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Original Article

Value of magnetic resonance and diffusion-weighted imaging for diagnosis and assessment of rectal cancer

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Abstract: Early diagnosis of rectal cancer is essential to improve patient survival, as advanced-stage patients have limited therapeutic options and poor prognosis. Imaging modalities, particularly magnetic resonance imaging (MRI), are important clinical tools for diagnosis and assessment of rectal cancer. This study analyzed the value of MRI conventional sequences and diffusion-weighted MRI (DWI) for diagnosis and assessment of rectal cancer. This study included 80 subjects: a case group of 40 subjects with rectal cancer, and a control group of 40 subjects with benign rectal tumors. MRI and DWI scans were used to detect apparent diffusion coefficients (ADC) of tumor tissue and normal tissue of the intestinal wall. Results were analyzed and compared with postoperative pathology staging and types. The area under the receiver-operating-characteristic curve (AUC) of MRI and DWI scans for diagnosis of rectal cancer were 0.921 and 0.992, respectively. ADC of rectal tumor tissue was significantly lower than that of normal rectal tissue ($t = 14.544$; $P<0.05$), and AUC of ADC values for rectal cancer was 0.995. Compared with postoperative pathology examination, Kappa values of pathology staging of rectal cancer assessed through MRI and DWI were 0.552 and 0.772, respectively. In addition, ADC values were significantly different among different rectal cancer pathologies ($F = 15.346$; $P<0.05$). ADC of highly differentiated adenocarcinoma was significantly higher than that of moderately differentiated adenocarcinoma or poorly differentiated adenocarcinoma. AUC of ADC values for poorly differentiated rectal adenocarcinoma was 0.744. In brief, DWI has higher value in diagnosis and assessment of rectal cancer than MRI conventional sequences. Quantitative measurement of ADC values can aid diagnosis of rectal cancer pathologies and can be used in preoperative assessments of degree of progression and malignancy of rectal cancer.

Keywords: Magnetic resonance imaging, MRI, diffusion weighted imaging, DWI, rectal cancer, diagnosis, pathology staging, disease assessment

Introduction

Colorectal cancer is one of the most common gastrointestinal malignancies. In the United States (US), colorectal cancer is the third most prevalent form of cancer and the second leading cause of cancer deaths [1-3]. Rectal cancer is difficult to diagnose-it has no specific symptoms during its early stages, making the disease easy to overlook or confuse with other diseases. Although new technology has increased the early diagnostic rate of rectal cancer, most patients still have progressed to late stage disease at diagnosis, leading to poor prognosis. Therefore, in Europe and the US, medical institutions call for screening and monitoring of rectal cancer to increase early diagnosis and improve patient prognosis [4, 5].

With recent clinical application of new surgical techniques (such as endoscopic submucosal dissection), new chemotherapy techniques, and new molecular targeted drugs, some progress has been made in rectal cancer therapies [6, 7]. However, therapeutic regimens specific to patients with advanced colorectal cancer remain restricted to chemotherapy and molecular targeted therapy, with no substantial extension of patient survival [8, 9]. Therefore, early diagnosis and proper disease monitoring are essential to improve the prognosis of rectal cancer patients.

Table 1. Diffusion weighted imaging (DWI) parameters

Parameter	Value
Repetition time	10300 ms
Echo time	76 ms
Field of view	350 mm × 350 mm
Layer thickness	3 mm
Number of layers	90
Matrix	128 × 128
Band width	1502 Hz/pixel
b-value	0.1000 s/mm^2
Number of collections	8
Collection time	6 min 2 s

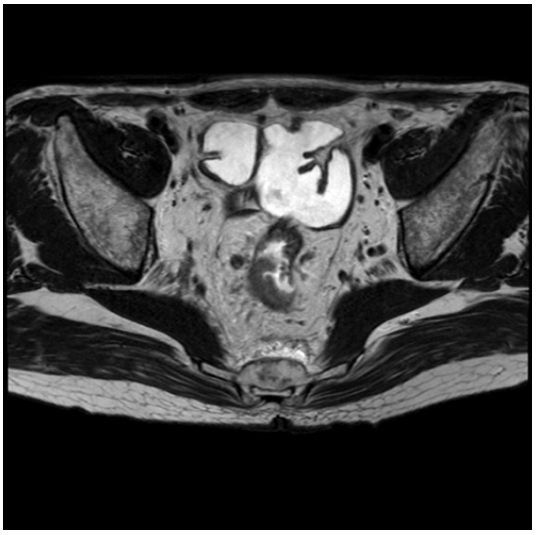

Figure 1. Representative pelvic magnetic resonance imaging (MRI) scan from an axial T2WI sequence. Right rear wall of the upper rectal segment is normally closed and thickening. Equisignal T2WI scan shows slightly higher signal intensity, muscularis propria signal is not continuous, and lymph nodes (diameter = 6 mm) are in mesentery fascia next to the right side of the intestine.

Development of molecular biotechnology, gene technology, endoscopic techniques, and imaging technology has afforded more methods for early diagnosis of rectal cancer. Imaging techniques are an effective means to assess and monitor rectal cancer. In particular, magnetic resonance imaging (MRI) is one of the best imaging modalities to accurately assess rectal cancer. MRI and other imaging methods are important clinical tools for preoperative noninvasive auxiliary diagnosis [10], which has important influence in directing the therapeutic course for patients diagnosed with rectal cancer. High-resolution MRI is also valuable in identifying tumor progression-through assessment of tumor staging and assessment of the relationship of the tumor with surrounding tissues-which also directs therapeutic course. For example, many doctors emphasize stratified therapies for T3 stage rectal cancer patients according to risk of recurrence [11]. Therefore, MRI examination plays an important role in diagnosis and evaluation of rectal cancer.

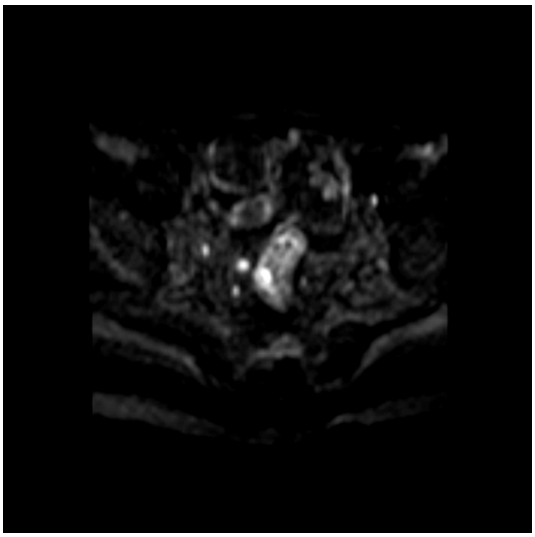

Figure 2. Representative axial diffusion weighted imaging (DWI) scan of the same layer as in **Figure 1**. Right rear wall of the upper rectal segment shows thickening, and equisignal nodules on the right side of the rectum show significantly higher signal. Postoperative pathology confirmation indicated T3 rectal adenocarcinoma with lymph node metastasis adjacent to the intestine.

Additional imaging varieties such as diffusion weighted MRI (DWI) have also shown value in the assessment of rectal cancer. Currently, DWI is the only noninvasive method able to detect diffuse movement of water molecules in living tissues, as the technique can assess transmembrane movement of water molecules based on Brownian motion. This is important for tumor imaging because areas of necrosis and inflammation have altered diffusion properties, making DWI valuable in assessment of differences in tumor pathology [12]. DWI can provide qualitative and quantitative functional information and evaluate biological characteristics of tumors through infusion parameters [13]. In addition, previous studies have shown that DWI can distinguish tumor boundaries better than conventional MRI and can predict patient

Table 2. Rectal and Non-rectal cancer cases diagnosed using magnetic resonance imaging (MRI) and diffusion weighted imaging (DWI) [n (%)]

	Method	n	Diagnosis score					U	P
			1	2	3	4	5		
Rectal cancer	MRI [n (%)]	40	0 (0.0)	2 (5.0)	3 (7.5)	16 (40.0)	19 (47.5)	5.132	<0.01
	DWI	40	0 (0.0)	1 (2.5)	1 (2.5)	6 (15.0)	32 (80.0)		
Non-rectal cancer	MRI	40	15 (37.5)	15 (37.5)	2 (5.0)	8 (20.0)	0 (0.0)	3.035	<0.01
	DWI	40	26 (65.0)	8 (20.0)	6 (15.0)	0 (0.0)	0 (0.0)		

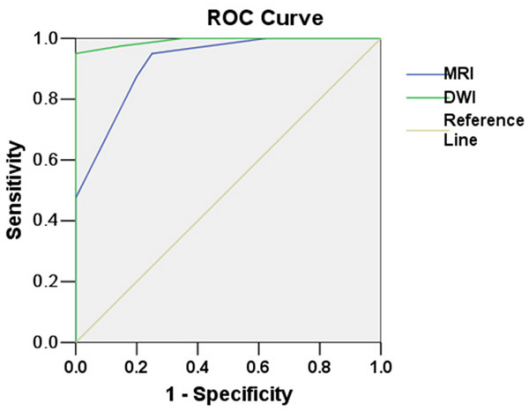

Figure 3. Receiver operating characteristic (ROC) curves of magnetic resonance imaging (MRI) and diffusion weighted imaging (DWI) scans for rectal cancer diagnosis.

Table 3. Performance of magnetic resonance imaging (MRI) and diffusion weighted imaging (DWI) in rectal cancer diagnosis

Method	AUC	Standard error	P	95% confidence interval	
				Upper limit	Lower limit
MRI	0.921	0.028	0.000	0.865	0.977
DWI	0.992	0.007	0.000	0.978	1.006

AUC = area under the curve.

response to chemotherapy [14]. Therefore, DWI techniques have application in evaluating clinical progression of malignant tumors [15, 16].

Studies have shown that combining DWI with conventional MRI can improve the ability of clinicians to evaluate response of advanced rectal cancer patients to chemotherapy and radiotherapy [17]. Other studies of recurrent rectal cancer have shown that DWI does not increase the diagnostic ability of conventional MRI, but does increase specificity and inter-observer agreement [18]. To more fully understand the clinical value of these imaging modalities, this study investigated the performance of MRI and DWI in diagnosis and evaluation of rectal cancer.

Materials and methods

Clinical data

The study included 80 patients treated in The Affiliated Hospital of Shanxi University of Traditional Chinese Medicine from January 2013 to January 2014. The case group included 40 subjects with rectal cancer, including 22 males and 18 females. Case group subjects were 35-81 years old with a mean age of 58.6±12.6 years. Patients who received radiotherapy and chemotherapy or other adjuvant therapy before MRI were excluded. All 40 subjects were confirmed by preoperative biopsy and postoperative pathology examination and received pelvic MRI and DWI scans before treatment. The control group consisted of 40 subjects who were diagnosed with suspicious rectal masses, including 20 males and 20 females. Control group subjects were 32-78 years old with a mean age of 56.8±3.7 years. Control group subjects received MRI and DWI scans and underwent rectoscopy biopsies to exclude rectal cancer. Case and control groups did not significantly differ in age and gender (P>0.05). All subjects gave informed consent to participate in the study. The hospital ethics committee of the Affiliated Hospital of Shanxi University of Traditional Chinese Medicine approved the study protocol.

Observational indexes and detection methods

Pelvic MRI and DWI scans were performed on a 3.0 T superconductive MRI apparatus (Siemens, Germany). MRI scans were done using conventional sequences, including pelvic plain transverse T1WI and sagittal, coronal, and transverse T2WI. DWI scans used single-shot echo planar imaging and frequency selection pulse

Table 4. Consistency of rectal cancer staging by magnetic resonance imaging (MRI) and postoperative pathology examination

MRI stage	Pathology stage				Total
	T1	T2	T3	T4	
T1 (n)	1	3	0	0	4
T2 (n)	2	12	1	0	15
T3 (n)	0	2	12	3	17
T4 (n)	0	0	1	3	4
Total (n)	3	17	14	6	40

Table 5. Consistency of rectal cancer staging by diffusion weighted imaging (DWI) andpostoperative pathology examination

DWI stage	Pathology stage				Total
	T1	T2	T3	T4	
T1 (n)	2	1	0	0	3
T2 (n)	1	15	1	0	17
T3 (n)	0	1	13	2	16
T4 (n)	0	0	0	4	4
Total (n)	3	17	14	6	40

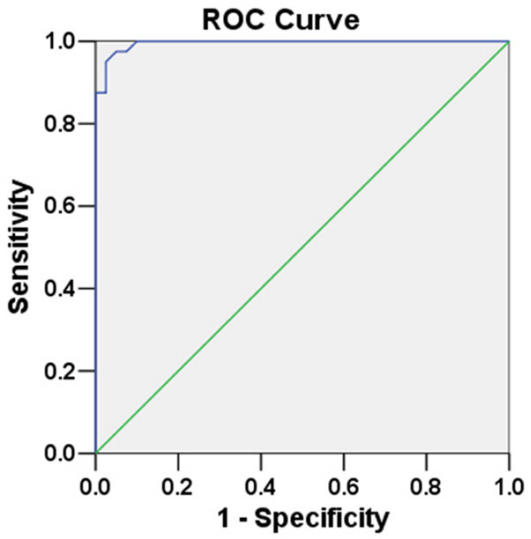

Figure 4. Receiver operating characteristic (ROC) curve of apparent diffusion coefficient (ADC) detection in rectal cancer diagnosis.

fat suppression techniques. Scanning parameters are provided in **Table 1**.

MRI diagnostic standards for rectal cancer were: mass in rectum or thickening wall of rectum; equal or slightly longer T1 signal intensity; and equal T1 or mixed with T2 signal intensity. DWI diagnostic standards for rectal cancer were: mass in rectum or restricted diffusion of thickening wall; and high signal. All cases were evaluated by the 5-score system: 1 = definitely not cancer; 2 = probably not cancer; 3 = uncertain; 4 = probably cancer; and 5 = definitely cancer. Tumors were staged according to MRI results using staging criteria: T1 = tumor invading rectal submucosa; T2 = tumor invading rectal wall muscularis propria; T3 = tumor penetrating rectal wall muscularis propria and reaching subserosa or invading surrounding tissues near rectum; and T4 = tumor penetrating peritonaeum viscerale or directly invading other organs or tissues.

Table 6. Efficiency of apparent diffusion coefficient (ADC) detection in diagnosis of rectal cancer

AUC	Standard error	P	95% confidence interval	
			Lower limit	Upper limit
0.995	0.004	0.000	0.986	1.004

AUC = area under the curve.

During DWI, a circular region of interest at the maximum level of the tumor lesion was selected and its apparent diffusion coefficient (ADC) was measured, avoiding necrosis or hemorrhage areas. This was repeated three times and the average was used as the final ADC value. The same method was used to measure ADC values of normal rectal segments. MRI results were blindly analyzed by two radiologists, with a third radiologist consulted in cases of inconsistency between the two. According to the "Applications Guidelines for Diagnosis and Treatment of Rectal Cancer (2013 revision)" developed by the American Society of Colon and Rectal Surgeons [19], pathology staging and pathology types of case group subjects were compared after surgery. Pathology types were divided using the following criteria: 1 = highly differentiated adenocarcinoma with adenoid tissue structure in the tumor accounting for >95%; 2 = moderately differentiated adenocarcinoma with adenoid tissue structure in the tumor accounting for 50%-95%; and 3 = poorly differentiated adenocarcinoma with adenoid tissue structure in the tumor accounting for <50%.

Statistical analysis

SPSS 13.0 software package was used for statistical analysis (IBM, Armonk, NY). Mea-

Table 7. Apparent diffusion coefficient (ADC) values of tumor tissues from different rectal cancer pathologies

Pathology	n	ADC value ($\times 10^{-3}$ mm^2/s)
Highly differentiated adenocarcinoma	9	0.87±0.07[b,c]
Moderately differentiated adenocarcinoma	22	0.71±0.06[a]
Poorly differentiated adenocarcinoma	9	0.66±0.12[a]

[a]P<0.05 *vs* highly differentiated adenocarcinoma; [b]P<0.05 vs moderately differentiated adenocarcinoma; [c]P<0.05 vs poorly differentiated adenocarcinoma.

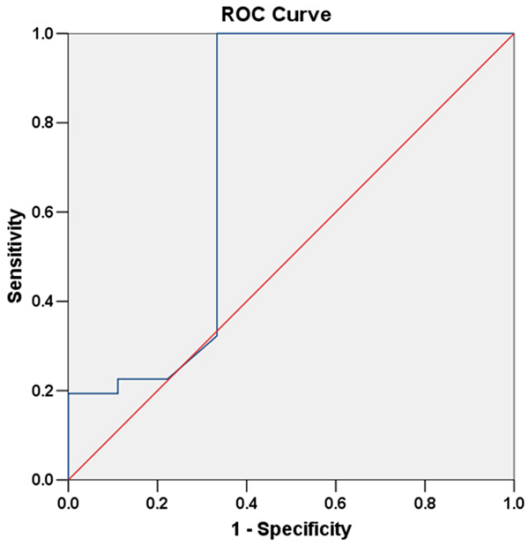

Figure 5. Receiver operating characteristic (ROC) curve of apparent diffusion coefficient (ADC) detection in diagnosis of poorly differentiated adenocarcinoma.

Table 8. Efficiency of apparent diffusion coefficient (ADC) detection in diagnosis of poorly differentiated rectal adenocarcinoma

AUC	Standard error	P	95% confidence interval	
			Lower limit	Upper limit
0.744	0.124	0.028	0.501	0.987

AUC = area under the curve.

surement data are expressed as mean ± standard deviation. Comparisons between the two groups were performed using independent samples t-test. Multiple group comparisons were performed using one-way analysis of variance. Pairwise comparisons were performed using least significant difference (LSD) method. Enumeration data are expressed as percentages. Enumeration data with rank correlation were compared using Mann-Whitney U method of frequency table. Effectiveness of MRI, DWI, and ADC values for diagnosis of rectal cancer was analyzed by receiver operating characteristic (ROC) curves. Area under the curve (AUC) was used as an index to evaluate effectiveness of diagnostic criteria. Cut-off value at maximum Youden index was used as the maximum screening cutoff. Consistency between MRI and DWI in evaluating tumor staging and pathology examination was compared using consistency coefficients (Kappa values) of the paired frequency table. *P*<0.05 was considered statistically significant.

Results

MRI and DWI for rectal cancer diagnosis

From imaging scans, 21 subjects had well-defined masses, while the remaining 59 subjects had fuzzy masses (**Figures 1**, **2**). MRI and DWI scans had significantly different diagnostic score distributions for rectal cancer (U = 5.132; P<0.01) and non-rectal cancer (U = 3.035; P<0.01, **Table 2**). ROC curves of MRI and DWI scans for diagnosis of rectal cancer (**Figure 3**) had AUC of 0.921 and 0.992, respectively (P<0.05) (**Table 3**).

MRI and DWI for evaluating staging and pathology of rectal cancer

Tumor staging was assessed via preoperative imaging scans and postoperative pathology examinations. While rectal tumor staging assessed via MRI corresponded with pathology staging relatively well (**Table 4**), tumor staging agreement between DWI and pathology examination was more precise (**Table 5**). Compared with postoperative pathology examination, Kappa values of rectal cancer pathology staging from MRI and DWI scans were 0.552 and 0.772, respectively (P<0.05).

ADC detection in diagnosis of rectal cancer pathology

Based on DWI, ADC values in rectal cancer tissues were (0.73±0.12) × 10^{-3} mm^2/s and ADC values in normal rectal tissues were (1.26±0.20) × 10^{-3} mm^2/s, which were significantly different (t = 14.544; P<0.05). ROC curve of ADC detection for diagnosis of rectal cancer (**Figure 4**) had an AUC of 0.995 (P<0.05, **Table 6**) and cut-off value of 0.935 × 10^{-3} mm^2/s (**Figure 4**). ADC

values were significantly different among tissues from different rectal cancer pathologies (F = 15.346; P<0.05). ADC of highly differentiated adenocarcinoma was significantly higher than that of moderately or poorly differentiated adenocarcinomas, while ADC values did not significantly differ between moderately and poorly differentiated adenocarcinomas (**Table 7**). ROC curve of ADC values for poorly differentiated rectal adenocarcinoma (**Figure 5**) had an AUC of 0.744 (P = 0.028) and cutoff value of 0.620 × 10^{-3} mm^2/s (**Table 8**).

Discussion

Accurate diagnosis and disease assessment are critical to improve the efficacy of cancer therapies. Development of medical imaging technology, computer tomography (CT), MRI, ultrasound, single photon emission computed tomography (SPECT), positron emission tomography (PET), PET/CT, and other medical imaging techniques have improved early diagnosis, clinical staging, and therapeutic monitoring of tumors. These advanced medical imaging techniques based on different imaging principles have their own unique performances and corresponding clinical applications [20].

In addition to continuing to improve early cancer diagnosis, some clinical researchers have recently tried using DWI combined with other imaging techniques for preoperative assessment of rectal cancer. For example, some studies found that combining DWI with MRI subtraction techniques in preoperative TN staging of rectal cancer is convenient, fast, and highly accurate [21]. Other studies have analyzed the effect of DWI and MRI in evaluating invasion, metastasis, recurrence, and prognosis of rectal cancer and found that DWI is highly valuable for diagnosis of lymph node metastasis in colorectal cancer; that ADC values can provide accurate quantitative information; and that standard T2WI has higher accuracy in estimating postoperative local recurrence of rectal cancer. That study also concluded that combining DWI and T2WI can improve diagnostic performance and is also an effective way to evaluate mesentery infiltration, invasion, and prognosis of rectal cancer [22].

Results of this study showed that MRI and DWI scans for diagnosis of rectal cancer had similar AUC values for ROC curves. However, AUC of ADC values for rectal cancer indicated that, compared to MRI conventional sequences, qualitative and quantitative data provided by DWI has higher diagnostic value and can be an important adjunct diagnostic method for rectal cancer.

Compared with postoperative pathology examination, pathology staging of rectal cancer detected and assessed with DWI was also more accurate than staging assessed with MRI. Further, ADC values differed with tumor pathologies-ADC of highly differentiated adenocarcinoma was significantly higher than that of moderately or poorly differentiated adenocarcinomas. AUC of ADC values for poorly differentiated rectal adenocarcinoma also indicated that, compared to MRI, DWI had higher value in evaluating pathology staging of rectal cancer patients and could be used to assist preoperative assessment of tumor progression and malignancy.

This study demonstrated benefits of DWI for diagnosis and assessment of rectal cancer over conventional MRI sequences. Quantitative measurement of ADC values from scans can aid diagnosis of rectal cancer pathologies and therefore should be used in preoperative assessment of degree of progression and malignancy of rectal cancer.

Disclosure of conflict of interest

None.

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