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Lymph node metastasis in rectal cancer: comparison of MDCT and MR imaging for diagnostic accuracy

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Abstract

Purpose To compare the diagnostic accuracies of MDCT and high-resolution MRI (HR-MRI) for regional nodal metastases with different short-axis diameter ranges in rectal cancer patients.

Methods Rectal adenocarcinoma patients who underwent both MDCT and HR-MRI before surgery were included. The maximum short-axis diameters of the nodes were measured, and were classified as benign or malignant on imaging findings. All of the nodes were subdivided as follows: ≤ 5 mm (Group A), > 5 mm and ≤ 10 mm (Group B) , and > 10 mm (Group C). The postoperative pathological reports were used as the standard, and the sensitivity, specificity, accuracy, ROC curve, and AUC value were calculated for each subgroup.

Results A total of 592 nodes were included in the node-to-node evaluation. In Group A, the specificity and accuracy of HR-MRI were significantly higher than those of MDCT (99.28% vs. 93.99%, $P < 0.001$; 95.78% vs. 89.56%, $P = 0.010$; respectively). In Group B, the specificity and accuracy of HR-MRI were also higher than those of MDCT (98.36% vs. 55.74%, $P < 0.001$; 80.45% vs. 66.17%, $P < 0.001$; respectively). For Groups A and B, the AUCs of MDCT were both 0.65, whereas those of HR-MRI were 0.76 and 0.82, respectively. In Group C, all nine malignant nodes were correctly diagnosed metastases on MDCT, whereas one was misjudged as benign on HR-MRI.

Conclusions The diagnostic value of HR-MRI is superior to that of MDCT, with higher specificity, accuracy, and AUC values for HR-MRI than for MDCT.

Keywords Rectal cancer · Regional lymph node · MDCT · High-resolution MRI · Comparison

Introduction

Lymph node (LN) status is important for determining the therapeutic strategy and constitutes one of the most important prognostic risk factors in patients with rectal cancer [1, 2]. Clinically, imaging modalities such as multiple-detector computed tomography (MDCT) and magnetic resonance imaging (MRI) are readily available methods with the capability of pretreatment assessment. Particularly, MRI has become the preferred modality in the multidisciplinary approach [3]. Most previous studies predicted nodal status by using MDCT or MRI only while neglecting to compare the diagnostic efficiency between MDCT and MRI in the same group of patients. In addition, although meta-analyses evaluating regional LNs with MRI and CT have been carried out, the degree of heterogeneity between studies, including differences in the methodologic quality, imaging protocols, diagnostic criteria of nodal metastases, and radiologist's

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experience in different inclusion studies, is still an important limitation of these analyses [4, 5].

There is considerable size overlap between benign and malignant LNs [6], and over 50% of the LNs involved in rectal cancer are less than 5 mm [7, 8]. Limited to spatial resolution, nodal size is always used as a criterion, but it is too unreliable as a predictor for malignancy [9]. High-resolution MRI (HR-MRI) can better assess morphologic features such as border and signal homogeneity. Improved accuracy has been reported when using morphologic criteria rather than size alone [10–12].

This study evaluated regional LN status with morphologic criteria in the same group of patients and compared the diagnostic accuracy of MDCT and HR-MRI for regional LN identification in patients with rectal cancer.

Methods

Study population

This study was performed in accordance with the recommendations of the institutional review board, and all the patients provided written informed consent. The inclusion criteria were as follows: (1) those with histopathology confirming primary rectal adenocarcinoma; (2) those who had undergone MDCT and rectal HR-MRI before total mesorectal excision (TME); (3) MDCT and rectal HR-MRI if performed earlier with identical imaging parameters, respectively; and (4) cases where the image qualities were good enough to observe LN morphology. The exclusion criteria were as follows: (1) those with histopathology confirming a special histopathological type, such as mucous adenocarcinoma or signet ring cell carcinoma, and (2) those who had a history of prior radiotherapy, chemotherapy, or chemoradiotherapy.

Image acquisition

MDCT

All the patients fasted for 4 h and drank one cup (300 mL) of 2.5% mannitol every 15 min for 1–2 h before the examination. After drinking four cups of mannitol, the patients received a rectal enema with 60–100 mL of 2.5% mannitol solution and drank 300 mL of 2.5% mannitol before the MDCT scan.

The MDCT examination was performed on a 160-slice CT system (Aquillion PRIME, TOSHIBA, Tokyo, Japan). The following scan parameters were used: tube current, 250 mA; voltage, 120 kV; slice thickness, 1 mm; gap, 0.8 mm. Images were reconstructed in the sagittal and coronal planes (slice thickness, 10 mm; gap, 5 mm). The contrast-enhanced pelvis scans were performed 70 s after the intravenous injection of 1.5 mL/kg nonionic contrast agent (Ultravist 300, Bayer) at a rate of 3.0 mL/s.

High-resolution MRI

According to the tumor location on colonoscopy, an appropriate amount (20-80 mL) of ultrasonic gel was poured into the rectum of each patient except those with low or large rectal tumors. Unless contraindicated, a dose of 20 mg of raceanisodamine hydrochloride was injected intramuscularly approximately 10 min prior to the MR examination to prevent intestinal peristaltic artifacts.

MRI was performed using a 3.0 T unit (Magnetom Verio, Siemens Healthcare, Erlangen, Germany) with a 6-channel phased-array wrap-around surface coil. The coil center was placed on the level of the pubic symphysis and adjusted according to the tumor location. Rectal MRI protocols included sagittal, coronal, and oblique axial high-resolution T2-weighted imaging (T2WI) using a turbo spin-echo sequence with the oblique axial plane orthogonal to the tumor basement. Details of the protocols are listed in Table 1.

Image evaluation

First, the MDCT images were reviewed independently by two radiologists who were experienced in reading the images of rectal cancer, and the maximum short-axis diameters (millimeters) of the LNs were measured. Rather than using size, we defined the criteria for LN metastasis as a LN of any size with an irregular border, a heterogeneous density, and/or heterogeneous enhancement (Fig. 1) [13]. Four weeks later, the two radiologists independently evaluated regional LNs based on HR-MRI. The maximum short-axis diameters (millimeters) of the LNs were measured again. The criteria for LN metastasis were an irregular border and/or a heterogeneous signal (Fig. 2) [14]. When a disagreement occurred, a consensus was reached by discussion. Only the LNs with matched images on MDCT and HR-MRI were evaluated.

Histopathologic assessment and nodal comparison

All visible LNs on preoperative images were localized by a radiologist and a surgeon with expertise in colorectal cancer. According to the agreement regarding nodal positions, the expert surgeon successively localized, removed, and numbered regional LNs one by one in different groups during surgery. For a node-to-node comparison, special attention was paid to the size and morphology of the LNs and the location of each LN relative to the tumor, rectal wall, mesorectal fascia, vessels, and adjacent LNs. Then, these LNs were isolated from the specimen and promptly submitted to the pathology department. All the LNs were analyzed by a

Table 1 Rectal high-resolution MRI protocols

Protocols	TR/TE (ms)	Slice thickness (mm)	Distance factor (%)	Slices	Flip angle (°)	Base resolution	Phase resolution (%)	FOV (mm)	Voxel size (mm)	Time acquisition
Sagittal T2WI	3000/87	3	0	19	150	320	80	180	0.7×0.6×3.0	2 min 30 s
Coronal T2WI	4000/77	3	0	25	137	384	80	220	0.7×0.6×3.0	2 min 52 s
Oblique axial T2WI	3000/84	3	0	24	150	320	100	180	0.6×0.6×3.0	3 min 18 s

TR repetition time, *TE* echo time, *FOV* field of view, *T2WI* T2-weighted imaging

pathologist with expertise in gastrointestinal diseases and evaluated as malignant for the presence of tumor cells under a light microscope. The LNs on preoperative images were excluded if they could not be matched with histopathologic findings to enable a node-to-node comparison. The pathological staging of rectal cancer was performed according to the rules for tumor-node-metastasis (TNM) staging of the American Joint Committee on Cancer [8].

Statistical analysis

Statistical analyses were performed using MedCalc software (version 15.8). All quantitative data were subjected to a normality test using the one-sample Kolmogorov–Smirnov test. Values with a nonnormal distribution are reported as medians with ranges. Based on the average nodal maximum short-axis diameters measured on MDCT and HR-MRI, all the LNs were subdivided as follows: ≤ 5 mm (Group A), > 5 mm and ≤ 10 mm (Group B) and > 10 mm (Group C). After receipt of the postoperative histopathologic results, the diagnostic sensitivity, specificity, and accuracy of MDCT and HR-MRI in the different subgroups were calculated and compared using McNemar's test. In addition, the receiver operating characteristic (ROC) curves for the two imaging modalities were analyzed. Areas under the curves (AUCs) were also calculated to assess the diagnostic utility. An AUC value of less than 0.5 indicated no diagnostic value, 0.5–0.7 indicated low diagnostic value, 0.7–0.9 indicated moderate diagnostic value, and more than 0.9 indicated high diagnostic value. Significance was set at a two-tailed P value < 0.05. Because all the LNs in Group C were metastatic, related statistical analyses in this group could not be conducted.

Results

Patient characteristics

A total of 80 patients (45 males and 35 females; median age: 61 years; range 31–80 years) were included in this study. The patients' demographic characteristics are listed in Table 2.

Nodal comparisons between imaging and histopathologic findings

The median interval between MDCT and HR-MRI was 2 days (range 0–12 days). All the patients underwent TME 6 days after MDCT or HR-MRI (range 1–20 days). Among the 80 enrolled patients, 1280 LNs were harvested from the rectal specimens (median number: 15; range 9–45), and 153 contained metastases. A total of 592 LNs were included in the node-to-node evaluation. The median

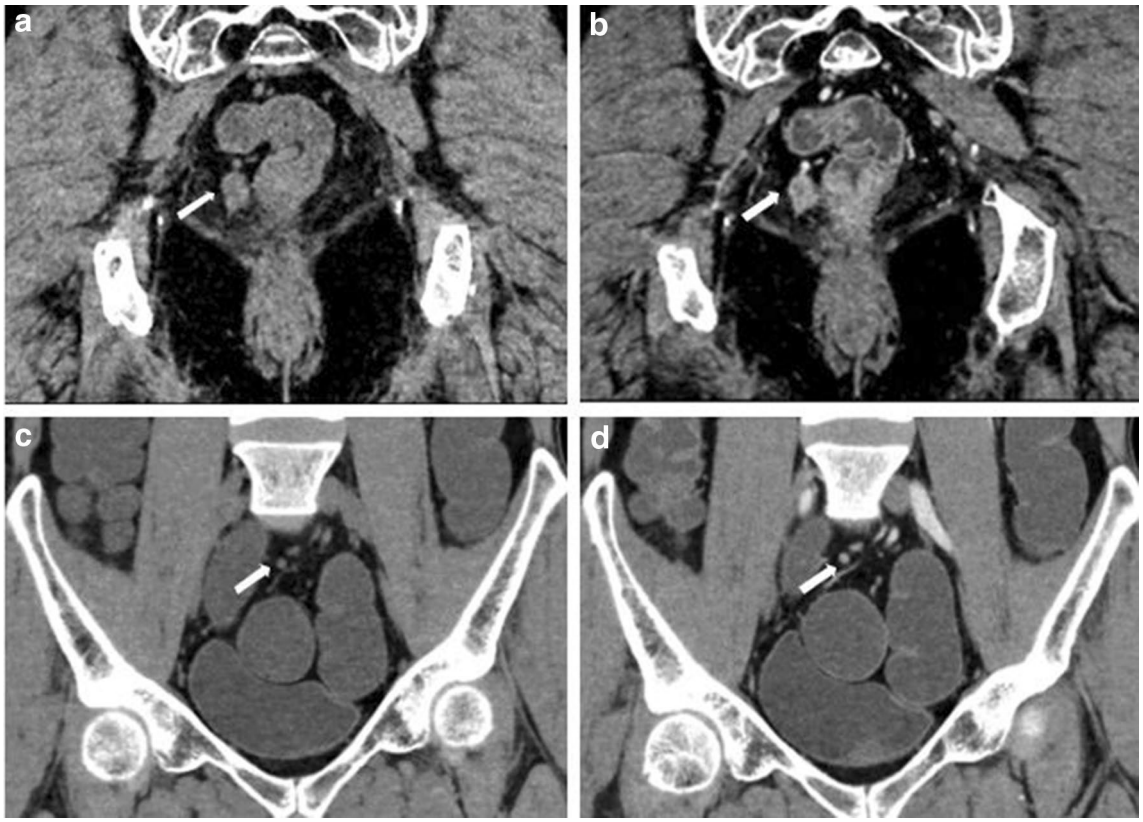

Fig. 1 **a** and **c** Unenhanced and **b** and **d** enhanced MDCT in coronal reconstruction images. **a** The malignant node (white arrow) had a short-axis diameter of 9.8 mm with an irregular border, a heterogeneous density, and **b** heterogeneous enhancement; **c** the benign node (white arrow) had a short-axis diameter of 4.0 mm with a regular border, a homogeneous density, and **d** homogeneous enhancement

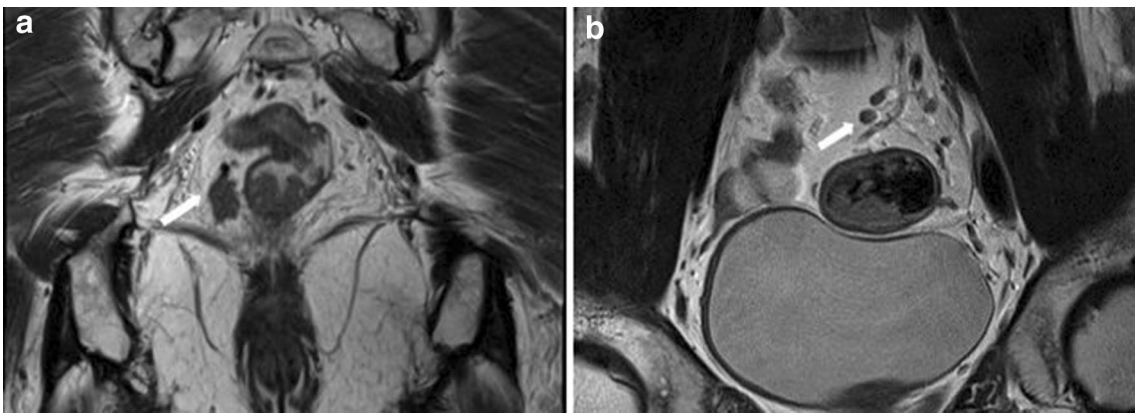

Fig. 2 Coronal high-resolution T2-weighted images. **a** The malignant node (white arrow) had a short-axis diameter of 9.8 mm with an irregular border and a heterogeneous signal; **b** the benign node (white arrow) had a short-axis diameter of 4.0 mm with a regular border and a homogeneous signal

short-axis diameter of the regional LNs retrieved was 3.8 mm (range 1.6–17.0 mm). Among the 477 benign LNs, the median short-axis diameter was 3.6 mm (range 1.6–8.7 mm) and 5.9 mm (range 2.9–17.0 mm) for the 115 malignant LNs.

Comparison of diagnostic performance for regional LN metastasis in different subgroups

As more than 50% of LNs with short-axis diameters < 5 mm are metastatic [15], and those > 10 mm are prone to

Table 2 Clinicopathologic features of 80 patients

Clinicopathologic feature	Number of patients
Age, median (range)	61 (31–80)
Gender	
Male	45 (56.3%)
Female	35 (43.8%)
Location	
Low	15 (18.8%)
Middle	33 (41.3%)
High	32 (40.0%)
Differentiation	
Well	0 (0.0%)
Moderate	70 (87.5%)
Poor	10 (12.5%)
pT stage	
T1	4 (5.0%)
T2	18 (22.5%)
T3	32 (40.0%)
T4	26 (32.5%)
pN stage	
N0	48 (60.0%)
N1	20 (25.0%)
N2	12 (15.0%)

The location of the rectal tumor depended on the distance from the most caudal margin of the tumor to the anal verge on MRI as follows: low < 5 cm, middle = 5–10 cm, high > 10 cm

p pathological

liquefactive necrosis, all the LNs were subdivided into three groups based on the maximum short-axis diameters as follows: ≤ 5 mm (Group A), > 5 mm and ≤ 10 mm (Group B) and > 10 mm (Group C).

Group A

Among the 450 LNs in Group A, 34 were metastatic. The specificity and accuracy of HR-MRI were significantly higher than those of MDCT (99.28% vs. 93.99%, $P < 0.001$; 95.78% vs. 89.56%, $P = 0.010$; respectively); however, there was no significant difference in sensitivity (52.94% vs. 35.29%, $P = 0.109$) (Table 3). The AUCs of MDCT and HR-MRI were 0.65 and 0.76, respectively, which were interpreted as low and moderate diagnostic values (Fig. 3a).

Group B

Among the 133 LNs in Group B, 72 contained metastases. The specificity and accuracy of HR-MRI were also significantly higher than those of MDCT (98.36% vs. 55.74%, $P < 0.001$; 80.45% vs. 66.17%, $P < 0.001$; respectively); however, there was no significant difference in sensitivity

Table 3 Comparison of diagnostic performances using MDCT and high-resolution MRI in Groups A and B

	MDCT	High-resolution MRI	*P*
Group A			
Sensitivity	35.29% (12/34)	52.94% (18/34)	0.109
Specificity	93.99% (391/416)	99.28% (413/416)	< 0.001
Accuracy	89.56% (403/450)	95.78% (431/450)	0.010
AUC	0.65	0.76	0.011
Group B			
Sensitivity	75.00% (54/72)	65.28% (47/72)	0.265
Specificity	55.74% (34/61)	98.36% (60/61)	< 0.001
Accuracy	66.17% (88/133)	80.45% (107/133)	< 0.001
AUC	0.65	0.82	0.001

(65.28% vs. 75.00%, $P = 0.265$). The diagnostic value of MDCT was low (AUC = 0.65), whereas that of HR-MRI was moderate (AUC = 0.82) (Fig. 3b).

Group C

All nine LNs in this group were malignant, and all were correctly considered metastatic on MDCT. However, one LN was incorrectly evaluated as benign using HR-MRI.

Discussion

The short-axis diameters of LNs were mostly used for the identification of malignant LNs in previous studies [16, 17], but there was no consensus on the size criterion for the prediction of metastatic LNs [18–20]. There is considerable size overlap between benign and malignant LNs [6], and approximately 50% of the LNs involved in rectal cancer are less than 5 mm [7, 8]. Therefore, the diagnostic value is limited when using size as the only criterion. It is reported that morphologic criteria employing the nodal border and signal characteristics are superior to size in predicting nodal status [13]. Although a previous meta-analysis compared CT and MRI in the evaluation of LNs in rectal cancer, importantly, the diagnostic criteria of LNs included in the meta-analysis differed.

In this study, MDCT and HR-MRI were used to compare their efficacy in evaluating regional LNs in patients with rectal cancer in the same sample. In this study, there was no significant difference in the sensitivity of MDCT and HR-MRI in Group A. Subjected to spatial resolution, the morphologic observation of small LNs would be affected [21, 22]. Despite the higher soft-tissue resolution, HR-MRI still cannot identify micrometastasis within LNs [23]. Therefore, the sensitivity of nodal involvement must be reduced [24]. In Group B, no significant difference in sensitivity was

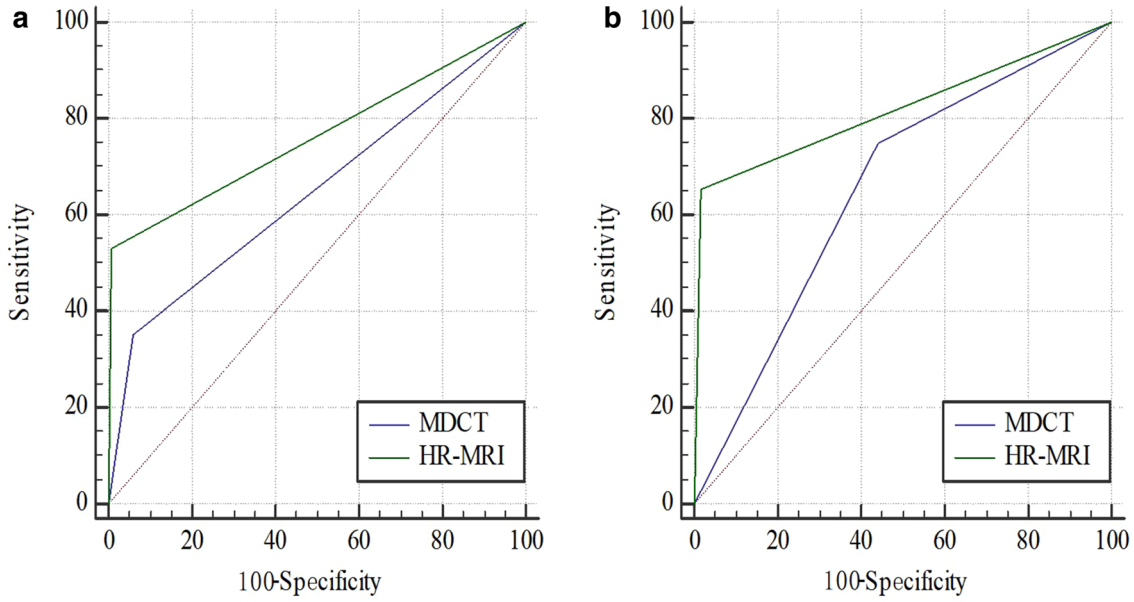

Fig. 3 ROC curves of the diagnostic performances for nodal metastasis in Group A (**a**) and Group B (**b**)

found between MDCT and HR-MRI. Larger LNs are prone to necrosis and liquefaction, which are important signs of nodal metastasis; hence, obvious heterogeneous or rim-like enhancement was observed on enhanced MDCT images [25]. Therefore, the sensitivity of MDCT improved with the additional criterion of the enhancement feature.

The specificity and accuracy of HR-MRI were both significantly higher than those of MDCT in Groups A and B. Because images were obtained with a 3-mm slice thickness without a gap in a small field of view and with the advantages of multidirectional and multiparameter imaging of HR-MRI, the ability to assess the border and internal architecture of LNs could help optimize LN staging. In addition, the lower soft-tissue resolution of MDCT made it impossible to observe the nodal morphological characteristics clearly [26]. Nevertheless, the diagnostic efficiency was improved with the addition of other nodal characteristics, such as border, attenuation, and enhancement, as criteria for LN metastasis on MDCT. Kulinna et al. [15] showed that the sensitivity, specificity, and accuracy of contrast-enhanced MDCT were 68%, 85%, and 78%, respectively, when LNs with a maximum short-axis diameter > 3 mm were assumed to be metastatic. Although the sensitivity was higher than that observed in our study, the specificity and accuracy were lower than those of ours. This result may be explained by the fact that LN involvement has been defined as a nodal maximum short-axis diameter > 3 mm without considering nodal morphological characteristics, which may lead to the misjudgment of certain normal or reactive hyperplastic LNs as metastatic, resulting in decreased specificity and accuracy. In addition, in the reports of different MRI studies, regional LN involvement was defined differently (LN > 3 mm, LN = 5 mm, LN > 8 mm and LN > 10 mm). Moreover, the long- or short-axis diameters for evaluating LN status were not explicit, and the accuracy ranged from 43 to 85%, which was inferior to that obtained in this study [7].

In the present study, all LNs > 10 mm were metastatic. All nine malignant LNs were correctly considered metastatic on MDCT, whereas one LN was incorrectly evaluated as benign on HR-MRI. The metastatic LN showed a regular border and homogeneous signal on HR-MRI and a regular border as well as homogeneous density on noncontrast MDCT images. However, the metastatic LN was assumed to be involved because of heterogeneous enhancement on contrast MDCT images. Due to a small amount of necrosis in LNs, slight signal inhomogeneity failed to be found on HR-MRI, while contrast MDCT images enhanced the internal density contrast in LNs and obtained more morphologic information on the basis of plain MDCT images [21, 27, 28].

There were several limitations to this study. First, the number of enrolled LNs with short-axis diameters > 10 mm was relatively small because most of them were definite metastatic, and neoadjuvant chemoradiotherapy is usually recommended for patients with nodal metastasis. Second, iliac LNs were not evaluated because extended pelvic lymphadenectomy is not performed in routine clinical TME. Finally, compared with nodal short-diameter, the diagnostic criteria used in this study are relatively more subjective, but the results were obtained after a consensus was reached by two experienced radiologists [4].

In conclusion, the specificity, accuracy, and AUC values of HR-MRI were higher than those of MDCT. The

diagnostic value of HR-MRI was superior to that of MDCT. However, the accuracy for detecting LN metastases on HR-MRI still needs to be improved. In the clinic, multiple imaging modalities should be combined with new techniques, and more informative signs should be observed to obtain a powerful predictive result.

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Compliance with ethical standards

Conflict of interest The authors do not have any possible conflicts of interest.

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