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The Value of High-Resolution MRI Technique in Patients with Rectal Carcinoma: Pre-Operative Assessment of Mesorectal Fascia Involvement, Circumferential Resection Margin and Local Staging

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A Study Design
B Data Collection
C Statistical Analysis
D Data Interpretation
E Manuscript Preparation
F Literature Search
G Funds Collection

Summary

Background: The purpose of the study was to identify the accuracy of high-resolution MRI in the pre-operative assessment of mesorectal fascia involvement, circumfrential resection margin (CRM) and local staging in patients with rectal carcinoma.

Material/Methods: The study included 56 patients: 32 male and 24 female. All patients underwent high-resolution MRI and had confirmed histopathological diagnosis of rectal cancer located within 15 cm from the anal verge, followed by surgery. MRI findings were compared with pathological and surgical results.

Results: The overall accuracy, sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of MRI-based T-staging were 92.8, 88.8%, 96.5%, 96%, and 90.3%, respectively**.** The accuracy, sensitivity, specificity, PPV, and NPV of MRI-based assessment of CRM were 94.6%, 84.6%, 97.6%, 91.4, and 94.6%, respectively. The accuracy, sensitivity, specificity, PPV, and NPV of MRI-based N-staging were 82.1%, 75%, 67.3%, 60%, and 86.1%, respectively.

Conclusions: Preoperative high-resolution rectal MRI is accurate in predicting tumor stage and CRM involvement. MRI is a precise diagnostic tool to select patients who may benefit from neo-adjuvant therapy and to avoid overtreatment in those patients who can proceed directly to surgery.

MeSH Keywords: Magnetic Resonance Imaging • Neoplasm Staging • Rectal Neoplasms

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Background

Rectal cancer is a common disease and a major cause of mortality. Its prevalence has consistently increased with changes of life style in recent years, where it is considered the third most common cancer worldwide. Rectal carcinoma is the most common type of all colorectal cancers and 65% and 98% of them are adenocarcinomas [1]. The local recurrence is related to the extramural tumor spread into the mesorectum and the distance from the tumor to the circumferential resection margin (CRM) [1–3].

Traditional rectal cancer surgery is associated with high rates of local recurrence, from 3% to 32% [4]. In recent years, the treatment of rectal cancer has changed dramatically with the introduction of total mesorectal excision (TME). The reinforcement of its value is by understanding the mesorectal involvement and CRM that lead to fewer positive

Table 1. Histopathological T-staging of rectal carcinoma with corresponding MR staging, quoted form Rao, 2007 [6].

Histopathological T-staging	MR T-staging appearance
T1: Tumor invades the submucosa	MRT1: Tumor signal intensity is confined to the submucosal layer
T2: 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
T3: 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
T4: Tumor directly invades other organs or structures or perforates the visceral peritoneum	MRT4: Tumor signal intensity extends into an adjacent structure or viscus

margins and consequently fewer local recurrences [4]. The overall recurrence rate has been reported to be below 10%, without the support of radiation therapy [5]. High-resolution magnetic resonance imaging (MRI) can visualize the layers of the rectal wall; accordingly it plays an important role in preoperative staging and thus in taking effective therapeutic decisions. High-resolution MRI can accurately delineate the extent of the primary tumor, providing information regarding the depth of tumor invasion, relationship of the tumor to mesorectal fascia, condition of CRM, whether involved or not, extramural vascular infiltration and lymph node (LN) status, thus helping the multidisciplinary teams to make effective decisions for patient management [5,6]. In the TNM staging for rectal cancer, the patients with cancer stage T1-2, N0 benefit from surgical treatment. The patients with stage T3-4 tumors require pre-operative radiation therapy, which reduces the rate of local recurrence. Furthermore, the treatment options do not depend merely on differentiating stage T2 from stage T3 cancer, since the studies have found that patients with extramural invasion greater than 5 mm have a 5-year survival rate of 54%, compared with 85% of the patients with invasion depth of less than 5 mm [7]. MRI can accurately determine the depth of extramural invasion and thus help in appropriate treatment selection.

The aim of the study

The purpose of the study was to identify the accuracy of high-resolution MRI in pre-operative assessment of mesorectal fascia involvement, circumfrential resection margin (CRM) and local staging in patients with rectal carcinoma.

Material and Methods

A prospective study was conducted between January 2012 and July 2014 in Hamad Medical Corporation hospitals in Doha, Qatar as well as in Zagazig University Hospital, Egypt. All subjects provided informed consent after receiving a full explanation of the nature of the study.

The study included 56 patients, 32 male and 24 female in the age range from 34 to 71 years and mean age of 50 years. All patients had confirmed histopathological diagnosis of rectal cancer located within 15 cm from the anal verge. The patients with pre-operative course of radiotherapy and patients with metastatic disease were excluded from the study. All patients underwent surgery within 1–3 weeks after MR examination.

All patients underwent high-resolution MRI using a phased-array surface coil. MR imaging was performed using a 1.5 Tesla machine (Avanto, Siemens, Germany). The patients underwent routine rectal cleansing 3–4 hours before MR examination to limit misinterpretation due to residual stool. All sequences were obtained with a non-breath-hold technique. After scout scanning, midline axial and sagittal T2-weighted turbo spin-echo (T2W-TSE) images were obtained. The scan protocol was TR 3000–4000 ms, TE 70–90 ms, field of view (FOV) 28–32×28–32 cm, matrix 276×384, slice thickness 5 mm and gap 1 mm. Those images were used to plan T2W-TSE high-resolution scans, which were perpendicular to the long axis of the rectum. High-resolution TSE (HR TSE) T2 sequences (TR 4200–5000 ms, TE 108 ms, FOV 180–240 mm, slice 3 mm, acquisition time 210–300 seconds) in axial, coronal and sagittal scans perpendicular to the long axis of the rectal tumor were acquired.

High-resolution MRI regarding T staging of rectal cancer is mainly based on the differences in T2 signal intensity between the tumor and the rectal wall layers. On T2-weighted images, three different layers can be recognized: an inner hyperintense layer representing the mucosa and submucosa, a hypointense intermediate layer corresponding to the muscularis propria and an external hyperintense layer that represents perirectal/mesorectal fat tissue. A thin low-intensity layer enveloping the mesorectum corresponds to the mesorectal fascia that is clearly visible on the lateral and posterior views [8,9].

Patient's T-staging was categorized according to the TNM classification (Table 1), [10] and was assessed according to the reported criteria. Considering that differentiation between T1 and T2 lesions is rather difficult, we combined both stages in the group of intramural lesions, which were characterized by tumor signal intensity limited to the muscular layer with an intact interface between the muscularis propria and the perirectal fat. The CRM is defined as the distance from the edge of the tumor to the margin of the resected specimen and it is considered one of the most important independent prognostic factors in the treatment of patients with rectal cancer [11].

The tumors were well visualized in all 56 patients. Thirty tumors were located in the upper rectum (10-15 cm from the anal verge, 53.6%), 10 in the mid rectum (5–10 cm from the anal verge, 17.9%), and 16 in the distal rectum

Table 2. MR-based T-staging in comparison with histopathological and surgery-based T-staging in 56 patients.

MRI staging	Histopathological staging			Total
	T1+T2	T3	T4	
T1+T2 (18/20)	18	4	0	22
T3 (22/26)	2	22	2	26
T4 (8/10)	0	0	8	8
Total (100%)	20 (35.7%)	26 (46.4%)	10 (17.9%)	56

Table 3. Accuracy, sensitivity, specificity, PPV, NPV for each T-stage by MRI.

	T1-T2 (n=20)	T3 (n=26)	T4 (n=10)
Accuracy	(50/56) 89.2%	(48/56) 85.7%	(54/56) 96.4%
Sensitivity	(18/20) 90.0%	(22/26) 84.6%	(8/10) 80.0%
Specificity	(32/36) 88.8%	(26/30) 86.7%	(46/46) 100.0%
PPV	(18/22) 81.8%	(22/26) 84.6%	(8/8) 100.0%
NPV	(32/36) 94.1%	(26/30) 86.7%	(46/48) 95.8%

Table 4. Concurrence between MRI and histopathological diagnosis.

MRI analysis	Accuracy	Sensitivity	Specificity	PPV	NPV
T-staging	92.8	88.8	96.5	96.0	90.3
CRM	94.6	84.6	97.6	91.6	95.4
N-staging	82.1	75.0	67.3	60.0	86.1

(less than 5 cm from the anal verge, 28.5%). The tumor size ranged between 2.0 and 9.0 cm, with the mean tumor size of 5.1 cm. The size of the resected tumor ranged from 0.8×2.0 cm to 5.0×7.0 cm (mean 3.5×4.4 cm).

CRM involvement has been defined as tumor or malignant lymph node presence within 1 mm of the mesorectal fascia. For N-staging, the presence of regional lymph nodes was evaluated based on their number and size [12]. Nodes with a short axis of 5 mm or greater and nodes with nodular irregular margins were considered metastatic, while those less than 5 mm were assumed to be uninvolved. The post-contrast and diffusion weighted images were not included in patient evaluation in this study.

Total mesorectal excision (TME) was performed. Histopathological studies were done immediately after surgery, resected specimens were opened on the opposite side of the tumor and fixed in formalin for 24 hours. 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.

Statistical analysis was carried out. The overall MRI T-staging accuracy was calculated. The accuracy, sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) for each T-stage, as well as for predicting CRM invasion and lymph node involvement were calculated using histopathological results as the gold standard. The agreement between MRI and histological results was assessed (Tables 2–4).

Results

Results of resected tumors showed adenocarcinoma in all patients. Twenty-five mucinous types were detected with focal (n=17) or diffuse (n=8) having significantly high signal intensity in the tumor on T2WI, which was correlated with the mucinous pool on pathologic specimens. Thirty-one non-mucinous types showed hyperintense signal (appearing higher than the muscle layer on T2WIs) less frequently than the mucinous types.

T-staging

The T-staging based on MRI findings is summarized in Table 1. Histopathological staging revealed intramural lesions (T1+T2 stage) in 20 patients (35.7%, Figure 1), T3 in 26 patients (46.4%, Figures 2–4) and T4 in 10 patients (17.9%, Figure 5). The histopathological staging is summarized in Table 2.

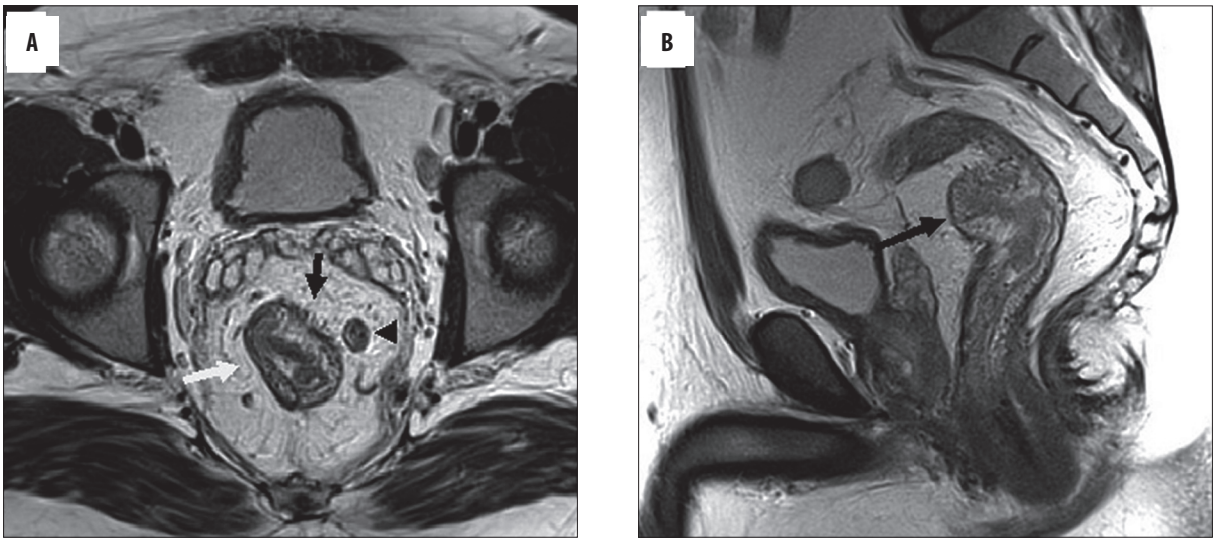


Figure 1. Male, 53 year-old with histopathologically proven T2 stage rectal carcinoma. (**A**) High resolution MRI axial T2WI: Concentric rectal mass (white arrow) with reticulo-nodular stranding of the mesorectal fat at the left antero-lateral aspect (black arrow). Enlarged lymph node on the left side of the mesorectal fat (arrow head), (**B**) sagittal T2WI: Rectal mass (arrow).

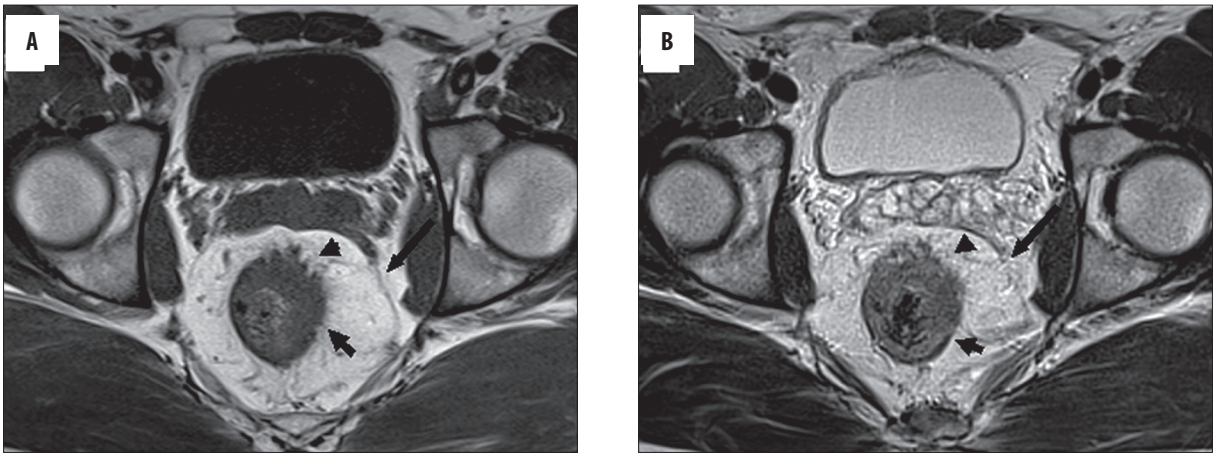


Figure 2. Male, 52 year-old with histopathologically proven T3 stage upper third rectal carcinoma. (**A**) High resolution MRI axial T1WI, (**B**) axial T2WI: Rectal mass (arrow) with disruption of outer layer and involvement of perirectal fat (arrow head), negative CRM (long black arrow).

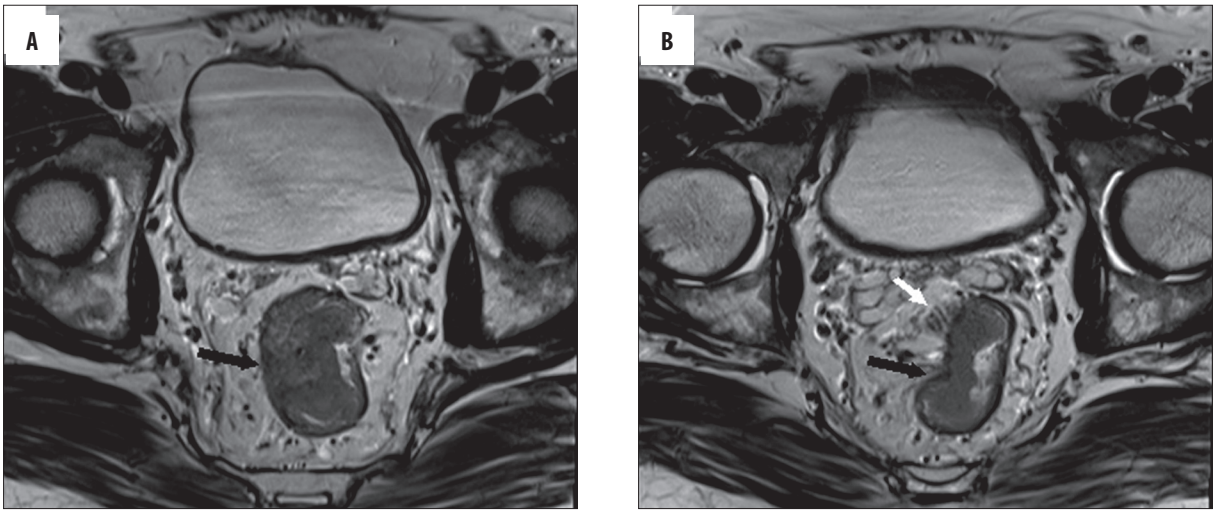


Figure 3. Male, 46 year-old male with histopathologically proven T3 stage rectal cancer. (**A**) High resolution T2WI axial, (**B**) high resolution T2WI axial in lower level: Rectal mass (black arrow) with mesorectal fat infiltration (white arrow).

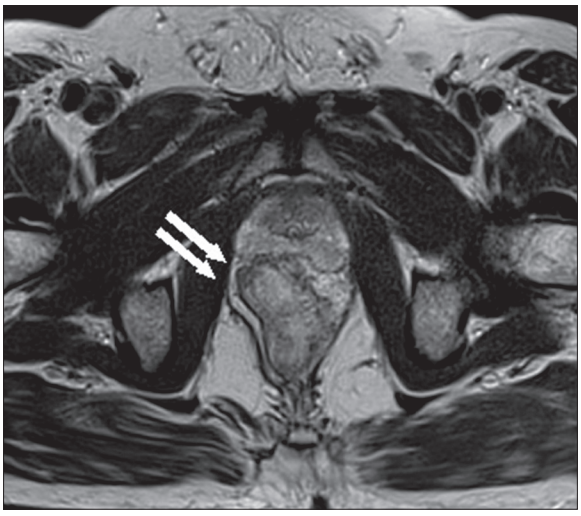
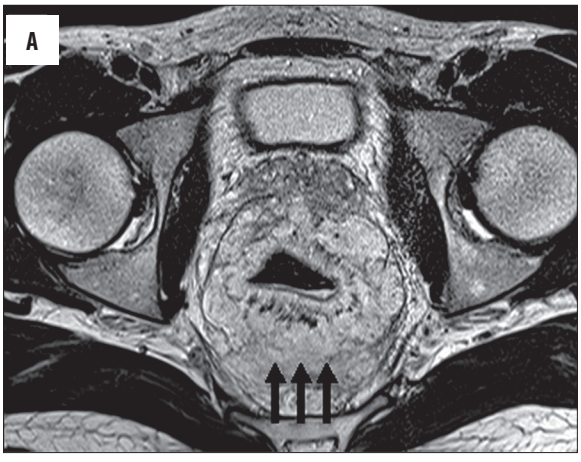


Figure 4. Male, 42 year-old with histopathologically proven T3 stage rectal cancer. High resolution axial T2WI: lower rectal mass with focal nodular outer layer involvement, peri-rectal fat and mesorectal fascia infiltration (white arrows).

Referring to Table 2, MRI correctly assessed T1-2 staging in 18 out of 22 intramural lesions (81.8%), in 22 out of 26 T3 lesions (84.6%) and in 8 out of 10 T4 lesions (80%). Two T2 lesions confirmed histopathologically were over-staged as T3 by MRI due to the presence of 1-2-mm reticulonodular tissue reaction that could not be differentiated from a true mesorectal fat tumor invasion (Figure 1). Four patients with histopathologically proved T3 tumor were under-staged by MRI as T2 due to a minimal mesorectal invasion that simulated the desmoplastic reaction (Figure 3). Two histologically proved T4 tumors were under-staged as T3 by MRI, because the seminal vesicle invasion was not recognized (Figure 5, Table 2). The accuracy, sensitivity, specificity, PPV, and NPV of MRI-based T-staging showed that the highest accuracy and specificity were at T4 stage, while the highest sensitivity in T1-T2 stage (Table 3). The overall accuracy, sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of MRI-based T-staging were 92.8, 88.8%, 96.5%, 96%, and 90.3%, respectively (Table 4).



CRM

MRI correctly predicted a tumor-free CRM in 41 patients out of the 43 patients with non-involved mesorectal fascia. Mesorectal fascia was well visualized on MRI in all patients, and was depicted as a thin, low-signal structure that envelops the mesorectum and surrounds the perirectal fat. Mesorectal fascia involvement in 13 patients was found in histopathological examination using a cut-off distance of 2 mm between the tumor and the mesorectal fascia. Two cases were not correctly recognized by MRI due to failure to identify nodal metastases of 2 mm recognizable in high-resolution MRI only (diffusion restriction and nodal enhancement can be helpful factors). One case of anterior rectal tumor which was suspected to have positive CRM based on MRI was confirmed by histopathology to be negative. The accuracy, sensitivity, specificity, PPV, and NPV of MRI-based assessment of CRM were 94.6%, 84.6%, 97.6%, 91.4, and 94.6%, respectively.

N-staging

Twenty out of 56 patients with rectal cancer showed metastatic nodes at histological examination. Twenty-five cases were diagnosed as having lymphadenopathy based on MRI. Fifteen of them were correctly categorized as metastasis. On the other hand, 10 cases were diagnosed as metastases in MRI due to lymph nodes size greater than 5 mm, and were found to be reactive lymphadenopathy in histopathological examination. The accuracy, sensitivity, specificity, PPV, and NPV of MRI-based N-staging were 82.1%, 75%, 67.3%, 60%, and 86.1%, respectively (Table 4).

Discussion

Accurate preoperative staging is crucial for management of patients with rectal cancer and for making effective

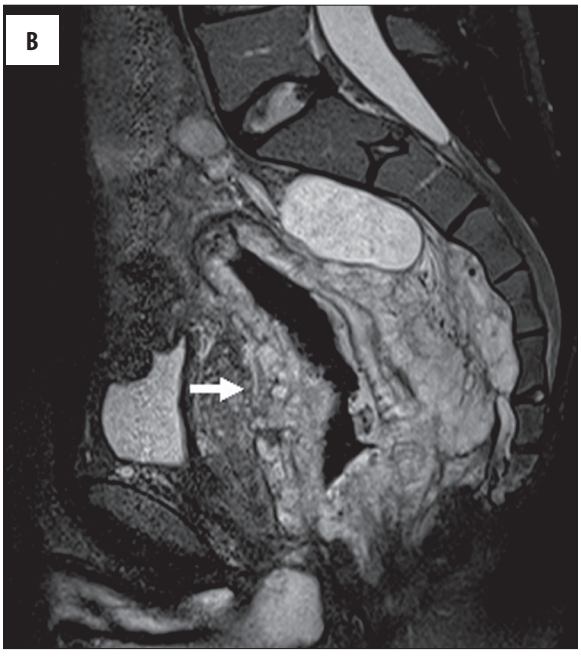


Figure 5. Male, 45 year-old male with histopathologically proven T4 stage rectal cancer. (**A**) High resolution T2WI axial, (**B**) high resolution T2WI sagittal with fat saturation: long segment rectal carcinoma with outer layer involvement (white arrow), infiltration of mesorectal fat and mesorectal fascia posteriorly denoting positive CRM (black arrows).

therapeutic decisions. High-resolution MRI with phased-array surface coil represents the most advanced staging modality providing physicians with the detailed information regarding the depth of tumor invasion, relationship of the tumor to the mesorectal fascia, CRM, extramural vascular invasion, and lymph node status, which are crucial points in the therapeutic planning of locally advanced tumors [5,6,8]. This enables the physicians to make correct decisions contributing to improvement in overall survival and quality of life in patients with rectal cancer. Rectal cancer has a higher recurrence rate than colon cancer, because of extensive lymphatic drainage of the pelvis [4].

TME removes the tumor-containing rectum and its draining lymph nodes as a distinct anatomic package, which results in reduced local recurrence rates [13]. Studies have reported that preoperative radiotherapy in combination with standardized TME reduces the local recurrence rate from 8.2% to 2.4% in a 2-year follow-up compared with TME only, but the significant beneficial effect was only observed for T3, T4 or node-positive tumors [14–16]. Hence, preoperative imaging is crucial to select patients for appropriate treatment [17–21]. The MR protocol is quite standardized and the HR TSE T2 sequences acquired in at least two planes are considered to be the fundamental part of the exam [22,23]; the axial plane orthogonal to the rectal tumor is essential, while gadolinium-enhanced T1 sequences do not appear to be an effective approach [24]. In other similar series, the overall agreement between MRI and histology for T-staging ranged from 66% to 94% [25–27].

In our study, MRI T-staging showed matching with histological T-staging in 48 out of 56 patients (85.7%). The T2 and T3 were present in most of our patients, i.e. 22 and 26 patients, respectively (35.7% and 46.4%), while the T4 stage was found in 10 patients (17.9%). Mismatch occurred in a total of 8 patients. The main difficulty in MRI staging was the differentiation between the T2 and T3 stage. In that group, six patients had a mismatch; four were staged as T2 in MRI, confirmed histopathologically as T3 due to minimal mesorectal invasion that simulated desmoplastic reaction favoring its staging with MRI as T2. Two patients with histopathologically proved T2 tumor were staged with MRI as T3 because the reticulo-nodular reactive tissue seen in MRI suggested muscle layer and perirectal fat involvement. Two patients with histopathologically proved T4 tumor were staged in MRI as T3 because no related organ invasion was found in MRI (seminal vesicle invasion in lower rectum mass). Complete matching between MRI and histopathology was seen in cases staged with MRI as T4. The accuracy, sensitivity, specificity, PPV, and NPV of MRI-based T-staging of each pathological stage showed that the highest accuracy and specificity were for stage T4, where the highest sensitivity for stage T1-T2. The overall accuracy, sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of MRI-based T-staging were 92.8, 88.8%, 96.5%, 96%, and 90.3%, respectively. That was in agreement with Ghieda et al. [28] and Iannicelli et al. [5] who stated that differentiation between intramural tumors and T3 borderline lesions still remains a diagnostic problem, based on the fact that it is often not possible to distinguish a true mesorectal tumor invasion from desmoplastic reaction or inflammatory peritumoral tissue that may or may not contain tumor cells.

MRI correctly predicted tumor-free CRM in 41patients out of 43 patients with non-involved mesorectal fascia (95.3%). Mesorectal fascia involvement in 13 patients was found in histopathological examination using a cut-off distance of 2 mm between the tumor/pathological lymph node and the mesorectal fascia. Two cases were not correctly recognized in MRI due to failure to identify nodal metastases of 2 mm recognizable in high-resolution MRI only. One case of anterior rectal tumor which, based on MRI, was suspected to have positive CRM was confirmed with histopathological examination to be negative. The accuracy, sensitivity, specificity, PPV, and NPV of MRI-based assessment of CRM were 94.6%, 84.6%, 97.6%, 91.4, and 94.6%, respectively which is in agreement with the findings of Rao [6] and Iannicelli et al. [5].

Some authors prefer to perform the examination without rectal lumen distension, hypothesizing that it may alter the distance between the tumor and the mesorectal fascia and potentially compromise the CRM evaluation [29]. Other authors advocate rectal distension with water, methylcellulose, superparamagnetic iron oxide solutions or warm ultrasound gel to improve depiction of the primary tumor [30–32]. In our series we did not use rectal distention agents.

Twenty out of 56 patients with rectal cancer showed metastatic nodes at histological examination. Twenty-five cases were diagnosed as having lymphadenopathy in MRI. Fifteen of them were correctly categorized as metastasis. On the other hand, 10 cases diagnosed in MRI were found to be reactive lymphadenopathy in histopathological exam. The accuracy, sensitivity, specificity, PPV, and NPV of MRI-based N-staging were 82.1%, 75%, 67.3%, 60%, and 86.1%, respectively. High-resolution MRI had relatively low specificity. Our results are comparable to other studies performed with rectal distention [5,6], or without rectal distension [29]. Adding diffusion-weighted images and post-contrast study to the examination may improve nodal involvement detection. However, the optimal and standardized MRI criteria to define local lymph-node metastatic involvement have not been established yet as highlighted in a recent meta-analysis that included 21 articles [10,33,34].

Conclusions

Preoperative high-resolution rectal MRI is accurate in predicting tumor stage and CRM involvement, which are the main factors affecting the outcome of surgery. MRI represents a precise diagnostic tool to select patients who may benefit from neo-adjuvant therapy and to avoid overtreatment in those patients who can proceed directly to surgery.

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