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RAPID COMMUNICATION

Assessment of T staging and mesorectal fascia status using high-resolution MRI in rectal cancer with rectal distention

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Abstract

AIM: To determine the accuracy of high-resolution magnetic resonance imaging (MRI) using phased-array coil for preoperative assessment of T staging and mesorectal fascia infiltration in rectal cancer with rectal distention.

METHODS: In a prospective study of 67 patients with primary rectal cancer, high-resolution magnetic resonance imaging (in-plane resolution, 0.66 × 0.56) with phased-array coil were performed for T-staging and measurement of distance between the tumor and the mesorectal fascia. The assessment of MRI was compared with postoperative histopathologic findings. Sensitivity, specificity, accuracy, positive predictive value, and negative predictive value were evaluated.

RESULTS: The overall magnetic resonance accuracy was 85.1% for T staging and 88% for predicting mesorectal fascia involvement. Magnetic resonance sensitivity, specificity, accuracy, positive predictive value, and negative predictive value was 70%, 97.9%, 89.6%, 93.3% and 88.5% for ≤ T2 tumors, 90.5%, 76%, 85.1%, 86.4% and 82.6% for T3 tumors, 100%, 95.2%, 95.5%, 62.5% and 100% for T4 tumors, and 80%, 90.4%, 88%, 70.6% and 94% for predicting mesorectal fascia involvement, respectively.

CONCLUSION: High-resolution MRI enables accurate preoperative assessment for T staging and mesorectal fascia infiltration in rectal cancer with rectal distention.

Key words: Magnetic resonance imaging; Rectum; Neoplasm; Staging; Mesorectal fascia

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INTRODUCTION

Rectal cancer is a common disease and a major cause of mortality in Western countries, and the prevalence in China has consistently increased with changes of life style in recent years[1]. Its poor prognosis is associated with risk both for local recurrence and metastases. The local recurrence is related to the extramural tumor spread into the mesorectum and the tumor distance to the circumferential resection margin (CRM)[2-4]. With the standardized total mesorectal excision (TME), the overall recurrence rate has been reported to be below 10%, without the help of radiation therapy[5]. Recent publications have suggested that preoperative radiotherapy enhanced local control[6-9] and improved prognosis[6] in T3 and resectable T4 rectal cancer, especially in the patients with involvement of the mesorectal fascia[8,10]. So accurate preoperative local staging is critical to determine the right patient for preoperative neoadjuvant therapy. High-resolution magnetic resonance imaging (MRI) using the phased coil can visualize the layers of the rectal wall, the mesorectal fascia and predict the depth of tumor invasion, however, the results and techniques were conflicting in the previous reports[11-13]. Some authors choose not to distend the rectum[12,14,15] whereas others advocate distension with air or water to improve depiction of the primary tumor[16-18]. The aim of our study was to assess the accuracy of MRI for preoperative T staging of rectal cancer and the distance to the mesorectal fascia with rectal distention.

MATERIALS AND METHODS

Patients

The study population consisted of 67 patients (37 men and 30 women, with a mean age of 62 years) with histopathologically proved rectal cancer by means of endoluminal biopsy. Rectal cancer was defined as carcinoma within 15 cm of the anal verge. All patients

underwent MRI 1-4 d before surgery. No patient had received preoperative chemoradiotherapy.

MRI examination

MRI was performed using 1.5T whole body system (Magnetom Avanto, Siemens) and a phased array multicoil in all patients. All patients underwent the hospital's standard cleaning enema procedure. Tepid water was then administered using a rectal enema tube, and the rectum was filled until the patient indicated a sensation of fullness in the rectum. The volume of water ranged from 150 to 400 mL. The rectal tube was removed after completion of instilling the water. No antispasmodic agents were used. The patients were placed in a supine position on an MR table with feet entering MR gantry.

After scout scanning, midline axial and sagittal T_2 weighted turbo spin-echo (T_2W-TSE) images were obtained. The scan protocol was TR 3000-4000 ms, TE 70-90 ms, field of view (FOV) 28-32 cm × 28-32 cm, matrix 276 × 384, slice thickness 5 mm and gap 1 mm. These images were used to plan T_2W-TSE high resolution scans, which were perpendicular to the long axis of the rectum. For a low third rectal tumor, an additional oblique coronal scan along the long axis of the anal canal was also acquired. The scan protocol was TR 2400-3500 ms, TE 90-100 ms, FOV 18 cm × 18 cm, matrix 272 × 320, slice thickness 3 mm and gap 0 mm, in-plane resolution 0.66 × 0.56. The whole examination took about half an hour.

MRI interpretation

Patient's T staging was categorized according to the TNM classification[4] and was assessed according to the reported criteria (Table 1)[11]. In our study, T1 and T2 tumors were combined to represent one T stage ⩽ T2, because of limitations at MRI in distinguishing T1 and T2 tumors[14]. T stage ⩽ T2 tumors were defined as tumors confined to the bowel wall with smooth margins. On the basis of a previous study[12], tumor with spiculation in the perirectal fat was considered to be a T3 lesion. The signal intensity of the tumor infiltrating the surrounding structures was thought to be T4 tumor.

The minimum distance between the outer margin of the tumor and the mesorectal fascia was measured on the Syngo Leonardo Workstation. Measurements for each patient were then categorized into < 2 mm or ⩾ 2 mm to assess whether the mesorectal fascia was involved. Two experienced abdominal radiologists who had no clinical and histopathologic information interpreted independently each MR image. Differences in assessment were resolved by means of consensus.

Surgery and histopathologic study

Total mesorectal excision (TME) was performed in 62 patients (anterior resection in 51 patients and abdominoperineal resection in 11 patients, pelvic exenteration in 5 patients). Immediately after surgery, resected specimens were opened on the opposite side of the tumor and fixed in formalin for 24 h. The specimens were then sliced transversely at an interval of 5 mm. The slices were embedded in paraffin, sectioned, and examined histologically after HE staining.

Table 1 Definitions used for staging rectal cancer

Histopathologic examination	MRI
pT1: Tumor invades the submucosa	MRT1: Tumor signal intensity is confined to the submucosal layer
pT2: Tumor invades the muscularis propria	MRT2: Tumor signal intensity extends into the muscle layer, with loss of the interface between the submucosa and circular muscle layer
pT3: Tumor invades through the muscularis propria into the subserosa or into the nonperitonealized pericolic or perirectal tissues	MRT3: Tumor signal intensity extends through the muscle layer into the perirectal fat, with obliteration of the interface between muscle and perirectal fat
pT4: Tumor directly invades other organs or structures or perforates the visceral peritoneum	MRT4: Tumor signal intensity extends into an adjacent structure or viscus

The depth of tumor invasion was classified according to the TNM classification (Table 1)[4] and the minimum distance between the tumor and the mesorectal fascia was measured macroscopically, and this distance was examined again under microscopy when the margin was assessed macroscopically to be close or involved. If this distance ⩽ 2 mm, the mesorectal fascia was considered to be involved[3,4]. The pathologist was blinded to the result of the MRI findings.

Statistical analysis

Accuracy, sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were calculated for each T stage and predicting CRM infiltration.

RESULTS

Appearance of rectal cancer

The MRI procedure took about half an hour and the patients were well tolerated. The tumors were well visualized in all patients. Forty-two tumors were located in the upper rectum (10-15 cm from the anal verge), 12 in the mid rectum (5-10 cm from the anal verge), and 13 in the distal rectum (less than 5 cm from the anal verge). The size of the resected tumor differed from 0.8 cm × 2 cm to 5 cm × 7 cm (mean 3.5 cm × 4.4 cm). Fifteen mucinous carcinomas were detected with focal (n = 8) or diffuse (n = 7) high signal (isointense or hyperintense to perirectal fat areas) in the tumor on T_2WI, which was correlated with the mucinous pool on pathologic specimens. In contrast, 52 nonmucinous carcinomas showed isointensity with the normal rectal wall or skeletal muscle on T_2WI.

T staging of rectal cancer

At histopathologic examination, 20 (29.9%) of 67 neoplasms were staged as ⩽ pT2 (Figure 1 and Figure 2), 42 (62.7%) of 67 as pT3 (Figure 3 and Figure 4), and 5 (7.5%) of 67 as pT4 (Figure 5). The overall MR accuracy was 85.1%. Over- and under-staging occurred in 9 (13.4%) of 67 patients and 1 (1.5%) of 67 patients, respectively. Accuracy for each T stage was ⩽ T2, 89.6%; T3, 85.1%; and T4, 95.5% (Table 2).

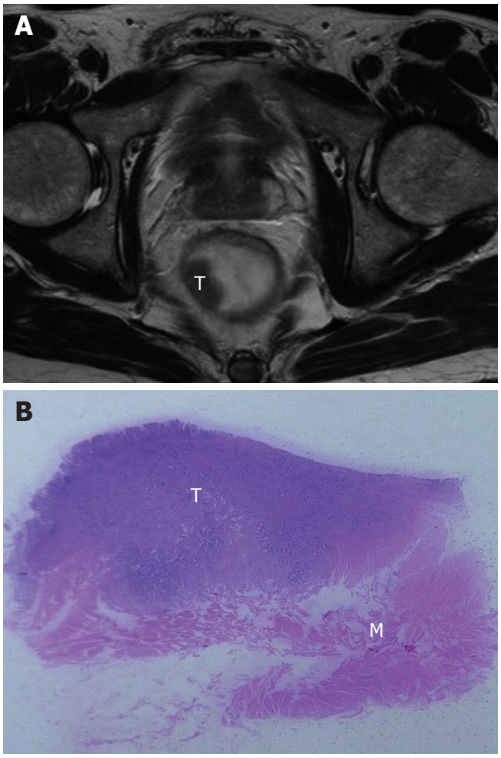
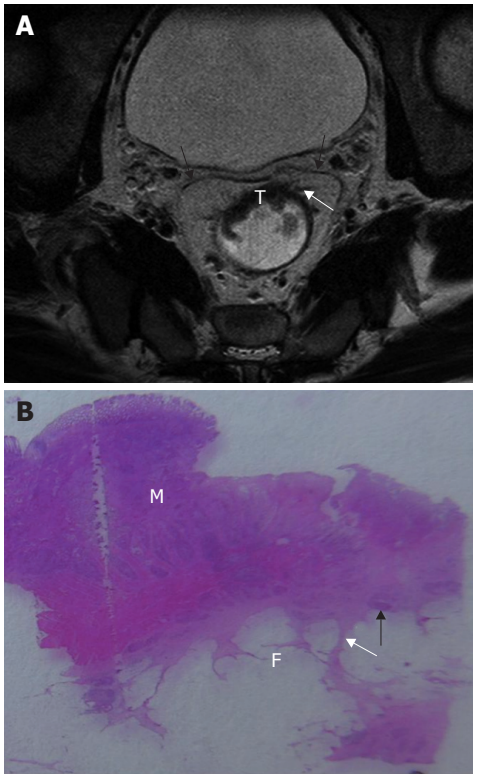


Figure 1 T2-stage rectal cancer in a 58-year-old male patient. **A**: Axial T_2W-TSE MR image (3500/94); **B**: Photograph of the corresponding histopathologic slice (hematoxylin-eosin stain; original magnification, x 10), showed T2-stage tumor (T) that was confined within the muscularis propria (M).

Figure 2 T2-stage rectal cancer overstaged at MR imaging (3000/98) as a T3-stage tumor in a 70-year-old male patient. MR image depicted tumor (T) with speculations (white arrow) which turned out to desmoplastic reaction without tumor cells at histology.

Mesorectal fascia status

Mesorectal fascia was visualized on MRI in all patients, which was depicted as a thin, low-signal-intensity structure that envelops the mesorectum and surrounds the perirectal fat. Mesorectal fascia was involved in 15 patients found by pathologists using a cutoff distance of 2 mm between a tumor and the mesorectal fascia[3,4]. The overall accuracy was 88% for predicting mesorectal fascia involvement (Figures 4B and C). The sensitivity, specificity, positive predictive value, and negative predictive value was 80% (12/15), 90.4% (47/52), 70.6% (12/17) and 94% (47/50), respectively. One false-negative case was due to failure



Figures 3 T3-stage rectal cancer without mesorectal fascia involvement in a 64-year-old female patient. **A**: Axial T_2W-TSE MR image (3000/98) showed tumor in anterior rectal wall (T) with transmural spiculation (black arrow) from tumor into perirectal fat, and the distance to mesorectal fascia (white arrow) is measured $\leqslant$ 2 mm; **B**: Photograph of the corresponding histopathologic slice (hematoxylin-eosin stain; original magnification, x 10) confirmed that tumor (black arrows) invaded the perirectal fat (F). Spiculations consist of desmoplastic reactions (white arrow) containing tumor cells (black arrows).

to identify nodal metastases within 2 mm, which is still a diagnostic problem for the radiologist, and the other two cases had more subtle invasion on MRI. Three false-positive cases were anterior rectal tumors (Figure 3A) and the remaining ones had ill-defined margins due to peritumor fibrosis and inflammatory reaction.

DISCUSSION

Colorectal cancer is one of the most common malignant tumors and its incidence is increasing, and rectal cancer is the main part of the colorectal cancer in China[1]. Rectal cancer has a higher recurrence rate than colon cancer, because of the extensive lymphatic drainage of the pelvis. TME removes the tumor-containing rectum and its draining lymph nodes as a distinct anatomic package, which results in reduced local recurrence rates[5]. Kapiteijn *et al*[8] reported that preoperative radiotherapy in combination with standardized TME reduces the local recurrence rate from 8.2% to 2.4% at a 2-year follow-up compared with TME only, but the significant beneficial effect was only observed for T3, T4 or node positive tumors. This study provides strong evidence that patients with T3, T4 or node positive rectal cancer indicated preoperative radiotherapy even when optimal surgery is performed. Recent reports provide convincing evidence of the superiority of preoperative chemoradiotherapy

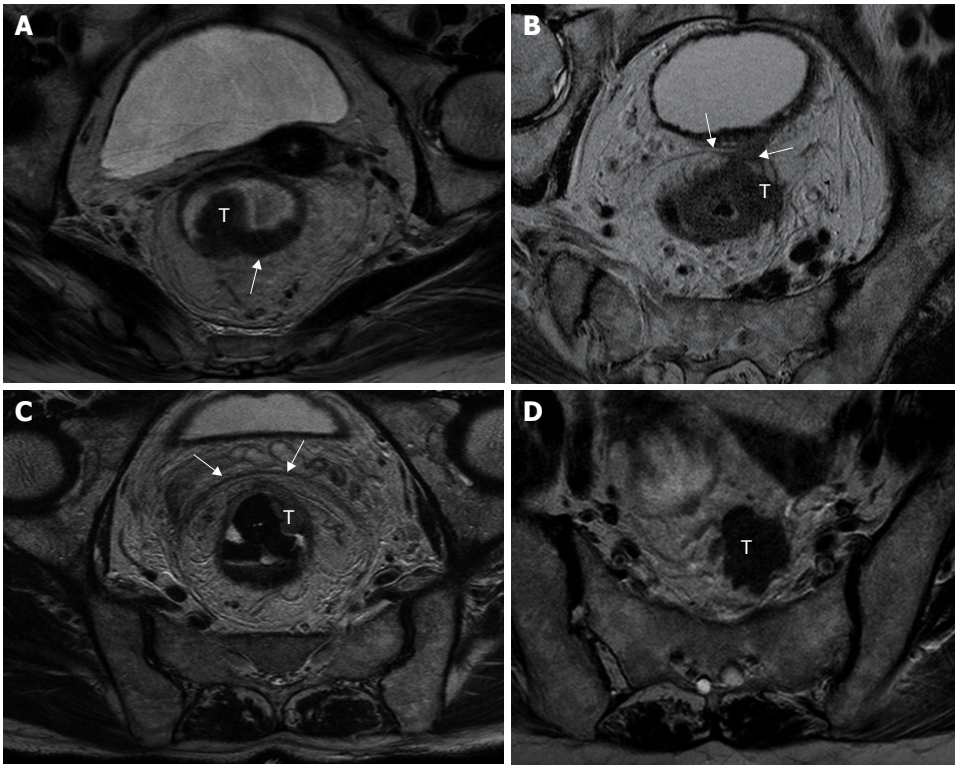


Figure 4 **A**: T3-stage rectal cancer without mesorectal fascia involvement in a 57-year-old female patient. Axial T_2W-TSE MR image (3000/98) manifested bulky tumor with broad-based nodular (T) with clear margin (white arrows); **B**: T3-stage rectal cancer with involved mesorectal fascia in a 79-year-old male patient. Axial T_2W-TSE MR image (3000/98) showed tumor (T) extending to mesorectal fascia (white arrows); **C**: T3-stage rectal cancer with involved mesorectal fascia in a 65-year-old male patient. Axial T_2W-TSE MR image (3000/98) showed heterogeneous strands are noted in the perirectal fat tissues with the thicken mesorectal fascia; **D**: T3-stage rectal cancer with extramural deposits in a 62-year-old female patient. Axial T_2W-TSE MR image (3000/98) showed extramural deposits (T) in the perirectal space with irregular shape.

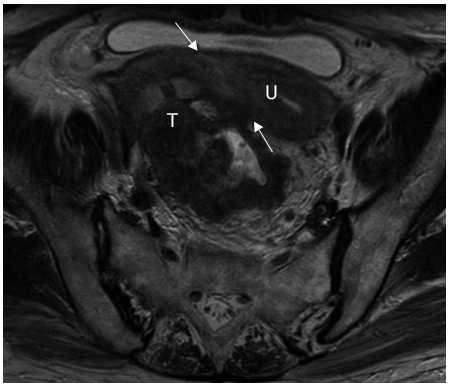


Figure 5 T4-stage rectal cancer with fixation to uterus in a 76-year-old female patient. Axial T_2W-TSE MR image (3000/98) showed direct invasion (white arrows) of tumour (T) into uterus (U).

Table 2 Accuracy for each T stage (*n*/*n*)%

	≤ pT2 (*n* = 20)	pT3 (*n* = 42)	pT4 (*n* = 5)
Accuracy	(60/67) 89.6	(57/67) 85.1	(64/67) 95.5
Sensitivity	(14/20) 70.0	(38/42) 90.5	(5/5) 100
Specificity	(46/47) 97.9	(19/25) 76.0	(59/62) 95.2
PPV	(14/15) 93.3	(38/44) 86.4	(5/8) 62.5
NPV	(46/52) 88.5	(19/23) 82.6	(59/59) 100

PPV: positive predictive value; NPV: negative predictive value.

over postoperative chemoradiotherapy[9,10], especially for patients with a close or involved resection margin at TME[10], So precise evaluation of mesorectal fascia involvement is a second important step for patients who are suitable for TME. However, one disadvantage of preoperative chemoradiotherapy is the possibility of over treatment for early-stage tumors. So with the increasing use of neoadjuvant therapy in patients with rectal cancer, accurate staging is needed to avoid unnecessary treatment for early stage tumors.

There have been studies on rectal cancer imaging comparing with endorectal ultrasonography (EUS), computed tomography (CT), and MR imaging[19,20]. Endoluminal US was considered to be the most accurate modality compared with CT and MR imaging for evaluation of local invasion of rectal cancer, however, it has several limitations: operator dependency; limitation to tumors located in the upper rectum when a rigid probe is used; no assessment of stenotic tumors; and inability to visualize the mesorectal fascia[19,21]. Although CT was the first technique introduced, it has limitations in differentiating and distinguishing different layers of the rectal wall, and has lower overall accuracy than EUS and MR. But multi-detector row spiral CT scanners, with reconstructions in multiplanar reformations (MPRs), are expected to provide a higher overall accuracy (83%, 34/41). The distance of the tumor to the mesorectal fascia was not assessed[22]. Studies of conventional MR with body coil in imaging rectal tumors were disappointing because of poor spatial resolution[23]. High resolution T_2-weighted MRI with phased-array coil is able to depict the detailed anatomy of rectal wall and perirectal structures related to TME[24], and seems to be the best single method[21].

Brown *et al*[11] demonstrated 100% accuracy in the T staging of 28 primary rectal cancers using high-resolution images with a 0.6 mm × 0.6 mm in-plane resolution, however this initial high accuracy and reproducibility were not confirmed. Poon *et al*[13] reported an overall accuracy of 74% using the similar technique. Our study with a 0.66 mm × 0.56 mm in-plane resolution showed that the

overall accuracy was 85.1% for T staging. Although low-risk T1 tumors may benefit from transanal endoscopic microsurgery (TEM), the clinical value is limited for those who already have a high risk of local recurrence and lymph node metastasis at the time of operation[25,26]. Differentiation between T1 and T2 tumors may be of little clinical consequence. On the other hand, high-resolution MRI is difficult in distinguishing T1 and T2 tumors, owing to loss of a clear interface between tumor within submucosa and circular muscle[14]. In addition, as there were few T1 patients (n = 3) in our study, we combined T1 and T2 tumors to ⩽ T2 stage. However, distinguishing T3 from T2 lesions seems to be very important for the use of preoperative therapy and its crucial criterion is infiltration of perirectal fat. The minimal criterion for assignment of pT3 is the absence of any mural muscle between the leading edge of the tumor and the extramural soft tissue. As Brown *et al*[11] described the presence of tumor signal intensity extending into the perirectal fat signal intensity with a broad-based bulging configuration and in continuity with the intramural portion of the tumor is correlated best with a T3 tumor on MR images[11], but it is difficult to distinguish spiculation in the perirectal fat caused by fibrosis only from that caused by fibrosis containing tumor cells. Over-staging occurred in 6 (30%) of 20 for T2 tumors in our study, similar to previous report (38.5%, 5/13)[13], because of extramural fibrosis and inflammatory reaction at the advancing edge of the tumor. It is important to remember that an inflammatory reaction at the expanding tumor margin occurs in about 25% of rectal cancers[27]. Although Brown *et al*[11] considered that peritumoral fibrosis has a distinct MR appearance that can be distinguished from the tumor itself, we retrospectively analyzed the over-staging images and failed to show any helpful distinguishing features. So spiculated lesions without preoperative treatment should be designated as T3 rather than T2 disease. In addition, extramural tumor nodules discontinuing from the primary tumor mass that are irregular in shape, are of the T category as pT3[4]. The irregular shape helps differentiate tumor deposit from lymph nodes with smooth contours.

In T3 tumor, the measurement of the minimum distance between the tumor and the mesorectal fascia is particularly important[12,14,20]. Histology of resection specimens has shown that the frequency of local recurrence greatly decreases when a tumor-free CRM of more than 1 mm can be obtained[2]. More recent data have suggested that the risk of local recurrence also is significantly increased with clearances of 2 mm or less. Thus, clearance of 2 mm or less should be considered a positive CRM[3,4]. Previous reports showed the evaluation of the mesorectal fascia and the CRM on the high-resolution phased-array MRI was highly accurate and reliable, however, the precise measurement is controversial[12,14,28]. Although these studies were performed without distending rectum, other authors recommended the use of distention to improve tumor visualization and T staging[16-18]. It is unclear if rectal distention has a detrimental effect on determining the distance between tumor margin and mesorectal fascia. So we distended rectum by administering tepid water of 150-400 mL, and we used the criterion of a cutoff distance of 2 mm between a tumor and the mesorectal fascia for predicting CRM infiltration since rectal distention reduces this distance. If the criteria (a cutoff distance of 6 mm) suggested by Beets-Tan *et al*[12] were used, many cases would be classified as CRM infiltration. Our performance with rectal distention is comparable with the high performance without rectal distention, with an accuracy of 88%, sensitivity 80% and specificity 90.4%. Torkzad[29] reported that there is a significant individual variation in the amount of mesorectal fat, which is probably subjected to mechanical pressure from the surrounding structures, so the distance measured from the tumor to the mesorectal fascia could also result in variations. Our study showed that rectal distention did not decrease the distance within 2 mm in most patients, perhaps because tumor invasion and desmoplastic reaction can stiffen adjacent tissues against the effects of the compression, and the amount of mesorectal fat compression is not enough to push the tumor so close to the mesorectal fascia. In our study, the problems in MRI evaluation of mesorectal fascia involvement is (1) the thin perirectal fat in the anterior part leading to difficulties in assessing anterior rectal tumors; (2) ill-defined margins due to peritumor fibrosis and inflammatory reaction leading to unprecise distance measurement; and (3) different volumes of water resulting in various rectal distentions and effects of mesorectal fat compression.

In the differentiation of T3 and T4 tumors, the crucial criterion is infiltration of adjacent structures. The MRI criterion for T4 stage was the obliteration of fat planes between tumor and adjacent organs, but sometimes a loss of fat planes occurred due to an inflammatory reaction or cachexia. Our results showed three T3 lesions were over-staged as MR-T4 disease. In one over-staged patient, the absence of fat planes between the tumor and bladder was due to an inflammatory reaction. The other two patients had large exophytic mucinous adenocarcinoma, pressing the uterus that simulated infiltrating uterus.

There were some limitations in this study. First, no comparison was made between those with and without the rectal distention; Second, the nodal involvement was not assessed, which is still a diagnostic problem for the radiologist depending on morphologic criteria[20]. Use of ultra-small superparamagnetic iron oxide (USPIO) contrast agents has shown promising results for staging nodal metastases, but need further evaluations[30]. Third, different volumes of water were used due to varying tolerance of the patients.

Notwithstanding these limitations, high-resolution MRI enables accurate preoperative assessment for T staging and mesorectal fascia infiltration in rectal cancer with rectal distention.

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