



**Karolinska  
Institutet**

**Institutionen för molekylär medicin och kirurgi**

# Preoperative radiotherapy in rectal cancer - aspects of different regimens

AKADEMISK AVHANDLING

som för avläggande av medicine doktorsexamen vid Karolinska Institutet offentligen försvaras i Rolf Luft Auditorium, Karolinska Universitetssjukhuset

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# ABSTRACT

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In Sweden approximately 2000 patients are annually diagnosed with a rectal cancer. The main treatment of the cancer is surgery. Radiotherapy (RT) is used as an adjuvant treatment in >60% of these patients to improve local control and in some patients to downsize a primary non resectable tumour to facilitate surgery. However RT has drawbacks as acute adverse events due to RT, increased risk of postoperative complications and mortality and late side-effects from RT. To optimise RT schedules regarding oncological and negative effects the Stockholm Colorectal Cancer Study Group initiated the Stockholm III Trial in 1998 to compare different fractionations of RT and the importance of timing to surgery. The trial is randomising patients with primary resectable tumours to one of three treatment schedules: short-course RT with immediate surgery (SRT); short-course RT with delayed surgery (SRT-delay); long-course RT with delayed surgery (LRT-delay).

In Paper I, III and IV patients randomised in the on-going Stockholm III Trial were studied. In Paper II were patients having SRT-delay outside the Stockholm III Trial in the Stockholm-Gotland region studied.

The papers conclude that the Stockholm III Trial is a feasible study with acceptable compliance to the protocol. Acute adverse events due to RT were low both within the Stockholm III Trial as well as after the SRT-delay schedule outside the trial.

In Paper II, patients outside the Stockholm III Trial had SRT-delay, a schedule still without strong scientifically support, mainly due to primary non-resectable tumours and co-morbidities. The short-term outcome of the treatment was in line with established schedules.

RT has been shown to impair the postoperative leucocytosis after surgery and increase complications and mortality. A depression of the bone marrow due to RT is one potential reason of these findings. In Paper III allocated treatment were related to postoperative complications and the leucocyte reaction to RT, measured as a ratio between leucocyte counts (LC) postoperative days 1 or 2 and the preoperative LC. Patients with low ratios had more complications compared to patients with intermediate and high ratios irrespective of RT regimen. Patients having SRT had more patients with low LC-ratios and more complications compared to the two other arms. There was no association between preoperative low (<4.0) LC and postoperative complications.

Short-course RT has been considered not to have a downstaging effect, however with surgery immediately after the end of RT. In Paper II with surgery delayed there were lower stages and less involved margins after the RT when the clinical stages and margins were compared to the pathological stages and resection margins, indicating downstaging. Also in Paper IV, comparing the arms with short-course RT, a downstaging effect were indicated when the patients in the SRT-delay arm had significantly lower TNM Stages and T-stages and in addition more tumour regression compared to patients in the SRT randomisation arm.

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