

Assessment of T and N staging with MRI₃T in lower and middle rectal cancer and impact on clinical strategy

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Abstract

Background: To determine the diagnostic accuracy of preoperative T/N stage using MRI in lower and middle rectal cancer patients and the impacts on clinical decision-making.

Patients and methods: There were 354 patients recruited from May 2017 to February 2019. MRI was performed within 2 weeks before surgery. Histopathologic results were evaluated for the postoperative T/N stage and MRI diagnostic accuracy was assessed based on the postoperative histopathologic results. Accuracy, sensitivity, specificity, positive predictive value, negative predictive value, and Kappa values were used to evaluate MRI diagnostic accuracy and analysis consistency compared with postoperative histopathologic staging.

Results: Overall MRI diagnostic accuracy was 78.2% and 56.8% for T1–4 and N0–2 staging. The Kappa values were 0.625 and 0.323 for T1–4 and N0–2 staging, respectively. After combination, MRI diagnostic accuracy was 85% and 69.5% for T and N staging. The Kappa values were 0.693 and 0.4 for T and N staging. The diagnostic accuracy of MRI for treatment decision-making was 79.1%.

Conclusion: MRI enables a highly accurate preoperative assessment of T stage but only a fairly accurate preoperative assessment of the N stage for rectal cancer with surgery. The diagnostic accuracy of MRI for treatment decision-making is promising.

Liping Xu, Zhaoyue Zhang, Qin Qin, and Chi Zhang contributed equally to this work.

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Keywords

Rectal cancer, magnetic resonance imaging staging, diagnostic accuracy, treatment decision-making, pathological staging, neoadjuvant chemoradiotherapy

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Introduction

Recently, rectal cancer has become a leading cause of cancer-related deaths in China and worldwide.^{1,2} Patients with rectal cancer undergo medical imaging examinations to determine the extent of the disease and to decide on the optimal treatment method. The tumor/node/metastasis (TNM) system is used to describe the extent of cancer.³ Endorectal ultrasonography (EUS), computed tomography (CT), and magnetic resonance imaging (MRI) are used to evaluate the T stage of the primary tumor and the N stage of the surrounding lymph nodes before treatment.^{4,5} These examinations help to determine the optimal approach: surgery first or neoadjuvant chemoradiotherapy (CRT) first.

High-resolution MRI has become one of the most important examinations for rectal cancer staging because of the high concordance between radiological data and pathological findings.^{6,7} The routine use of MRI provides clinicians the ability to determine which selective management strategies to implement, including surgery alone for patients with low-risk tumors (pT2, N0, and no risk factors) or neoadjuvant therapy followed by surgery for those with locally advanced rectal cancer (i.e., \geq T3 and/or N+ stage and/or other risk factors).^{8,9} However, the accuracy of all current imaging modalities remains limited. Misdiagnoses of the T and N stages, including overestimation and underestimation, lead to overtreatment or undertreatment based on the current National Comprehensive Cancer Network (NCCN) guidelines, resulting in unexpected outcomes. The purpose of the present study was to assess the accuracy of MRI for

preoperative TN staging of lower and middle rectal cancer patients, compare the results with the postoperative histological stage, and evaluate the impacts on clinical decision-making.

Materials and methods

Patients

The study population consisted of patients who underwent radical surgery between May 2017 and February 2019 at the First Affiliated Hospital of Nanjing Medical University. The inclusion criteria were as follows: (1) confirmed pathological diagnosis of rectal cancer by endoscopy-guided biopsy before surgery; (2) tumor located \leq 10 cm from the anal verge; (3) preoperative MRI T/N staging within 2 weeks before surgery; and (4) postoperative pathological T/N staging. Patients were excluded if they met the following criteria: (1) no original rectal tumor (second or recurrent tumor); (2) received neoadjuvant treatment before surgery; (2) tumor location $>$ 10 cm from the anal verge; and (3) had no MRI exam or MRI T/N staging. The present study was performed in accordance with the ethical standards of the World Medical Association Declaration of Helsinki, and the study was approved by the Institutional Research Ethics Committee at the First Affiliated Hospital of Nanjing Medical University. Eligible patients were asked whether they would consider participating in the study. Oral and written information was provided to each potential participant, and each patient provided written informed consent if they agreed to participate.

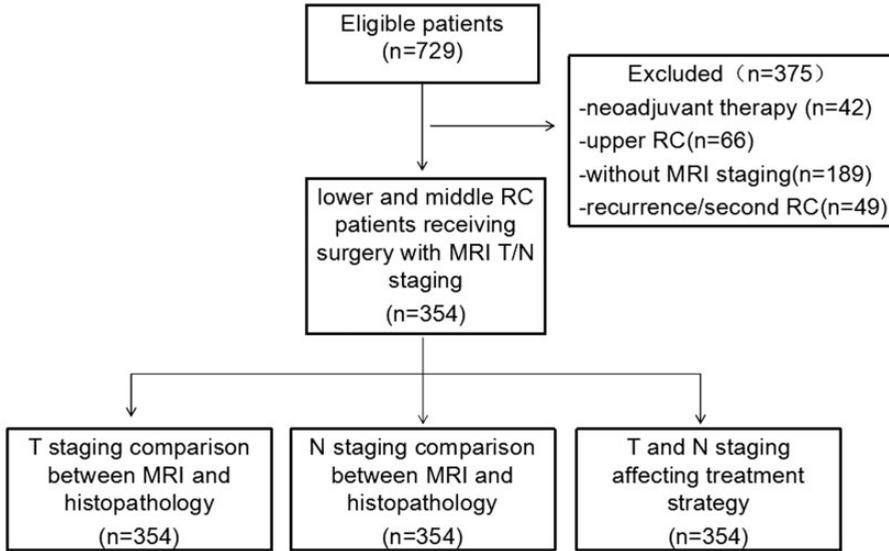


Figure 1. Flow chart of the study.

Among the 729 patients, the following patients were excluded: 42 who received neoadjuvant CRT or chemotherapy; 66 patients with inadequate tumor locations; 189 patients who did not receive MR scans; and 49 patients who were confirmed with no original rectal cancer (Figure 1).

MRI examination

MRI was performed for all patients using a Siemens Syngo 3.0 T whole-body system (Magnetom Avanto, Siemens, Erlangen, Germany) with a phased-array multicoil. The patients were placed in a supine position on an MR table with their feet entering the MR gantry. After the scout scan, mid-line axial and sagittal T2-weighted turbo spin-echo (T2W-TSE) images were obtained. The parameters of the scan protocol were as follows: repetition time (TR), 3000 to 4000 ms; echo time (TE), 70 to 90 ms; field of view (FOV), 28 to 32 cm × 28 to 32 cm; matrix, 276 × 384; slice thickness, 5 mm; and gap, 1 mm. These images were used to plan the high-resolution T2W-TSE

scans, which were perpendicular to the long axis of the rectum. For the lower third rectal tumors, an additional oblique coronal scan along the long axis of the anal canal was also acquired. The scan protocol was as follows: TR, 2400 to 3500 ms, TE, 90 to 100 ms; FOV, 18 cm × 18 cm; matrix, 272 × 320; slice thickness, 3 mm; gap, 0 mm; and in-plane resolution, 0.66 × 0.56. The whole examination took approximately 30 minutes.

T/N stage assessment criteria. The criteria that were used to determine the T stage were based on the American Joint Committee on Cancer seventh TNM classification. T/N staging evaluation was performed based on previously published articles.^{6,7,10}

Surgery and histopathologic study

Surgery was performed in 354 patients. The resected specimens were opened on the opposite side of the tumor and fixed in formalin for 24 hours after surgery. The specimens were then sliced transversely at 5-mm

intervals. The slices were embedded in paraffin, sectioned, and examined histologically after hematoxylin and eosin (HE) staining. The depth of tumor invasion was classified based on the TNM classification.⁹ The pathologist was blinded to the MRI findings.

Statistical analysis

The diagnostic accuracy, sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were calculated for each T stage and N stage. A weighted Kappa value was calculated. A weighted Kappa value less than 0 indicated poor agreement, 0 to 0.2 indicated slight agreement, 0.21 to 0.40 indicated fair agreement, 0.41 to 0.60 indicated moderate agreement, 0.61 to 0.80 indicated substantial agreement, and 0.81 to 1.0 indicated almost perfect agreement. Receiver operator characteristics (ROC) curve analyses were performed and the area under the curve (AUC) was calculated. Statistical analyses were performed with using SPSS version 19.0 (SPSS Inc., IBM Corp., Armonk, NY, USA).

Results

Patient demographics and clinical data

There were 354 patients (236 men and 118 women) with a mean age of 62.30 ± 10.77 years, and a range of 29 to 89 years who were included in the final analysis. Overall, 48 (13.6%) patients had ultra-low rectal cancer (≤ 3 cm), 108 (30.5%) patients had lower rectal cancers (3 to 5 cm from the anal verge), and 198 (55.9%) patients had mid-rectal cancer (5 to 10 cm from the anal verge) (Table 1).

T staging of rectal cancer. After histopathologic examinations of the 354 neoplasms, 31 (8.76%) were staged as pT1, 113 (31.92%) as pT2, 196 (55.37%) as pT3, and 14 (3.95%) as pT4 (Table 2). The accuracy by

Table 1. Patient characteristics.

Characteristics	Number of patients (%)	
Sex		Age, Median
Male	236 (66.7%)	62.74
Female	118 (33.3%)	61.42
Age, median ± SD (years)		62.30 ± 10.769
Tumor size		
≤3 cm	48 (13.6%)	
3–5 cm	108 (30.5%)	
5–10 cm	198 (55.9%)	

N = 354.

SD, standard deviation.

MRI of each T stage was 94.6% for T1, 79.7% for T2, 83.6% for T3, and 98.6% for T4 (Table 2). The sensitivity of each T was 48.4% for T1, 78.8% for T2, 82.7% for T3, and 78.6% for T4. The specificity of each T stage was 99.1% for T1, 80.1% for T2, 84.8% for T3, and 99.4% for T4. The PPV of each T stage was 83.3% for T1, 65.0% for T2, 87.1% for T3, and 84.6% for T4. The NPV for each T stage was 95.2% for T1, 88.9% for T2, 79.8% for T3, and 99.1% for T4. The overall MR accuracy was 78.2%. The Kappa value for T staging was 0.625.

After combining T1 and T2 as T1–2 and combining T3 and T4 as T3–4, the results for the 354 patients were as follows: 144 (40.68%) were staged as pT1–2 and 210 (59.32%) were pT3–4. The overall MR accuracy for T staging was 85.0%, and the Kappa value for T staging was 0.693 (Table 3).

N staging of rectal cancer. After histopathologic examinations of the 354 patients, the N stage was determined. The overall MR accuracy for each N stage was 56.8%. The accuracy of each N stage was 49.8% for N0, 43.7% for N1, and 64.2% for N2. The sensitivity for N0, N1, and N2 was 58.1%, 60%, and 47.6%, respectively. The specificity for N0, N1, and N2 was 82.8%, 68.1%, and 84.9%, respectively. The PPV

Table 2. T staging of rectal cancer with MRI compared with the histopathology results.

MRI T staging	Histopathologic T staging			
	T1	T2	T3	T4
T1	15	3	0	0
T2	16	89	32	0
T3	0	21	162	3
T4	0	0	2	11
Accuracy rate (%)	94.6% (335/354)	79.7% (282/354)	83.6% (296/354)	98.6% (349/354)
Sensitivity (%)	48.4% (15/31)	78.8% (89/113)	82.7% (162/196)	78.6% (11/14)
Specificity (%)	99.1% (320/323)	80.1% (193/241)	84.8% (134/158)	99.4% (338/340)
PPV (%)	83.3% (15/18)	65.0% (89/137)	87.1% (162/186)	84.6% (11/13)
NPV (%)	95.2% (320/336)	88.9% (193/217)	79.8% (134/168)	99.1% (338/341)

N = 354.

Total accuracy = 78.2%.

PPV, positive predictive value; NPV, negative predictive value; MRI, magnetic resonance imaging.

Kappa = 0.625, P = 0.000, P < 0.05.

Table 3. T staging of rectal cancer: Comparison of the MRI and histopathologic findings.

MRI T staging	Histopathologic T staging	
	T1–2	T3–4
T1–2	123	32
T3–4	21	178
Accuracy rate (%)	85% (301/354)	
Sensitivity (%)	85.4% (123/144)	84.8% (178/210)
Specificity (%)	84.8% (178/210)	85.4% (123/144)
PPV (%)	79.4% (123/155)	89.4% (178/199)
NPV (%)	89.4% (178/199)	79.4% (123/155)

N = 354.

PPV, positive predictive value; NPV, negative predictive value, MRI, magnetic resonance imaging.

Kappa = 0.693, P = 0.000, P < 0.05.

for N0, N1, and N2 was 79.9%, 42.6%, and 40.5%, respectively. The NPV for N0, N1, and N2 was 62.8%, 81.2%, and 88.2%, respectively. The Kappa value for N staging was 0.323 (Table 4).

N1 and N2 were combined as N+. For the 354 operative specimens, the overall MR accuracy for N staging was 69.5%. For N0 and N+, the sensitivity was 58.1% and 82.8%, the specificity was 82.8% and 58.1%, the PPV was 79.9% and 62.8%, and the NPV was 62.8% and 79.9%. The Kappa value for N staging was 0.4 (Table 5).

Effects on treatment strategy of MRI imaging staging. The accuracy rate of MRI for treatment decision-making was 79.1% (Table 6). The accuracy rate for MRI staging in determining which patients should receive surgery first was 66.28% (57/86). The sensitivity for patients receiving surgery first determined by MRI staging was 55.9%. The probability of underestimation was 33.72% (29/86) (Table 6, Figure 2). The accuracy of MRI staging for determining which patients should receive neoadjuvant therapy first was 83.2% (223/268), and the sensitivity for patients receiving

Table 4. N staging of rectal cancer: Comparison of the MRI and histopathologic findings.

MRI N staging	Histopathologic N staging		
	N0	N1	N2
N0	111	22	6
N1	54	60	27
N2	26	18	30
Accuracy rate (%)	49.8% (107/215)	43.7% (94/215)	64.2% (138/215)
Sensitivity (%)	58.1% (111/191)	60% (60/100)	47.6% (30/63)
Specificity (%)	82.8% (135/163)	68.1% (173/254)	84.9% (247/291)
PPV (%)	79.9% (111/139)	42.6% (60/141)	40.5% (30/74)
NPV (%)	62.8% (135/215)	81.2% (173/213)	88.2% (247/280)

N = 354.

PPV, positive predictive value; NPV, negative predictive value; MRI, magnetic resonance imaging.

Kappa = 0.323, P = 0.000, P < 0.05.

Table 5. N staging of rectal cancer: Comparison of the MRI and histopathologic findings.

MRI N staging	Histopathologic N staging	
	N0	N+
N0	111	28
N+	80	135
Accuracy rate (%)	69.5% (246/354)	
Sensitivity (%)	58.1% (111/191)	82.8% (135/163)
Specificity (%)	82.8% (135/163)	58.1% (111/191)
PPV (%)	79.9% (111/139)	62.8% (135/215)
NPV (%)	62.8% (135/215)	79.9% (111/139)

N = 354.

PPV, positive predictive value; NPV, negative predictive value; MRI, magnetic resonance imaging.

Kappa = 0.400, P = 0.000, P < 0.05.

Table 6. Effects of MRI imaging staging on the treatment strategy.

MRI staging	Histopathologic staging	
	Surgery	Neoadjuvant CRT
Surgery	57 (66.28%)	29 (33.72%)
Neoadjuvant CRT	45 (16.79%)	223 (83.21%)
Accuracy	79.1% (280/354)	79.1% (280/354)
Sensitivity	55.9% (57/102)	88.5% (223/252)
Specificity	88.5% (223/252)	55.9% (57/103)
PPV	66.3% (57/86)	83.2% (223/268)
NPV	83.2% (223/268)	66.3% (57/86)

N = 354.

PPV, positive predictive value; NPV, negative predictive value; MRI, magnetic resonance imaging; CRT, chemoradiotherapy.

Kappa = 0.665, P = 0.000, P < 0.05.

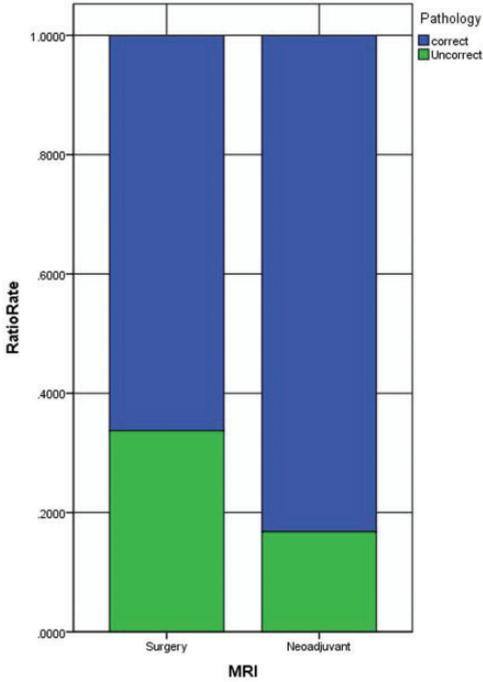


Figure 2. Accuracy and error rate of MRI for clinical decision compared with pathologic results. MRI, magnetic resonance imaging.

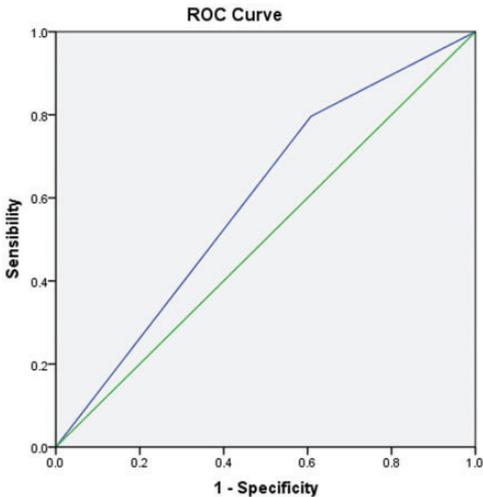


Figure 3. The ROC curve of MRI assessment for decision-making. AUC = 0.594. ROC, receiver operating characteristics; MRI, magnetic resonance imaging; AUC, area under the curve.

neoadjuvant therapy first determined by MRI staging was 88.5%. The probability of overestimation was 16.79% (45/268) (Table 6, Figure 2). MRI is more likely to underestimate the stage and result in undertreatment compared with overestimating the stage and result in overtreatment.

Figure 3 shows the ROC curves of MRI assessment for decision-making. ROC analysis revealed that the AUC was 0.594.

Discussion

Currently, neoadjuvant chemotherapy and radiotherapy before surgery are crucial for the treatment of locally advanced rectal cancer. The overstaging of rectal tumors may lead to the overtreatment for patients with T1 or T2 tumors and an elevated risk for therapy-related morbidity and mortality.¹⁰ Understaging means sacrificing local control. Therefore, with the increasing use of neoadjuvant therapy in patients with rectal cancer, accurate staging is needed to avoid unnecessary treatment for early stage tumors.

The accuracy of MRI for T staging of rectal cancer ranged from 67% to 83%,^{11–14} which mainly depended on the difficulty in differentiating between T1 and T2 tumors as well as the desmoplastic response of some tumors that might lead T2 tumors to be misdiagnosed as T3 tumors.¹⁵

Brown et al.¹⁶ demonstrated 100% accuracy in T staging of 28 primary rectal cancers using high-resolution images. Poon et al.¹⁷ reported an overall accuracy of 74% using a similar technique. Rao et al.¹⁸ showed that the overall accuracy was 85.1% for T staging. Our study showed that the total accuracy of T1–4 staging by MRI was 78.2%. The Kappa value for T1–4 staging was 0.625, indicating substantial agreement with the histopathologic results. After combining T1 and T2 together as T1–2 and T3 and T4 together

as T3–4, the overall MR accuracy was 85.0% for T1–2 and T3–4. The Kappa value for T1–2 and T3–4 staging was 0.693, indicating substantial agreement with the histopathologic results. Our results suggest that MRI has become one of the most accurate T staging modalities for rectal cancer.

Overall, MR tended to be less accurate for N staging of rectal cancer than for T staging. In our study, the overall MR accuracy for all N0, N1, and N2 stages was 56.8%. The Kappa value for all N stages was only 0.323, indicating fair agreement with the histopathologic results. After combining N1 and N2 together as N+, the overall MR accuracy for N staging was 69.5%. The Kappa value for N staging was 0.4, indicating fair agreement with the histopathologic results. Up to 15% of perirectal lymph nodes are too small to be identified using MRI.¹⁹ Therefore, detecting lymph node metastases is difficult.

The sensitivity and specificity of MRI for T staging of the tumor varies considerably, with the sensitivity that ranges from 29% to 57% and a specificity that ranges from 50% to 83%.^{11–14} Moreover, the diagnostic sensitivity and specificity of MRI are also largely dependent on the experience of the radiologists.²⁰ Thus, the results differ greatly among different institutes worldwide, and they are not helpful for clinical practice. The impact of MRI staging on treatment decision-making needs to be determined. However, few reports about this topic exist.

In our study, the diagnostic accuracy rate of MRI for treatment decision-making was 79.1%. The understaging rate was 33.72%. The over-staging rate was 16.79%, which was similar to that in previous reports (which ranged from 15% to 30%),²¹ but lower compared with Maas et al.¹⁰ who found a mean overstaging rate of 43% at 1.5 T and 57% at 3 T. MRI is more likely to underestimate the TN stages

and result in undertreatment compared with overestimation of the TN stages, which would result in overtreatment.

There were some limitations in this study. First, this retrospective study included an uncontrolled methodology and a limited number of patients from a single institution. Second, mesorectal fascia infiltration in rectal cancer was not assessed, which is also an important factor for treatment decision-making.

Conclusion

MRI enables the highly accurate preoperative assessment of T stages and fairly accurate preoperative assessment of N stage for mid–low rectal cancer. The diagnostic accuracy of MRI for treatment decision-making was reliable.

Declaration of conflicting interest

The authors declare that there is no conflict of interest.

We declare that this manuscript have not been copyrighted or published previously, and it is not under consideration for publication elsewhere, in whole or in part.

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