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Modern multidisciplinary treatment of rectal cancer based on staging with magnetic resonance imaging leads to excellent local control, but distant control remains a challenge

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Abstract ***Aim:*** The purpose of this multicenter cohort study was to evaluate whether a differentiated treatment of primary rectal cancer based on magnetic resonance imaging (MRI) can reduce the number of incomplete resections and local recurrences and improve recurrence-free and overall survival.

Methods: From February 2003 until January 2008, 296 patients with rectal cancer underwent preoperative MRI using a lymph node specific contrast agent to predict circumferential resection margin (CRM), T- and N-stage. Based on expert reading of the MRI, patients were stratified in: (a) low risk for local recurrence (CRM > 2 mm and N0 status), (b) intermediate risk and (c) high risk (close/involved CRM, N2 status or distal tumours). Mainly based on this MRI risk assessment patients were treated with (a) surgery only (TME or local excision), (b) preoperative 5 × 5 Gy + TME and (c) a long course of chemoradiation therapy followed by surgery after a 6–8 week interval.

Results: Overall 228 patients underwent treatment with curative intent: 49 with surgery only, 86 with 5 × 5 Gy and surgery and 93 with chemoradiation and surgery. The number of complete resections (margin > 1 mm) was 218 (95.6%). At a median follow-up of 41 months the

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three-year local recurrence rate, disease-free survival rate and overall survival rate is 2.2%, 80% and 84.5%, respectively.

Conclusion: With a differentiated multimodality treatment based on dedicated preoperative MR imaging, local recurrence is no longer the main problem in rectal cancer treatment. The new challenges are early diagnosis and treatment, reducing morbidity of treatment and preferably prevention of metastatic disease.

1. Introduction

In the past decades studies have shown that the risk for recurrence after resection of rectal cancer is substantially reduced with the surgical technique of the total mesorectal excision (TME). In this technique, popularised by Heald, the tumour is removed as a complete package including the surrounding mesorectal fat and lymph nodes.[1] Additionally, neoadjuvant (chemo)radiation has improved local control and, in some studies, survival.[2–5] Intensifying treatment of rectal cancer however is at the expense of treatment-induced morbidity and even mortality. Therefore, individualisation of treatment taking into account characteristics such as age, co-morbidity, stage and location of the tumour might provide an optimal balance between minimising treatment related morbidity and best oncological outcome. Until now, there is however no definite evidence that the outcome is better than applying a single standard treatment for all patients. Subgroup analyses within the large randomised trials can provide clues as to what factors can be used to guide treatment decisions for individual patients. In most of the trials patients with stage I disease (T1-2N0) have a negligible risk for local recurrence, and therefore do not need preoperative irradiation.[6] On the other hand, in patients with a combination of unfavourable characteristics like a tumour extending into the mesorectal fascia, positive lymph nodes and a very distal location, a short course of preoperative radiation and immediate surgery does not provide enough protection against local recurrence, and a long course of preoperative chemoradiation (CRT) is required.[2,3,6]

Reliable preoperative imaging is essential for a differentiated treatment according to risk factors for local recurrence. Although endorectal ultrasound is good in assessing the extent of the primary tumour in small lesions,[7] magnetic resonance imaging (MRI) has repeatedly shown to provide the best information on the relation of the tumour to the mesorectal fascia.[8–12] Assessing nodal involvement however has been suboptimal, and until now all three imaging modalities (endoscopic ultrasound, computed tomography (CT) and MRI) lack sufficient accuracy for clinical decision-making.[13] MRI studies with lymph node-specific contrast agents have shown promising results for the prediction of nodal involvement.[14,15] This would enable MRI to assess the two most important risk factors for local recurrence: relation of the tumour to the mesorectal fascia and nodal stage.

The primary aim of our prospective cohort study was to assess the outcome as defined by the number of complete resections of a differentiated treatment protocol for rectal cancer, based on MRI. The secondary aim was the assessment of long-term outcome as defined by three-year local recurrence, disease-free and overall survival, compared to the data of the Dutch TME trial.

2. Patients and methods

2.1. Patients

Between February 2003 and January 2008, a prospective multicentre cohort study was performed in patients with primary rectal cancer in whom a differentiated treatment protocol was primarily based on MRI. In February 2003 the study started as a single centre pilot study at the Maastricht University Medical Centre, and was continued as a multicentre study from December 2005 onwards ($n = 117$). Three regional hospitals joined the study: Laurentius Hospital Roermond (start of inclusion: 12–2005, $n = 38$), St. Jans Hospital Weert (start of inclusion: 12–2005, $n = 17$) and VieCuri Medical Center Venlo (start of inclusion: 02–2006, $n = 58$). Institutional review board approval was obtained for all hospitals. All patients gave a written informed consent.

2.1.1. Inclusion criteria

Histologically proven adenocarcinoma of the rectum.

2.1.2. Exclusion criteria

Patients were excluded from the study if they had locally recurrent rectal cancer, were pregnant, were younger than 18 years, had a contra-indication for MR imaging (pacemaker, neurostimulator, insulin pump and certain vascular clips (e.g. used in brain surgery), cochlear implants, metal fragments in the eye or any other metal implant not securely fixed or electronic device), or did not give informed consent for participation. For the present analyses that include long-term outcome, patients who received palliative treatment or who had a previous or coexisting malignancy were excluded.