Diffusion Kurtosis Imaging Versus DWI in the Clinical Assessment of Rectal Carcinoma: A Retrospective Study

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Research Article

Keywords: Intestinal tumor, diffusion imaging, microstructure

Posted Date: May 17th, 2021

DOI: https://doi.org/10.21203/rs.3.rs-466182/v1

Abstract

Background: To perform an analysis of mean diffusivity(MD)、mean kurtosis(MK) demonstrating the diagnostic value of diffusion kurtosis imaging (DKI) and diffusion weighted imaging (DWI) with respect to rectal carcinoma.

Methods: A total of thirty-nine rectal carcinoma cases and thirty-nine healthy subjects (Normal control group) were enrolled in our study. All the subjects underwent multi-parameter (DWI, DKI)magnetic resonance examination. The acquired images were individually analysed by two readers. The obtained images were input into the corresponding software, then an analysis of the subjects' apparent diffusion coefficient(ADC), MD and MK values was performed. A receiver-operating charasterictic (ROC) analysis was used to assess the diagnostic efficiency of the MK, MD and ADC parameters. The Mann-Whitney U test was used to contrast the parameters in both groups. Spearman correlation analysis was used to analyse the correlation between ADC and MD, MK. The Kappa consistency test was used to evaluate the consistency between each reader's evaluation.

Results: Reflecting their diagnostic values with respect to rectal carcinoma, the AUC for MK, MD, and ADC were 0.911, 0.888, and 0.827 (all $P < 0.05$), respectively. Using 0.59, 2.15×10^{-3} mm^2/s, 1.35×10^{-3} mm^2/s as thresholds, the sensitivities of MK, MD, ADC were 89.50%, 78.90%, and 76.30%, respectively; meanwhile their respective specificities were 84.20%, 73.70%, and 73.70%.The ADC was directly proportional to MD ($r = 0.994$, $P < 0.05$) and inversely proportional to MK ($r = -0.460$, $P < 0.05$). Analysis of the imaging data revealed consistent results from both readers,Kappa=0.737.

Conclusion: The ADC、MK and MD parameters were effective in diagnosing rectal carcinoma. Moreover, the MK and MD parameters were found to provide even more valid information regarding the microenvironment with a higher diagnostic performance.

Introduction

Rectal carcinoma is a common malignant tumor of the digestive tract. In the United States, colorectal cancer is the third most common type of cancer and the third leading cause of cancer mortality[1] .Recent, evidence has revealed that the popularity of screening and changes in treatment strategies have delayed the progression of disease and decreased the overall mortality rates of patients with rectal carcinoma[2].Correct diagnosis and assessment of rectal cancer are crucial factors when determining the choice of treatment.

According to the diffusion-weighted imaging(DWI) single index and diffusion-tensor imaging(DTI) models, the diffusion of water molecules follows a Gaussian distribution and water molecules are found to move freely and unrestricted in biological tissues[3]. DWI has been shown to be effective for the qualitative and quantitative analysis of lesions, and can be used for the diagnosis and staging of rectal cancer at the molecular level[4].Diffusion kurtosis imaging(DKI) is based on the non-gaussian diffusion theory[5]; it is primarily applied in the neurological field[6],with its prominent role being tumor identification and grading. However, the technique is gradually being applied in the diagnosis of prostate lesions and disease affecting other organs[7]. Up to nowno comparison had been made between DKI and apparent diffusion coefficient(ADC) in terms of colorectal cancer diagnosis, thus we aimed to investigate the ADC values of DWI and DKI parameters in the diagnosis of rectal cancer, and the relationship between ADC values and DKI parameters.

Methods

Patients

The pathological results were considered as the gold standard for diagnosis, a retrospective analysis was conducted on the data of patients (carcinoma of the rectum group)admitted to our hospital from January to June 2017 with a confirmed diagnosis of rectal cancer by surgical pathology, including twenty-nine males and ten females (Mean age = 54.6 ± 12.9 years; age range = 25 to 80 years).Case inclusion criteria: Patients who had not received surgery or chemoradiotherapy for at least a week before the examination;The image had no motion artifactsPostoperative pathological biopsy confirmed adenocarcinoma of the rectum. Case exclusion criteriaThe image’s artifacts were serious and did not meet the diagnosis requirementsNo surgical treatment was performed within 10 days of the examinationChemoradiotherapy was performed before surgeryThe postoperative pathological results reported mucinous adenocarcinomaadenoma and inflammationThe lesion was too small to conduct an ROI measurement

Thirty-nine healthy volunteers matched with the rectal carcinoma group in terms of age and sex were enrolled as the normal control group, including twenty-nine males and ten females(Mean age = 53.1 ± 11.2 years; age range = 25 to 80 years old).Inclusion criteria: Tolerance test; No intestinal disease;No chemoradiotherapy; MRI showed no obvious abnormalities. This study was approved by the medical ethics committee of our hospital, and all the subjects signed an informed consent.

Imaging Protocols

All the MR examination were performed on a 1.5T MR scanner(MAGNETOM Aera, Siemens Healthineers, Erlangen,Germany) with a 32 channe body coil. The routine scan sequence was as follows; Axial T1WI in-opp phase GRE sequence: TR 262ms,TE 2.62msFOV 400 mm×320mmmatrix 256×256slice thickness 6 mminter-layer spacing 1.2 mmAverage 1; Axial T2WI sequenceTR 7520 msTE 96 msFOV 160 mm×160 mmmatrix 360×512slice thickness 3 mminter-layer spacing 0.6Average 2voxel 0.3 mm×0.3 mm×0.3mm

DWI and DKI MRI images were acquired using a free-breathing single-shot echo-planar imaging pulse sequence with diffusion gradients applied in three orthogonal directions with the following parameters: DWI: TR 5498 ms,TE 76 msb value 0,1000 s/mm^2FOV 330 mm×258 mmmatrix 256×256slice thickness 6 mminter-layer spacing 1.2average 2DKI: TR 6200 msTE 78 msb value 0250500750

1000�1500�2000 s/mm^2�the averages for b values were 1 2 3 4 5 6 7, FOV 330 mm×258 mm�matrix 192×192�slice thickness 6.5 mm�inter-layer spacing 1.3 mm�,scanning time 10 min 42 s.

Data Extraction

The MRI images were saved in a DICOM format. ADC values were automatically generated after DWI sequence scanning, the DKI raw date was post-processed through a prototyped Diffusion Toolbox software (Siemens Healthineers), then the mean diffusivity(MD)�mean kurtosis(MK) parameters were generated. Two radiologists with more than 5 years of working experience in the diagnosis of pelvic diseases conducted an ROI analysis (Area range 7.12 to 9.68 mm^2)on the largest surface area covered by the tumor to measure the MK and MD values, avoiding necrotic and cystic areas as much as possible. Whenever a great difference between the two measurements made by the two radiologists was identified, a corresponding discussion was initiated and a unanimous decision made. Additionally, two radiologists with more than 5 years of working experience in the diagnosis of pelvic diseases also performed an ROI analysis(Area range 6.58 to 9.47 mm^2)on the largest surface area covered by the tumor to measure the ADC values, avoiding necrotic and cystic areas as much as possible. Whenever a great difference between the two measurements made by the two radiologists was identified, a corresponding discussion was initiated and a unanimous decision made. All the parameters were measured for 3 times and the mean value was taken.

Statistical Analysis

The SPSS 21.0 software was used for statistical analysis,and measurement data were expressed as $\pm s$� The collected data did not follow a normal distribution. The *Mann-Whitney U* test was used to compare the differences between the two groups. Using the pathological results as the gold standard, ROC curves were drawn, and the respective values for the AUC were calculated. Threshold values were determined according to the most probable index, and the diagnostic efficacy of each parameter for carcinoma of the rectum was evaluated. The *Spearman* rank correlation was used to analyse the relationship between ADC values and MD�MK values. The kappa test was used to evaluate the consistency of the ROI results measured by the two physicians.A value of kappa lower than 0.20 was interpreted as poor agreement,0.41–0.60 as moderate,0.61–0.80 as substantial,and 0.81-1 as almost perfect agreement according to Cohen's kappa coefficient[8] The difference was statistically significant if $P < 0.05$�

Results

The consistency of the ROI measured by the two diagnostic radiologists was good, Kappa=0.737.

Postoperative pathology confirmed that among the thirty-nine cases of rectal carcinoma,11 cases were highly differentiated adenocarcinoma,13 cases were moderately differentiated adenocarcinoma, and 15 cases were poorly differentiated adenocarcinoma. Pathological T stage was ≤T2 in 8 cases, T3 in 18 cases and T4 in 13 cases.

Compared with the control group, an increment in the MK values and a decrement in the MD, ADC values were observed in the rectal carcinoma group, with statistically significant differences, as displayed in table 1 and figure 1 and 2.

Table 1 Comparison of parameters between the two groups

Groups	MK value(n=39)	MD value ($\times 10^{-3}$ mm^2/s)(n=39)	ADC value ($\times 10^{-3}$ mm^2/s)(n=39)
Rectal carcinoma group	0.73±0.15	1.69±0.57	0.90±0.56
Normal/control group	0.51±0.10	2.54±0.50	1.75±0.54
Z value	−6.163	−5.014	−4.801
P value	<0.001	<0.001	<0.001

Values in parentheses are percentages.Values are presented as mean±standard deviation where applicable.MK mean kurtosis,MD mean diffusion,ADC

The ROC curves representing the MK, MD and ADC values for the diagnosis of rectal carcinoma were illustrated in figure 3; the respective AUC values were 0.911,0.888,and 0.827.($P<0.05$), and MK value of 0.59, MD value of 2.15×10^{-3} mm^2/s, ADC value of 1.35×10^{-3} mm^2/s were taken as the threshold values. The sensitivity and specificity values for the diagnosis of rectal carcinoma were listed in table 2 and figure 3.

Table 2 The diagnostic efficacy of rectal carcinoma n term of MK, MD, ADC values

Parameters	AUC	Threshold	Sensitivity(%)	Specificity(%)
MK	0.911	0.59	89.50%	84.20%
MD	0.834	2.15×10^{-3} mm^2/s	78.90%	73.70%
ADC	0.820	1.35×10^{-3} mm^2/s	76.30%	73.70%

The AUC values in parentheses are percentages.MK mean kurtosis,MD mean diffusion,ADC apparent diffusion coefficient.

ADC values were negatively correlated with MK values ($r=-0.460$, $P<0.05$), and positively correlated MD values ($r=0.994$, $P<0.05$).

Discussion

Accurate staging and grading of rectal tumors can facilitate the treatment process and improve the prognosis of patients. DWI is a non-invasive functional imaging technology that provides information about the diffusion of water molecules in the tumor microenvironment. DKI provides more effective clinical information about lesions. Studies have shown that[9] DKI can be used to assess the non-gaussian distribution of molecules in patients with brain diseases such as stroke and Parkinson's disease. The purpose of this study was to compare the application value of DKI and DWI in the clinical evaluation of rectal carcinoma.

ADC values reflect the state of limited diffusion of water molecules. The higher the density of tissue cells, the more limited the diffusion of molecules, the lower the ADC value and vice versa. Malignant cells elicit a fast differentiation rate, thus the diffusion of water molecules in such lesions are limited by the restriction of macromolecular substances and cell membranes[10],resulting in a decrease in the ADC value. This study's results reveal that ADC values in the rectal carcinoma group were lower than those depicted in the control group($P < 0.001$)，which was consistent with the previous theoretical hypotheses[11].Sun YS et al [12] confirmed that the optimal b value of DWI in rectal cancer was 1000 s/mm^2，which could better overcome the influence of perfusion and T2 penetration effects. However, measurement of the ADC value is based on the fact that the diffusion of water molecules conforms to the gaussian distribution. Withal, the human body is composed of several tissues, hence the cell types, cell density and blood supply of each tissue are different. The diffusion of water molecules follows a non-gaussian distribution[12]，DKI represents the plane echo sequence of a single excitation, with 7 different b values and 3 scanning directions perpendicular to each other;The MK value is calculated by the apparent kurtosis coefficient (AKC) in each direction. The larger the MK value is, the more complex the structure is in the target organization, so it is used to measure the complexity of the organizational structure， the larger the MK value is, the more complex the structure is in the target organization, so it is used to measure the complexity of the organizational structure[13]. Moreover, malignant lesions have an abundant supply of interstitial blood vessels, so it was speculated that the MK values of malignant lesions should be higher than those of normal tissues, which was confirmed by the results of this study. On the other hand, MD values were similar to the ADC values of the DWI single index model, which reflects the diffusion state of water molecules in the human body. Malignant cells are compactly arranged, which limits the diffusion of water molecules, leading to a subsequent decrease in their MD values. Based on the aforementioned observations, we speculate that the MD values of malignant lesions should be lower than those of normal tissues. In this study, differences in ADC, MD and MK values between the two groups were statistically significant, indicating that the three parameters were all effective parameters for the diagnosis of rectal carcinoma and could reflect the changes of lesion tissue structures at the microstructure level.

The ROC analysis conducted in this study suggested that the AUC for the MK value was the largest and that of the ADC value was the smallest. The sensitivity and specificity values of MK value were higher than those of the MD and ADC values, so DKI was more effective in diagnosing rectal carcinoma. At present, the preoperative diagnosis of rectal cancer is mainly based on the combination of DWI and T2WI[14], and DKI can also provide similar diffusion images. Rectal tumors delineate a significantly high signal on images with high b values, while the normal intestinal wall, bezoars and surrounding normal structures exhibit a low signal when inhibited, and the higher b the value, the more obvious the inhibition;On the image with a b value of 2000 s/mm^2, only the tumor elicited a significantly high signal. Thence, DKI sequences can also highlight the tumor lesions and has a higher SNR, which can display a more intuitive image of the tumor compared to conventional MRI images, making up for the deficiency of conventional scan sequences in the diagnosis of rectal cancer.

DKI and DWI are both magnetic resonance functional imaging technologies, and the diffusion limitation degree of water molecules has an impact on the MK, MD and ADC values. The results obtained in this study showed that ADC values were positively correlated with MD values, and negatively correlated with MK values. Due to the rapid proliferation of malignant cells, the extracellular volume is rapidly depleted, leading to a drop in both the ADC and MD values. However, the more complex the arrangement structure of tumor cells, the further the diffusion of water molecules from the gaussian distribution, hence increasing the MK value.

Limitations of this study: This study used a retrospective study design, with the possibility of selection bias. Rectal carcinoma was not subdivided according to the pathological grading, and different differentiation grades may affect the DKI model parameters and ADC values;This study's sample size is relatively small, which may be affected by validation bias. Intrarectal coils were not used in this study to increase the SNR. Thus, future studies should expand the sample size in order to increase the reliability of the conclusions.

Conclusion

Withal, DKI has a high diagnostic efficiency and could provide useful clinical information about the characteristics of tumor microenvironment through simultaneous quantitative measurements of MK and MD values based on the diffusion of water molecules.

Abbreviations

DWI:diffusion-weighted imaging;DTI:diffusion-tensor imaging;DKI:Diffusion kurtosis imaging; ADC:apparent diffusion coefficient;MD:mean diffusivity;MK:mean kurtosis;ROC:A receiver-operating charasterictic.

Declarations

Acknowledgements

Not applicable

Authors’contributions

LY and MZ designed the research.LL,SW and JZ collected and analyzed the data.MZ wrote and revised the paper.The authors read and approved the final manuscript.

Funding

This research did not receive any specific grant from funding agencies in the public,commercial,or not-for-profit sectors.

Availability of data and materials

All studies were retrieved from PubMed,EMBASE,Web of Science,Cochrane Library,China National Knowledge Infrastructure(CNKI),Wanfang,and VIP databases

Ethics approval and consent to participate

All procedures used in this research were approved by the Ethics Committee of the Sichuan Provincial People’s Hospital.

Consent for publication

Not applicable

Competing interests

The authors declare that they have no competing interests.

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Figures

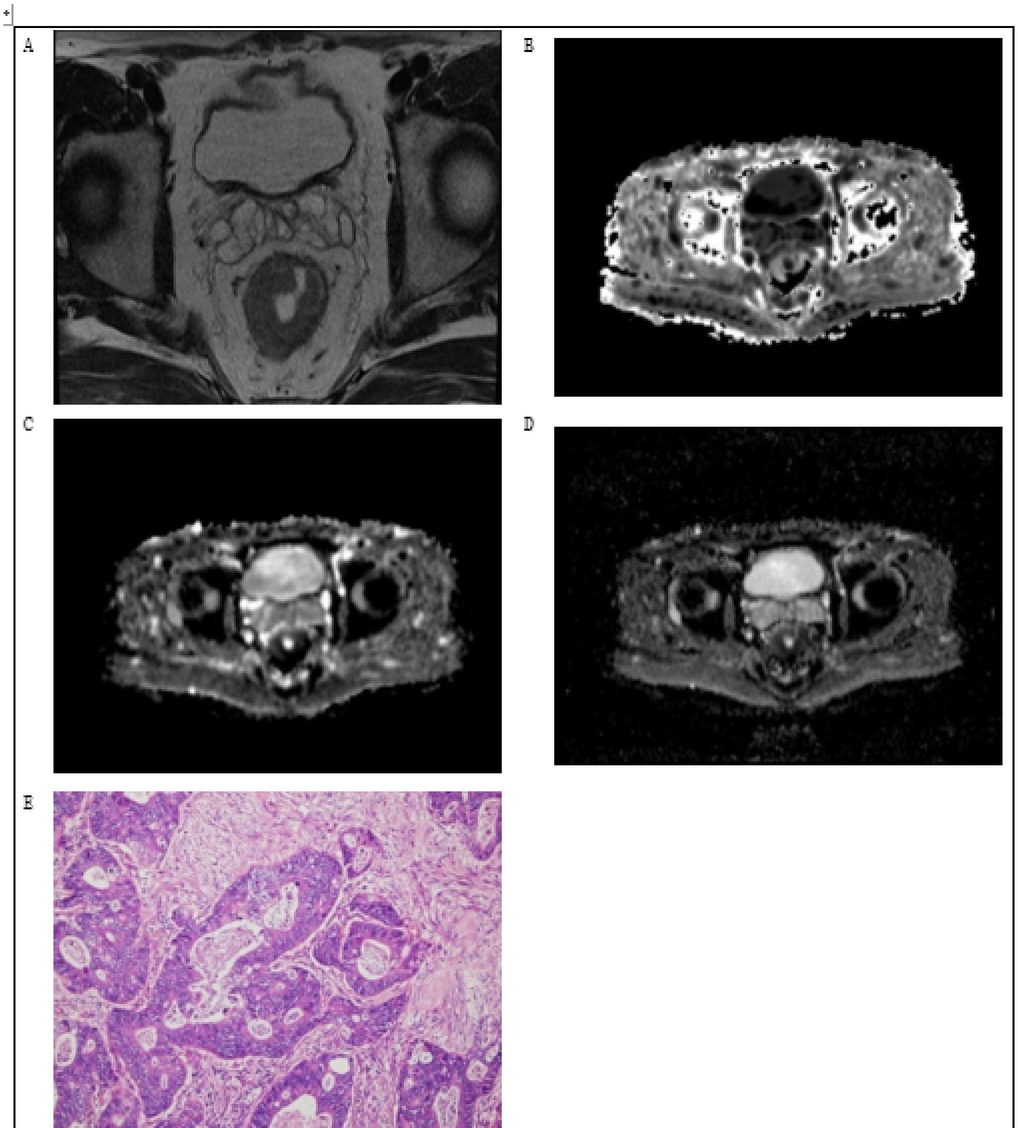

Figure 1

Figure 1

58 year-old man, with stage T3 a middle rectal differentiated adenocarcinoma. The wall of the rectal cancer showed irregular thickening and the tumor elicited a slightly longer T2 signal， b-d.MK, MD, ADC maps, respectively; MK、MD、ADC values were 0.89, 1.61×10−3 mm/s2, and 0.91×10−3 mm/s2 respectively; e. Pathological features.(HE，×200)

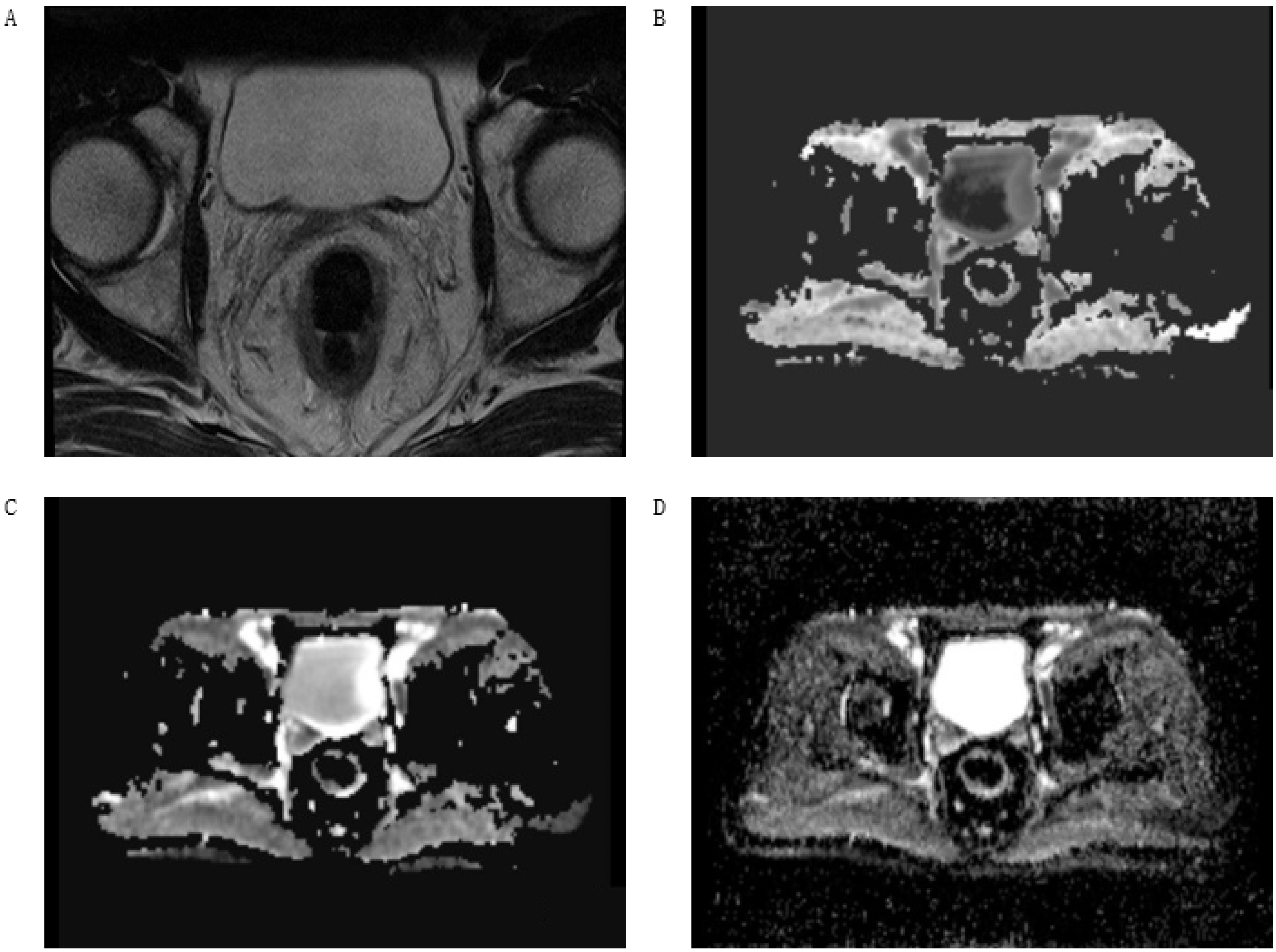

Figure 2

Figure 2

50 year-old man, normal volunteer. a. Axial T2WI shows normal rectal wall divided into three layer. b-d.MK, MD, and ADC maps, respectively; MK, MD, ADC values were 0.485, 2.37×10^{-3} mm/s2, and 1.61×10^{-3} mm/s2 respectively.

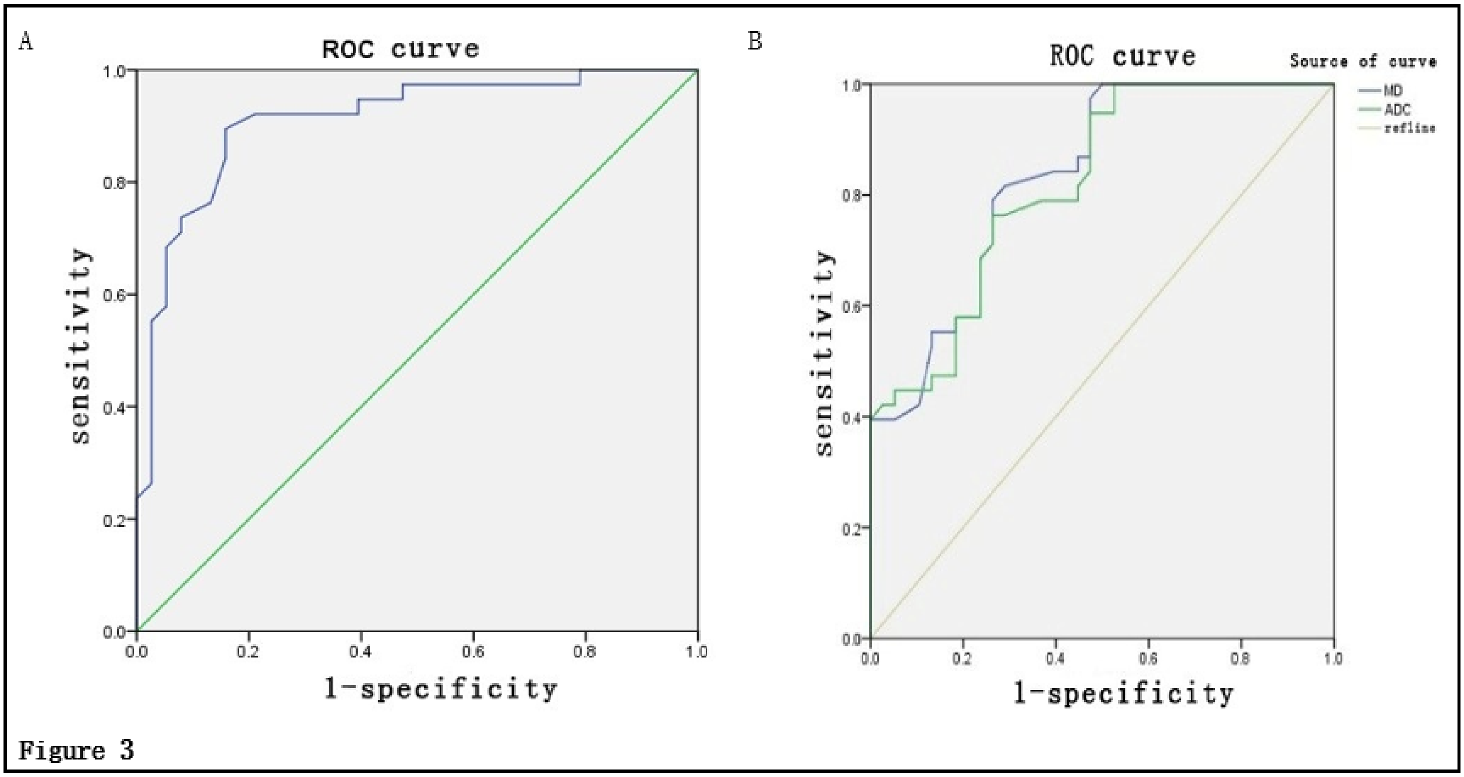

Figure 3

ROC curves of rectal carcinoma diagnosis in terms of MK, MD and ADC values a. The AUC diagnosed with respect to the MK value was 0.911b.The AUC values diagnosed in term of MD and ADC were 0.834 and 0.820, respectively.