Postoperative radiotherapy reduced local recurrence after surgery for rectal cancer

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 Dec 14;348:1610-14.

Objective
To determine whether postoperative radiotherapy reduces local recurrence and increases survival in patients who have surgery for nonfixed rectal cancer.

Design
Randomised controlled trial with a minimum follow-up of 5 years.

Setting
46 hospitals in the United Kingdom and the Republic of Ireland.

Patients
469 patients (62% men) who were suitable for either abdominoperineal excision or anterior restorative resection and had a tumour that was not fixed within the pelvis on clinical examination. Inclusion criteria were age < 80 years, confirmed Dukes stage B or C adenocarcinoma, and no evidence of extrapelvic cancer. Follow-up was 95%. Accrual occurred from 1984 to 1989.

Intervention
After surgery, 234 patients were randomised to radiotherapy and 235 patients to usual care. Megavoltage radiotherapy (40 Gy given in 20 fractions of 2 Gy over 4 wk) was started between 30 and 60 days after surgery and was delivered to the pelvis with 2 parallel opposed fields, 18 cm (length) by 15 cm (width), positioned to cover the former site of the primary tumour with an adequate proximal margin (usually 5 cm).

Main outcome measures
Local recurrence, distant recurrence, survival, disease-free survival, and complications. The study was stopped early (only 469 of the 500 planned patients had been entered) in favour of a subsequent study of combined radiation and chemotherapy. All analyses were by intention to treat.

Main results
The groups did not differ for disease-free survival (hazard ratio [HR] 0.85, 95% CI 0.65 to 1.08, $P = 0.18$) or overall survival (HR 0.84, CI 0.65 to 1.07, $P = 0.17$). Patients who received radiotherapy had fewer local recurrences than patients who did not receive radiotherapy (HR 0.54, CI 0.38 to 0.77, $P = 0.001$) (Table). The groups did not differ for late complications or distant recurrences (HR 0.85, CI 0.63 to 1.14, $P = 0.29$).

Conclusion
Patients who received radiotherapy after surgery for Dukes stage B or C rectal cancer had a lower rate of local recurrence; but disease-free survival, survival, and distant recurrence rates were not improved.

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Surgery followed by radiotherapy vs surgery alone*

Outcome at 5 years	Surgery and radiotherapy EER	Surgery alone CER	RRR (95% CI)	ARR |EER − CER|	NNT (CI)
Local recurrences	21%	34%	39% (17 to 55)	13%	8 (5 to 20)

*Abbreviations defined in Glossary; RRR, ARR, NNT, and CI calculated from data in article.

Commentary

The 2 trials of adjuvant radiation therapy for rectal cancer done by the United Kingdom Medical Research Council (MRC) provide further evidence of the ability of radiation to reduce the risk for pelvic recurrence, whether radiation is given before or after surgery. These trials are also consistent with previous studies because they report only limited improvement in survival (1).

The risk for pelvic recurrence after surgery alone for rectal cancer is generally reported in the range of 5% to 50%, with a median of approximately 20%. Better pelvic control has recently been reported, apparently because of wide, sharp dissection around the primary cancer (2). It is not yet known whether the general adoption of such techniques would obviate the need for pelvic radiation. No details are provided about the surgical techniques used in the MRC trials. At present, adjuvant radiation continues to play a central role in the management of rectal cancer.

The propensity for rectal cancer to recur outside the pelvis indicates the need for effective systemic adjuvant therapy. The 2 MRC studies were designed before the first evidence became available to indicate that combining radiation and cytotoxic chemotherapy could reduce the risk for both pelvic and extrapelvic recurrence and was more likely to improve survival than single-modality adjuvant therapy. Many current adjuvant studies are based on a trial by the North Central Cancer Trials Group in which the combination of radiation with 5-fluorouracil and methylCCNU (subsequent studies showed methylCCNU to be unnecessary) improved recurrence rates and survival (3). Combined-modality adjuvant treatment resulted in a 34% relative reduction of recurrence (CI 12% to 50%, $P = 0.002$) and a 29% relative improvement in overall survival (CI 7% to 45%, $P = 0.04$).

The juxtaposition of the MRC trials highlights an unresolved controversy regarding whether adjuvant radiation should be given before or after surgery (1). Although the radiation fields and doses used in the 2 studies were identical, the relative merits of preoperative and postoperative radiation cannot be deduced because of differences in patient eligibility. Currently, interest in preoperative radiation is strong. High-dose post-

(continued on page 119)