Randomized clinical trial

Long-term results of a randomized trial comparing preoperative short-course radiotherapy with preoperative conventionally fractionated chemoradiation for rectal cancer

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Background: **Neoadjuvant chemoradiotherapy does not alter anal sphincter preservation or postoperative complications compared with short-course radiotherapy alone in patients with clinical stage T3 or T4 resectable rectal cancer. The aim of this study was to compare survival, local control and late toxicity in the two treatment groups.**

Methods: **The study randomized 312 patients to receive either preoperative irradiation (25 Gy in five fractions of 5 Gy) and surgery within 7 days or chemoradiation (50·4 Gy in 28 fractions of 1·8 Gy, bolus 5-fluorouracil and leucovorin) and surgery 4–6 weeks later. The median follow-up of living patients was 48 (range 31–69) months.**

Results: **Early radiation toxicity was higher in the chemoradiation group (18·2 *versus* 3·2 per cent; $P < 0·001$). The actuarial 4-year overall survival was 67·2 per cent in the short-course group and 66·2 per cent in the chemoradiation group ($P = 0·960$). Disease-free survival was 58·4 *versus* 55·6 per cent ($P = 0·820$), crude incidence of local recurrence was 9·0 *versus* 14·2 per cent ($P = 0·170$) and severe late toxicity was 10·1 *versus* 7·1 per cent ($P = 0·360$) respectively.**

Conclusion: **Neoadjuvant chemoradiation did not increase survival, local control or late toxicity compared with short-course radiotherapy alone.**

Presented in part to the 13th European Cancer Conference, Paris, France, October–November 2005

Paper accepted 10 May 2006

Published online in Wiley InterScience (www.bjs.co.uk). **DOI:** 10.1002/bjs.5506

Introduction

Randomized trials have demonstrated superior local control, lower toxicity and better compliance of radiotherapy or radiochemotherapy administered before rather than after surgery[1–4]. Conventionally fractionated chemoradiation with delayed surgery or short-course irradiation (25 Gy in five fractions) with immediate surgery are probably the most frequent regimens in the preoperative treatment of patients with resectable rectal cancer[2,4,5–10]. Similar long-term survival, local control and late morbidity have been reported for both these methods in non-comparative studies[4,8–12]. The benefit of the short-course schedule is a lower rate of early toxicity than with chemoradiation[4,13–16]. In addition, short-course irradiation is less expensive and more convenient, especially in centres with a long waiting list. On the other hand, the use of high doses per fraction raises concern about late toxicity[17]. Conventionally fractionated chemoradiation might be better than the short-course radiation schedule at reducing local recurrences. Another advantage of chemoradiation is better sphincter preservation because the tumour bulk is reduced before surgery[17,18]. However, there is no firm evidence to support this[18].

A randomized study was conducted to determine whether greater tumour shrinkage after chemoradiation would result in an improved rate of sphincter-preserving surgery compared with short-course radiotherapy. The