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Research article

Performance comparison between MRI and CT for local staging of sigmoid and descending colon cancer

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ABSTRACT

Purpose: To compare the diagnostic performance of MRI and CT for local staging of sigmoid and descending colon cancer, with pathological results as the reference standard.

Method: This retrospective study included 116 patients with sigmoid or descending colon cancer who underwent both MRI and CT before surgery. MRI and CT images were separately reviewed by two independent and blinded radiologists to assess the following features: T-stage, presence of extramural extension (T3-4 disease), lymph node metastases (N+), and extramural vascular invasion (EMVI+). Diagnostic performance with sensitivity and specificity for detecting positive status (T3-4, N+ or EMVI+) were assessed using receiver-operating-characteristic (ROC) curve, and compared between MRI and CT.

Results: MRI achieved correct T-stage in 81 of 116 patients (69.8 %) while CT in 66 (56.9 %). For detecting T3-4 disease, MRI showed better performance than CT with area under the curve (AUC) of 0.888 versus 0.712 ($P = 0.002$) and specificity of 81.82 % versus 54.6 % ($P = 0.011$). No significance was found in sensitivity between two modalities (89.2 % versus 83.1 %, $P = 0.302$). For detecting N+ disease, performance of MRI and CT were similar (AUC, 0.670 versus 0.650, $P = 0.412$). For detecting EMVI+, MRI showed better performance than CT (AUC, 0.780 versus 0.575, $P = 0.012$) with significantly higher sensitivity (68.6 % versus 40.0 %, $P = 0.031$) and similar specificity (both are 84.3 %).

Conclusions: MRI may offer more superior diagnostic performance than CT for detecting T3-4 disease and EMVI, thereby supporting its alternative application to CT in local staging of colon cancer.

1. Introduction

Colon cancer is one of the most frequent causes of cancer-related death worldwide [1]. During the past few years, advanced techniques and concepts have been introduced in the treatment strategy. The principle of complete mesocolic excision (CME) has been initially implemented in colon cancer surgery and been proved associated with better disease-free survival than conventional resection, particularly for stage I-II disease [2]. In addition, numbers of recent studies including the Foxtrot trial demonstrate that preoperative chemotherapy is feasible and may achieve superior R_0 resection rates as well as improved overall survival in locally advanced colon cancer [3–6]. Progress in treatment has led to the requirement of accurate preoperative staging approaches to determine the optimal surgical plane and select patients who may benefit most from these advanced techniques.

Contrast-enhanced computed tomography (CT) is the current main modality used for preoperative local staging in colon cancer. However, due to limited soft-tissue contrast, its performance for staging primary tumor (T stage) or detecting extramural extension is generally dissatisfactory with accuracy range from 60 % to 80 % [7–10]. Moreover, the value for assessing regional nodal involvement also remains poor and unreliable [11,12]. Magnetic resonance imaging (MRI) has better soft-tissue contrast than CT, and by scanning with high-resolution techniques, it allows for showing the layer structure of bower wall. In rectal cancer, MRI has been confirmed to obtain more detailed imaging of the regional tumor [13,14]. But usefulness of MRI for local staging in colon cancer is not yet well established, and to date, only a few studies with small sample size have evaluated the feasibility [15–17].

The purpose of this study was to compare the diagnostic performance of MRI and CT for local staging of sigmoid and descending colon cancer, with postoperative histological results as the reference standard.

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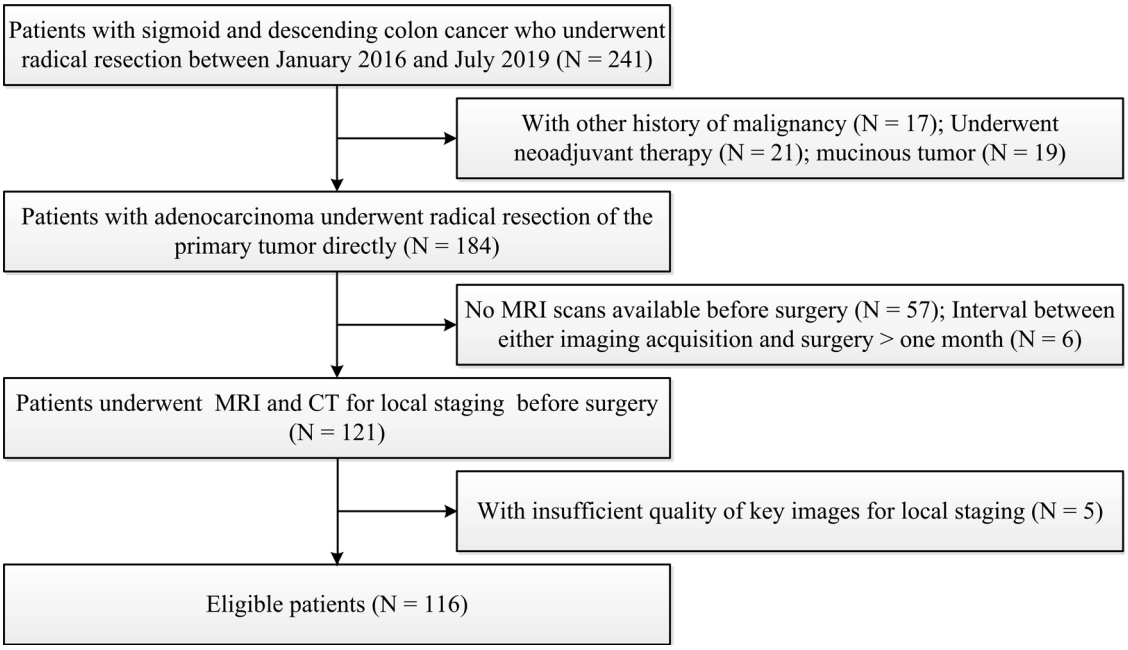

Fig. 1. Recruitment pathway for study population.

2. Materials and methods

2.1. Patient selection

This study was approved by local institutional review board and informed consent was waived according to the retrospective design. We searched the medical database for records of consecutive patients with sigmoid or descending colon adenocarcinoma (between rectosigmoid junction and splenic flexure of the colon) who underwent radical resection between January 2016 and July 2019. Exclusion criteria were as follows: (1) with other history of malignancy; (2) underwent neoadjuvant therapy; (3) mucinous tumor; (4) without either MRI or CT scans before surgery; (5) underwent surgery beyond one month after imaging acquisition; or (6) insufficient quality of key images for staging tumor. The patient selection process was shown in Fig. 1. Finally, 116 eligible patients were included. Study population characteristics were listed in Table 1.

Table 1
Basic characteristics of study population.

Items	Total *N* = 116
Age, mean ± sd (range)	60.9 ± 9.9 (36-83)
Gender, n (%)	
Male	78 (67.2)
Female	38 (32.8)
Pathological primary tumor stage, n (%)	
T1	4 (3.4)
T2	29 (25.0)
T3	66 (56.9)
T4	17 (14.7)
Pathological nodal stage, n (%)	
N0	54 (46.6)
N+	62 (53.4)
p-EMVI status available, n (%)	86 (74.1)
p-EMVI-	51 (59.3)
p-EMVI+,	35 (40.7)
Location	
Sigmoid colon	94 (81.0)
Descending colon	22 (19.0)

Abbreviation: sd, standard deviation; p-EMVI, pathological extramural vascular invasion.

2.2. MRI and CT protocol

In our institution, the current overall principle for initial imaging examination of colon cancer is as follows: abdominopelvic contrast-enhanced CT has been used as the standard imaging modality for the initial evaluation; when the multidisciplinary team has any doubt about the primary tumor staging or decision-making with CT, colon MRI will be recommended; in addition, colon MRI is performed simultaneously in some cases with liver MRI which was used to rule out or to determine the management of liver metastasis. The examination strategy provides a unique opportunity to compare the diagnostic performance of MRI with CT in this study.

Bowel preparation was based on a low-residue diet for two days and fasted for 4 – 5 h before MRI or CT examination, and intravenous antispasmodic agents were performed before imaging acquisition. To achieve moderate distention of small intestine, 600 – 800 ml tap water was ingested at 20 min prior to examination.

MRI was performed using one of three magnet scanners (Avanto 1.5 T, Aera 1.5 T, Verio 3.0 T, Siemens Healthineers, Erlangen, Germany) with 32-channel phased-array coils. The MRI protocol for primary staging of colon cancer consisted of: (1) axial and sagittal T2-weighted imaging (T2WI), (2) axial diffusion-weighted imaging (DWI), and (3) axial and coronal post-contrast T1-weighted imaging (T1WI). The total examination duration was approximately 24 min. Detailed parameters were summarized in Table 2.

CT was performed using one of three multi-detector scanners (Somatom Definition AS + 128, Siemens Healthineers, Erlangen, Germany; Brilliance 128, Philips Healthcare, Best, The Netherlands; and Aquilion one 320, Toshiba Medical Systems, Tokyo, Japan). Contrast-enhanced scanning was conducted after a bolus intravenous injection of 1.5 ml/kg of non-ionic contrast agent (Ultravist 350, Bayer Healthcare, Berlin, Germany) followed by 30 ml saline flush at a rate of 3 ml/s. Scans were started at 6 s (arterial phase), 46 s (venous phase) after a trigger threshold of 100 Hounsfield unit (HU) was reached at abdominal aorta. Scanning parameters were set as 120 kVp, 200–250 mA s and detector collimation of 0.6-0.625 mm. CT Images were reconstructed with slice thickness/reconstruction interval of

Table 2
MRI protocol used in this study.

Sequence	Parameter	Avanto 1.5-T	Aera 1.5-T	Verio 3-T
Axial TSE T2WI	TR/TE	4050/97 ms	4890/80 ms	3080/90 ms
	Thickness	4 mm		
	FOV/matrix	20 cm × 20 cm/320 × 320		
Sagittal TSE T2WI	TR/TE,	3480/97	5740/83	3200/88
	Thickness	4 mm		
	FOV/matrix	20 cm × 22 cm/ 272 × 320		
Axial SS-EPI DWI	TR/TE	3200/74 ms	5200/58 ms	3300/70 ms
	Thickness	5 mm		
	FOV/matrix	29 cm × 24 cm/150 × 120		
	B-values (sec/mm^2)	0, 500, 1000	0, 500, 1000	0, 800
Axial and coronal Contrast enhanced 3-D VIBE T1WI	TR/TE	5.04/2.31ms	6.98/ 2.38 ms	4.15/1.41 ms
	Thickness	3 mm		
	FOV/matrix	36 cm × 27 cm/320 × 182		

Abbreviation: T2WI, T2-weighted imaging; T1WI, T1-weighted imaging; TSE, turbo spin echo; SS-EPI, single-shot echo planar imaging; VIBE, volume interpolated body examination; p-EMVI, pathological extramural vascular invasion.

3 mm.

2.3. Imaging interpretation

At first, images were independently analyzed by two board-certified gastrointestinal radiologists (with 12 and 7 years of experience, respectively) and their own results were recorded. Then, the final results were determined by their consensus discussion. The radiologists were blinded to the detailed postoperative pathological data. To control readers' recall bias, MRI and CT images were separately reviewed with an interval of at least six weeks. To enhance consistency between the two readers' interpretations, external examples with typical imaging features were given before performing study interpretations. Before a result was given, the readers should review all sequences/phases of MRI or CT data.

The following imaging features were evaluated: T-stage (T1, T2, T3, T4), primary tumor extramural extension (T3-4 versus T1-2), lymph node metastases (N+ versus N0), and extramural vessel invasion status (EMVI+ versus EMVI-). When determining presence of extramural extension (T3-4) and EMVI, a five-level confidence scoring system (0-4: from definitely absent to definitely present; scoring 3 or 4 regarded as positive) was used.

T-stage (T1, T2, T3, T4) was determined according to the 7th TNM system [18]. The staging criteria using MRI were [17,19]: (T1) on T2WI, intermediate-signal tumor limited in the submucosal layer without extending into the low-signal muscular layer; on DWI, high-signal tumor limited in the inner half of the bowel wall; (T2) on T2WI, low-signal muscular layer is partially replaced by the intermediate-signal tumor but without breaking through; on DWI, high-signal tumor extending into the outer half of bowel wall but still with a low-signal margin; (T3) on T2WI, the low-signal muscular layer is completely replaced and penetrated through by bulge or nodular tumor signal; on DWI, high-signal tumor invading the whole colon wall or extending into the pericolic space; and (T4) tumor invades serosa or other organ, the distance of tumor is less than 1 mm to the adjacent organ or the recognized serosa on either T2WI or DWI. The staging criteria using CT were [17]: (T1) enhanced tumor does not extend into the muscular layer; (T2) enhanced tumor limited in the colon wall with smooth of muscle layer and clear pericolic fat; (T3) presence of irregular out margin or nodular extension of the mass beyond the bowel wall; and (T4) tumor invades serosa or other organ, the distance of tumor is less than 1 mm to the adjacent organ or the recognized serosa.

Lymph nodes were evaluated based on their size and morphologic features. N+ status was defined as at least one of regional lymph nodes with diameter of ≥ 7 mm, irregular margin or heterogeneous signal/enhancement [12]. This was assessed on T2WI, DWI and post-contrast T1WI of MRI data, and on each phase of CT images.

EMVI+ was considered to be present on T2WI when tumor penetrates through the bowel wall and invades at least one extramural vascular structure. A five-level confidence scoring system described in previous researches was used [20,21]. On CT, EMVI+ was defined as tumor connecting to an extramural vascular with abnormally extended contour, or presence of filling defect within an extramural vascular [22].

2.4. Surgery and pathology

Radical resection was performed in an elective setting within one month after imaging acquisition for each patient. Pathologic results including T-stage, N-stage and EMVI status were examined and recorded. Tumors were staged according to the 7th TNM system [18]. EMVI was considered when tumor tissue was present within a tubular structure that was lined by endothelial cells, smooth muscles, or elastic fibers. Expression of CD31, CD34, F8, and D2-40 was assessed immunohistochemically to help for detecting EMVI. All pathological reports were determined in consensus by at least two pathologists who underwent special training on colorectal carcinoma pathology.

2.5. Statistical analyses

Postoperative pathological results were used as the reference standard, and patient data were dichotomized as T3-4 versus T1-2, N+ versus N0 or EMVI+ versus EMVI-. Receiver-operating-characteristic (ROC) curve was constructed to assess the diagnostic performance of each imaging modality for identifying T3-4, N+ and EMVI+, respectively. The difference in performance between MRI and CT was analyzed by comparing the corresponding areas under the ROC curves (AUC). The sensitivity and specificity for detecting T3-4 disease, N+ and EMVI+ were calculated, then, were compared between MRI and CT using the McNemar test for paired proportions. Interobserver reliability on subjective scores for identifying T3-4 disease and EMVI+ was evaluated using kappa (κ) calculation ($\kappa < 0.40$, poor agreement; $0.40 \leq \kappa < 0.60$, moderate agreement; $0.60 \leq \kappa < 0.80$, good agreement; and $\kappa \geq 0.80$, perfect agreement). Statistical analyses were conducted with MedCalc for Windows, version 12.0 (MedCalc Software). A P value of less than 0.05 indicated a significant difference.

3. Results

3.1. Patients and histopathology

The study population included 116 patients (78 men and 38 women) with a mean age of 60.9 years. Basic demographics and distribution of tumor features are shown in Table 1.

3.2. Overall T-stage and detection of extramural extension (T3-4)

Compared to pathological T stage as the reference standard (Table 3), MRI correctly diagnosed T-stage in 81 of 116 patients (69.8 %) while CT in 66 patients (56.9 %). In the detection of T3-4 tumor, MRI significantly outperformed CT with AUCs of 0.888 and 0.712, respectively ($P = 0.002$, Fig. 2A). The corresponding specificity was significantly higher with MRI than with CT (81.8 % versus 54.6 %, $P = 0.011$, Table 4). No significance was found in sensitivity between the two modalities (89.2 % versus 83.1 %, $P = 0.302$). There was good interobserver agreement on subjective scores for identifying T3-4 tumor

Table 3
Numbers of patients correctly staged using CT or MRI (T-stage).

Pathological T-stage, (*N*)	Correctly staged using MRI, *N* (%)	Correctly staged using CT, *N* (%)
T1 (4)	0 (0)	0 (0)
T2 (29)	23 (79.3)	14 (48.3)
T3 (66)	53 (80.3)	46 (69.7)
T4 (17)	5 (29.4)	6 (35.3)
Total (116)	81 (69.8)	66 (56.9)

with both MRI and CT (κ = 0.67; 95 % confidence interval [95 % CI], 0.56-0.78 versus κ = 0.65; 95 % CI, 0.55-0.76).

3.3. Detection of regional nodal involvement (N+)

MRI was similar to CT in its performance for detecting patients with regional nodal involvement (AUC, 0.670 versus 0.650, P = 0.412). The sensitivity and specificity for identifying nodal involvement were 70.9 % and 72.6 % with MRI, 62.9 % and 57.4 % with CT.

3.4. Detection of extramural vessel invasion (EMVI+)

Of the 116 patients, pathological EMVI status was examined in 86 patients with 35 positive (EMVI+) cases. For the detection of EMVI + disease, MRI was significantly superior to CT (AUC, 0.780 versus 0.575, P = 0.012, Fig. 2B). The sensitivity of MRI was significantly higher than that of CT (68.6 % versus 40.0 %, P = 0.031) while the specificities of the two modalities were similar (both are 84.3 %). There was good interobserver agreement on subjective scores for identifying EMVI with MRI (κ = 0.68; 95 % CI, 0.60-0.77) and (κ = 0.58; 95 % CI, 0.48-0.67). Examples of images are illustrated in Figs. 3 and 4.

4. Discussion

This is a study with a sample size of 116 patients to compare the performance between MRI and CT for local staging of sigmoid and descending colon cancer by using pathological results as reference standard. Our results revealed significantly better performance of MRI than CT for identifying extramural extension (T3-4) with a higher specificity, and for identifying EMVI+ with a higher sensitivity. The performance of MRI for detection nodal involvement was comparable with that of CT.

Table 4
Comparison of diagnostic values between CT and MRI by using McNemar's test.

Items	Sensitivity			Specificity		
	MRI	CT	*P*-value	MRI	CT	*P*-value
T3-4	89.2(80.4-94.9)	83.1(73.3-90.5)	0.302	81.8(64.5-93.0)	54.6(36.4-71.9)	**0.011**
N+	70.9(58.1-81.8)	72.6(59.8-83.2)	0.982	62.9(48.7-75.7)	57.4(43.2-70.8)	0.250
EMVI+	68.6(50.7-83.1)	40.0(23.8-57.8)	**0.031**	84.3(71.4-92.9)	84.3(71.4-92.9)	1.000

In era of precision therapy of colon cancer, accurate T-stage is increasingly needed for planning optimal operative route and selecting patients for neoadjuvant therapy. CT remains the current standard staging modality, and the feasibility and good accuracy of MRI have also been verified [15]. In the present study, MRI achieved an AUC of 0.888 with sensitivity of 89.2 % and specificity of 81.8 % for identifying T3-4 disease; the performance is superior to CT with the corresponding values of 0.712, 83.1 % and 54.6 %. A previous study also confirmed the advantage of MRI for T staging, in that study of 29 tumors, authors reported an accuracy of 90 % for predicting locally advanced colon cancer with MRI and 76 % with CT [23].

T2WI plays an important role in the process of T staging. In most cases of the present study, T2WI could recognize the low-signal muscular layer which may be distinct from intermediate-signal tumor and used as a landmark for distinguishing T3-4 versus T1-2. If the low-signal layer is clearly showed and remains intact, extramural invasion could be safely ruled out; this may contributed to the higher specificity and accuracy for detecting T3-4 tumor with MRI. Nerad and colleagues [15] also reported a high specificity of 84%–89% for detecting T3-4 tumor with MRI (N = 55), which is even higher than our results. The reasons for this difference might due to their additionally performed coronal T2WI and more experience of the expert readers in interpreting colon MRI.

In contrast to MRI, it is more difficult for CT to distinguish the muscular layer of bowel wall; this may limited its value and objectivity for assessing early wall penetration. In the present study, 10 of the 116

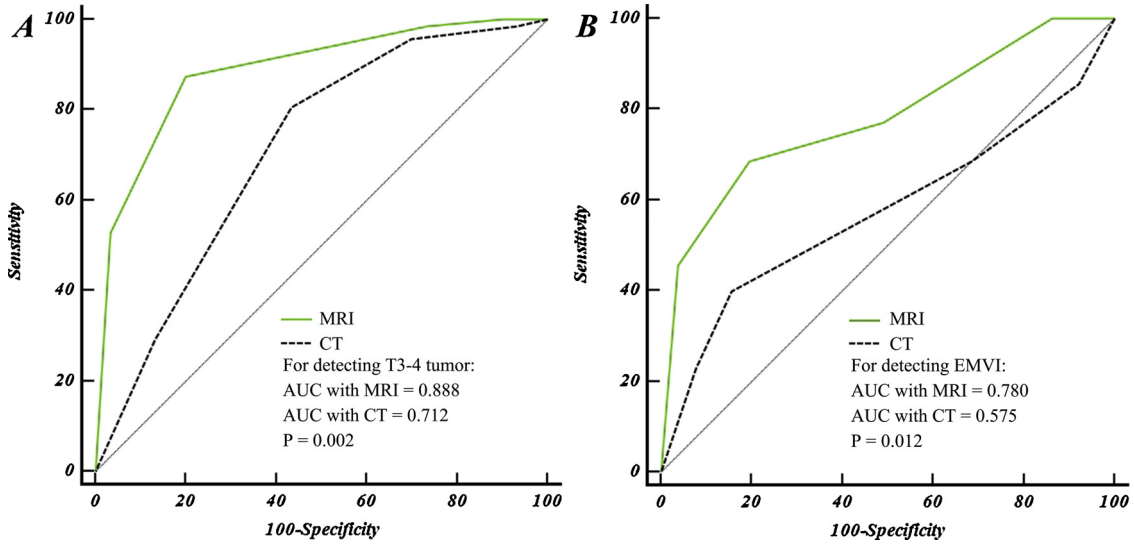

Fig. 2. A: Receiver-operating-characteristic curves constructed with the confidence level scores for identifying T3-4 tumor via MRI or CT. Areas under the curves (AUC) were compared between the two modalities. MRI was more effective than CT for identifying T3-4 tumor in colon cancer. **B:** ROC curves constructed with the confidence level scores for identifying extramural vascular invasion (EMVI) via MRI or CT. AUCs were compared between the two modalities. MRI was more effective than CT for identifying EMVI in colon cancer.

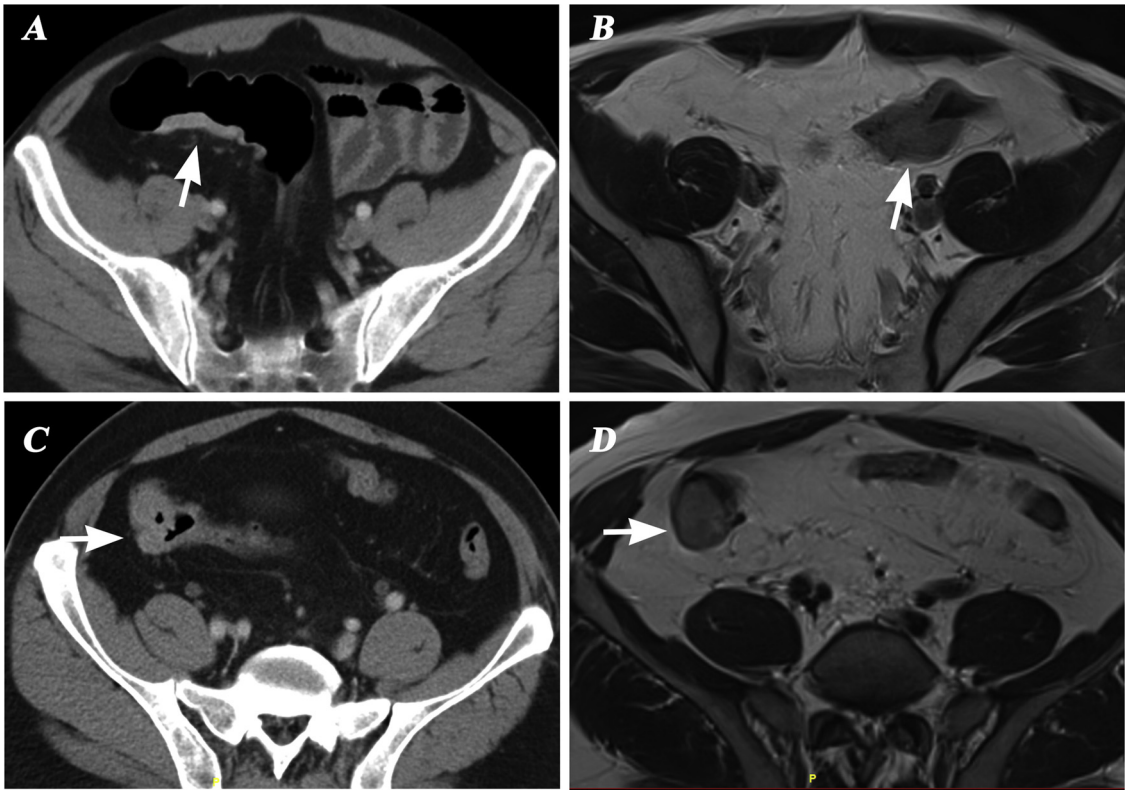

Fig. 3. A–B: Pathologically proved stage T3 colon carcinoma. Axial post-contrast CT (A) shows the smooth outer margin representing a T1-2 disease (subjective score of 1, under-staged), but Axial T2-weighted imaging (B) accurately displays the absence of the muscular layer as T3-4 disease (score of 3). **C-D:** Pathologically proved stage T2 colon carcinoma. Axial post-contrast CT (C) shows mildly coarse outer margin as T3-4 disease (score of 3, over-staged), while axial T2-weighted imaging (D) correctly displays the low signal of muscular layer as T1-2 disease (score of 0).

patients with CT-based T1-2 tumor were correctly diagnosed as T3-4 (confirmed by pathological results) using MRI. The main challenge of MRI in colon is the motion artifacts caused by bowel mobility and vulnerability to breathing motions. In our study, five patients were excluded because of the low-quality MRI.

In the detection of EMVI, CT is of limited use with sensitivity as low as 8 % has been reported by a most recent study [24]. In contrast, the present study demonstrated that MRI was significantly better than CT in detecting EMVI of colon cancer. EMVI was detected with MRI in 68.6 % of these patients with pathological confirmed EMVI but with CT in 40.0 %. Our result is equivalent to that reported from Rollve and colleagues [23]. Of the enrolled eight cases with EMVI in that study, MRI predicted six cases and CT predicted only three. In addition, the study by Nerad et al. [15] also showed a very high sensitivity (88%–100%) for detecting EMVI with MRI. These results indicate MRI may be a superior approach to CT in identifying EMVI in colon cancer. As the link between pathological EMVI and patient' oncologic outcome has been well established [25–27], it is of clinical implications to use MR-detected EMVI as a pre-operative prognostic predictor for patients stratification and therapeutic tailoring.

For N+ disease detecting, MRI had comparable diagnostic performance with CT, and their sensitivity and specificity ranged 57.4%–72.6% in the present study. Similar results and accuracy have been reported by previous studies [15,23]. Actually, there is no reliable imaging modality for detecting nodal involvement. In addition to nodal size, morphologic features may play a role. However based on the limited resolution of current imaging techniques, it is challenging to accurately evaluate the morphology and internal signal intensity or density within a normal-sized lymph node. Moreover, effect of functional imaging is limited by its even lower spatial-resolution than conventional imaging. A previous study has shown advantages of DWI in detecting more lymph nodes, but it cannot offer help for distinguishing between negative and positive nodes [28]. Accurate N staging may depend on future advances in imaging techniques regarding improvements resolution. Nevertheless in the current clinical practice of colon cancer, MRI can provide performance that is not inferior to CT for detecting nodal involvement. Actually, even if not significant, MRI achieved a higher specificity than CT; this could be attributed to the DWI sequence which can help to more reliably predict N-status [29].

There are several limitations in the present study. First, colon MRI scans were generally performed in patients who had uncertain staging results on CT images or who were suspected of having liver metastases, thus a large proportion (125/241, 51.9 %) of patients with no colon MRI were excluded from this study. Our findings therefore should be interpreted with caution due to the highly selected study population. Second, T3 tumor with extramural depth ≥ 5 mm (T3cd) was used as an indicator for neoadjuvant therapy in the Foxtrot trial [5] and may be of clinical importance. But performance of MRI and CT for detecting T3cd disease has not been evaluated in the present study because this item was not available from the previous pathological database of our institution. Third, as a retrospective study, some patients had only CT images of 3 mm slice thickness and multi-planar reformation was not available; this may influence the performance of CT for local staging. But the same is likely true for the MRI protocol which has not been optimally designed (high-resolution axial T2WI was perpendicular to the long axis of human body but not tumor-involved colon, and coronal T2WI has not been performed). Hence, further well-designed prospective research is warranted to validate the present results, as well as to establish the optimal MRI and CT protocols for colon cancer staging.

In conclusion, our data indicate that MRI may offer better diagnostic performance than CT for detecting T3-4 disease and EMVI in sigmoid and descending colon cancer. Moreover, in the identification of nodal involvement, MRI performed comparably with CT. Our findings suggest

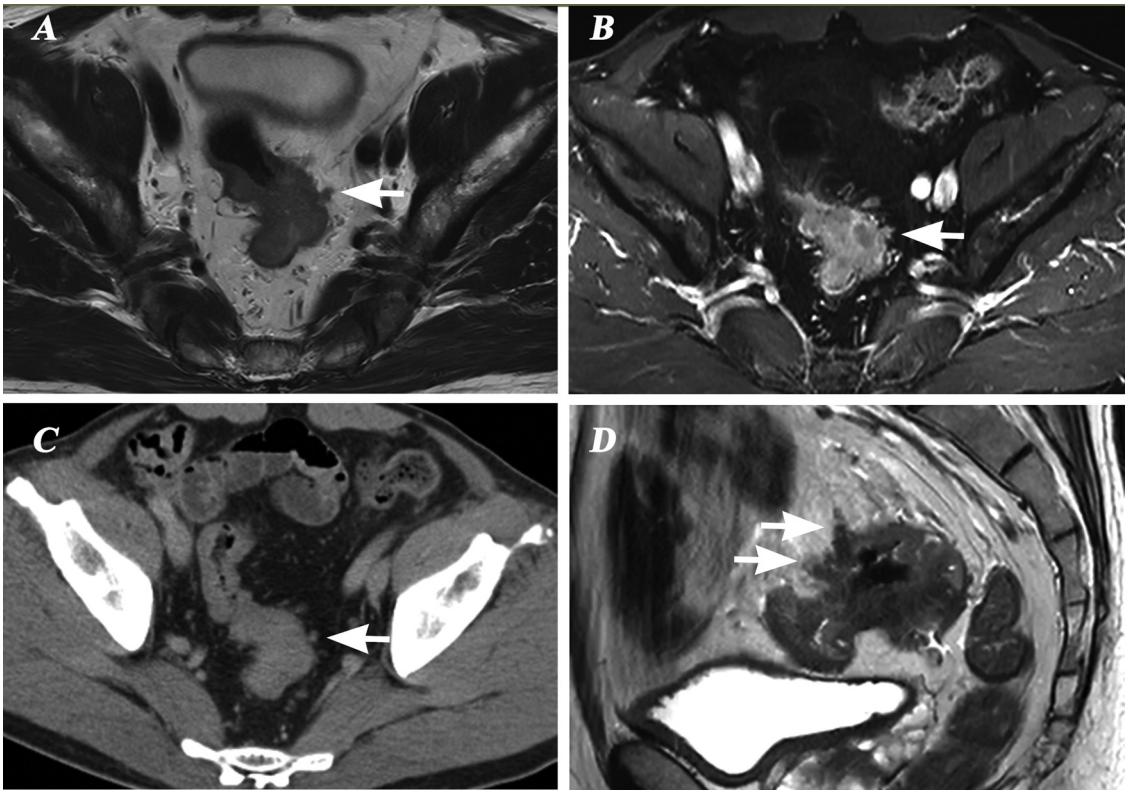

Fig. 4. A–C: Colon carcinoma with pathologically proved extramural vascular invasion (EMVI). Axial T2-weighted imaging (A) and post-contrast T1-weighted imaging (B) display a small vascular containing intermediate signal with expanded caliber (EMVI+, subjective score of 3), which was mistaken for a small lymph node in axial post-contrast CT (arrow in C) by readers. **D:** Another case with pathologically proved EMVI. Sagittal T2-weighted imaging (D) shows the more obvious EMVI than that in A and B, which was also missed by readers with CT (not shown).

that MRI may be acceptable as an alternative tool for local staging and risk-stratifying in patients with colon cancer, especially in those with uncertain tumor stage based on CT alone.

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Disclaimers

The authors indicated no potential conflicts of interest.

Declaration of Competing Interest

It was officially stated that we all authors have participated sufficiently in the intellectual content, the analysis of data and reviewed the final version of the paper. There are no commercial associations that might be a conflict of interest in relation to the resubmitted article.

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