Original Article

Relationship between apparent diffusion coefficient values and clinicopathologic features in rectal cancer: a cross-sectional study

Chunyu Zhang[1,2,3,4#], Ting Lu[1,2,3,4#], Hongyu Zhang[1,2,3,4], Yuting Zhang[1,2,3,4], Long Yuan[1,2,3,4], Junlin Zhou[1,2,3,4]

[1]Department of Radiology, Lanzhou University Second Hospital, Lanzhou, China; [2]Second Clinical School, Lanzhou University, Lanzhou, China; [3]Key Laboratory of Medical Imaging of Gansu Province, Lanzhou, China; [4]Gansu International Scientific and Technological Cooperation Base of Medical Imaging Artificial Intelligence, Lanzhou, China

Contributions: (I) Conception and design: C Zhang, T Lu, J Zhou; (II) Administrative support: J Zhou; (III) Provision of study materials or patients: C Zhang, T Lu, J Zhou; (IV) Collection and assembly of data: C Zhang, Y Zhang; (V) Data analysis and interpretation: C Zhang, T Lu, H Zhang, Y Zhang, L Yuan; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

[#]These authors contributed equally to this work as co-first authors.

Correspondence to: Junlin Zhou, MD, PhD. Department of Radiology, Lanzhou University Second Hospital, Cuiyingmen No. 82, Chengguan District, Lanzhou 730030, China; Second Clinical School, Lanzhou University, Lanzhou, China; Key Laboratory of Medical Imaging of Gansu Province, Lanzhou, China; Gansu International Scientific and Technological Cooperation Base of Medical Imaging Artificial Intelligence, Lanzhou, China. Email: ery_zhoujl@lzu.edu.cn.

Background: The prognosis of rectal cancer is closely related to its clinicopathologic features. Accurate preoperative assessment of these features is crucial for treatment planning and prognosis prediction. The apparent diffusion coefficient (ADC), derived from diffusion-weighted imaging (DWI), has shown potential as a noninvasive imaging biomarker for evaluating tumor characteristics. This study aimed to explore the relationship between ADC values and the clinicopathological features of rectal cancer.

Methods: We retrospectively recruited 97 eligible patients with rectal adenocarcinoma who underwent magnetic resonance imaging (MRI) and surgical resection at our institution between January 2023 and December 2023. Each patient was evaluated for the presence of extramural vascular invasion (EMVI) or circumferential resection margin (CRM) on MRI, and the mean (ADC_{mean}), minimum (ADC_{min}), and maximum (ADC_{max}) ADC values were calculated. Moreover, the relationship between the ADC values and clinicopathological features, including tumor stage, histologic grade, lymphovascular invasion, perineural invasion, and lymph node metastasis, were statistically analyzed.

Results: Among 97 patients with rectal cancer, the mean age was 61.40±10.46 years and 60 (61.9%) were males. ADC_{mean}, ADC_{min}, and ADC_{max} were significantly lower in patients with EMVI or CRM than in those without EMVI or CRM (P<0.05). Pathologic T1–2 staging exhibited higher ADC_{mean} (0.79±0.26 *vs.* 0.61±0.22, P=0.001), ADC_{min} (0.71±0.26 *vs.* 0.55±0.22, P=0.002) and ADC_{max} (0.89±0.26 *vs.* 0.75±0.22, P=0.004) compared with T3–4 staging. Highly and moderately differentiated tumors had higher ADC_{mean}, ADC_{min}, and ADC_{max} than less-differentiated tumors (P<0.05). Patients with lymphovascular invasion, perineural invasion, and lymph node metastasis showed significantly lower ADC_{mean}, ADC_{min}, and ADC_{max} than those without these conditions (P<0.05). ADC_{mean}, ADC_{min} and ADC_{max} were negatively correlated with EMVI (r=–0.334, –0.340, –0.302), CRM (r=–0.362, –0.414, –0.276), pathologic T-stage (r=–0.324, –0.313, –0.276), histologic grade (r=–0.353, –0.352, –0.289), lymphovascular invasion (r=–0.405, –0.384, –0.421), perineural invasion (r=–0.428, –0.407, –0.265), and lymph node metastasis (r=–0.347, –0.316, –0.268) in rectal cancer.

Conclusions: ADC values were negatively associated with different clinicopathological features of rectal cancer, suggesting their potential role as noninvasive imaging markers for preoperative tumor assessment.

Keywords: Extramural vascular invasion (EMVI); circumferential resection margin (CRM); colorectal cancer; preoperative assessments

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Introduction

Colorectal cancer is the third most prevalent cancer worldwide and the second leading cause of cancer-related deaths, accounting for nearly 900,000 deaths annually (1,2). Globally, the number of new cases of colorectal cancer was more than doubled from 1990 to 2019 (3). Rectal cancer accounts for approximately 1/3 of colorectal cancers, and its incidence increases every year (4).

Recent studies have identified a correlation between the prognosis of rectal cancer and the clinicopathological features of the tumor (5). For example, extramural vascular invasion (EMVI) in rectal cancer is associated with a poor prognosis and low overall survival (6,7). The circumferential resection margin (CRM) has been shown to be an independent prognostic factor in patients with cT3 stage low rectal cancer (8). Additionally, high clinical stage, low degree of differentiation, lymphovascular invasion, perineural invasion, and lymph node metastasis not only indicate the presence of more aggressive tumors but are also closely correlated with patient prognosis (9-11). Given their prognostic significance, accurate preoperative assessment of these clinicopathological features is crucial for optimizing treatment strategies and predicting patient outcomes.

Magnetic resonance imaging (MRI) is an important clinical examination tool for the diagnosis and staging of rectal cancer (12,13). MRI can help in clinical risk stratification by identifying high-risk characteristics of rectal cancer, such as EMVI and CRM (13,14). Diffusion-weighted imaging (DWI), a non-contrast MRI technique, quantifies the diffusion of water molecules in biological tissues, providing functional tumor information (15,16). The apparent diffusion coefficient (ADC), derived from DWI, has been investigated as a potential imaging biomarker for assessing tumor aggressiveness and predicting histopathological features (15-17).

Several studies have explored the correlation between ADC values and clinicopathological characteristics of rectal cancer (18-20). Lower ADC values have been associated with poor differentiation, advanced T stage, and lymph node metastasis, suggesting that ADC could serve as a marker of tumor aggressiveness (18-20). However, most previous studies have focused on individual pathological factors rather than providing a comprehensive analysis of ADC's association with multiple clinicopathological features (18-20). Therefore, the correlation between ADC values and the multiple clinicopathological characteristics of patients with rectal cancer is still being explored.

In this study, we measured the mean (ADC_{mean}), minimum (ADC_{min}), and maximum (ADC_{max}) ADC values in patients with rectal cancer to investigate their relationship with different clinicopathological features of rectal cancer. Moreover, we evaluated the diagnostic value of ADC values in determining the different biological behaviors of rectal cancers. By identifying significant correlations, we aim to evaluate the potential of ADC values as noninvasive quantitative imaging markers for preoperative tumor assessment, which could contribute to

Highlight box

Key findings

- The apparent diffusion coefficient (ADC) values were negatively associated with different clinicopathological features of rectal cancer.

What is known and what is new?

- The majority of prior research has examined individual pathological factors instead of conducting a comprehensive analysis of ADC's relationship with multiple clinicopathological characteristics.
- Our study reveals that mean, minimum, and maximum ADC values were negatively correlated with rectal cancer extramural vascular invasion, circumferential resection margin, pathological T stage, histological grading, lymphovascular invasion, perineural invasion, and lymph node metastasis.

What is the implication, and what should change now?

- ADC values can be used for preoperative noninvasive assessment of clinicopathological features of rectal cancer to better guide clinical risk stratification and personalized treatment.
- ADC values should be used as an important indicator of the clinicopathology of rectal cancer during preoperative evaluation.

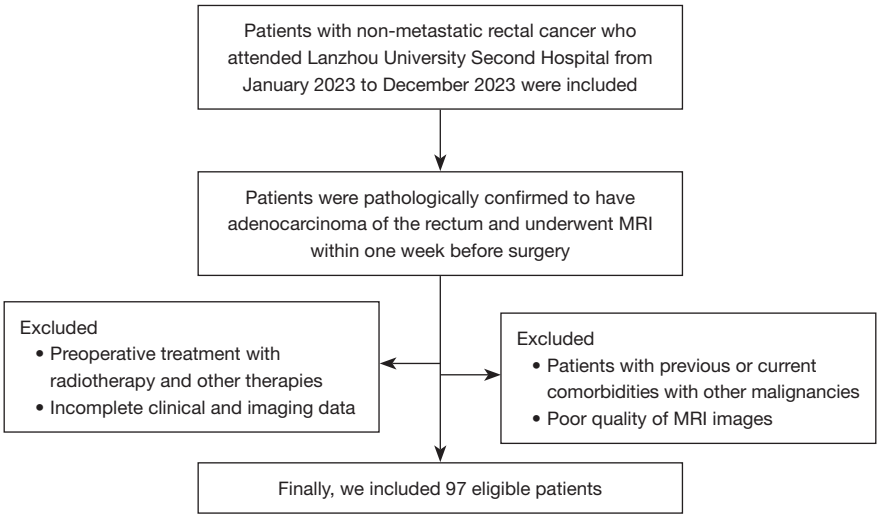

Figure 1 Patient selection process. MRI, magnetic resonance imaging.

more precise treatment planning and prognostic evaluation in rectal cancer. We present this article in accordance with the STARD reporting checklist (available at https://jgo.amegroups.com/article/view/10.21037/jgo-24-831/rc).

Methods

Study design and patient selection

This was a cross-sectional, single-center retrospective study. The study was conducted in accordance with the Declaration of Helsinki and its subsequent amendments. This retrospective study was approved by the Medical Ethics Review Board of Lanzhou University Second Hospital (No. 2024A-927), and the need for informed consent was waived owing to the retrospective nature of the study. Data on patients with non-metastatic rectal cancer who attended Lanzhou University Second Hospital from January 2023 to December 2023 were obtained from hospital's information management system. All patients were pathologically confirmed to have adenocarcinoma of the rectum and underwent MRI within one week before surgery. The exclusion criteria were as follows: (I) preoperative treatment with radiotherapy and other therapies; (II) previous or current comorbidities with other malignancies; (III) incomplete clinical and imaging data; and (IV) poor quality MRI images. Finally, we included 97 eligible patients (*Figure 1*).

Sample size estimation

The required sample size was estimated based on previous studies investigating the correlation between ADC values and clinicopathological features in rectal cancer (18-20). Assuming an expected effect size of r=0.3 (moderate correlation), a significance level of α=0.05, and a power of 80% (1–β=0.8), the minimum required sample size was calculated as 84 patients using G*Power software (version 3.1.9.7). Our final sample size of 97 patients meets this requirement.

Clinical information and laboratory data collection

Preoperative clinical baseline information was obtained including patients' sex, age, smoking, alcohol consumption, body mass index (BMI), and serum tumor marker levels. Serum carcinoembryonic antigen (CEA), carbohydrate antigen 125 (CA125), and carbohydrate antigen 199 (CA199) levels were measured using a chemiluminescent immunoassay (Roche Cobas e601 analyzer, Roche Diagnostics, Mannheim, Germany). Levels were considered to be abnormally high when CEA >3.4 ng/mL, CA125 >35 U/mL, and CA199 >27 U/mL.

Clinicopathological feature assessment

Baseline postoperative pathological evaluations were

performed independently by two experienced pathologists who were blinded to the imaging results. If the two disagreed, the decision was made by consultation. The following parameters were assessed:

(I) Histologic grade: tumors were classified as well-differentiated, moderately differentiated, or poorly differentiated according to the World Health Organization (WHO) classification;
(II) Pathologic T-stage: determined based on the American Joint Committee on Cancer (AJCC) 8th edition tumor node metastasis (TNM) staging system;
(III) Lymphovascular invasion: defined as the presence of tumor cells within endothelial-lined lymphatic or vascular spaces;
(IV) Perineural invasion: defined as tumor cell infiltration within or surrounding nerve structures;
(V) Lymph node metastasis: presence of metastatic tumor cells in regional lymph nodes.

MRI image acquisition

All MRI scans were performed using a Philips 3.0 T superconducting MRI system with a 32-channel linear array surface coil. The main sequences and parameters were as follows: repetition time =3,000 ms, echo time =80 ms, layer thickness =3 mm, matrix =260×260, field of view =260 mm × 260 mm, voxel =1 mm × 1 mm, excitation number =1, and flip angle =90°. Sagittal images of the tumor lesion were obtained to locate the lesion in the rectum, and then axial and coronal T2 weighted image (T2WI) scans and oblique axial and coronal DWI scans were performed. For DWI scanning, a single excitation spin-plane echo sequence was selected, and the b value was chosen to be 0, 1,000 s/mm^2.

MRI image analysis

The MRI images were automatically uploaded to a picture archiving and communication system after scanning was completed, and independent reviews and measurements were performed on this system by two radiologists each with 10 years of experience in diagnostic abdominal imaging. Two radiologists without knowledge of the pathological diagnosis evaluated the maximum diameter, tumor location, EMVI, and CRM. In cases of disagreement between the two reviewers, the final result was determined after deliberation. The distance from the anal verge to the fold of the lower edge of the tumor was measured on the T2 sagittal image. If the distance was <5 cm, it was considered low rectal cancer, 5–10 cm was considered intermediate cancer, and >10 cm was high cancer (18). EMVI was diagnosed as a moderate signal within vessels, a slight dilatation of vessel contours and diameters, a marked irregular nodular dilatation of vessel contours, and an internally defined tumor signal (19). Tumors were considered to have CRM invasion if they were present within 1 mm of the rectal mesenteric fascia (20).

ADC image evaluation

The ADC_{mean}, ADC_{min}, and ADC_{max} values were calculated by two radiologists. Specifically, a circular region of interest was plotted on the axial ADC image using T2WI and DWI as references. The region of interest was positioned at the highest level of the tumor and was sized to contain as many solid portions of the lesion as possible and avoid blood vessels, necrosis/cysts, and calcifications (*Figure 2*). Subsequently, the average of the measurements obtained by the two radiologists was recorded as the final value.

Statistical analysis

All data analyses were conducted using SPSS 26.0 (IBM Corp., Armonk, NY, USA) and Origin 2020 (Northampton, MA, USA). Categorical variables were presented as frequencies (percentages) and were compared using Fisher's exact test or Chi-squared test. Continuous variables were expressed as mean ± standard deviation or median (interquartile range) and were compared using the Wilcoxon-Mann-Whitney *U* test or independent *t*-test. The agreement of the measurements between the two radiologists was assessed using the interclass correlation coefficient. Correlations between ADC values and clinicopathologic features of rectal cancer were assessed using Pearson or Spearman correlation analysis. The receiver operating characteristic curve analysis was used to assess the diagnostic ability of ADC values for the clinicopathologic features of rectal cancer. The area under the curve (AUC) value, sensitivity, specificity and Youden index were calculated. The AUC was classified as follows: 0.5–<0.7 (low), ≥0.7–<0.8 (moderate), ≥0.8–<0.9 (good), and ≥0.9 (excellent) diagnostic accuracy. P<0.05 (bilateral) was regarded as statistically significant.

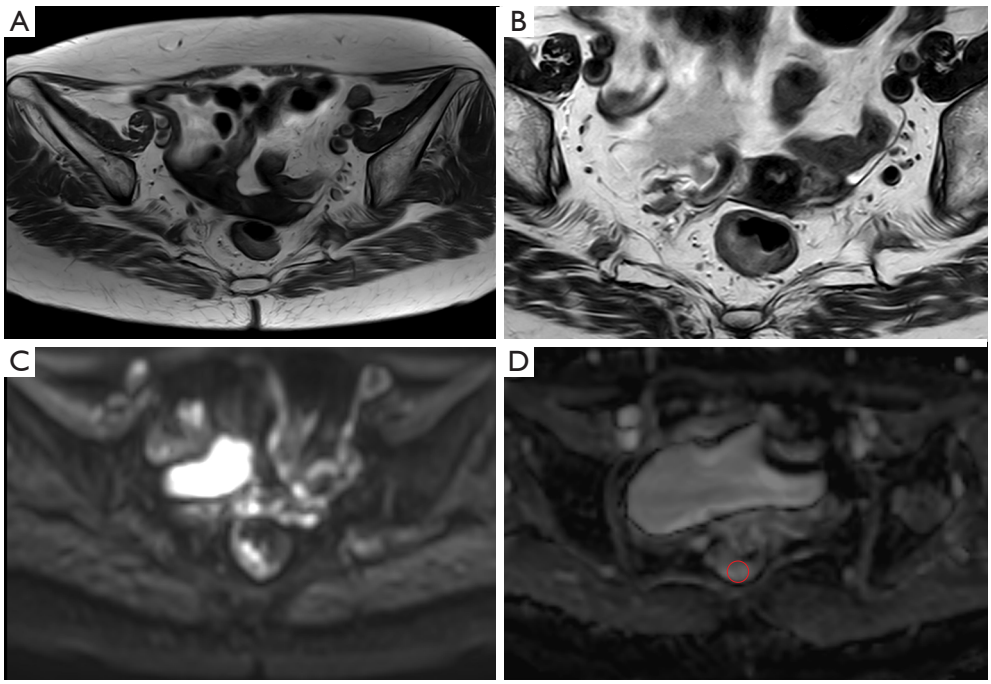

Figure 2 The schematic diagram of the ADC value measurement of the tumor. (A) T1 weighted image of axial lesions; (B) T2 weighted image of axial lesions; (C) diffusion-weighted image of axial lesions; (D) ADC image of axial lesions. The red circle indicates the area of interest for ADC measurement. ADC, apparent diffusion coefficient.

Results

Clinicopathologic characteristics of all patients

Among 97 patients with rectal cancer, the mean age was 61.40±10.46 years and 60 (61.9%) were males. The clinicopathologic features of the patients are shown in *Table 1*. EMVI was present in 71 (73.2%) of the tumors, and CRM was present in 53 (54.6%) of the tumors. Regarding pathological T-stage, 39 (40.2%) of the tumors were T1–2 and 58 (59.8%) were T3–4. Regarding histological grading, 65 (67.0%) of the tumors were highly/moderately differentiated and 32 (33.0%) were lowly differentiated. In addition, 60 (61.9%) tumors had lymphovascular invasion, 61 (62.9%) had perineural invasion, and 33 (34.0%) had lymph node metastasis.

Comparison of ADC values for clinicopathologic features

The ADC values, including ADC_{mean}, ADC_{min}, and ADC_{max}, measured by the two radiologists were in good agreement (all intra-class correlation coefficient values >0.80). We found that ADC_{mean} (0.63±0.22 *vs.* 0.83±0.26, P<0.001), ADC_{min} (0.56±0.22 *vs.* 0.76±0.27, P<0.001), and ADC_{max} (0.76±0.22 *vs.* 0.94±0.26, P=0.001) were significantly lower in patients with EMVI than in patients without EMVI. Patients with CRM had significantly lower ADC_{mean} (0.60±0.21 *vs.* 0.78±0.25, P<0.001), ADC_{min} (0.52±0.21 *vs.* 0.73±0.25, P<0.001), and ADC_{max} (0.74±0.22 *vs.* 0.89±0.25, P=0.004) than those without CRM. Furthermore, patients with pathologic T1–2 staging exhibited higher ADC_{mean} (0.79±0.26 *vs.* 0.61±0.22, P=0.001), ADC_{min} (0.71±0.26 *vs.* 0.55±0.22, P=0.002), and ADC_{max} (0.89±0.26 *vs.* 0.75±0.22, P=0.004) compared to patients with T3–4 staging. Higher ADC_{mean} (0.74±0.21 *vs.* 0.57±0.29, P=0.005), ADC_{min} (0.67±0.20 *vs.* 0.50±0.30, P=0.005), and ADC_{max} (0.85±0.22 *vs.* 0.72±0.27, P=0.01) were also observed in patients with high/moderate differentiation compared those with low differentiation. Furthermore, rectal cancer with either lymphovascular invasion, perineural invasion, or lymph node metastasis showed significantly lower ADC values (ADC_{mean}, ADC_{min}, and ADC_{max}) compared to patients without lymphovascular invasion, perineural invasion, or lymph node metastasis (P<0.05; *Table 2*, *Figure 3*). However, ADC values were not significantly different in terms of age, sex, BMI, current smoking, alcohol consumption, CEA, CA125, CA199, maximum tumor diameter, and location (P>0.05).

Table 1 Clinicopathologic characteristics of all patients

Parameters	Values (n=97)
Age (years)	61.40±10.46
Sex	
Male	60 (61.9)
Female	37 (38.1)
BMI (kg/m^2)	22.58±3.44
Current smoking	16 (16.5)
Alcohol consumption	11 (11.3)
CEA (ng/mL)	
>3.4	37 (38.1)
≤3.4	60 (61.9)
CA125 (U/mL)	
>35	3 (3.1)
≤35	94 (96.9)
CA199 (U/mL)	
>27	22 (22.7)
≤27	75 (77.3)
Maximum diameter (cm)	4.49±1.72
Tumor location	
Low/middle	69 (71.1)
High	28 (28.9)
EMVI	
(–)	26 (26.8)
(+)	71 (73.2)
CRM	
(–)	44 (45.4)
(+)	53 (54.6)
ADC_{mean} ($\times10^{-3}$ mm^2/s)	0.68±0.25
ADC_{min} ($\times10^{-3}$ mm^2/s)	0.62±0.25
ADC_{max} ($\times10^{-3}$ mm^2/s)	0.81±0.24
Pathologic T stage	
T1–2	39 (40.2)
T3–4	58 (59.8)
Histological grade	
HD/MD	65 (67.0)
LD	32 (33.0)
Lymphovascular invasion	
(–)	37 (38.1)
(+)	60 (61.9)
Perineural invasion	
(–)	36 (37.1)
(+)	61 (62.9)
Lymph node metastasis	
(–)	64 (66.0)
(+)	33 (34.0)

Data are presented as mean ± standard deviation or n (%). ADC_{max}, maximum apparent diffusion coefficient value; ADC_{mean}, mean apparent diffusion coefficient value; ADC_{min}, minimum apparent diffusion coefficient value; BMI, body mass index; CA125, carbohydrate antigen 125; CA199, carbohydrate antigen 199; CEA, carcinoembryonic antigen; CRM, circumferential resection margin; EMVI, extramural vascular invasion; HD, highly differentiated; LD, low differentiated; MD, moderately differentiated.

Correlation of ADC values with clinicopathologic features

Correlation analysis showed that not only EMVI was negatively correlated with ADC_{mean} (r=–0.334, P=0.001), ADC_{min} (r=–0.340, P=0.001), and ADC_{max} (r=–0.302, P=0.003), but also CRM was negatively correlated with ADC_{mean} (r=–0.362, P<0.001), ADC_{min} (r=–0.414, P<0.001) and ADC_{max} (r=–0.276, P=0.006). Additionally, pathologic T-stage and histologic grading were negatively correlated with ADC_{mean} (r=–0.324, –0.353; P=0.001, <0.001), ADC_{min} (r=–0.313, –0.352; P=0.002, <0.001), and ADC_{max} (r=–0.276, –0.289; P=0.006, 0.004), indicating that the higher the stage and lower the degree of differentiation, the lower the ADC value. The lymphovascular invasion, perineural invasion, and lymph node metastasis also revealed negative associations with ADC_{mean} (r=–0.405, –0.428, –0.347; all P<0.05), ADC_{min} (r=–0.384, –0.407, –0.316; all P<0.05), and ADC_{max} (r=–0.421, –0.265, –0.268; all P<0.05). These findings indicate that the ADC values are negatively correlated with the invasiveness of rectal cancer (*Table 3*, *Figure 4*). However, ADC values did not correlate with patient age, sex, BMI, current smoking, alcohol consumption, CEA, CA125, CA199, maximum tumor diameter, or location (P>0.05).

Table 2 Comparison of ADC values for clinicopathologic features

Parameters	ADC_{mean} ($\times10^{-3}$ mm^2/s)		ADC_{min} ($\times10^{-3}$ mm^2/s)		ADC_{max} ($\times10^{-3}$ mm^2/s)	
	Mean ± SD	P value	Mean ± SD	P value	Mean ± SD	P value
Age (years)		0.14		0.24		0.14
≥55	0.70±0.25		0.63±0.25		0.83±0.25	
<55	0.62±0.23		0.56±0.24		0.74±0.22	
Sex		0.38		0.44		0.38
Male	0.70±0.25		0.63±0.25		0.83±0.24	
Female	0.65±0.25		0.59±0.25		0.78±0.25	
BMI (kg/m^2)		0.82		0.97		0.65
≥24	0.69±0.25		0.62±0.27		0.82±0.24	
<24	0.68±0.25		0.62±0.24		0.80±0.25	
Current smoking		0.52		0.29		0.82
Yes	0.72±0.23		0.68±0.23		0.82±0.24	
No	0.68±0.25		0.60±0.25		0.81±0.25	
Alcohol consumption		0.80		0.74		0.79
Yes	0.69±0.15		0.63±0.13		0.79±0.16	
No	0.68±0.26		0.61±0.26		0.81±0.25	
CEA (ng/mL)		0.28		0.11		0.94
>3.4	0.65±0.25		0.57±0.26		0.81±0.25	
≤3.4	0.70±0.24		0.65±0.24		0.81±0.25	
CA125 (U/mL)		0.53		0.72		0.40
>35	0.60±0.23		0.57±0.22		0.69±0.19	
≤35	0.69±0.25		0.62±0.25		0.81±0.25	
CA199 (U/mL)		0.77		0.69		0.82
>27	0.67±0.28		0.60±0.29		0.82±0.26	
≤27	0.69±0.24		0.62±0.24		0.81±0.24	
Maximum diameter (cm)		0.76		0.61		0.84
≥4.5	0.69±0.26		0.63±0.26		0.81±0.25	
<4.5	0.68±0.24		0.60±0.24		0.80±0.24	
Tumor location		0.09		0.07		0.15
High	0.62±0.23		0.54±0.25		0.75±0.22	
Low/middle	0.71±0.25		0.65±0.25		0.83±0.25	
EMVI		<0.001		<0.001		0.001
(–)	0.83±0.26		0.76±0.27		0.94±0.26	
(+)	0.63±0.22		0.56±0.22		0.76±0.22	
CRM		<0.001		<0.001		0.004
(–)	0.78±0.25		0.73±0.25		0.89±0.25	
(+)	0.60±0.21		0.52±0.21		0.74±0.22	

Table 2 (*continued*)

Table 2 (*continued*)

Parameters	ADC_{mean} ($\times10^{-3}$ mm^2/s)		ADC_{min} ($\times10^{-3}$ mm^2/s)		ADC_{max} ($\times10^{-3}$ mm^2/s)	
	Mean ± SD	P value	Mean ± SD	P value	Mean ± SD	P value
Pathologic T stage		0.001		0.002		0.004
T1–2	0.79±0.26		0.71±0.26		0.89±0.26	
T3–4	0.61±0.22		0.55±0.22		0.75±0.22	
Histological grade		0.005		0.005		0.01
LD	0.57±0.29		0.50±0.30		0.72±0.27	
HD/MD	0.74±0.21		0.67±0.20		0.85±0.22	
Lymphovascular invasion		<0.001		<0.001		<0.001
(–)	0.82±0.27		0.75±0.27		0.94±0.27	
(+)	0.60±0.19		0.53±0.20		0.73±0.19	
Perineural invasion		<0.001		<0.001		0.006
(–)	0.82±0.22		0.75±0.21		0.90±0.25	
(+)	0.60±0.23		0.54±0.24		0.76±0.23	
Lymph node metastasis		0.001		0.003		0.01
(–)	0.74±0.24		0.67±0.24		0.85±0.24	
(+)	0.57±0.23		0.51±0.23		0.72±0.24	

ADC, apparent diffusion coefficient; ADC_{max}, maximum apparent diffusion coefficient value; ADC_{mean}, mean apparent diffusion coefficient value; ADC_{min}, minimum apparent diffusion coefficient value; BMI, body mass index; CA125, carbohydrate antigen 125; CA199, carbohydrate antigen 199; CEA, carcinoembryonic antigen; CRM, circumferential resection margin; EMVI, extramural vascular invasion; HD, highly differentiated; LD, low differentiated; MD, moderately differentiated; SD, standard deviation.

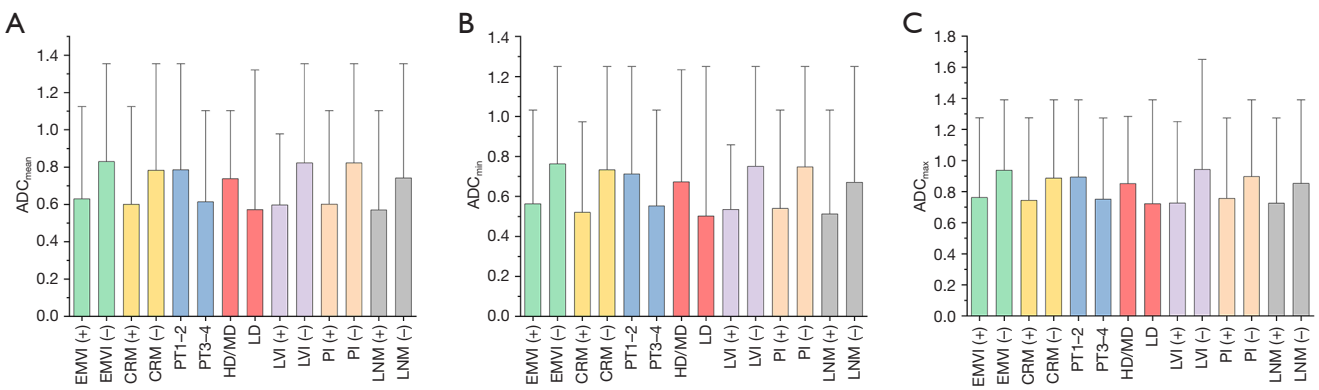

Figure 3 The histograms demonstrate the comparison of ADC_{mean} (A), ADC_{min} (B) and ADC_{max} (C) values among different clinicopathologic features. ADC_{mean}, mean apparent diffusion coefficient value; ADC_{min}, minimum apparent diffusion coefficient value; ADC_{max}, maximum apparent diffusion coefficient value; CRM, circumferential resection margin; EMVI, extramural vascular invasion; HD, highly differentiated; LD, low differentiated; LNM, lymph node metastasis; LVI, lymphovascular invasion; MD, moderately differentiated; PI, perineural invasion; PT, pathologic T stage.

Table 3 Correlation of ADC values with clinicopathologic features

Parameters	ADC_{mean} ($\times10^{-3}$ mm^2/s)		ADC_{min} ($\times10^{-3}$ mm^2/s)		ADC_{max} ($\times10^{-3}$ mm^2/s)	
	r value	P value	r value	P value	r value	P value
Age (years)	0.143	0.16	0.113	0.27	0.147	0.15
Sex	0.102	0.32	0.086	0.40	0.111	0.28
BMI (kg/m^2)	0.032	0.75	–0.003	0.97	0.073	0.48
Current smoking	0.060	0.56	0.100	0.33	0.021	0.84
Alcohol consumption	0.042	0.68	0.045	0.66	–0.003	0.97
CEA	–0.111	0.28	–0.171	0.10	–0.009	0.93
CA125	–0.062	0.55	–0.029	0.78	–0.089	0.38
CA199	–0.041	0.69	–0.049	0.63	0.007	0.94
Maximum diameter (cm)	0.029	0.78	0.047	0.65	0.019	0.86
Tumor location	–0.171	0.10	–0.185	0.07	–0.141	0.17
EMVI	–0.334**	0.001	–0.340**	0.001	–0.302**	0.003
CRM	–0.362**	<0.001	–0.414**	<0.001	–0.276**	0.006
Pathologic T stage	–0.324**	0.001	–0.313**	0.002	–0.276**	0.006
Histological grade	–0.353**	<0.001	–0.352**	<0.001	–0.289**	0.004
Lymphovascular invasion	–0.405**	<0.001	–0.384**	<0.001	–0.421**	<0.001
Perineural invasion	–0.428**	<0.001	–0.407**	<0.001	–0.265**	0.009
Lymph node metastasis	–0.347**	0.001	–0.316**	0.002	–0.268**	0.008

**, at the 0.01 level (two-tailed), the correlation was significant. ADC, apparent diffusion coefficient; ADC_{max}, maximum apparent diffusion coefficient value; ADC_{mean}, mean apparent diffusion coefficient value; ADC_{min}, minimum apparent diffusion coefficient value; BMI, body mass index; CA125, carbohydrate antigen 125; CA199, carbohydrate antigen 199; CEA, carcinoembryonic antigen; CRM, circumferential resection margin; EMVI, extramural vascular invasion.

Diagnostic performance of ADC values for clinicopathologic features

The receiver operating characteristic analysis showed that ADC_{mean} had AUC values of 0.717, 0.710, 0.691, 0.717, 0.741, 0.755, and 0.711 for predicting EMVI, CRM, pathological T stage, histological grade, lymphovascular invasion, perineural invasion, and lymph node metastasis, respectively. The diagnostic performance of ADC_{min} in assessing EMVI, CRM, pathologic T stage, histologic grading, lymphovascular invasion, perineural invasion, and lymph node metastasis was 0.722, 0.740, 0.684, 0.716, 0.728, 0.743, and 0.692, respectively. Furthermore, the AUC values of ADC_{max} for predicting EMVI, CRM, pathological T stage, histological grade, lymphovascular invasion, perineural invasion, and lymph node metastasis were 0.697, 0.660, 0.662, 0.678, 0.750, 0.658, and 0.663, respectively (*Table 4*, *Figure 5*).

Discussion

As a clinical quantitative parameter, the ADC value has attracted increasing research attention and has been widely used to assess the biological characteristics of tumors, such as brain tumors, cervical cancer, esophageal cancer, and prostate cancer (21-24). In the present study, we explored the correlations between different clinicopathological features and ADC_{mean}, ADC_{min}, and ADC_{max} in patients with rectal cancer. Our primary findings showed that all measured ADC values were negatively correlated not only with EMVI and CRM of rectal cancer but also with the pathological T-stage of the tumor, histological grading, lymphovascular invasion, perineural invasion, and lymph node metastasis. However, ADC_{mean}, ADC_{min}, and ADC_{max} were independent of the patient's age, sex, and BMI. Therefore, our study revealed that ADC values can indicate the invasiveness of rectal cancer.

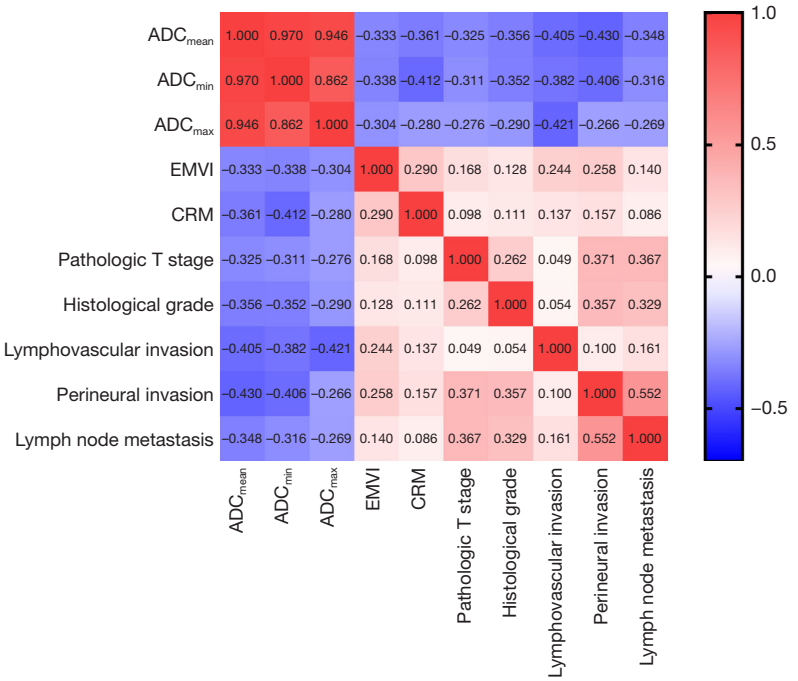

Figure 4 Heat map of the correlation between ADC values and different clinicopathologic features. ADC, apparent diffusion coefficient; ADC$_{mean}$, mean apparent diffusion coefficient value; ADC$_{min}$, minimum apparent diffusion coefficient value; ADC$_{max}$, maximum apparent diffusion coefficient value; CRM, circumferential resection margin; EMVI, extramural vascular invasion.

Table 4 Diagnostic performance of ADC values for clinicopathologic features

Parameters	ADC$_{mean}$			ADC$_{min}$			ADC$_{max}$		
	AUC	Sen (%)	Spe (%)	AUC	Sen (%)	Spe (%)	AUC	Sen (%)	Spe (%)
EMVI	0.717	52.11	88.46	0.722	54.93	88.46	0.697	52.11	80.77
CRM	0.710	83.02	56.82	0.740	83.02	56.82	0.660	88.68	38.64
Pathologic T stage	0.691	56.90	82.05	0.684	63.79	74.36	0.662	62.07	69.23
Histological grade	0.717	59.38	89.23	0.716	65.62	90.77	0.678	59.38	78.46
Lymphovascular invasion	0.741	96.67	54.05	0.728	95.00	54.05	0.750	81.67	67.57
Perineural invasion	0.755	59.02	91.67	0.743	65.57	80.56	0.658	55.74	77.78
Lymph node metastasis	0.711	48.48	90.62	0.692	60.61	79.69	0.663	60.61	70.31

ADC, apparent diffusion coefficient; ADC$_{max}$, maximum apparent diffusion coefficient value; ADC$_{mean}$, mean apparent diffusion coefficient value; ADC$_{min}$, minimum apparent diffusion coefficient value; AUC, area under the curve; CRM, circumferential resection margin; EMVI, extramural vascular invasion; Sen, sensitivity; Spe, specificity.

EMVI and CRM are significant prognostic factors affecting the survival of patients with rectal cancer (25,26). MRI can assess the presence of EMVI and CRM in rectal cancer with high sensitivity and specificity (27,28). A meta-analysis showed that MRI-based radiomics modeling can be used to preoperatively determine EMVI in patients with rectal cancer, with good diagnostic performance (29). Cai *et al.* (30) found that an automated deep learning process constructed based on DWI and T2WI images could classify EMVI states. Additionally, Ju *et al.* (31) found that a joint model constructed using radiomics features extracted from T2WI images combined with clinical features could be

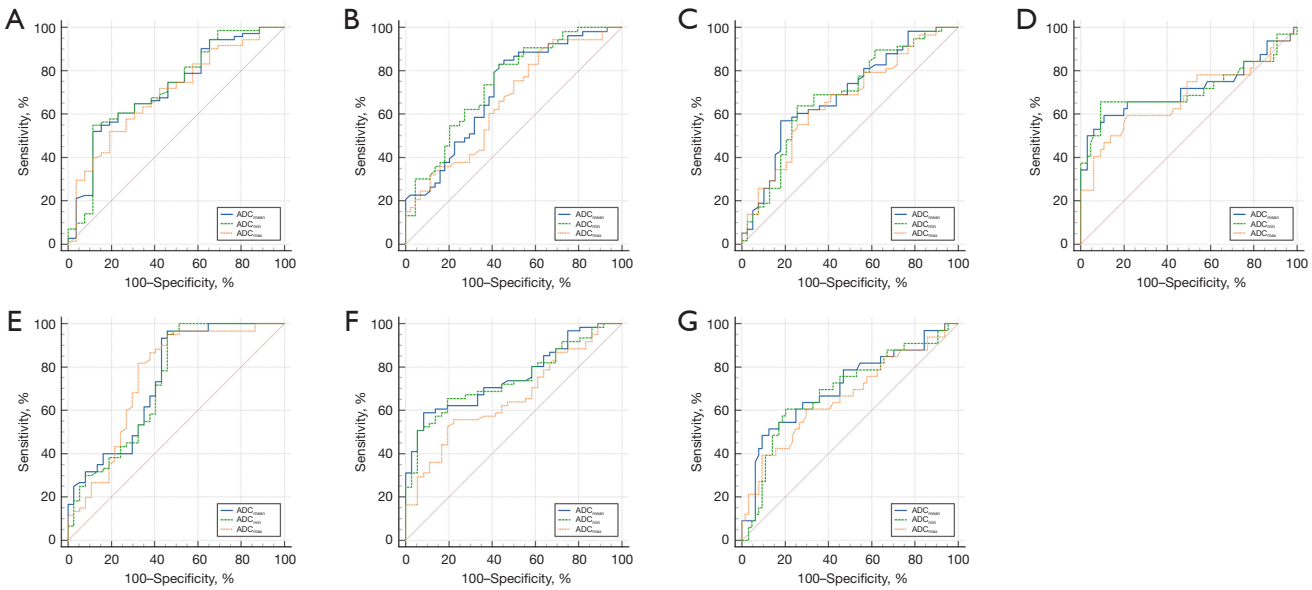

Figure 5 Diagnostic performance of ADC values for EMVI (A), CRM (B), pathologic T-staging (C), histologic grading (D), lymphovascular invasion (E), perineural invasion (F), and lymph node metastasis (G) in rectal cancer. ADC, apparent diffusion coefficient; ADC_{mean}, mean apparent diffusion coefficient value; ADC_{min}, minimum apparent diffusion coefficient value; ADC_{max}, maximum apparent diffusion coefficient value; CRM, circumferential resection margin; EMVI, extramural vascular invasion.

used to clinically determine CRM in patients with low-to-moderate rectal cancer. These studies demonstrated the value of MRI in the diagnosis of EMVI and CRM. In the present study, we observed that ADC_{mean}, ADC_{min}, and ADC_{max} were negatively associated with EMVI and CRM and that ADC values could be used to diagnose EMVI and CRM.

Preoperative staging is important for the personalized treatment of rectal cancer (32). Moreover, preoperative determination of the histological grade of rectal tumors can be used to assess the response to therapy (33). Recent studies have affirmed the value of rectal MRI in TNM staging and histological grading of rectal cancer (18,34). Liu *et al.* (35) reported that ADC values, including mean and minimum ADC values, were related to the T classification and histologic grading of rectal cancer. A retrospective study also showed that ADC values are associated with rectal cancer staging and could be a useful tool for preoperative tumor staging (36). Furthermore, Zhou *et al.* (34) demonstrated that the ADC value of the rectal cancer pathologic T1–2 stage was significantly higher than that of the T3–4 stage, whereas the ADC value of high-grade rectal cancer was significantly lower than that of low-grade cancer. Consistent with the above studies (34-36), our study demonstrated that ADC values are helpful in the preoperative evaluation of rectal cancer staging and grading.

Lymphovascular and perineural invasion and lymph node metastasis are markers of poor prognosis in rectal cancer (37,38). Cho *et al.* (39) found that ADC values can be used to determine whether lymph nodes in rectal cancer are metastatic. Liu *et al.* (35) identified a negative relationship between mean and minimum ADC values and perineural invasion. A retrospective study found that a combined model constructed on the basis of intravoxel incoherent motion-DWI histogram features may be useful in assessing the status of rectal cancer perineural invasion (40). In the present study, we established that patients with rectal cancer with lymphovascular and perineural infiltration and lymph node metastases usually had lower ADC values (ADC_{mean}, ADC_{min}, and ADC_{max}). This suggests that ADC values are associated with the aggressiveness of rectal cancers.

There are some limitations in this study. First, as the data in this study were collected retrospectively, there may be unavoidable selection and recall bias. We plan to design prospective studies to further explore this topic in the future. Second, the sample size was relatively small; we will subsequently include more data and additional centers for further validation in the future. Finally, we only explored the relationship between ADC values and clinicopathological features in rectal cancer. Gene mutation

data are also important for prognostic assessment of patients with rectal cancer, and thus the association between ADC values and gene mutations in rectal cancer warrants further investigation.

Conclusions

In conclusion, ADC_{mean}, ADC_{min}, and ADC_{max} were negatively correlated with rectal cancer EMVI, CRM, pathological T stage, histological grading, lymphovascular invasion, perineural invasion, and lymph node metastasis. This suggests that ADC values can be used for preoperative noninvasive assessment of the clinicopathological features of rectal cancer to better guide clinical risk stratification and personalized treatment.

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Footnote

Reporting Checklist: The authors have completed the STARD reporting checklist. Available at https://jgo.amegroups.com/article/view/10.21037/jgo-24-831/rc

Data Sharing Statement: Available at https://jgo.amegroups.com/article/view/10.21037/jgo-24-831/dss

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://jgo.amegroups.com/article/view/10.21037/jgo-24-831/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki and its subsequent amendments. This retrospective study was approved by the Medical Ethics Review Board of Lanzhou University Second Hospital (No. 2024A-927), and the need for informed consent was waived owing to the retrospective nature of the study.

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