Radiotherapy in Rectal Cancer

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One of the major advances in cancer therapy during the 1990s is the curative multimodality treatment of colorectal cancer. First, adjuvant chemotherapy has been established in colon cancer Dukes' C; second, adjuvant postoperative chemoradiotherapy and preoperative radiotherapy have proved to be effective in rectal cancer Dukes' B and C; third, multimodality treatment including several treatment modalities has been shown to cure a fairly high percentage of patients with locally advanced and recurrent rectal cancer; and fourth, a change in the surgical technique in rectal cancer has in several institutions reduced local recurrence rate and improved survival.

Although most agree that radiotherapy plays an important part in the current curative treatment of rectal cancer, its role and scheduling in the multimodality treatment of the disease remains controversial, among oncologists as well as surgeons. The American tradition employing long-term radiotherapy and long-term chemotherapy in addition to surgery is also advocated in certain parts of Europe. On the other hand, simpler and less resource-demanding regimens aimed at avoiding toxicity and over-treatment have been established in some countries in Europe, but with little impact outside these countries.

In this issue of Acta Oncologica two articles (1, 2) review the role of perioperative radiotherapy in rectal cancer. The article by Gunderson (1) gives a comprehensive review of several aspects of multimodality treatment of colorectal cancer, operable cases as well as locally advanced and local recurrent ones. The article by Glimelius & Påhlman (2) discusses in detail the theoretical background for and current evidence on perioperative adjuvant radiotherapy of rectal cancer.

Is there any consensus on indications for and scheduling of perioperative radiotherapy in rectal cancer? And, what are the principal questions still under discussion that should be answered in future trials? Let us first consider the adjuvant situation in operable rectal cancer.

ADJUVANT TREATMENT IN OPERABLE CASES

The role of adjuvant treatment depends on the type of surgery being used and the results obtained by surgery alone in the particular institution. Almost all data published on adjuvant treatment are based on conventional surgery with a high local recurrence rate (20–40%) in the surgery alone group (3–7). With this type of surgery, postoperative radiotherapy (45–50 Gy, 1.8–2.0 Gy per fraction) combined with fluorouracil-based chemotherapy has reduced the local recurrence rate in Dukes' B and C cases to about 10% and reduced the risk of death by 30–40% compared with surgery alone (3, 5) or surgery combined with postoperative radiotherapy (4). Similarly, preoperative radiotherapy has reduced local recurrence rate (6, 7), but has not improved overall survival, except for the recent large Swedish trial (using 25 Gy with 5 Gy per fraction) that showed a reduction in death risk of about 20% (7). So far, we do not have any data deriving from the combination of this preoperative regimen and postoperative chemotherapy.

But what is the benefit of adjuvant radiotherapy when surgery is optimal with a low local recurrence rate (5–10%) by surgery alone, as obtained with the TME procedure (8)? Probably we cannot extrapolate from the previous trials, but we are hopeful that a Dutch trial will give us an answer within a few years. When surgery alone gives such excellent results with respect to local recurrence rate, it does not seem reasonable to give routinely perioperative radiotherapy in operable cases, as 90–95% of the patients will be overtreated and at risk of acute and late morbidity. Probably, a subgroup of the rectal cancer patients operated with the TME procedure will have a relatively high local recurrence rate with poor prognosis, and this group of patients should be offered perioperative radiotherapy and probably chemotherapy as well. This group includes patients with positive lateral resection margins (R1 resections) and with perforation during surgery. In addition, the group may include other groups of pa-

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tients that will be identified during the next years of TME practice (e.g. patients with low tumours, abdominoperineal resection, stage Dukes' C, neural infiltration). If these risk factors can be identified prior to surgery, preoperative radiotherapy will probably be preferred. However, if the risk factors are identified intraoperatively or postoperatively, postoperative radiotherapy should be given, together with chemotherapy.

LOCALLY ADVANCED AND RECURRENT CASES

As reviewed by Gunderson (1), combined modality treatment can cure a fairly high proportion of patients with locally advanced T4 rectal cancers and also patients with a local recurrence. Five-year survival rates of about 40% are reported in patients with primary tumours, and about 20–40% in patients with local recurrences. Results like this require proper selection of patients, close collaboration between oncologists, specialist surgeons, radiologists, and a rather 'aggressive' attitude among the surgeons. Preoperative external radiotherapy to 45–50 Gy is required in combination with extensive surgery. The best results are when the resection margins are free (R0 resection) and the poorest when macroscopic tumour is left (R2 resection). The main controversies here are the roles of additional concomitant and maintenance chemotherapy (1, 9) and intraoperative radiotherapy (IORT) as a boost (1, 10). None of these modalities have been properly addressed in randomized clinical trials, although a few are currently being performed.

REFERENCES

1. Gunderson LL. Indications for and results of combined modality treatment of colorectal cancer. Acta Oncol 1999; 38: 5–19.
2. Glimelius B, Påhlman L. Perioperative radiotherapy in rectal cancer. Acta Oncol 1999; 38: 21–30.
3. Gastrointestinal Tumor Study Group. Survival after postoperative combination treatment of rectal cancer. N Engl J Med 1986; 315: 1294–5.
4. Krook JE, Moertel CG, Gunderson LL, et al. Effective adjuvant therapy for high-risk rectal carcinoma. N Engl J Med 1991; 324: 709–15.
5. 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. Br J Surg 1997; 84: 1130–5.
6. Stockholm Rectal Cancer Study Group. Preoperative short-term radiation therapy in operable rectal carcinoma. A prospective randomized trial. Cancer 1990; 66: 49–55.
7. Swedish Rectal Cancer Trial. Improved survival with preoperative radiotherapy in resectable rectal cancer. N Engl J Med 1997; 336: 980–7.
8. MacFarlane JK, Ryall RDH, Heald RJ. Mesorectal excision for rectal cancer. Lancet 1993; 341: 457–60.
9. Minsky BD, Cohen AM, Kemeny N, et al. Enhancement of radiation-induced downstaging of rectal cancer by fluorouracil and high-dose leucovorin chemotherapy. J Clin Oncol 1992; 10: 79–84.
10. Gunderson LL, Martin JK, Beart RW, et al. External beam and intraoperative electron irradiation for locally advanced colorectal cancer. Ann Surg 1988; 207: 52–60.