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Spacer in rectal cancer

Acute toxicity after a diverting stoma and spacer prior to chemoradiation in locally advanced rectal cancer

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ABSTRACT

Background and purpose: Chemoradiotherapy (CRT) followed by surgery is the standard of care for locally advanced rectal cancer (LARC). For grade ⩾3 acute diarrhea there is a relationship between dose and irradiated small bowel volume. The aim of this study was to evaluate whether combined placement of a diverting stoma and sigmoid spacer (DSSS) led to reduced irradiated small bowel volume and less grade ⩾3 acute diarrhea in the treatment of LARC.

Materials/methods: Between 2003 and 2010, 54 of 189 LARC patients treated with CRT in two institutions had a DSSS prior to CRT. Data on patient and treatment characteristics and outcomes were collected retrospectively. Delineation of small bowel was performed with planning CT-scans. CTCAE version 4.0 was used for acute toxicity.

Results: Patients with a DSSS had significantly less small bowel volume irradiated up to doses of 20 Gy. This difference was not observed for the higher dose levels. CRT induced grade ⩾3 acute diarrhea was not different between the two groups (8.3% vs. 12.8%; $p = 0.41$).

Conclusion: DSSS is not clearly beneficial to reduce grade ⩾3 acute diarrhea, and it must be considered whether placement of a DSSS is justified for this purpose.

After the introduction of total mesorectal excision (TME) in the treatment of rectal cancer, local recurrence rates and survival have improved substantially [1,2]. Additional reduction in local recurrence rate has been achieved with preoperative radiotherapy [3,4]. For locally advanced rectal cancer (LARC), several randomized trials show that preoperative chemoradiotherapy (CRT) with 5-fluorouracil (5-FU) leads to downstaging and downsizing, [5–8] and subsequently leads to a higher probability of local control [5]. However, several studies show that acute toxicity after preoperative chemoradiotherapy for locally advanced rectal cancer is more common than after short-course preoperative radiotherapy [9–11]. Approximately 18–21% of patients will develop grade 3–4 toxicity during CRT treatment [10–11].

In an attempt to minimize small bowel volume in the radiotherapy fields, several surgical techniques have been introduced. Spacers can be brought into position to move small bowel out of the small pelvis [12]. Usually, patients will receive a diverting colostomy in the same procedure. The benefit of a diverting colostoma prior to neoadjuvant therapy is that patients are instantly relieved of obstruction symptoms and it may reduce discomfort due to perineal radiation dermatitis. In general the sigmoid is used as a spacer, but also a breast-prosthesis can be used [12].

The aim of this retrospective study is to evaluate whether a spacer reduces irradiated small bowel volume and whether this results in less grade ⩾3 acute diarrhea in patients with locally advanced rectal cancer.

Patients and methods

Study population

Patients with newly diagnosed LARC between January 2003 and October 2010 who were referred to two different radiotherapy departments in the Netherlands were included in this retrospective study. Patients were identified from departmental cancer registries at the University Medical Center Leiden (LUMC) and the Radiotherapy Center West (RCW). In the LUMC, 162 patients were identified, of whom 39 were excluded for the following reasons: prior malignancy ($n = 14$); treatment for local recurrence ($n = 13$); metastatic disease at diagnosis ($n = 10$) and prior pelvic

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radiotherapy ($n = 2$). In the RCW, a total of 85 patients were identified of whom 19 were excluded (10 due to prior malignancy, 6 local recurrences and 3 patients with a dose exceeding 50.4 Gy).

Tumors were considered locally advanced when magnetic resonance imaging indicated a tumor with overgrowth into an adjacent organ, close proximity to the mesorectal fascia or any tumor stage accompanied by N2-status. Data such as patient characteristics, type and date of surgery and adjuvant treatment received were collected retrospectively from patient charts. For determination of acute toxicity, the Common Terminology Criteria for Adverse Events (CTCAE version 4.0) were used. Patients were seen weekly during their CRT and clinical findings were written down by the treating physician. The highest toxicity score has been taken and grading was retrospectively done.

Delineation of small bowel and bladder

Data on patient small bowel and bladder volume were acquired from treatment-planning CT scans (Philips Pinnacle 3.0 and Helax treatment planning systems). Delineation of small bowel loops was performed under supervision of the same radiologist at both institutions. The delivered radiation dose superior to the L4/L5 junction was negligible for all patients. Therefore, only small bowel loops on each slice of the planning CT scan inferior to the L4/L5 junction were contoured. A small bowel dose volume histogram was calculated for the initial intended pelvic treatment to 50–50.4 Gy, with the absolute volume of small bowel to be treated to each dose between 5 Gy and 50 Gy reported at 5 Gy intervals. For 34 of the 189 patients the dose volume histograms could not be retrieved (11.1% of patients with a DSSS and 19.3% of patients without a DSSS). The reason that 34 of the treatment plans could not be retrieved was due to the fact that planning for these patients was performed in an older Pinnacle version and it was not possible to restore the plans in the current Pinnacle 3.0 Philips treatment planning system. All of the lost plans were from patients treated at the LUMC. To predict the likelihood of grade $\geqslant 3$ acute diarrhea, patients were regarded as "low risk" if the irradiated volume of small bowel for each increment of 5 Gy remained below the threshold volumes as determined by Robertson et al. The threshold volumes for grade $\geqslant 3$ acute diarrhea as defined by Roberston et al. are the following, 425 cc for 5 Gy, 265 cc for 10 Gy, 120 cc for 15 Gy, 112 cc for 20 Gy, 105 cc for 25 Gy, 92 cc for 30 Gy, 85 cc for 35 Gy and 71 cc for 40 Gy [13]. No model exists for the prediction of acute grade $\geqslant 3$ diarrhea for the dose ranges of 45–50 Gy. For the dose range of 45–50 Gy the mean irradiated small bowel volume in this study was well under 50 cc. Once the irradiated volume of small bowel exceeded the threshold volume for one or more dose level(s) patients were regarded as "high risk".

Diverting stoma/spacer placement (DSSS)

In one institution, patients with locally advanced rectal cancer were often treated with a diverting stoma and spacer (46 of 66 patients, 69.7%), whereas in the other institution patients were only treated with a stoma and a diverting stoma (8 of 123 patients, 6.5%) when considered necessary due to serious obstructing symptoms. Serious obstructing symptoms were regarded as a clinical suspicion of an impending obstructive ileus. CRT treatment generally started 3–5 weeks after spacer placement.

Radiotherapy

Preoperative radiotherapy consisted of 50–50.4 Gy in daily fractions of 1.8–2.0 Gy five days a week. The clinical target volume (CTV) was defined as the gross tumor volume (GTV) and the mesentery with vascular supply, containing the perirectal, presacral, and the internal iliac nodes (up to the S1/S2 junction). The recommended upper border was the promontory. The anal canal was included when an abdominoperineal resection (APR) was likely, whereas the lower border included at least 3 cm of mesorectum caudal to the primary tumor if the planned operation was a low anterior resection (LAR). The treatment was delivered with a four-field conformal box technique and the majority of patients were treated in supine position.

Chemotherapy

A total of 147 of 189 patients received concurrent chemotherapy (77.8%). Of these patients 83.0% received twice daily oral Capecitabine 825 mg/m^2, including weekends. Other chemotherapy regimens were Capecitabine and Oxaliplatin (9.5%), 5-Fluorouracil with Leucovorin (2.0%) and Capecitabine with Bevacizumab (5.4%). The patients that did not receive chemotherapy received radiation therapy (50–50.4 Gy) prior to surgical resection.

Definitive surgery

Definitive surgery was performed 5–8 weeks after the last radiation treatment. Standard exploratory laparotomy with thorough examination of the intraperitoneal cavity was performed. All surgeons were TME trained and performed LAR (33 patients), APR (103 patients), Hartmann (35 patients) or a proctocolectomy (1 patient) at their own discretion. For 15 patients no resection was performed due to disease progression or refusal by the patient. For 2 patients it was unknown if a resection had occurred.

Statistical analysis

All data were entered in a database and analyzed with the SPSS package (SPSS 17.0, Inc, Chicago, IL). A x^2 test was used for categorical variables, and a Mann–Whitney–Wilcoxon test for continuous variables. The clinical variables included general patient and tumor characteristics, as well as treatment related variables. Clinically significant variables with $p \leqslant .10$ in univariate analysis were included in the multivariate linear regression analysis for numerical data and in the logistic regression analysis for categorical data. All reported p values were two-sided, and differences were considered statistically significant when $p \leqslant .05$.

Results

Patient characteristics

Patient and tumor characteristics are shown in Table 1. A diverting stoma and spacer of the sigmoid (DSSS) were implemented in 54 individuals from the cohort of 189 patients with locally advanced rectal cancer. In total 46 of 54 patients with a DSSS (85.2%) originated from one institute ($p < 0.001$). In the LUMC 8 of 123 patients (6.5%) received a DSSS while 46 of 66 patients (69.7%) in the RCW received a DSSS. Patients with a DSSS had higher tumor stage (42.6% cT4), underwent more APR (66.0%) since tumors were in closer proximity to the anal verge and had relatively low incidence of advanced lymph node involvement (15.7% N2). At multivariate analysis, two risk factors independently predicted the presence of a DSSS. Ranked in order of statistical significance these were: institution, and the level of the inferior tumor margin.