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Rectal cancer

Reirradiation, surgery and IORT for recurrent rectal cancer in previously irradiated patients

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Abstract

A total of 11 patients with recurrent rectal cancer who had been previously irradiated were treated with preoperative reirradiation (median dose 30 Gy), surgery and IORT. This treatment was related with high morbidity, a short pain-free survival (5 months) and poor local control (27% after 3 years), although some patients have long-term distant control and survival.

Keywords: Rectal cancer; Recurrent; Radiotherapy; Reirradiation; Surgery; IORT

Background and purpose

Preoperative short-term radiotherapy (5×5 Gy) has evolved into an integrated factor in the treatment of T2-3 rectal tumours because of beneficial effects on local control [1]. Long-term radiotherapy (44–50 Gy) has become standard of care in the treatment of T4 tumours because of improved local control and the effect of downsizing/-staging, thereby facilitating less invasive surgery in a subgroup of patients [2].

The 3–15 percent of patients who do develop a local recurrence confront us with a new problem; the treatment of previously irradiated tumours [1]. In previously non-irradiated recurrent tumours the combination of preoperative radiotherapy with a dosage of 50 Gy and surgery leads to improved local control [3]. This high radiation dose cannot be administered in previously irradiated patients, thus a lower dose of radiation must be applied not exceeding the maximum tolerated dosage. Previously Mohiuddin et al. demonstrated that reirradiation of a rectal recurrence with 15×2 Gy is feasible and a large multicentre study reported excellent results with this treatment schedule [4,5].

On the other hand, data from the Dutch TME trial suggested that the clinical nature and prognosis of patients with locally recurrent rectal cancer has changed since the introduction of preoperative radiotherapy. The majority of patients who presented with a local recurrence after previous preoperative radiotherapy had simultaneous distant metastases and a poor survival (median 6 months) [6].

In our tertiary referral centre patients with locally recurrent rectal cancer are treated with reirradiation followed by surgery in combination with intraoperative radiotherapy. The aim of this study is to analyse the results of this multimodality treatment protocol for patients with recurrent rectal cancer.

Material and methods

In the period 1984–2006, 117 patients with recurrent rectal cancer were treated in our tertiary-referral cancer hospital, of which 11 patients were previously irradiated and treated with reirradiation before surgery of the recurrence. The group consisted of 7 male and 4 female with a median age of 62 years (range 41–77).

The median dosage of external beam radiotherapy (EBRT) applied during treatment of the primary tumour was 50 Gy (range 25–60). Six patients received preoperative radiation (3 patients 5×5 Gy, 2 patients 25×2 Gy and 1 patient 25×2 Gy in combination with 10 Gy intraoperatively). Primary surgery consisted of low anterior resection (LAR) in 6 patients and abdominoperineal resection (APR) in 5 patients. Primary pathologic TNM stages were T2N0 ($n = 2$), T3N0 ($n = 3$), T3N1 ($n = 2$), T3N2 ($n = 1$), T4N0 ($n = 1$) and T4N1 ($n = 1$). Five patients received postoperative radiotherapy (25×2Gy) during the primary treatment due to a microscopically incomplete (R1) resection ($n = 3$) or preoperative tumourspill ($n = 2$). None of the patients received chemotherapy for treatment of the primary tumour.

Patients were preoperatively analyzed and selected using a pelvic CT- and MRI-scan of the pelvis. On indication a

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cystoscopy was used to identify tumour growth in the bladder. Screening for distant metastases was performed using thoracic and abdominal CT-scans. Based on the preoperative examination and imaging, 5 patients were graded as Wanebo Tr4 (e.g. tumour penetrating adjacent organs) and 6 as Wanebo Tr5 (invasion of bony structures, of low pelvic side walls) [7].

EBRT was administered in doses of 1, 8 or 2 Gy per fraction up to a median dose of 30 Gy (range 27—40). EBRT was delivered by either a three-field technique, using one posterior and two lateral portals or a four-field box technique. The pelvic field borders were defined as follows: the lateral borders extend 1.5 cm lateral of the bony pelvis, with the cranial border the promontory (L5—S1), and the caudal border was at least below the foramina obturatoria to 2 cm under the anus, depending on the tumour position. The dorsal border encompassed the sacrum, and the anterior border was chosen in such a way that the tumour region was widely covered.

In 1997, an intraoperative radiation therapy (IORT) program was started in our hospital. IORT with HDR brachytherapy was given to patients who had a minimal circumferential free resection margin equal to or less than two millimetres. The resection margin was judged on frozen sections taken during surgery. IORT was performed using the Flexible Intraoperative Template (FIT) developed at our department, delivering a dose of 10 Gy, usually at 1 cm depth from the applicator surface [8].

Patient characteristics, operation techniques and follow-up were studied using the database and hospital charts. Surgery, related morbidity was divided into major and minor complications. Major morbidity was defined as complications that required reintervention. All other complications were classified as minor.

All patients were bi-annually seen at our outpatient-clinic for follow-up. Survival time was calculated from the date of resection of the rectal cancer until the last follow-up attendance or until death. Local control was calculated from the date of resection of the rectal cancer until the histological or evident radiological presence of a local recurrence. The cumulative survival, disease-free survival and local control rate after surgery were calculated using the Kaplan—Meier method. Because of the small size of the patient cohort no statistical analyses for prognostic significant factors were performed.

Results

Of the 11 patients in this study, 10 were diagnosed after presentation with complaints; 6 patients presented with perineal pain, 3 with an altered pattern of defecation and 1 patient with urinary problems. One patient did not have any complaints, but presented with a rise of carcinoembyonic antigen (CEA). Median interval between primary surgery and date of recurrence was 22 months (range 9—117). Preoperative workup did not reveal any distant metastases and all patients were operated on with curative intent. Neo-adjuvant chemotherapy was applied to one patient with a presacral recurrence before reirradiation (40 Gy) in combination with hyperthermia. One patient underwent a staging laparotomy with construction of a diverting colostomy before the start of radiation to identify the resectability of the local recurrence and to avoid tumour obstruction in the preoperative workup.

All but one operation were performed in our cancer centre. In 2 patients a resection of a recurrence was performed after a previous APR, in 4 patients an APR was performed and 4 patients underwent a total pelvic exenteration. In one patient the tumour showed massive growth into the lateral pelvic walls with fixation to bilateral ureters and fixation to the presacral plane and was therefore defined as not resectable. The median duration of operation was 420 min (range 360—540) and the median loss of blood 3500 ml (range 1100—21,000).

All patients received intraoperative radiotherapy; 9 patients were treated with HDR-IORT (10Gy) and 1 patient with IOERT (12.5 Gy) because of incomplete or marginal complete resection margins as judged preoperatively. The radiotherapy was applied to the presacral plane in 3 patients, ventral plane in 1 patient, right lateral pelvic wall in 8 patients and left lateral pelvic wall in 5 patients.

In one of the operated patients a microscopically complete resection could be obtained; 6 patients underwent a microscopically incomplete resection (R1) and 3 patients a macroscopically incomplete resection (R2). Pathological examination identified invasion into prostate ($n = 1$), vesicles ($n = 2$), bladder ($n = 2$), vagina ($n = 2$), sacral bone ($n = 2$) and the lateral pelvic wall ($n = 6$). Seven patients were without metastatic lymph nodal involvement, 3 patients were N1 and 1 patient N2.

There was no postoperative mortality. The two most common postoperative complications were urinary tract infection (50%) and wound infection (40%). Two patients (20%) developed sepsis due to a central venous catheter, one patient (10%) a pneumonia and one patient (10%) post-radiation neuropathic pain. One patient experienced a major complication with bilateral postoperative renal stasis based on postradiation fibrosis for which bilateral renal catheters were placed. The median hospital stay was 14 days (range 11—49).

Median follow-up is 22 months (range 2—66). Local control rates after 1 and 3 year were 66% and 27%, respectively. The distant metastasis-free survivals after 1 and 3 years were 100% and 50% and the overall 1- and 3-year survivals were 77% and 51%, respectively (Fig. 1).

Postoperatively four patients (40%) were free of pain, after a mean follow-up of 22 months (range 3—54). Three of these patients remained without recurrence and one developed a local recurrence. One patient developed complaints of local perineal pain in combination with neuropathic pain in the left leg during preoperative radiotherapy that persisted after surgery (Fig. 2).

Six other patients with recurrent disease developed complaints of severe local perineal/pelvic pain ($n = 6$) and neuropathic pain in the lower extremities ($n = 5$). The patients were all treated in collaboration with a specialized ''pain-team'' that consisted of a neurologist and an anaesthesiologist. All patients were treated with medication; one patient was treated with an opioid, one patient Amitriptyline (tricyclic antidepressant) and the other 4 patients