (IQR 4–12 days) for patients allocated immediate surgery and 73 days (64–84) for those allocated preoperative radiotherapy. The distribution of type of surgery done was very similar in the two treatment groups (table 2), with about half the patients in each group having

	Surgery only (n=140)	Radiotherapy plus surgery (n=139)
Sepsis		
Abdominal wound	18 (13%)	8 (6%)
Pelvic	16 (12%)	22 (17%)
Haemorrhage	12 (9%)	5 (4%)
Obstruction		
Intestinal	3 (2%)	. .
Urinary	15 (11%)	7 (5%)
Anastomotic leak	10 (7%)	9 (7%)
Other complications		
Perineal wound	5	10
Gastrointestinal	4	4
Genitourinary	7	7
Respiratory	10	4
Cardiovascular	2	3
Colostomy	. .	4
Cerebrovascular	2	. .
Anastomosis	1	1
Psychiatric	1	1
Postoperative death	10	5

Table 3: **Postoperative complications by allocated treatment**

	Surgery only	Radiotherapy plus surgery
Grade of tumour*		
Low	15 (12%)	16 (14%)
Average	94 (74%)	93 (79%)
High	18 (14%)	8 (7%)
Unknown	. .	4
Local invasion		
None	8 (6%)	14(12%)
Slight	23 (18%)	20 (17%)
Moderate	47 (37%)	54 (46%)
Extensive	49 (39%)	29 (25%)
Unknown	. .	4
Venous spread		
None found	91 (73%)	98 (84%)
Submucosal veins	4 (3%)	4 (3%)
Extramural veins	30 (24%)	14 (12%)
Unknown	2	5
Dukes' classification		
A	9 (7%)	19 (16%)
B	43 (34%)	64 (54%)
C	75 (59%)	35 (30%)
Unknown	. .	3
Primary tumour size (cm)		
1–4	45 (36%)	78 (68%)
5–7	66 (52%)	33 (29%)
⩾8	15 (12%)	3
Unknown	1	7
Lymph nodes examined		
None	5 (4%)	12 (10%)
1–3	19 (15%)	31 (27%)
4–6	36 (29%)	47 (41%)
⩾7	65 (52%)	25 (22%)
Unknown	2	6
Number of lymph nodes involved		
None	54 (43%)	83 (71%)
1–3	37 (29%)	23 (20%)
4–6	21 (17%)	9 (8%)
⩾7	15 (12%)	2 (2%)
Unknown	. .	4
Number of quadrants involved		
1	8 (6%)	22 (20%)
2	6 (5%)	10 (9%)
3	32 (26%)	27 (24%)
4	79 (63%)	52 (47%)
Unknown	2	10
Total resections	127	121

*Low, average, and high=well, moderately, and poorly differentiated, respectively.

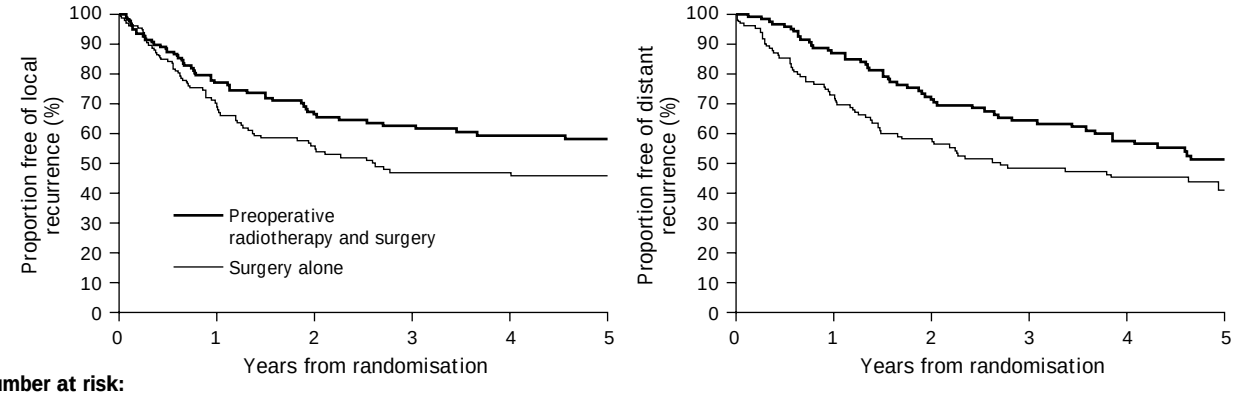
Table 4: **Pathological assessments by allocated treatment**

abdominoperineal excision. The presence of residual disease in the pelvis, abdomen, or both, was assessed. Of patients allocated radiotherapy, 73 (55%) were found to have no residual disease, compared with 66 (48%) of the patients who had surgery alone. Surgeons were asked to assess whether the operation had been curative, palliative, or indeterminate. Of patients allocated surgery alone, 56 (40%) of 140 were thought to have had curative operations compared with 66 (47%) of 139 patients allocated radiotherapy (p=0·21).

Three patients allocated surgery alone were considered unfit for surgery. Nine patients allocated preoperative radiotherapy did not have surgery—seven were not fit, one patient refused, and one was not referred back after radiotherapy.

The presence or absence of each of six specific postoperative (occurring within 30 days of surgery) complications was recorded, together with any postoperative deaths (table 3). Surgeons were also asked to report any other complications. There was no evidence of an excess of complications in the radiotherapy group.

Pathological assessment of the resected tissue was done for patients from both treatment groups (table 4).



Number at risk:

Surgery alone	140	84	61	43	38	29
Preoperative radiotherapy	139	93	71	59	48	36

	140	86	61	45	38	28
	139	90	70	61	48	39

Figure 2: **Survival free of local and distant recurrence by allocated treatment**

Tumours were significantly smaller in the radiotherapy group (Mann-Whitney, p<0·0001). The proportion of tumours graded as Dukes' C was significantly lower in the radiotherapy group than in the surgery alone group (29 *vs* 59%, p=0·0002) and the number of involved lymph nodes was also smaller. However, the number of lymph nodes examined was lower in the radiotherapy group.

At follow-up, surgeons were asked to report on the status of the patients' abdominal and (if applicable) perineal wounds, and to describe, in broad terms, any late complications. Again, there was no evidence of an increased number of late complications in the radiotherapy group, two patients in each treatment group still had complications of the abdominal wounds 12 months after surgery. Among those who had abdominoperineal excision, four of 49 patients who had surgery alone who were assessable at 12 months had complications of the perineal wound compared with seven of 56 patients allocated radiotherapy. The most common complications that occurred throughout follow-up were of the genitourinary system; these occurred in 18 patients in each treatment group. Complications associated with the colostomy were reported in ten surgery alone patients and eight radiotherapy patients, and five patients in each group had anastomosis-related complications after anterior restorative resection.

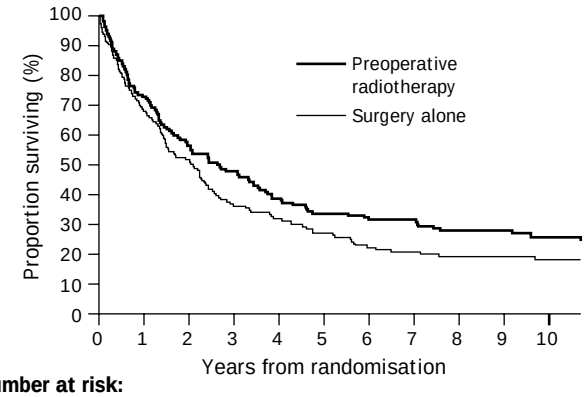
Figure 2 shows Kaplan-Meier curves for time free of local recurrence. 65 patients allocated surgery alone had a recurrence compared with 50 of those allocated radiotherapy. The log-rank comparison suggests an advantage for the radiotherapy group of borderline statistical significance (p=0·04). The hazard ratio is 0·68 (95% CI of 0·47–0·98), which suggests that preoperative radiotherapy reduces the risk of local recurrence by a third. However, the data are compatible with a reduction in the risk of as much as a half or as little as 2%.

Survival free of distant recurrence is also shown in figure 2. 67 patients allocated surgery alone had a distant recurrence compared with 49 of those allocated radiotherapy. A reduction in the risk of metastatic recurrence was found which was, rather unexpectedly, of a similar order to the reduction in local recurrence (hazard ratio 0·66 [0·46–0·95]; log-rank p=0·02).

Consistent with the results of the individual endpoints, results for disease-free survival also suggest a benefit to the radiotherapy patients (hazard ratio 0·76 [0·58–1·0], log-rank p=0·05). Disease recurrence or death within 5 years occurred in 108 patients allocated surgery alone and 96 of those allocated radiotherapy.

Of the 279 patients randomised, 217 have died; 114 (81%) of 140 patients allocated surgery alone and 103 (74%) of 139 patients allocated radiotherapy, median survival times are 24 months and 31 months, respectively. Median follow-up time for the patients who survived is 10 years. Although less than two thirds of the planned sample size was achieved, 217 (86%) of the 251 deaths anticipated, if the planned 450 patients had been entered and followed up for 3 years, have occurred. The hazard ratio for death from any cause is 0·79, giving an estimated reduction in the risk of death for patients allocated radiotherapy of 21% (log-rank p=0·10). However, the 95% CI for this hazard ratio is wide (0·6–1·04) indicating that the data are also compatible with no advantage to radiotherapy (figure 3).

We attempted to classify causes of death, taking the principal cause named on the trial death form or the OPCS death certificate. Necropsy was done rarely and so causes of death should be interpreted with caution. However, cause-specific survival analysis suggests a larger benefit for radiotherapy. Fewer deaths were reported to have been from colorectal cancer or complications of the disease or its treatment among patients allocated preoperative radiotherapy than among those allocated



Number at risk:

Surgery alone	140	50	37	27	14
Preoperative radiotherapy	139	66	46	39	18

Figure 3: **Overall survival by allocated treatment**

surgery alone (85 *vs* 103; hazard ratio 0·71 [0·54–0·97], p=0·02). This estimate indicates a substantial decrease in the risk of death from colorectal cancer in patients allocated radiotherapy, although the data are compatible with a halving of the risk of death from colorectal cancer at one extreme or as little as 3% reduction in risk at the other.

Discussion

The extended follow-up period of the study enabled us to come close to achieving our objectives despite failure to enrol the 450 patients required for the trial design. The effects of radiotherapy on recurrence of cancer and survival are similar to the estimates on which the trial design was based. Failure to recruit the planned number of patients is reflected in the wide 95% CI seen for each of the main endpoints.

There was evidence of benefit from preoperative radiotherapy before the trial.[4–7] The reasons for investigating preoperative radiation therapy were: reduction in size of the primary tumour and frequency of regional node metastases before resection; a reduction in the frequency of local pelvic recurrence and of distant metastasis from cancer cells released during resection (preoperative treatment can inhibit the proliferation of malignant cells whether they remain local or spread outside the pelvis after radiation); radiation responsiveness of cancer cells may be greater before surgery when they are normally oxygenated than afterwards when they may be hypoxic because of surgical effects on the vasculature; and a lower frequency of late radiation enteritis because the small bowel is less likely to be adherent in the pelvis.[8]

In line with the earlier trials we found no increased frequency of early or late complications in the patients who received radiotherapy. There were significant reductions in tumour size and grade and in the rates of local recurrence and distant metastases in the radiotherapy group. There was a suggestion that the risk of death from colorectal cancer was reduced, and a trend towards an improvement in overall survival. However, the trial was of sufficient size to detect only substantial improvement in overall survival.

The trial was aimed at a specific disease subgroup—patients with locally advanced but otherwise operable rectal cancer (defined in the first MRC trial[1] as fixed or partially fixed). Patients in this subgroup have a much lower potential for curative surgery as well as a much poorer rate of survival even when curative surgery appeared to have been achieved. In the earlier trial[1] surgeons were asked only to record their preoperative findings with respect to fixity, but in this trial they were asked to base a crucial decision on type of treatment on these observations. Patients in the preoperative radiotherapy treatment group, in which a moderately high dose of radiation was to be used, had their surgery delayed by 2 months (1 month to cover the radiotherapy fractionation and a further month for tumour regression to occur and for the normal tissues to recover from the radiation). Whereas surgeons showed little reluctance to accept the 2 weeks of low-dose radiation of the first trial, especially because there was no requirement for further delay before the operation, they were reluctant to allow their patients to be open to what they saw as the risks of delayed surgical treatment in this trial. This reluctance may have hindered recruitment to the trial. Also there was a general misinterpretation of the outcome of the initial trial of low-dose radiotherapy. In addition, the patients selected for this study represent only a small proportion of total operable cases.

The case for preoperative adjuvant radiotherapy has been supported by several trials published since this trial started, including the European trial reported by Gerard and colleagues.[9] In that study of 466 patients, the survival benefit of 69% in the treated group versus 59% in the surgery-only group also failed to achieve statistical significance (log rank p=0·08). Several Swedish studies[10–14] have advanced the case for the use of preoperative rather than postoperative radiation in terms of better patient compliance, greater reduction in local recurrence rates, and lower morbidity. None of these studies has concentrated specifically on locally advanced tumours. Pahlman and Glimelius[11] reported evidence that the reduction in volume of tissue irradiated through three portals instead of the two used in this and most other trials, has resulted in reduced postoperative morbidity and mortality. Moreover, current practice is to give a short course of high-dose radiation (25 Gy over 5–7 days) and to proceed to immediate surgery, thus avoiding the long delay before surgery.

Since the trial was closed, surgeons have been entering patients in large numbers into the AXIS trial in which there is randomisation with respect to preoperative radiation for patients with rectal cancer, with the Swedish model of short, high-dose therapy. The combined evidence from all these trials should yield sufficient numbers to answer precisely the questions of the effect of preoperative radiotherapy on local and distant recurrence, and above all the effect on survival.

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Randomised trial of surgery alone versus surgery followed by radiotherapy for mobile cancer of the rectum

*Medical Research Council Rectal Cancer Working Party**

Summary

Background Although surgery is the treatment of choice for rectal cancer, local recurrence is common even after apparently curative resection. We aimed to assess the role of postoperative radiotherapy in reducing rates of local recurrence, and improving disease-free and overall survival in patients with mobile Dukes' stage B and C rectal cancers.

Methods We carried out a prospective, randomised trial of surgery alone (n=235) versus surgery followed 4–6 weeks later by radiotherapy (n=234), of 40 Gy in 20 fractions of 2 Gy over 4 weeks. The 469 patients, from 46 hospitals in the UK and the Republic of Ireland, were randomised between 1984 and 1989, and followed up for a minimum of 5 years or to death.

Findings 284 patients died, 145 of 235 allocated surgery alone and 139 of 234 allocated postoperative radiotherapy. The hazard ratio for overall survival was 0·84 (95% CI 0·65–1·07, p=0·17). At 5 years' follow-up 79 patients who received surgery alone and 48 who received postoperative radiotherapy had had local recurrence (hazard ratio 0·54 [0·38–0·77], p=0·001). The corresponding numbers with distant recurrence were 83 and 75 (hazard ratio 0·85 [0·63–1·114], p=0·18). The hazard ratio for disease-free survival was 0·85 (0·65–1·08; p=0·18). Radiotherapy was generally well tolerated; assessment of late events showed serious late bowel complications to be rare and not significantly increased after radiotherapy, even when this followed anterior resection.

Interpretation Our results have provided further evidence of the ability of postoperative radiotherapy to delay and prevent local recurrence of rectal cancer. Although the local recurrence rate in the control group is in keeping with other multi-centre trials of the mid to late 1980s, it is undoubtedly higher than would be regarded as acceptable now. The combination of larger trials required to provide definitive answers on the impact that postoperative radiotherapy will have on survival.

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See Commentary page 1600

Introduction

Radical surgery is the treatment of choice for the majority of patients with rectal cancer. However, even after an apparently curative operation, recurrence—particulary local recurrence—is common. In an attempt to improve the results of surgery, adjuvant therapies have been under investigation for several decades, yet survival rates have changed little, remaining around 40% at 5 years from diagnosis. The incidence of local recurrence of rectal cancer is dependent on Dukes' stage (and possibly surgeon). Local recurrence has been reported to occur in about 25% of patients with stage B disease, and 50% of patients with stage C disease. Local recurrence is difficult to treat, and is a major cause of morbidity and impairment to quality of life. Local recurrence leads to the death of many patients directly or indirectly. Attempts to prevent local recurrence through the use of radiotherapy have a long history, with early trials concentrating on the use of preoperative radiotherapy. The first major randomised trial to assess preoperative radiotherapy began in 1964,[1] and at least 18 randomised trials have been completed since. Trials of postoperative radiotherapy began 10 years later, and have been fewer in number. Although preoperative radiotherapy may be given with the hope of enabling more curative resections to be done, there will

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