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Local recurrence in rectal cancer : mechanisms of development, patterns of relapse and treatment options

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Chapter



Preoperative MRI can predict tumor invasion into pelvic structures in locally recurrent rectal cancer

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Abstract

Purpose: To assess the accuracy of preoperative MRI for identification of tumor invasion into pelvic structures in patients with locally recurrent rectal cancer (LRRc) scheduled for curative resection.

Patients and Methods: Preoperative MRIs of 40 consecutive patients with LRRc scheduled for curative treatment between October 2003 and November 2006 were analyzed retrospectively. Four observers with different experience in reading pelvic MRI assessed tumor invasion into the following structures: bladder, uterus/seminal vesicles, vagina/prostate, left and right pelvic walls and sacrum. Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) were calculated and a ROC curve was constructed. Surgical and/or histopathological findings were used as reference standard. Interobserver agreement was measured using kappa statistics.

Results: Preoperative MRI was accurate for the prediction of tumor invasion into structures with NPVs of 93 - 100% and AUCs of 0.79 - 1.00 for all structures and observers. PPVs were 53 - 100%. Overstaging occurred in 11 (observer 1), 22 (observer 2), 10 (observer 3) and 9 (observer 4) structures and understaging in 9 (observer 3) and 2 (observer 4) structures. Assessment failures were mainly due to misinterpretation of diffuse fibrosis, especially at the pelvic side walls. Interobserver agreement ranged between 0.64 and 0.99 for experienced observers.

Conclusion: Preoperative MRI is accurate for the prediction of tumor invasion into pelvic structures. MRI may be useful as preoperative road map for the surgical procedure and may thus increase the chance of a complete resection. Interpretation of diffuse fibrosis remains difficult.

Introduction

Locally recurrent rectal cancer (LRRC) has long been regarded as a rarely curable disease. Patients were treated palliatively and subsequent median survival was 14 months and 5-year survival rate 5%¹. However, during the last twenty to thirty years, more patients were considered candidate for curative treatment², such as neoadjuvant chemoradiation with extensive surgery and sometimes intra-operative radiotherapy³. Using these techniques, 5-year survival rates of 30 - 40% were obtained⁴⁻⁶, but at the cost of a substantial treatment related morbidity. Therefore, only patients in whom the chance of a radical resection is high are likely to benefit from this aggressive approach. Otherwise, optimal palliative treatment should be considered.

Most of the imaging studies on locally recurrent rectal cancer with PET, CT or hybrid PET-CT techniques have focused on the detection of local recurrence after treatment of the primary tumor⁷⁻⁹. Tertiary referral centers who regularly treat these patients often perform additional magnetic resonance imaging (MRI) to establish whether or not a tumor is resectable. Although MRI has proven to be the preferred first choice staging modality of primary rectal cancer¹⁰⁻¹², little is known about its performance for predicting tumor extent in patients with a local recurrence. Therefore, the goal of our study was to assess the accuracy of a preoperative MRI for predicting tumor invasion into pelvic structures in patients with locally recurrent rectal cancer scheduled for a curative resection.

Patients and Methods

Patients

The institutional review board approved this study and waived informed consent because of the retrospective nature of the study. Between October 2003 and November 2006, 56 consecutive patients diagnosed with non metastasized, locally recurrent rectal cancer were scheduled for curative treatment with neoadjuvant chemoradiation, extended surgery and intraoperative radiotherapy in the Catharina hospital in Eindhoven, the Netherlands, a national referral center for these patients^{5,13}. In 45 of the 56 patients, a MRI was performed preoperatively after the chemoradiation and 28 of these patients also had a baseline MRI before chemoradiation. Five of these 45 patients did not undergo a resection, because of widespread disease and were excluded. Overall, in 40 patients MRI could be correlated with final histopathology findings.

Neoadjuvant treatment

Patients received preoperative chemoradiation with a radiotherapy dose of 50.4 Gray (Gy), 5 times a week in 28 doses of 1.8 Gy. Patients who had received radiotherapy for the primary tumor were re-irradiated (30.6 Gray, 5 times a week in 17 doses of 1.8 Gy). EBRT was delivered with a linear accelerator (10 MeV) using a three-field box technique (one posterior and two lateral portals). The pelvic field borders used were described earlier⁵. Chemotherapy consisted of either capecitabine (2 x 825 mg/m²/d) 5 days a week for three weeks alone or combined with oxaliplatin (50 mg/m²) on day 1, 8 and 15.

MR imaging techniques

MR imaging was performed at 1.5 T (Achieva and Intera, Philips Medical Systems, Best, the Netherlands) using a quadrature phased array spine coil, a cardiac or body phased array coil (Philips Medical Systems, Best, the Netherlands). Sequences used were axial T2-weighted TSE (T2W 2D TR/TE 3882/125; TSE factor 16; slice thickness 3.0; slice gap 0.3; NSA 6; acq matrix 256 x 176; FOV 180; scan time 7:36), sagittal T2W 2D TSE (TR/TE 3882/125; TSE factor 23, slice thickness 3.0; slice gap 1.0; NSA 4; FOV 250; acq matrix 304 x 241; scan time 5:41), axial T1W 2D TSE (TR/TE 550/7; TSE factor 4; slice thickness 4; slice gap 0.4; NSA 1; FOV 410; acq matrix 368 x 306; scan time 1:32) and sagittal T1W 2D TSE (TR/TE 600/13; TSE factor 3; slice thickness 4.0; slice gap 0.8; NSA 2; FOV 320 x 208; acq matrix 320 x 145; scan time 4:00). Patients did not receive any bowel preparation, air insufflation or intravenous spasmolytic medication.

MR evaluation

The MR images were retrospectively evaluated for extent of tumor growth into surrounding pelvic structures/organs by 4 observers. Observer 1 (R.G.B.) is a dedicated pelvic MR radiologist with 12 years of experience in reading pelvic MRI in a university medical center. Observer 2 (A.W.D.) is a pelvic MR radiologist with 5 years of experience in a general hospital which serves as a national referral center for locally advanced and recurrent rectal cancer. Observer 3 (V.C.C.) is a general radiologist with special interest in gastrointestinal malignancies and 1 year of experience in this field. Observer 4 (H.J.R.) is a surgical oncologist with 20 years expertise in management and surgery of (recurrent) rectal cancer. The MR images were made anonymous and were presented in a random order. The observers were blinded to surgical, histopathological and each other's results. Tumor invasion was defined as diffuse or nodular isointense tissue on the T2W FSE MR images that was at a distance of ≤ 1 mm from the structure/organ. All observers used confidence levels for the prediction of tumor invasion (1 = definitely not invaded, 2 = probably not invaded, 3 = possibly invaded, 4 = probably invaded and 5 = definitely invaded). The following structures were evaluated: vagina/ prostate, uterus/ seminal vesicles, urinary bladder, sacral bone, left and right (dorso)lateral pelvic side walls. The pelvic side walls were defined as the piriform and the internal obturator muscles, the sacrotuberous and sacrospinal ligaments.

Surgery and intraoperative radiotherapy

At the start of the laparotomy, the abdomen was checked for liver, nodal or peritoneal metastases. The type of surgery was determined by the location of the tumor and the extent of tumor growth into surrounding structures (Table 8.1). The goal was to obtain an en bloc resection of the tumor and the involved structures with a tumor free margin of at least 1 mm. All patients received intraoperative radiotherapy at the area of the closest resection margin, at highest risk for residual tumor¹⁴.

Table 8.1 Patient and treatment characteristics

| | No. | % |
|---|-----|------------------|
| All | 40 | 100 |
| Median age in years (range) | | 61 (47-77) |
| Sex | | |
| Male | 26 | 65.0 |
| Female | 14 | 35.0 |
| Neoadjuvant therapy for primary tumor | | |
| No | 13 | 32.5 |
| Short course (5x5 Gy) | 17 | 42.5 |
| Long course (45-50.4 Gy) | 10 | 25.0 |
| Type of primary surgery | | |
| LAR | 25 | 62.5 |
| APR | 15 | 37.5 |
| Median interval primary-recurrence surgery in months (range) | | 34.0 (13-100) |
| MRI | | |
| Both pre and post neoadjuvant therapy | 28 | 70.0 |
| Only post neoadjuvant therapy | 12 | 30.0 |
| Neoadjuvant therapy for recurrence | | |
| Re-irradiation + chemotherapy | 27 | 67.5 |
| Full course + chemotherapy | 13 | 32.5 |
| Type of recurrence surgery | | |
| LAR | 6 | 13.3 |
| APR | 6 | 13.3 |
| ASR | 12 | 26.7 |
| Exenteration | 9 | 20.0 |
| Nonanatomic resection | 7 | 15.6 |

MRI; magnetic resonance imaging, LAR; low anterior resection, APR; abdominoperineal resection, ASR; abdominosacral resection.

Histopathology

The circumferential resection margin (CRM) of the fresh specimen was inked, the specimen was fixed in 10% formalin for 48 hours and then cut in 5 - 10 mm transversal slices. Slices were embedded in blocks and processed for hematoxylin and eosin (HE) staining in 5 µm sections. On the HE stained slides the distance between the tumor and the resected organs, structures and CRM was evaluated. If the CRM in the direction of a nonresected organ / structure was free of tumor, the organ / structure was scored as noninvaded. If it showed tumor within 1 mm the organ / structure was considered as invaded. If the surgical and histopathological findings could not be reconstructed for a specific site by reviewing the reports and the HE slides, this site was excluded from analysis.

Statistical analysis

The reference standard consisted of a detailed reconstruction of all available surgical and histopathological information retrieved from the reports and by reviewing the HE slides if necessary. ROC curves were constructed for the prediction of tumor invasion of pelvic structures for all observers and the areas under the ROC curves (AUC) were calculated. The AUCs were compared using the method of DeLong¹⁵. After dichotomization of the confidence levels (1 - 2 = no invasion, 3 - 5 = invasion) sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) for the prediction of tumor invasion of pelvic structures were calculated. Interobserver agreement was measured using linear weighted kappa statistics^{16,17} with kappa-values of 0.2 - 0.4 indicating fair, 0.4 - 0.6 moderate, and > 0.6 excellent agreements. A difference was

Table 8.2 Prediction of tumor invasion of pelvic structures
(cut-off level between 2 and 3)

| Obs. | AUC 95% CI | Accuracy 95% CI | Sensitivity 95% CI | Specificity 95% CI | PPV 95% CI | NPV 95% CI |
|--------------------------------|---------------|--------------------|-----------------------|-----------------------|---------------|---------------|
| Anterior | | | | | | |
| 1 | 1.00 | 100 (36/36) | 100 (5/5) | 100 (31/31) | 100 (5/5) | 100 (31/31) |
| | 1.00-1.00 | 100-100 | 100-100 | 100-100 | 100-100 | 100-100 |
| 2 | 0.97 | 92 (33/36) | 100 (5/5) | 90 (28/31) | 63 (5/8) | 100 (28/28) |
| | 0.91-1.02 | 78-98 | 100-100 | 74-98 | 24-91 | 100-100 |
| 3 | 0.80 | 94 (34/36) | 60 (3/5) | 100 (31/31) | 100 (3/3) | 94 (31/33) |
| | 0.53-1.07 | 81-99 | 15-95 | 100-100 | 100-100 | 80-99 |
| 4 | 0.79 | 92 (33/36) | 60 (3/5) | 97 (30/31) | 75 (3/4) | 94 (30/32) |
| | 0.52-1.07 | 78-98 | 15-95 | 83-100 | 19-99 | 79-99 |
| Uterus/ Seminal vesicles | | | | | | |
| 1 | 0.98 | 94 (34/36) | 100 (11/11) | 92 (23/25) | 85 (11/13) | 100 (23/23) |
| | 0.93-1.03 | 81-99 | 100-100 | 74-99 | 55-98 | 100-100 |
| 2 | 0.93 | 86 (31/36) | 100 (11/11) | 80 (20/25) | 69 (11/16) | 100 (20/20) |
| | 0.85-1.01 | 71-95 | 100-100 | 59-93 | 41-89 | 100-100 |
| 3 | 0.94 | 94 (34/36) | 91 (10/11) | 96 (24/25) | 91 (10/11) | 96 (24/25) |
| | 0.83-1.05 | 81-99 | 59-100 | 80-100 | 59-100 | 80-100 |
| 4 | 1.00 | 97 (35/36) | 100 (11/11) | 96 (24/25) | 92 (11/12) | 100 (24/24) |
| | 1.00-1.00 | 85-100 | 100-100 | 80-100 | 62-100 | 100-100 |
| Urinary bladder | | | | | | |
| 1 | 0.99 | 98 (39/40) | 100 (4/4) | 97 (35/36) | 80 (4/5) | 100 (35/35) |
| | 0.95-1.02 | 87-100 | 100-100 | 85-100 | 28-99 | 100-100 |
| 2 | 0.98 | 98 (39/40) | 100 (4/4) | 97 (35/36) | 80 (4/5) | 100 (35/35) |
| | 0.94-1.02 | 87-100 | 100-100 | 85-100 | 28-99 | 100-100 |
| 3 | 0.86 | 95 (38/40) | 75 (3/4) | 97 (35/36) | 75 (3/4) | 97 (35/36) |
| | 0.60-1.12 | 83-99 | 19-99 | 85-100 | 19-99 | 85-100 |
| 4 | 0.98 | 95 (38/40) | 100 (4/4) | 94 (34/36) | 67 (4/6) | 100 (34/34) |
| | 0.94-1.02 | 83-99 | 100-100 | 81-99 | 22-96 | 100-100 |

Values are percentages. Values in parenthesis are absolute numbers. Obs.; observer, 95% CI; 95% confidence interval; AUC; area under the receiver operating characteristic curve, PPV; positive predictive value, NPV; negative predictive value.

Table 8.2 Continued

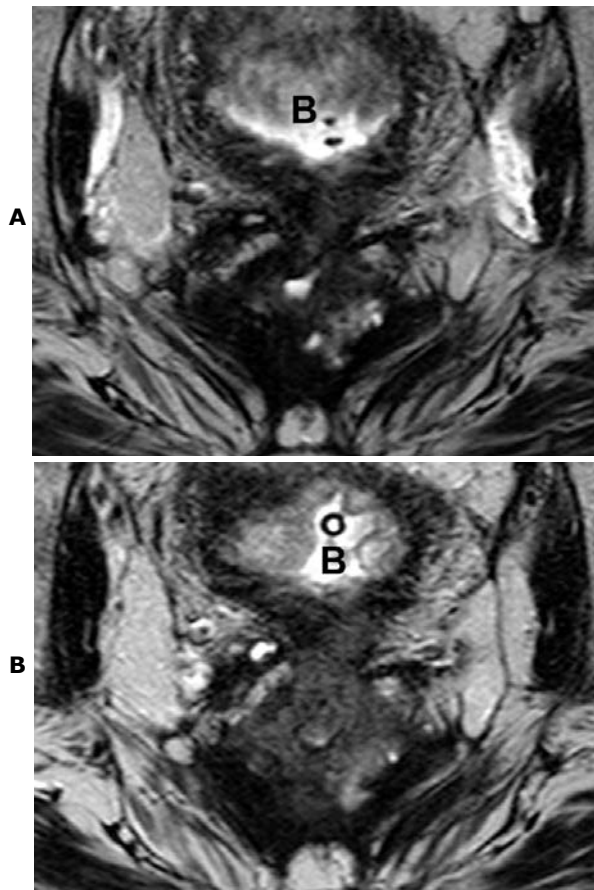
| Obs. | AUC | Accuracy | Sensitivity | Specificity | PPV | NPV | |
|--|---------------|-------------------|------------------------|------------------------|------------------------|------------------------|------------------------|
| | 95% CI | 95% CI | 95% CI | 95% CI | 95% CI | 95% CI | |
| Lateral | | | | | | | |
| Left pelvic side wall | 1 | 0.96 0.91-1.02 | 92 (36/39) 79-98 | 100 (11/11) 100-100 | 89 (25/28) 72-98 | 79 (11/14) 49-95 | 100 (25/25) 100-100 |
| | 2 | 0.96 0.91-1.02 | 85 (33/39) 69-94 | 100 (11/11) 100-100 | 79 (22/28) 59-92 | 65 (11/17) 38-86 | 100 (22/22) 100-100 |
| | 3 | 0.85 0.70-1.00 | 87 (34/39) 73-96 | 82 (9/11) 48-98 | 89 (25/28) 72-98 | 75 (9/12) 43-95 | 93 (25/27) 76-99 |
| | 4 | 0.96 0.90-1.02 | 95 (37/39) 83-99 | 100 (11/11) 100-100 | 93 (26/28) 77-99 | 85 (11/13) 55-98 | 100 (26/26) 100-100 |
| Right pelvic side wall | 1 | 0.94 0.87-1.01 | 87 (34/39) 73-96 | 100 (8/8) 100-100 | 84 (26/31) 66-95 | 62 (8/13) 32-86 | 100 (26/26) 100-100 |
| | 2 | 0.96 0.90-1.02 | 82 (32/39) 66-92 | 100 (8/8) 100-100 | 77 (24/31) 59-90 | 53 (8/15) 27-79 | 100 (24/24) 100-100 |
| | 3 | 0.80 0.61-1.00 | 82 (32/39) 66-92 | 75 (6/8) 35-97 | 84 (26/31) 66-95 | 55 (6/11) 23-83 | 93 (26/28) 77-99 |
| | 4 | 0.96 0.90-1.02 | 95 (37/39) 83-99 | 100 (8/8) 100-100 | 94 (29/31) 79-99 | 80 (8/10) 44-97 | 100 (29/29) 100-100 |
| Posterior | | | | | | | |
| Sacral bone | 1 | 1.00 1.00-1.00 | 100 (40/40) 100-100 | 100 (10/10) 100-100 | 100 (30/30) 100-100 | 100 (10/10) 100-100 | 100 (30/30) 100-100 |
| | 2 | 1.00 1.00-1.00 | 100 (40/40) 100-100 | 100 (10/10) 100-100 | 100 (30/30) 100-100 | 100 (10/10) 100-100 | 100 (30/30) 100-100 |
| | 3 | 0.95 0.84-1.06 | 98 (39/40) 87-100 | 90 (9/10) 56-100 | 100 (30/30) 100-100 | 100 (9/9) 100-100 | 97 (30/31) 83-100 |
| | 4 | 0.98 0.94-1.02 | 98 (39/40) 87-100 | 100 (10/10) 100-100 | 97 (29/30) 83-100 | 91 (10/11) 59-100 | 100 (29/29) 100-100 |
| Values are percentages. Values in parenthesis are absolute numbers. Obs.; observer, 95% CI; 95% confidence interval,; AUC; area under the receiver operating characteristic curve, PPV; positive predictive value, NPV; negative predictive value. | | | | | | | |

considered statistically significant if $p \leq 0.05$ (two-sided). Statistical analyses were performed using the SPSS statistical software program (SPSS® for Windows Release 15.0, SPSS Inc, Chicago, IL, USA).

Results

Patient, treatment and tumor characteristics

The study population consisted of 26 men and 14 women with a median age of 61 years (range 47 - 77). The median interval between primary and recurrent surgery was

Figure 8.1

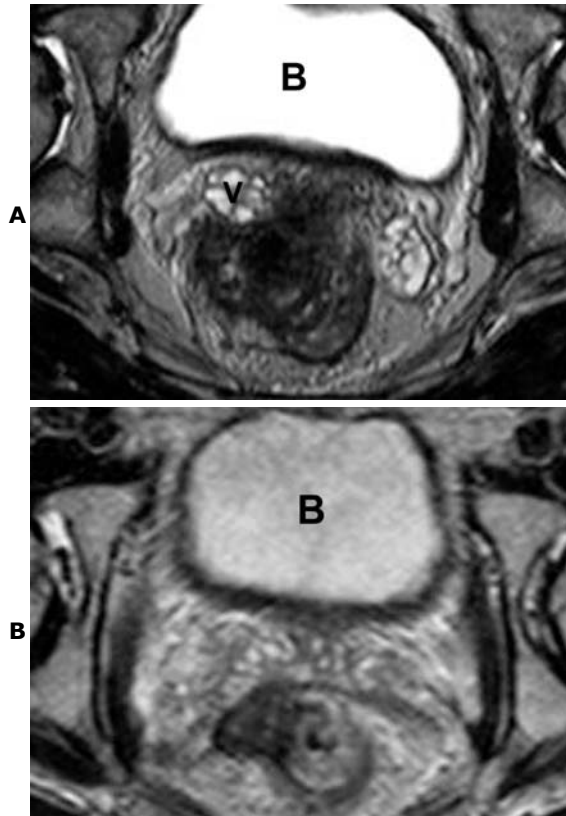
An example of volume downsizing and overstaging on T2W TSE (3882/125) images before (a) and after chemoradiation (b). Although the tumor volume decreased due to neoadjuvant chemoradiation, no change in the appearance of the peripheral pushing fibrotic mass was seen. Invasion into the lateral pelvic side walls and bladder was scored with the same confidence level by all observers on both pre and post chemoradiation MR images. All observers overstaged the bladder and both pelvic side walls. Histopathology revealed only limited intramucosal residual tumor cells. B; bladder.

34 months (range 13 - 100). The median interval between the MRI and surgery was 33 days (range 7 - 105). The details about primary and recurrent (neoadjuvant) treatment are described in Table 8.1. In total, 236 structures were evaluated in 40 patients. In 6 structures (2.5%) the reference standard could not be reconstructed, because there was no information in the surgical or histopathological reports on these structures and no HE slides available containing this structure that would allow revision of the structures.

Assessment of invaded structures

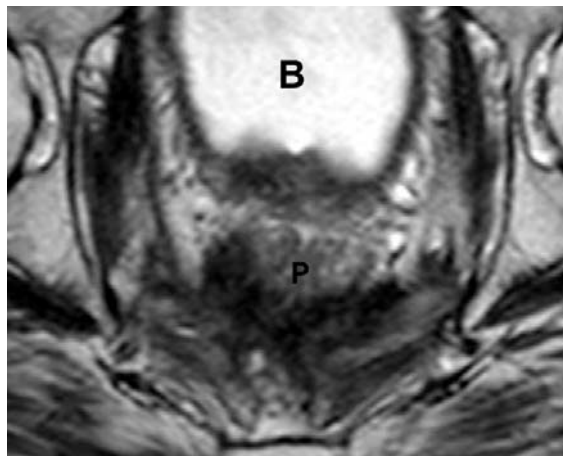
Table 8.2 gives the AUCs, sensitivities, specificities, PPVs and NPVs of all observers for the prediction of tumor invasion into various pelvic structures at anterior, lateral and

Figure 8.2



An example of a true positive T2W MR image (3882/125) before (a) and after (b) neoadjuvant chemoradiation. All observers correctly scored invasion into the seminal vesicle on both pre and post chemoradiation MR images. B, bladder; V; seminal vesicle

Figure 8.3



An example of understaging on a T2W MR image (3882/125). Observer 3 understaged the prostate interpreting the lesion as preexisting fibrosis rather than recurrent tumor. B; bladder, P; prostate.

posterior locations. The AUCs for prediction of tumor growth into the left and right pelvic wall of the observer with the least experience (observer 3) were significantly lower (0.85 and 0.80 respectively) compared to those of the more experienced observers (≥ 0.94 , $p < 0.05$). Sensitivities ranged from 60 - 100%, with the lowest scores for the vagina/prostate (observer 3 and 4). Specificities ranged from 80-100%. PPVs ranged from 53 - 100%, with the lowest scores for the pelvic side walls (all observers). NPVs ranged from 93 - 100% (observer 1 and 2 scored 100% for all structures).

Although tumor volume decreased substantially in the 28 patients who received both a pre and a post chemoradiation MRI, invasion into structures as judged by the observers generally remained identical on both MRIs (data not shown, example in Figure 8.1).

Assessment of failures

Overall, 82.5% (33/40) of patients were correctly assessed by observer 1, 72.5% (29/40) by observer 2, 70% (28/40) by observer 3 and 85% (34/40) by observer 4 (Figure 8.2). Observer 1 overstaged 11 structures in 7 patients and observer 2 overstaged 22 structures in 11 patients. Neither of these observers ever understaged. Observer 3 had 9 false negatives in 6 patients and 10 false positives in 6 patients. Observer 4 showed 2 false negatives in 2 patients and 9 false positives in 4 patients.

The majority of overstaging was due to prediction of a diffuse hypo-intense mass on T2W TSE images as fibrosis that may contain remaining tumor, while histopathology showed complete or nearly complete response without significant tumor load left (Figure 8.1). This occurred for observer 1 in 8 of the 11 overstaged cases (73%), for observer 2 in 55% (12/22), for observer 3 in 80% (8/10) and for observer 4 in 89% (8/9). The site where this error occurred most frequently was the lateral pelvic side wall. In two cases the right seminal vesicle was scored as definitely invaded by observer 1, 2 and 3 but histopathology showed a 4 mm free margin between the tumor and the seminal vesicle in one case and no relationship between the tumor and the seminal vesicle in the other.

Understaging also occurred in the presence of a hypo-intense mass on T2W TSE MR images, which was interpreted by observer 3 as preexisting fibrosis rather than recurrent tumor (Figure 8.3). Observer 4 understaged 2 patients who had tumor invasion of both the uterus (cervix) and the vagina. Although this observer respected the uterine invasion, the invasion of the posterior fornix was missed.

Interobserver agreement

The kappas between the observers for the bladder ranged between 0.74 and 0.98, for the uterus / seminal vesicles between 0.69 and 0.88, for the vagina / prostate between 0.31 and 0.72, for the left lateral pelvic wall between 0.84 and 0.96, for the right lateral pelvic wall between 0.73 and 0.88 and for the sacrum between 0.88 and 0.99 (Table 8.3).

Table 8.3 Interobserver agreement for the prediction of tumor invasion of pelvic structures

| Obs. | Bladder | Uterus/ Seminal | Vagina/ Prostate vesicles | Left pelvic wall | Right pelvic wall | Sacrum |
|--------|-----------|--------------------|---------------------------------|---------------------|----------------------|-----------|
| 1-2 | 0.98 | 0.88 | 0.72 | 0.93 | 0.88 | 0.99 |
| 95% CI | 0.97-1.00 | 0.74-1.00 | 0.45-1.00 | 0.85-1.00 | 0.76-1.00 | 0.98-1.00 |
| 1-3 | 0.87 | 0.82 | 0.61 | 0.87 | 0.83 | 0.92 |
| 95% CI | 0.63-1.00 | 0.62-1.00 | 0.20-1.00 | 0.71-1.00 | 0.65-1.00 | 0.78-1.00 |
| 1-4 | 0.86 | 0.86 | 0.64 | 0.96 | 0.83 | 0.91 |
| 95% CI | 0.50-1.00 | 0.70-1.00 | 0.27-1.00 | 0.89-1.00 | 0.65-1.00 | 0.78-1.00 |
| 2-3 | 0.91 | 0.69 | 0.52 | 0.79 | 0.73 | 0.91 |
| 95% CI | 0.75-1.00 | 0.46-0.93 | 0.14-0.91 | 0.62-0.97 | 0.52-0.94 | 0.77-1.00 |
| 2-4 | 0.85 | 0.72 | 0.54 | 0.88 | 0.81 | 0.90 |
| 95% CI | 0.62-1.00 | 0.51-0.93 | 0.16-0.93 | 0.78-0.99 | 0.64-0.98 | 0.76-1.00 |
| 3-4 | 0.74 | 0.81 | 0.31 | 0.84 | 0.84 | 0.88 |
| 95% CI | 0.42-1.00 | 0.62-1.00 | 0.24-0.85 | 0.67-1.00 | 0.67-1.00 | 0.72-1.00 |

Obs.; observers, 95% CI; 95% confidence interval.

Discussion

Patients with locally recurrent rectal cancer benefit from accurate information on the extent of tumor growth into pelvic structures. With the exact preoperative knowledge of which pelvic structures are invaded, a detailed operative plan can be made for an en bloc resection with wide margins around the tumor, maximizing the chance of a complete resection. In patients in whom it is anticipated that this cannot be achieved, palliative treatment can be considered, with less treatment related morbidity. Our study showed that MRI was highly accurate for predicting absence of invasion into pelvic structures with NPVs of 93 - 100% for all observers. In other words, when MRI predicted that a structure was not invaded, it was true in 9 to 10 out of 10 cases regardless the experience of the observer. The PPV however tended to be lower, especially at the lateral pelvic side walls (PPVs 53 - 85%), even for expert observers. Generally, there was high interobserver agreement.

To the best of our knowledge only one other study has investigated the role of MRI in surgical treatment planning of recurrent rectal cancer¹⁸. In this study of 49 patients, MRI showed NPVs of 84 - 100% and PPVs of 71 - 100% for the prediction of tumor invasion into pelvic structures. Histopathology was only available for 51% of the correlations with MRI and 98/343 (28.6%) of structures were excluded because no reference standard of surgery/histopathology could be reconstructed, opposed to only 2.5% in our study. The authors reported that the main difficulty was assessment of tumor involvement of the pelvic side wall, with both false negative and false positive findings, especially after previous radiotherapy. Our findings confirm this, although the errors in pelvic side wall

involvement in our study were mostly overstaging errors. After chemoradiation, tumor tissue has often been replaced by fibrosis, and it is difficult to interpret on T2W images whether or not there is still viable tumor invading the piriform and obturator muscles. To a lesser extent this fibrosis also caused staging failures of the anterior structures. Posteriorly, staging was almost perfect, probably because an intact hypointense periosteal line on the T2W TSE images almost guarantees a non involved sacral bone (Figure 8.4).

Figure 8.4



An example in which the presacral periosteal line helped to decide that the tumor did not invade the sacrum (T2W TSE MR image 3882/125). S; sacrum.

MR interpretation of fibrosis in recurrent rectal cancer

From studies in the setting of primary rectal cancer it is known that fibrosis after chemoradiation can cause interpretation difficulties in judging the extent of a tumor¹⁹. Within a mass of hypointense fibrotic tissue small areas of vital tumor, too small to be visible on MRI, can remain. For recurrent rectal cancer the problem of fibrosis is even more complex. The normal pelvic anatomy is often distorted because of the treatment of the primary tumor, with fibrotic changes that can be due to the primary operation, infectious complications, and prior radiotherapy. This not only hampers the detection of recurrences, but also the defining of the exact tumor extent, as it is often located within preexisting fibrosis in the presacral or lateral area. In our experience the pushing or invading fibrotic mass in front of the recurrent tumor most often did not contain malignant cells at the definitive histological examination. Our hypothesis is that this fibrosis in front of a pushing growing recurrence often is old scar tissue rather than recurrent tumor that has responded to chemoradiation. This in contrast to the fibrosis seen after chemoradiation of a primary rectal cancer, that replaces tumor and where small remnants of vital tumor can be found throughout the fibrotic tissue¹⁹. This hypothesis is supported by the fact that MR imaging showed no change in the pushing fibrotic mass after chemoradiation.

Many criteria have been proposed to differentiate between fibrosis and recurrent

tumor. It has been suggested that tumor has a high and fibrosis a low signal intensity on T2-weighted images, tumor has a round border and fibrosis straight angular margins and that tumor has contrast enhancement of > 40% of the mass or a typical rim-enhancement pattern after gadolinium²⁰. Although these criteria are helpful, they are not very specific as they may occur in tumor, fibrosis, inflammation or hematoma^{21,22}.

Radiological decision making

Apart from the inherent difficulty to distinguish fibrosis from tumor, other factors can influence the judgment of the radiologist. An important factor is the understanding of the clinical consequences of the radiological report. Overstaging can lead to overtreatment, and to unnecessary treatment related morbidity, but without compromising oncological outcome. Understaging can have more serious consequences and could lead to an incomplete resection, jeopardizing the patients' cure. In our study, the least experienced radiologist had about the same number of understaging and overstaging errors, while the two experienced radiologists and the surgeon had far more overstaging errors. This probably reflects the incorporation of clinical management issues in the radiological decision. It is our belief that active participation of radiologists in multidisciplinary meetings increases the understanding between radiologists and clinicians.

Limitations

The retrospective nature of this study presents some inherent limitations. Although the reference standard was based on detailed reconstruction of surgical and histopathological reports and review of HE slides when required, it was sometimes difficult to reconstruct the exact relation between the tumor and the surrounding structures. In the cases where the reconstruction was definitely impossible the structures were excluded from the analysis. This occurred in only 2.5% of the structures.

In conclusion, preoperative MRI in patients with locally recurrent rectal cancer treated with neoadjuvant chemoradiation is reliable for the prediction of extent of tumor growth into surrounding pelvic structures. It can serve as a road map for the surgical procedure and increases the chance of a complete resection. Interpretation of fibrotic tissue at the latero-dorsal pelvic side walls remains difficult.

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