Received: 2 November 2019 | Accepted: 28 April 2020 | Published on: 6 August 2020

DOI: 10.1111/ajco.13368

ORIGINAL ARTICLE

WILEY

Value of 3Tesla MRI in the preoperative staging of mid-low rectal cancer and its impact on clinical strategies

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Funding information
National Natural Science Foundation of China, Grant/Award Numbers: 81874217, 81703028; Young Medical Key Talents of Jiangsu Province, Grant/Award Number: QNRC2016572; Priority Academic Program Development of Jiangsu Higher Education Institutions, Grant/Award Number: JX10231801; Suzhou Clinical Medical Expert Team, Grant/Award Number: SZYJTD201824

Abstract

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

Patients and methods: A total of 211 patients were recruited from October 2015 to March 2017 in this retrospective study. High-resolution MRI was performed within 2 weeks before surgery. Histopathologic results were evaluated for the postoperative T/N stage and the diagnostic accuracy of MRI was assessed according to the postoperative histopathologic results. The accuracy, sensitivity, specificity, positive predictive value and negative predictive value were evaluated for T/N staging and κ values were used to evaluate MRI consistent analysis compared with postoperative histopathologic staging.

Results: The overall MRI diagnostic accuracy was 79.62% for T1-4 staging and 54.50% for N0-2 staging. The κ values were 0.619 and 0.255 for T1-4 and N0-2 staging, respectively. The diagnostic accuracy of MRI for treatment decision-making was 80.57%.

Conclusion: MRI allows a highly accurate preoperative assessment of T stage but only a fairly accurate preoperative assessment of N stage for rectal cancer. The diagnostic accuracy of MRI for treatment decision-making is promising, but additional studies are needed to validate these findings in a larger sample size from multiple centers.

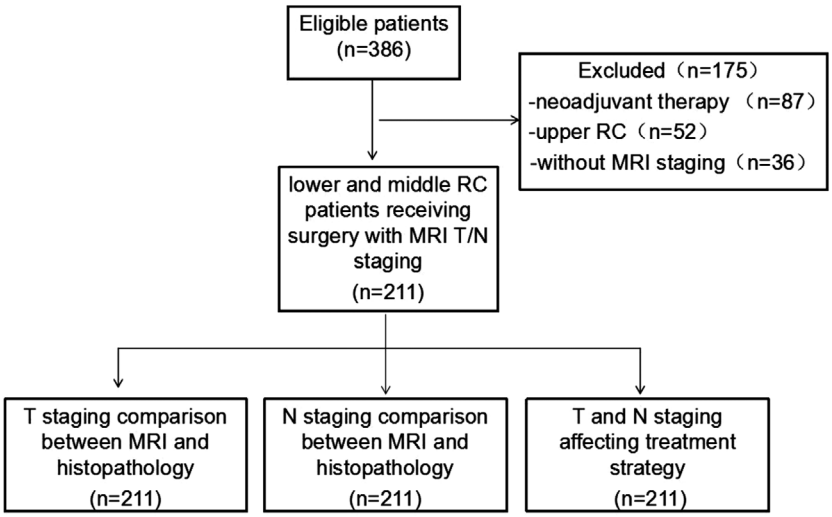
KEYWORDS
diagnostic accuracy, histopathology, magnetic resonance imaging staging, rectal cancer

1 | INTRODUCTION

In recent years, rectal cancer has become a leading cause of cancer-related deaths both 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

FIGURE 1 Flow diagram of the study



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., ≧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 on the basis of the current National Comprehensive Cancer Network (NCCN) guidelines, resulting in unexpected outcomes. Therefore, the purpose of this study was to assess the accuracy of MRI for the 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.

2 | MATERIALS AND METHODS

2.1 | Patients

This retrospective study was approved by the Institutional Research Ethics Committee of the First Affiliated Hospital of Nanjing Medical University. The study population consisted of patients who underwent radical surgery between October 2015 and March 2017 at the First Affiliated Hospital of Nanjing Medical University. The inclusion criteria were as follows: (1) preoperative pathological diagnosis of rectal adenocarcinoma diagnosed by endoscopy-guided biopsy; (2) tumor located ≤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) received previous neoadjuvant CRT or chemotherapy before the MRI scan or surgical resection; (2) tumor located >10 cm from the anal verge and (3) had no MRI staging. Among the 386 patients, the following patients were excluded: 87 who received neoadjuvant CRT (nCRT) or chemotherapy; 52 who had unsuitable tumor locations; and 36 who did not receive MR scans (Figure 1).

2.2 | MRI examination

MRI was performed for all patients using a Siemens Syngo 3.0 T whole-body system (Magnetom Avanto, Siemens) with a phased-array multicoil. The patients were placed in a supine position on an MR table with their feet entering the MR gantry. Then scout scan, midline 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): 3000–4000 ms, echo time (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 the high-resolution T2W-TSE scans, which were perpendicular to the long axis of the rectum. For lower third rectal tumors, an additional oblique coronal scan along the long axis of the anal canal was also obtained. The scan protocol was as follows: TR: 2400–3500 ms, TE: 90–100 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 half an hour.

2.3 | T/N stage assessment criteria

The criteria used for determining the T stage were based on the American Joint Committee on Cancer eighth TNM classification. T/N staging evaluation was performed by previously published papers.[6,7,10]

For MRI T stage, the criteria are as follows. T1, tumor invades submucosa but does not extend into circular muscle layer. T2, tumor invades but does not penetrate muscularis propria (MP). T3, tumor invades subserosa through MP. T4, tumor invades peritoneal refection or other organs. Normal rectum layers and examples of T1-4 are showed in Figures 2 and 3.

Criteria for positive lymph node metastasis included a short-axis diameter of ≥5 mm, an irregular border, mixed signal intensity or the presence of a high intensity nodule within the lymph node.

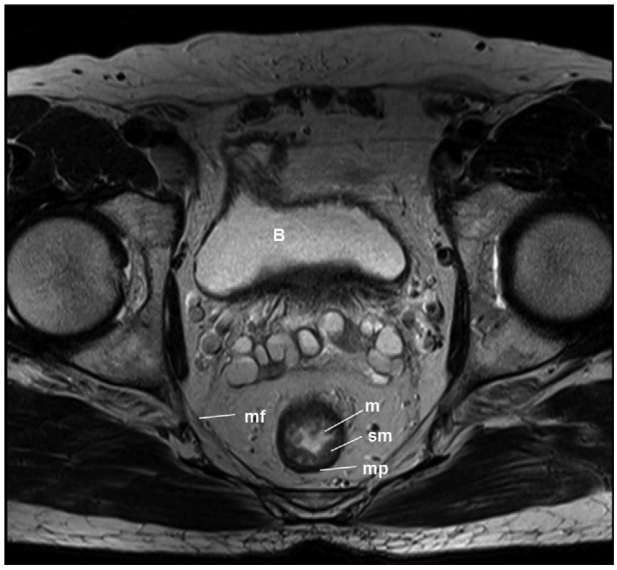


FIGURE 2 T2WI TSE MR image of normal rectal structure. m, rectum mucosa; sm, submucosa; mp, muscularis propria; mf, mesorectal fascia; B, bladder

Two experienced abdominal diagnostic radiologist who are blind to clinical and histopathologic information interpreted each MRI image independently on the workstation monitor. Differences in assessment were resolved by means of consensus.

2.4 | Surgery and histopathologic study

Total mesorectal excision (TME) was performed in 211 patients. Resected specimens were opened on the opposite side of the tumor and fixed in formalin for 24 h after surgery. The specimens were then sliced transversely at intervals of 5 mm. The slices were embedded in paraffin, sectioned and examined histologically after hematoxylin and eosin (HE) staining. The depth of tumor invasion was classified according to the TNM classification.[9] The pathologist was blinded to the MRI findings.

2.5 | 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. The weighted κ value was also calculated. A weighted κ value less than 0 indicated poor agreement, 0–0.2 indicated slight agreement, 0.21–0.40 indicated fair agreement, 0.41–0.60 indicated moderate agreement, 0.61–0.80 indicated substantial agreement and 0.81–1.0 indicated almost perfect agreement. Statistical analyses were performed with SPSS version 19.0 (SPSS Inc., Chicago, IL, USA).

3 | RESULTS

3.1 | Patient demographics and clinical data

A total of 211 patients (125 males and 86 females) with a mean age of 60.52 ± 11.20 years and a range of 22–85 years were included in the final analysis. In total, 97 (45.97%) patients had mid-rectal cancer (5–10 cm from the anal verge), and 114 (54.03%) patients had lower rectal cancers (less than 5 cm from the anal verge) (Table 1).

The histologic diagnoses were well-differentiated adenocarcinoma for one (0.47%) patient, moderately differentiated adenocarcinoma for

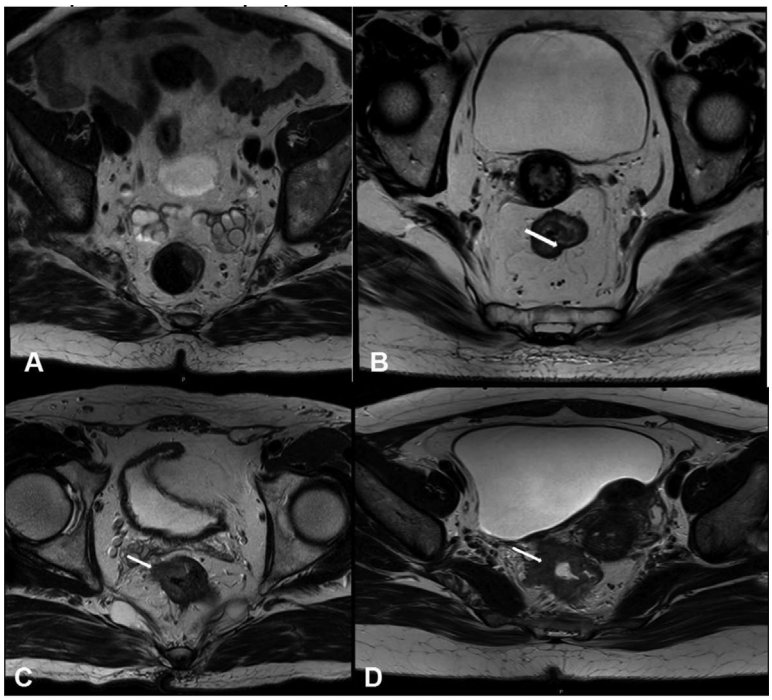


FIGURE 3 T2WI-TSE MR images of rectal cancer. (A) T1 stage, (B) T2 stage, (C) T3 stage, (D) T4 stage

TABLE 1 Patient characteristics ($n = 211$)

Characteristics	Number of patients (%)	
Sex		Age, median
Male	125 (59.2%)	60.50 ± 12.76
Female	86 (40.8%)	60.54 ± 10.05
Age, median ± SD (years)		60.52 ± 11.20
Tumor location (cm)		
≤5 cm from anal verge	97 (45.97%)	
5–10 cm from anal verge	114 (54.03%)	
Pathology		
Adenocarcinoma	185 (87.68%)	
Mucinous adenocarcinoma	23 (10.90%)	
Signet-Ring cell carcinoma	3 (1.42%)	
Tumor differentiation, *n* (%)		
Well	1 (0.47%)	
Moderate	99 (46.9%)	
Poor	111 (52.6%)	

99 (46.9%) patients, and poorly differentiated adenocarcinoma for 111 (52.6%) patients. Regarding histologic type, 185 (87.68%) tumors were common adenocarcinomas, 23 (10.90%) were mucinous adenocarcinomas and 3 (1.42%) were signet-ring cell carcinomas (Table 1).

3.2 | T staging of rectal cancer

Of all the 211 cases, 4 (1.90%) were staged as cT1, 72 (34.12%) as cT2, 133 (63.03%) as cT3 and 2 (9.5%) as cT4 with MRI staging. After histopathologic examinations of the 211 neoplasms, 12 (5.69%) were staged as pT1 (Table 2), 69 (32.70%) as pT2, 118 (55.92%) as pT3 and 12 (5.69%) as pT4. The accuracy of each T stage was 96.21% for T1, 85.31% for T2, 83.41% for T3 and 94.31% for T4 (Table 2). The overall MR accuracy was 79.62%. The κ value for T staging was 0.619.

TABLE 3 N staging of rectal cancer: comparison of the MRI and histopathologic findings ($n = 211$)

	Histopathologic N staging		
MRI N staging	N0	N1	N2
N0	70	22	7
N1	37	27	12
N2	13	5	18
Accuracy (%)	63.03 (133/211)	63.98(135/211)	82.46 (174/211)
Sensitivity (%)	58.33 (70/120)	50 (27/54)	48.64 (18/37)
Specificity (%)	68.48 (63/92)	68.79 (109/157)	89.66 (156/174)
PPV (%)	70.71 (70/99)	35.53 (27/76)	50.00 (18/36)
NPV (%)	55.75 (63/113)	80.00 (108/135)	89.14 (156/175)

Total accuracy rate = 54.50%; $\kappa = 0.255$, $P = 0.000$, $P < 0.05$.

3.3 | N staging of rectal cancer

Of all the 211 patients, 99 (46.92%) were staged as cN0, 76 (36.02) as cN1 and 36 (17.06%) with MRI. After histopathologic examination of the 211 neoplasms, 120 (56.87%) were staged as pN0 (Table 3), 54 (25.59%) as pN1 and 37 (17.54%) as pN2. The accuracy of each N stage was 63.01% for N0, 63.98% for N1 and 82.46% for N2 (Table 3). The overall MR accuracy for N staging was 54.50%. The κ value for N staging was 0.255 (Table 3).

3.4 | Effects of MRI staging on the treatment strategy

Since nCRT was recommended therapy for LARC basis of the current NCCN guidelines, however, actually, a large percentage of LARC patients choose surgery as their first choice for different reasons. We presumed all 211 patients received the standard treatment as guidelines base on preoperative MRI T/N stage. And then we obtained the correct and error rate of MRI accuracy on treatment decision

TABLE 2 T staging of rectal cancer with MRI compared with the histopathology results ($n = 211$)

	Histopathologic T staging			
MRI T staging	T1	T2	T3	T4
T1	4	0	0	0
T2	8	55	9	0
T3	0	14	108	11
T4	0	0	1	1
Accuracy (%)	96.21 (203/211)	85.31 (180/211)	83.41 (176/211)	94.31 (199/211)
Sensitivity (%)	33.33 (4/12)	79.71 (55/69)	91.53 (108/118)	8.33 (1/12)
Specificity (%)	100 (199/199)	85.62 (125/142)	73.12 (68/93)	99.50 (198/199)
PPV (%)	100 (4/4)	72.37 (55/76)	81.20 (108/133)	50.00 (1/2)
NPV (%)	96.14 (199/207)	89.93 (125/139)	87.18 (68/78)	94.76 (198/209)

Total accuracy rate = 79.62%; PPV, positive predictive value; NPV, negative predictive value. $\kappa = 0.619$, $P = 0.000$, $P < 0.05$.

TABLE 4 Effects of MRI staging on the treatment strategy ($n = 211$)

	Histopathologic staging	
MRI staging	Surgery	Neoadjuvant CRT
Surgery	38	14
Neoadjuvant CRT	27	132
Accuracy (%)	80.57 (170/211)	80.57 (170/211)
Sensitivity (%)	58.46(38/65)	90.41 (132/146)
Specificity (%)	90.41 (132/146)	58.46(38/65)
PPV (%)	73.76 (38/52)	83.02 (132/159)
NPV (%)	83.02 (132/159)	73.76 (3//52)

Total accuracy rate = 80.57%; $\kappa = 0.517$, $P = 0.000$, $P < 0.05$.

compared to the golden standard–pathological results. The diagnostic accuracy of MRI for treatment decision-making was 80.57% (Table 4). The diagnostic accuracy of MRI staging for determining which patients should receive surgery first was 73.08% (38/52), and the underestimation rate was 26.92% (14/52) (Figure 4). The diagnostic accuracy of MRI staging for determining which patients should receive neoadjuvant therapy first was 83.02% (132/159) (Table 4), and the overestimation rate was 16.98% (27/159) (Figure 4). MRI is more likely to underestimate the stage and result in undertreatment than overestimate the stage and result in overtreatment.

4 | 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 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 the T staging of rectal cancer ranges from 67% to 83%,[11–14] which mainly depends 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 a 100% accuracy in the 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 79.62%. The κ value for T1-4 staging was 0.619, 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.

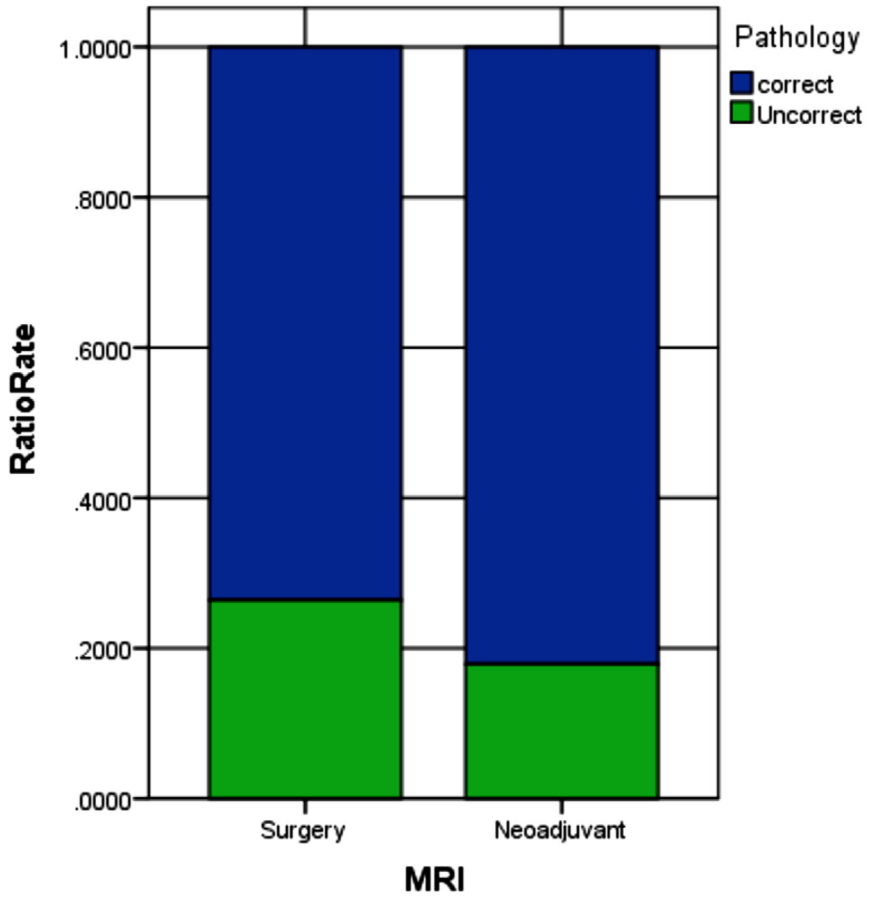


FIGURE 4 Accuracy and error rates of MRI for clinical decision compared to pathological results. The diagnostic accuracy of MRI staging for determining which patients should receive surgery first was 73.08%, and the underestimation rate was 26.92% (14/52). The diagnostic accuracy of MRI staging for determining which patients should receive neoadjuvant therapy first was 83.02%, and the overestimation rate was 16.98% (27/159) [Colour figure can be viewed at wileyonlinelibrary.com]

Overall, MR was inclined 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 54.50%. The κ value for all N stages was only 0.255, indicating fair agreement with the histopathologic results. Up to 15% of perirectal lymph nodes are too small to be depicted by MRI.[19] Therefore, detecting lymph node metastases is highly difficult.

The sensitivity and specificity of MRI for tumor T staging varies considerably, with a 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 radiologist.[20] Thus, the results differ greatly among institutes worldwide and are not helpful for clinical practice. The impact of MRI staging on treatment decision-making is greatly needed. However, few reports about this topic exist.

For the first time, to our knowledge, we evaluated the impact on clinical decision based on MRI preoperative T/N staging. In our study, the diagnostic accuracy of MRI for treatment decision-making was 80.57%. The accuracy of MRI staging for determining which patients should receive surgery first was 73.08%. The understaging rate was 26.92%. The accuracy of MRI staging for determining which patients should receive neoadjuvant therapy first was 83.02%. Although the overstaging rate in this study was 16.98%, which was similar to that in previous reports (ranging from 15% to 30%),[21] it was lower than that reported in Monique Maas's study (the mean overstaging rate was 43% at 1.5 T and 57% at 3 T).[10] Overestimation and underestimation of T and N stage could be result from the fact that interpretation difficulties in the distinction between malignant tumor stranding in a T3 tumor and desmoplastic benign reactions in a T2 tumor with MRI. Besides, according to NCCN guideline, nCRT was recommended once the patient was staged as T3 or T4 or N+, whereas only when the patient was staged as T1-2 and nodal negative, surgery was their first treatment choice. Therefore, MRI is more likely to underestimate the TN stages and result in undertreatment than overestimate the TN stages and result in overtreatment.

This study had some limitations that should be mentioned. First, this was a retrospective study performed at a single institute. Second the study included an uncontrolled methodology and enrolled a limited number of patients from a single institution. Third, circumferential resection margin (CRM), extramural vascular invasion (EMVI) and mesorectal fascia infiltration in rectal cancer was not assessed, which is also very important factors for treatment decision-making. All these factors would have influenced our findings, we expect an advantage for clinical treatment decision-making.

5 | CONCLUSION

MRI allows a highly accurate preoperative assessment of T stage but only a fairly accurate preoperative assessment of N stage for rectal cancer. The diagnostic accuracy of MRI for treatment decision-making could be promising, but additional studies are needed to validate these findings in a larger sample size from multiple centers.

6 | DECLARATIONS

6.1 | Ethical approval and consent to participate

This retrospective study was approved by the Institutional Research Ethics Committee of the First Affiliated Hospital of Nanjing Medical University. Both Chinese and English editions of the Ethical files (No: 2019-SR-316) are attached.

6.2 | Consent for publication

All authors of this paper have read and complied with author guidelines. The contents of this manuscript have not been copyrighted or published previously. The contents of this manuscript are not under consideration for publication elsewhere. The contents of this manuscript will not be copyrighted, submitted, or published elsewhere while acceptance by the manuscript is under consideration. All authors approve to publish this article in *Asia-Pacific Journal of Clinical Oncology*.

COMPETING INTERESTS

The authors declare that no competing interests exist.

FUNDING

This work was funded by grants from the National Natural Science Foundation of China (Nos. 81874217 and 81703028), the Young Medical Key Talents of Jiangsu Province (No. QNRC2016572), and Priority Academic Program Development of Jiangsu Higher Education Institutions (PAPD) (No. JX10231801); Suzhou Clinical Medical Expert Team, Award Number: SZYJTD201824.

AUTHORS' CONTRIBUTIONS

XLP, ZC and ZZY performed the data collection and data analysis and drafted the manuscript; SXC and QQ supervised the research program and edited the manuscript; and SXC and QQ had significant roles in the study design and manuscript review. All authors read and approved the final manuscript.

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How to cite this article: Xu L, Zhang C, Zhang Z, et al. Value of 3Tesla MRI in the preoperative staging of mid-low rectal cancer and its impact on clinical strategies. *Asia-Pac J Clin Oncol*. 2020;16:e216–e222. https://doi.org/10.1111/ajco.13368