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ABDOMINAL IMAGING

ORIGINAL ARTICLE

The ability of phased-array MRI in preoperative staging of primary rectal cancer: correlation with histopathological results

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PURPOSE
This study evaluated the accuracy of phased-array magnetic resonance imaging (MRI) for preoperative local tumor staging in primary rectal cancer and emphasized the importance of the preoperative differentiation of T2 tumors from T3 tumors so the appropriate treatment can be applied.

MATERIALS AND METHODS
Twenty-four patients with primary rectal cancer were examined preoperatively using 1.5 T MRI with a phased-array coil. Multiplanar T2-weighted images were obtained. Rectum anatomy, depth of tumor invasion, mesorectal involvement and lymph nodes were assessed. All patients underwent radical surgery. The histological sections were evaluated microscopically. The correlation of magnetic resonance imaging and histopathology was assessed using the kappa statistic. Overstaging with MRI was compared with Fischer's exact test.

RESULTS
Histopathological examination of the tumors revealed adenocarcinoma. When the tumors were staged, there was one patient with a pT1 tumor, six patients with pT2 tumors, and 17 patients with pT3 tumors. Using MRI, four patients with pT2 were overstaged as T3, and one patient with pT3 was overstaged as T4. In the remaining cases (one pT1, two pT2, and 16 pT3), MRI correctly assessed the stage of transmural invasion. The accuracy of T staging and metastatic lymph node detection with MRI was calculated as 79.2% and 58.5%, respectively.

CONCLUSION
Phased-array MRI is a valuable technique for the preoperative staging of rectal cancer, especially in the differentiation of T2 and T3 tumors.

Key words: • *rectal neoplasms* • *magnetic resonance imaging* • *neoplasm staging*

The prognosis and treatment of rectal carcinoma depends on the tumor stage at presentation (1). Local tumor extent, involved lymph nodes, and the presence of distant metastases are the main factors that influence prognosis (1–5). A poor prognosis of rectal cancer is associated with a high risk of metastases and local recurrence (6). Incomplete removal of the tumor is the major cause of local recurrence, which varies from 3% to 32% (7, 8). Total mesorectal excision (TME) is the standard surgical approach in primary rectal cancer. TME involves the removal of the mesorectum, which contains the rectal tumor, all local draining nodes and the mesorectal fat by sharp dissection along the mesorectal fascia (9–12). This minimizes the chance of any tumor being left behind and results in a substantial reduction of the high local recurrence rate to less than 10% (8, 13) even without adjunctive treatment (13, 14). When performing TME, knowledge of the relationship of the tumor to the circumferential resection margin (CRM) is important. When the CRM is involved with the tumor, the risk of local recurrence is high (9, 15–17).

Chemoradiation therapy is the standard adjunctive preoperative treatment for patients with a high likelihood of curative resection failure (14, 18). According to the recent literature, patients who received preoperative chemoradiation therapy had a lower rate of local recurrence compared to patients who received postoperative chemotherapy and radiation therapy (1, 19). Therefore, there is a need for preoperative imaging methods to aid in the identification of patients with extrarectal spread who may benefit from preoperative chemoradiation therapy (20).

Magnetic resonance imaging (MRI) is the most promising diagnostic method for the preoperative local staging of rectal cancer (8, 21). Spatial resolution has dramatically improved with advances in MRI techniques, such as the use of endorectal and phased-array coils (22, 23). Current evidence suggests that MRI is the most accurate technique for predicting tumor stage (24) because it provides an assessment of the local prognostic factors, including the extent of extramural tumor spread, the involvement of the lateral resection margin, the involvement of neighboring organs in the pelvis, the presence of local lymph node metastases, extramural lymphovascular infiltration and peritoneal involvement (9, 25, 26).

The purposes of this study were to evaluate the accuracy of MRI performed with phased-array coil for preoperative local tumor staging in patients with rectal cancer and emphasize the importance of the preoperative differentiation of T2 tumors from T3 so the appropriate treatment plan can be applied.

Materials and methods

Patients

Twenty-four patients with histopathologically proven primary rectal cancer were prospectively examined using MRI with a phased-array

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coil for preoperative staging. The patients included 14 men and 10 women with a median age of 57.1 years (range, 25–80 years). None of the patients had received neoadjuvant radiochemotherapy.

MRI technique

MRI was performed using a 1.5 T MRI scanner (Signa, GE Medical Systems, Milwaukee, Wisconsin, USA) equipped with a phased-array coil. All patients underwent the hospital's standard cleaning enema procedure. No rectal distension, antispasmodic medication or rectal or intravenous contrast agent administration was performed. The patients were placed in a supine position on the MRI table with their feet first entering the gantry.

Axial, coronal and sagittal T2-weighted fast spin-echo (T2W-FSE) images without fat suppression were obtained. The literature indicates that tumors are slightly better evaluated without fat suppression in T2-weighted images because perirectal fat has a high signal intensity that provides an excellent contrast to the tumor (27). The scan protocol was TR 4000 ms, TE 110 ms, echo train length 16, field of view (FOV) 260×260 mm, matrix 288–384, slice thickness 4 mm and Nex 2. The whole examination took approximately 30 min.

Image analysis

MRI images were evaluated on a workstation. The tumors were subcategorized into two groups according to their anatomic location: low rectal tumors were less than 5 cm from the anal verge, and upper-middle rectal tumors were more than 5 cm from the anal verge. Distances were measured using electronic calipers. The rectal mucosa and submucosa (inner hyperintense layer), muscularis propria (hypointense intermediate layer), perirectal fat tissue (external hyperintense layer), mesorectal fascia (thin low intensity structure that envelops the mesorectum and surrounding perirectal fat tissue) and the mesorectal and extramesorectal lymph nodes were visualized. The depth of the transmural invasion by the tumor, mesorectal involvement of the tumor, the number of detected lymph nodes and the smallest short-axis diameters of the lymph nodes were assessed. The lateral and posterior boundaries of the mesorectal fascia were clearly delineated, but its anterior aspect was difficult to differentiate from Denonvilliers' fascia in some of the male patients.

The tumor itself was recognized by an intermediate signal intensity between the high signal intensity of the fat tissue and the low signal intensity of the muscular layer. Each rectal tumor was staged according to the MRI findings and was later correlated with the operative and pathological findings. The depth of transmural invasion by each tumor was categorized according to the TNM classification (28) and was assessed according to the reported criteria (29). We characterized T1 tumors by an infiltration of the submucosal layer and a sparing of the muscularis propria. When the tumor invades muscularis propria we accepted the tumor as T2. T2 lesions were differentiated from T3 lesions by the identification of a smooth outer tumor border within the rectal wall with no invasion into the fat surrounding the rectum. T3 lesions had irregular outer borders and invaded the fat surrounding the rectum with a plaque, mass, or cordlike signal intensity that projected into the perirectal fat. The presence of spiculation within the fat alone was not sufficient evidence of an extramural invasion (29, 30). In T4 lesions, fat planes between the rectal carcinoma and surrounding organs disappeared. Mesorectal fascia involvement and the invasion of adjacent organs were also noted as indicators of T4 tumors. CRM involvement was defined as a tumor that was <2 mm from the mesorectal fascia. This crucial distance of at least 2 mm can be predicted with 97% confidence when the distance on MRI is at least 6 mm (24).

Mesorectal and extramesorectal lymph nodes with irregular margins and/or a short axis greater than 5 mm were accepted as metastatic (31).

Histopathological study

All patients underwent radical surgery. TME was performed in patients with T2 and T3 tumors, and local excision was performed in one patient with a T1 tumor. TME was performed according to standardized techniques using a low anterior resection or abdominoperineal resection (2). The sections were evaluated microscopically for determinations of the depth of transmural tumor invasion and lymph node metastasis according to TNM classification (28).

Statistical study

Agreement between MRI- and histologically determined tumor stages was assessed using the weighted kappa statistic. Overstaging and understaging of the tumors by phased-array MRI were compared using Fischer's exact test. The sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of MRI in the differentiation of stage T2 and T3 tumors and CRM were calculated.

Results

Sixteen tumors were located in the upper-middle rectum, and eight tumors were present in the lower rectum. The histopathological evaluation of resected tumors revealed adenocarcinoma in all of the patients. The pathological T stages of the lesions were pT1 in one patient, pT2 in six patients and pT3 in 17 patients. Using MRI, four patients with pT2 tumors were overstaged as T3 tumors (Figs. 1 and 2), and one patient with a pT3 was overstaged as a T4 tumor. In the remaining cases, MRI correctly assessed the stage of transmural tumor invasion (pT1 tumor in one patient, pT2 tumor in two patients and pT3 tumor in 16 patients) (Fig. 3). The accuracy of T staging with MRI was 79.2% (19 out of 24). Five cases were overstaged with MRI. Four of these cases had lower localized tumors and were overstaged as T3 tumors, and one case had an upper-middle anterior localized tumor that was overstaged as a T4 tumor. The accuracy of MRI in determining the CRM involvement and the NPV was 95.83% and 100%, respectively. In the differentiation of T2/T3 tumors, the sensitivity, specificity, PPV, and NPV were 100%, 33.3%, 80% and 100%, respectively (McNemar test $P > 0.05$). Statistically, there was a poor correlation between histopathological and MRI tumor staging in the differentiation of T2/T3 tumors (κ=0.421; P = 0.015). The concordance of MRI and the histopathological findings was evaluated using the kappa statistic, which was greater in upper-middle located tumors than tumors that were located in the lower rectum (κ=0.84 and κ=0, respectively).

In 15 of 24 cases, MRI detected 65 metastatic lymph nodes with irregular margins and/or a short axis

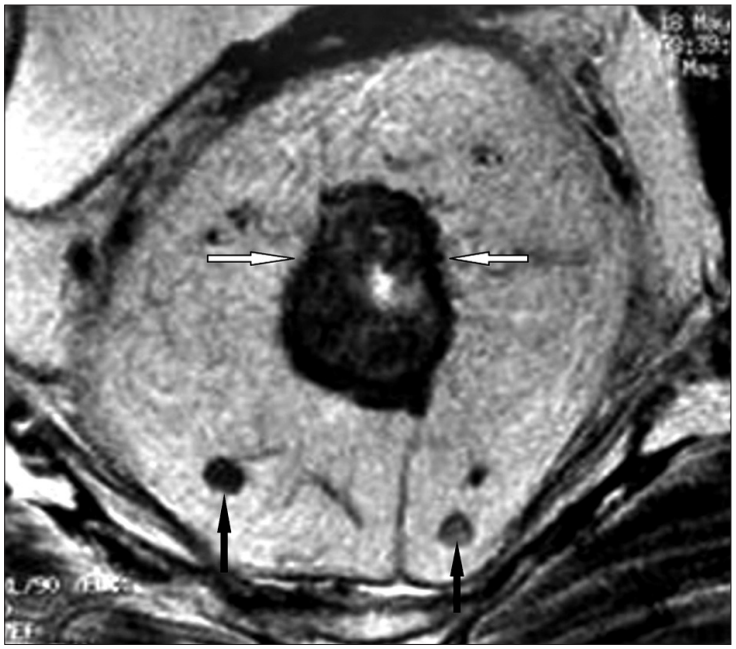

Figure 1. Axial T2-weighted image shows rectal tumor with millimetric spicular extensions *(white arrows)* into the perirectal fat tissue, which is consistent with a T3 tumor. Two mesorectal hypointense spherical lymph nodes are visible *(black arrows)*. Histopathologically, this tumor was pT2, N1.

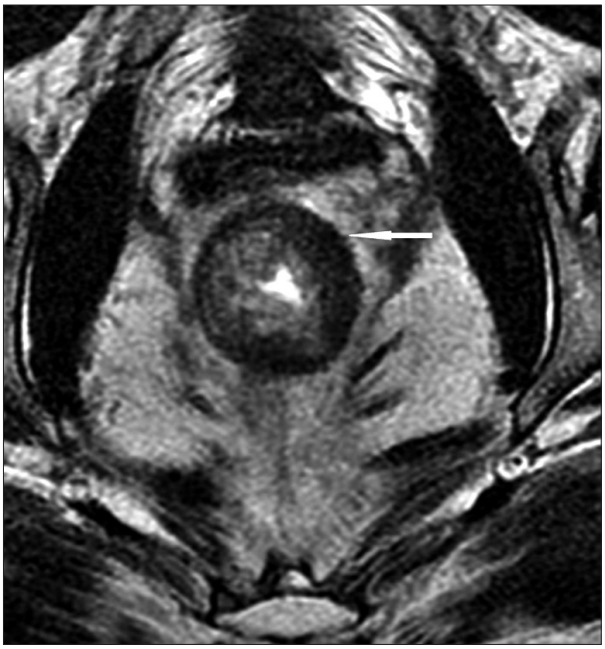

Figure 2. Axial T2-weighted image shows rectal tumor with millimetric spicular extensions *(white arrow)* into the perirectal fat mainly left anterolaterally and posteriorly with no evidence of lymph node involvement. This tumor was assessed as a T3, N0 tumor radiologically. On histopathological examination, the tumor was pT2, N0.

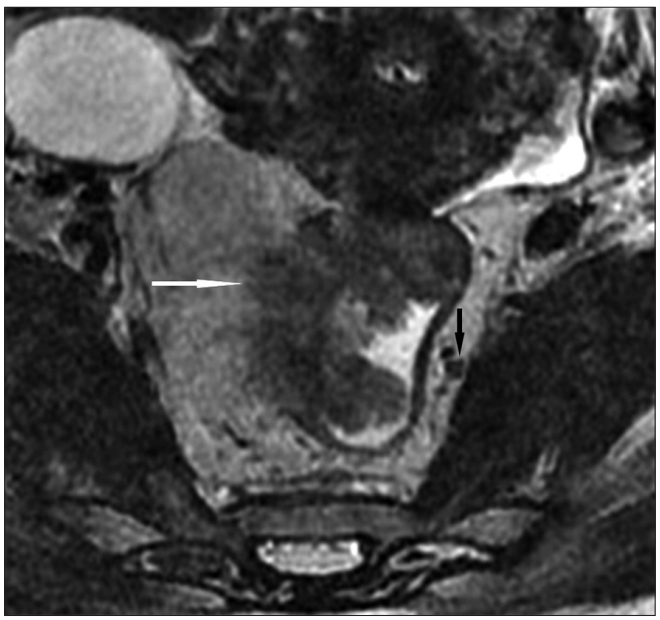

Figure 3. Axial T2-weighted image shows a rectal tumor mainly involving the right lateral side of the rectum with obvious extensions into the perirectal fat *(white arrow)*, which is consistent with T3. T3 was also confirmed histopathologically. There are a few millimetric spherical lymph nodes in the left perirectal fat tissue in this axial image *(black arrow)*; histopathologically, the tumor was N1.

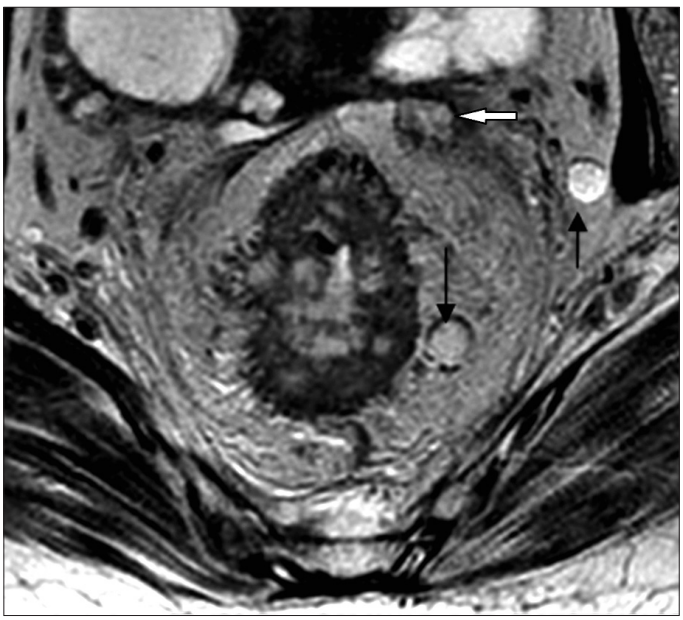

Figure 4. Axial T2-weighted image shows a rectal tumor leading to concentric luminal stenosis. The tumor extends into the perirectal fat tissue. Left anterolaterally, there is a nodular hyperintense lesion adjacent to the mesorectal fascia, which is consistent with a lymph node or an extramural tumor deposit *(white arrow)*. There are also mesorectal and extramesorectal hyperintense metastatic lymph nodes on the left side *(black arrows)*. The tumor was a pT3, N2 mucinous adenocarcinoma histopathologically.

that was greater than 5 mm (Fig. 4). Histopathologically, 38 of these 65 lymph nodes were metastatic, and the remaining lymph nodes were reactive. Detection of lymph node metastasis using phased-array MRI gave an accuracy of 58.5%. According to TNM classification, NX indicates that the regional lymph nodes cannot be evaluated, N0 indicates that there is no metastasis in the regional lymph nodes, N1 indicates that there is metastasis in

1 to 3 regional lymph nodes, and N2 indicates that there is metastasis in 4 or more regional lymph nodes (28). Using MRI and histopathological assessment, nine of the patients were N0. Four patients were diagnosed as N1 by MRI, but 12 N1 patients were detected using histopathology. Three of the 11 patients who were staged as N2 with MRI were confirmed histopathologically.

Discussion

Although rectal tumors can be diagnosed using digital examination, barium enema, and either colonoscopy or sigmoidoscopy, these endoluminal techniques do not provide sufficient information about the extraluminal spread of the tumor for preoperative planning. Therefore, several imaging methods have been studied to assess the spread of the tumor, such as endorectal ultrasonography (EUS), computed tomography (CT), and MRI (24, 32). EUS is the most widely used imaging technique. It depicts the anatomic layers of the rectal wall with high accuracy and enables a precise determination of the tumor extent. Reported accuracy rates of EUS for the assessment of the T stage are in the range of 69%–97% (33). However, EUS is invasive and operator dependent. It cannot be performed in stenotic tumors or in tumors that are localized close to the sigmoid colon. The assessment of the mesorectal fascia and tumor extension into neighboring organs is not possible because of the limited field of view (27, 34).

CT has limitations in differentiating and distinguishing different layers of the rectal wall, and it has a lower overall accuracy rate than EUS and MRI (35). Ju et al. (36) concluded that EUS is superior to spiral CT for the judgment of tumor infiltrate depth and concluded that neither modality provides a satisfactory assessment of lymph node metastasis for rectal cancer. However, Ahmetoğlu et al. (37) showed that multidetector CT can be highly accurate in the prediction of T staging, N staging, International Union Against Cancer (IUCC) staging, and mesorectal fascia involvement in the preoperative local staging of rectal cancer. In contrast to these results, Juchems et al. (38) stated that multidetector CT fails to reliably identify IUCC I in rectal cancer patients. Therefore, they concluded that a strategy for identifying patients who would benefit from neoadjuvant therapy that was based solely on multidetector CT did not seem appropriate. They do not recommend CT as the primary examination for the staging of rectal cancer. Several studies have stated that MRI shows excellent overall accuracies in the diagnosis of mesorectal fascia and adjacent organ invasion of 88%–100% and 100%, respectively (39–41). This high accuracy rate has not been achieved by EUS, conventional CT or multidetector CT (32). In a comparative study by Mathur et al. (42), CT correctly staged patients with T1/T2 rectal cancers more often than MRI (77% vs. 43%, respectively, $P = 0.226$), and these patients were overstaged more often by MRI compared to CT (54% vs. 23%, respectively, $P = 0.226$). In this study, the majority of patients with T3 tumors were correctly staged by MRI compared to CT (76% vs. 41%, respectively, $P = 0.08$), and more T3 disease was understaged by CT than MRI (54% vs. 18%, respectively, $P = 0.032$). CT and MRI staged T4 tumors equally well. In another study, MRI with a phased-array coil was highly accurate and superior to CT for the prediction of tumor infiltration in surrounding structures in locally advanced primary or recurrent rectal cancer. The sensitivity and specificity were 97% and 98% for MRI and 70% and 85% for CT, respectively. The accuracy was 80% for MRI and 19% for CT (43).

Because of its poor spatial resolution, MRI using a standard body coil does not provide sufficient data in rectal tumors (35). MRI using an endorectal coil has the same limitations as EUS, including a poor resolution of the pelvic structures surrounding the rectum due to the small field of view and the inability to insert the coil into patients with stenosing tumors (34).

MRI using a phased-array coil combines the advantages of the body and endorectal coils and provides a large field of view with high spatial resolution, which optimizes local and distant staging of rectal carcinoma during a single MRI session (21). This MRI technique depicts the detailed anatomy of the rectal wall and perirectal structures that are related to TME (35). Phased-array MRI also has the advantage of minor patient discomfort because no endorectal coil is inserted (21). For T-staging, the accuracy of phased-array MRI is similar to MRI with an endorectal coil (21). Although the initial results of phased-array MRI were poor, with an accuracy of 55% for Dukes classification and T-staging, subsequent studies using different techniques have reported sensitivity values above 90%, specificities of 70% to 98%, and an overall accuracy of 90% (29, 43–45).

Several techniques have been suggested for the use of phased-array MRI of the rectum. Rectal cleansing has been performed to prevent image misinterpretation due to stool residues. However, distension of the rectal lumen is controversial (20). In a study by Brown et al. (29), optimal results were obtained without rectal luminal distension. Two approaches have been defined for the basic sequence protocols for MRI of the rectum: the use of only T2-weighted sequences and the use of both T1- and T2-weighted sequences. For the use of T1-weighted sequences, the administration of a contrast agent is also suggested. However, contrast-enhanced T1-weighted sequences are not effective for the local staging of rectal cancer (8). A ferristene-based supermagnetic contrast medium has also been used for luminal distension of the rectum in conjunction with the acquisition of gadolinium-enhanced MRI. This double-contrast MRI method results in a sensitivity of 100%, specificity of 90%, and an accuracy of 90% for distinguishing tumor stages more severe than Dukes A (44). Different studies (8, 46, 47) have stated that contrast-enhanced T1-weighted images can be helpful for the differentiation of different rectal wall layers, which is impossible in plain T1-weighted images. However, the potential advantages of contrast-enhanced T1-weighted images in lesion staging are questionable because of discordant results and the lack of a clear comparison with nonenhanced T2-weighted images (48). In a study by Beets-Tan et al. (40), contrast-enhanced thin section MRI with a phased-array coil was helpful for the differentiation of reactive changes from true tumor invasion; they also reported that MRI could not be used to reliably distinguish between fibrosis with and without tumor cells.

In our study, we did not perform rectal distension, and no intravenous or rectal contrast agent was used. The overall accuracy of phased-array MRI for T-staging was 79.2%; the accuracies were 42.8% for T1 and T2 tumors and

94% for T3 tumors. The accuracy rate for staging T1 and T2 tumors in our study was low. Previous studies reveal that the differentiation of T1 from T2 lesions is difficult (21). One T1 tumor in our study was correctly staged by phased-array MRI with a sparing of the muscularis propria.

However, distinguishing T3 from T2 lesions is very important for the use of preoperative therapy, and the crucial criterion is the infiltration of perirectal fat. An absence of hypointensity of the muscle layer between the edge of the tumor and the extramural soft tissue is the minimal criterion for an assignment of pT3 (35). The presence of tumor signal intensity that extends into the perirectal fat is correlated best with a T3 tumor on MRI images, but it is difficult to distinguish spiculation in the perirectal fat that is caused by fibrosis only from spiculation that is caused by fibrosis containing tumor cells (29).

The mesorectal fascia represents the CRM, and tumoral involvement of the CRM has a high recurrence rate (49). Therefore, the main purpose of the preoperative staging of rectal tumors with MRI is to identify patients with T3 lesions, a subset of whom have potential CRM involvement and may benefit from neoadjuvant treatment (e.g., radiation therapy and chemotherapy) (20).

In our study, the low accuracy rate in the staging of T2 tumors was due to an overstaging of these lesions as T3 tumors. The literature states that this mistake is the most frequent pitfall because of the inability of MRI to distinguish the spiculation in the perirectal fat that is caused by fibrosis alone from spiculation that is caused by fibrosis containing tumor cells. Peritumoral fibrosis can be seen as spiculation with a lower signal intensity compared to the broad-based or nodular appearance of an advancing tumor margin (50). Furthermore, understaging between T3 and T2 tumors is a less common problem that may occur because of a microscopic infiltration of perirectal fat (21).

TME is the standard surgical approach in primary rectal cancer (9–12). With this surgical approach, the precise T-staging is less important than a correct diagnosis of mesorectal fascia involvement and the determination of the relationship between the tumor and anal sphincters (21). Invasion of the mesorectal fascia leads to adjunct radiochemotherapy to reduce the recurrence rate, but the invasion of anal sphincters changes the surgical technique (21). Recent studies reveal accuracy rates between 91%–100% for the prediction of mesorectal fascia invasion (24, 29, 41, 51, 52). In our study, one case with upper-middle anterior localized tumor was overstaged as a T4 tumor with mesorectal fascia invasion and a closeness to the prostate gland; the remaining 23 cases were T1, T2 and T3 tumors without mesorectal fascia involvement.

When assessing T3 tumors, it is very important to depict the minimum distance between the tumor edge and the mesorectal fascia for the accurate assessment of CRM. CRM involvement is associated with a higher risk of pelvic recurrence and poorer survival (17). According to Beets-Tan et al. (43), CRM can be predicted using MRI with a high accuracy and consistency, which allows for the preoperative identification of patients who are at risk of recurrence. Even with a successful TME, CRM positivity was 15%–20% (53).

A distance of 1 mm or less between the tumor edge and the lateral resection margin is significant for CRM positivity (21, 54, 55). Peschaud et al. (55) accepted a distance as 2 mm or less in their study because the study of Nagtegaal et al. (16) had emphasized that a tumor-free area of 2 mm was more clinically important for local and far recurrence. In our study, we used a criterion of 2 mm for CRM involvement, and the majority of cases were diagnosed correctly without CRM positivity. Only one case was overstaged as T4 using MRI. Overstaging with MRI is a common difficulty for the assessment of low localized rectal tumors due to the small amount of mesorectal fat tissue. This anatomic feature leads to a misdiagnosis of T-staging and CRM assessment. Peschaud et al. (55) reported that phased-array MRI findings in low localized tumors was not as accurate as in middle localized tumors. In our study, the overall accuracy of phased-array MRI in 8 low localized rectal tumors was 50%, with an overstaging in 4 of these cases.

The low accuracy of MRI in the distal rectum, especially in anterior localized tumors, has been stated in several studies (40, 41). Posterior perirectal adipose tissue is thicker than anterior perirectal adipose tissue (56). This difference leads to the excellent visualization of posterior mesorectal fascia and makes it difficult to assess the anterior mesorectal fascia together with Denonvilliers' fascia (57).

Phased-array MRI has a larger field of view, which allows for the evaluation of lymph nodes that are outside the field of view of EUS and endorectal MRI (21). However, the overall accuracy of MRI for the detection of lymph node involvement ranges between 59% and 95% (34). Many studies suggest an increase in lymph node size as a predictor of nodal involvement (58, 59). More recent studies suggest that multiple criteria should be used to improve accuracy (60). Brown et al. (31) confirmed that morphological criteria, such as an irregular borders and mixed signal intensity, in mesorectal lymph nodes greater than 3 mm and 5 mm are a better predictor of lymph node status than size alone. In our study, we obtained an accuracy of 58% in the assessment of nodal involvement in which we evaluated the lymph node as metastatic with a short axis that was greater than 5 mm.

The main limitation of our study was the small number of patients. The number of T2 lesions was low. There was only one T1 lesion and no T4 lesions. The small number of patients had a negative effect on the general preoperative tumor staging purpose of the study. Because of a lack of T4 lesions, we were unable to assess the real accuracy of MRI for the detection of mesorectal fascia involvement. With the exception of one case that was overstaged as T4 using MRI, all of the cases lacked mesorectal fascia involvement. This deficiency biased the assessment of the accuracy of MRI for the prediction of mesorectal fascia involvement, which was 95.8%. However, this study, together with Beets-Tan et al. (40) and Branagan et al. (61) shows that MRI can predict patients in whom the CRM is not involved, which allows them to proceed to surgery without the need for preoperative radiotherapy.

With minimal patient discomfort and the ability to assess stenosing tumors and mesorectal lymph node involvement, phased-array MRI has obvious advantages over other imaging techniques, such as EUS and endorectal MRI. Phased-array MRI is the best modality for the preoperative staging of rectal tumors, especially for the differentiation of T2 and T3 tumors

because it detects mesorectal fascia involvement, which is very important for treatment planning. Unfortunately, phased-array MRI can overstage low localized rectal tumors. Larger studies that evaluate the mesorectal fascia and mesorectal fat involvement will aid in the determination of definite involvement criteria for the use of MRI. Additionally, low localized rectal tumors must be further studied to reduce misstaging with MRI.

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Conflict of interest disclosure

The authors declared no conflicts of interest.

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