

Original Article

Study on diagnostic value of quantitative parameters of intravoxel incoherent motion diffusion-weighted imaging (IVIM-DWI) in prostate cancer

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Abstract: Objective: To investigate the diagnostic value of quantitative parameters of intravoxel incoherent motion diffusion-weighted imaging (IVIM-DWI) in prostate cancer. Methods: From January 2019 to June 2020, 96 patients with prostatic tumor admitted in the department of urological surgery of our hospital were selected as subjects. Magnetic resonance imaging data of 48 cases of benign prostatic hyperplasia and 48 cases of prostate cancer were retrospectively analyzed. The patients included in this study received conventional MRI and IVIM-DWI examinations. Quantitative parameters of IVIM-DWI including D value, D* value, apparent diffusion coefficient (ADC) value and f value in lesions of prostatic tumor were calculated through the double exponential model fitting algorithm. D value, D* value, ADC value and f value were compared between benign prostatic hyperplasia (BPH) group and prostate cancer group. Quantitative parameters of IVIM-DWI were also compared among patients from different Gleason scores groups. The correlation of quantitative parameters of IVIM-DWI with Gleason scores and PSA concentration was analyzed. Diagnostic efficiency of quantitative parameters of IVIM-DWI for prostate cancer was evaluated by ROC curve. Results: Compared with those in BPH group, D value, ADC value and f value in prostate cancer group were significantly lower, but D* value was obviously higher. With the Gleason score increased, D value, ADC value and f value gradually decreased, while D* value gradually increased. The diagnostic efficiency of parameters ADC and D was higher among other parameters. D value, ADC value and f value of prostate cancer were negatively correlated with Gleason score and PSA concentration, respectively (all $P < 0.05$), while D* value was positively correlated with Gleason score and PSA concentration. Conclusions: Quantitative parameters of IVIM-DWI could be used for the diagnosis and evaluation of prostate cancer, and quantitative parameters of IVIM-DWI were associated with Gleason score and PSA concentration.

Keywords: Diffusion-weighted MR imaging, intravoxel incoherent motion, prostate cancer, differential diagnosis

Introduction

Prostatic cancer is one of the most common malignant tumors in middle-aged and elderly men [1]. In recent years, with the population ages, the incidence of prostatic cancer has been increased year by year. It has seriously threatened physical and psychological health of middle-aged and elderly men [2, 3]. It was reported that the treatment plan and prognosis of patients differ according to risks. Patients with prostatic cancer in early phase could be treated actively to reach a higher 5-year survival rate and the patients with prostatic cancer in advanced phase had a significantly lower

5-year survival rate [4, 5]. Thus, early diagnosis and accurate prognosis evaluation of prostatic cancer is very crucial for improvement of life quality and decrease of mortality.

Magnetic resonance imaging is currently the optimal imaging examination method for diagnosing prostate cancer. The use of conventional magnetic resonance imaging technology alone has certain limitations. It could only obtain morphological information and could not reflect the internal microstructure of tumor tissues, which led to difficulty in evaluating the risk of prostate tumors [6, 7]. Some studies reported that conventional T2WI and T1WI enhanced examina-

Diagnostic value of IVIM-DWI in prostate cancer

tions could well show tumor tissue rich in blood vessels, but its diagnostic efficiency for prostate cancer was low because the prostate itself was one of tissues rich in blood supply [8, 9]. In recent years, with the development of magnetic resonance imaging technology, Intravoxel incoherent motion diffusion-weighted imaging (IVIM-DWI) has gradually been used clinically, which could more accurately reflect the microstructure and pathological features of lesions [10]. Some studies reported that IVIM-DWI imaging has been successfully applied for diffuse and tumorous diseases in liver, kidney, pancreas, and so on, and the obtained conclusions have confirmed the IVIM theory from a clinical perspective [11-13]. At present, there are few reports on IVIM research of prostate. Therefore, this study aimed to explore the diagnostic value of IVIM-DWI quantitative parameters for prostate cancer and its correlation with Gleason score and PSA concentration. The results of this study would provide clinical guidance for the diagnosis and evaluation of prostate cancer.

Material and methods

Subjects

From January 2019 to June 2020, 96 patients with prostatic tumor admitted in the department of urological surgery in our hospital were selected as subjects. The inclusion criteria were follows: (1) The age was over 18 years; (2) There was only a solitary lesion; (3) Patients underwent the transrectal ultrasound guided biopsies or surgical resection and tumorous types were confirmed by histopathological methods. (4) Patients voluntarily underwent conventional MRI and IVIM-DWI examinations and the image data was complete. The exclusion criteria were as follows: (1) Biopsies or surgical resection of prostate were conducted within two months of MRI examination. (2) Patients had contraindications of MRI examination such as metal implants in the body. (3) Patients had previous radiotherapy and endocrinotherapy. (4) The clinical data of patients was not complete. (5) Patients were allergic to contrast agents. (6) Patients were accompanied with severe hepatic and renal dysfunctions, cardio-and cerebrovascular disease, other types of malignant tumors and cognition impairment. This study was approved by the

hospital ethics committee and written informed consent was obtained from patients included in this study.

Method of MR examination

All patients were in the supine position. All examinations were performed on 1.5T 48-channel magnetic resonance scanner (Siemens, Germany). The scanned area was from the bottom to the tip of the prostate. The international standards for multi-parametric magnetic resonance imaging (Mp-MRI) technology in prostate were applied. T1WI and T2WI scans were obtained according the following parameters: TR 5500 ms, TE 100 ms, Matrix 320×256, FOV 240×240, slice thickness 3.0 mm, and intersection gap 0 mm. The quantitative parameters of IVIM-DWI were acquired with 7 b values (0, 50, 100, 200, 400, 800 and 1000 s/mm²). The single-shot echo planar image (Matrix 150×141, FOV 280×224, slice thickness 4.0 mm, and intersection gap 0 mm) and dynamic contrast-enhanced MR (Three-dimensional volumetric interpolated breath-hold examination, TR 4.52 ms, TE 1.43 ms, Matrix 224×179×150, FOV 300×300 mm, slice thickness 3.0 mm, NEX 2, A total of 20 rounds, scanning time for each round was 13 s) were performed. The original image of IVIM-DWI was transmitted to a workstation. And the IVIM-DWI fitting pseudo-color image of prostate tissue was obtained through parameter setting and threshold adjustment. According to the method of three-dimensional volume of interest, a circular region of interest (ROI) was drawn in the corresponding area of prostate tumor. The following parameters of IVIM-DWI such as D value, D* value, ADC value and f value were calculated by software. The analysis of data was performed by two experienced radiologists.

Statistical analysis

All the data included in this study were analyzed by SPSS 22.0 statistical software. The measurement data were presented by mean ± standard deviation (SD). The comparison of results from two groups was performed by independent t test. And the comparison among three groups was conducted by One-way ANOVA. The count data were expressed by percentages or cases. The comparison between two groups was performed by χ^2 test. The correlation of quantitative parameters of IVIM-DWI

Diagnostic value of IVIM-DWI in prostate cancer

Table 1. Basic information of patients included in this study

Parameters	Values
Age (years)	72.83±7.63
Duration of diseases (years)	2.18±0.34
BMI (kg/m ²)	21.4±0.87
PSA (ng/mL)	19.70±1.29
BPH (Cases)	48
Prostate cancer (Cases)	48
Gleason scores (Cases)	
Less than 7 points	16
Equal to 7 points	8
More than 7 points	24
Hypertension (Cases)	20
Diabetes (Cases)	14
Hyperlipidemia (Cases)	10

Note: BMI: Body mass index, PSA: Prostate specific antigen, BPH: Benign prostatic hyperplasia.

with Gleason score and PSA concentration were performed by Pearson correlation analysis. Diagnostic efficiency of quantitative parameters of IVIM-DWI for prostatic cancer was evaluated by receiver operating characteristic (ROC). $P < 0.05$ showed that there was statistically significant difference.

Results

General information

As shown in **Table 1**, the average age of patients enrolled in this study was 72.83±7.63 years. Duration of disease was 2.18±0.34 years. Body mass index (BMI) was 21.4±0.87 kg/m². The concentration of prostate specific antigen (PSA) was 19.70±1.29 ng/mL. There were 48 patients with benign prostatic hyperplasia (BPH) and 48 cases with prostate cancer. Meanwhile the cases of Gleason scores less than 7 points, equal to 7 points and more than 7 points were 16, 8 and 24, respectively. In addition, there were 20 patients with hypertension, 14 patients with diabetes and 10 patients with hyperlipidemia.

Comparison of quantitative parameters of IVIM-DWI between BPH group and prostate cancer group

As seen **Table 2**, compared with those in BPH group, D value, ADC value and f value in pros-

tate cancer group were significantly lower, and D* value was obviously higher. And there were significant differences (all $P < 0.05$).

Comparison of quantitative parameters of IVIM-DWI among patients from different Gleason scores groups

There were significant differences for D value, D* value, ADC value and f value among patients from different Gleason scores groups, as shown in **Table 3**. With the Gleason score increased, D value, ADC value and f value gradually decreased while D* value gradually increased.

Diagnostic efficiency of quantitative parameters of IVIM-DWI

The results of ROC curves showed that the sensitivity of D value for diagnosis of prostate cancer was 74.8%, and the specificity was 94.9% with the area under the ROC curve of 0.908; the sensitivity of D* value for diagnosis of prostate cancer was 69.4%, and the specificity was 84.9% with the area under the ROC curve of 0.739; the sensitivity of f value for diagnosis of prostate cancer was 79.3%, and the specificity was 88.6% with the area under the ROC curve of 0.806; the sensitivity of ADC value for diagnosis of prostate cancer was 77.1%, and the specificity was 96.8% with the area under the ROC curve of 0.926, as shown in **Table 4** and **Figure 1**.

The correlation analysis between quantitative parameters of IVIM-DWI and Gleason score and PSA concentration

The results of Pearson correlation analysis showed that there were positive correlations of D value, ADC value and f value with Gleason scores and PSA concentration, while there were negative correlations of D* value with Gleason scores and PSA concentration, as shown in **Table 5**.

Discussion

Prostate cancer and prostate hyperplasia have many similar manifestations. Clinically, the differential diagnosis between them was confirmed by the transrectal ultrasound guided biopsies. However, the complications such as pain and bleeding caused by needle biopsy

Diagnostic value of IVIM-DWI in prostate cancer

Table 2. Comparison of quantitative parameters of IVIM-DWI between BPH group and prostate cancer group

Groups	D value ($\times 10^{-3}$ mm ² /s)	D* value ($\times 10^{-3}$ mm ² /s)	ADC value ($\times 10^{-3}$ mm ² /s)	f value
BPH group	1.18±0.82	5.19±1.27	1.39±0.34	10.27±1.64
Prostate cancer group	0.74±0.15	5.82±1.43	1.09±0.29	9.57±1.45
t value	3.732	2.329	4.747	2.261
P value	<0.001	0.022	<0.001	0.026

Table 3. Comparison of quantitative parameters of IVIM-DWI among patients from different Gleason scores groups

Groups	D value ($\times 10^{-3}$ mm ² /s)	D* value ($\times 10^{-3}$ mm ² /s)	ADC value ($\times 10^{-3}$ mm ² /s)	f value
Gleason score less than 7 points group	1.32±0.85	4.93±1.12	1.56±0.39	11.08±1.54
Gleason score equal to 7 points group	0.80±0.17	5.38±1.09	1.20±0.28	10.41±1.22
Gleason score more than 7 points group	0.68±0.12	6.14±1.23	0.94±0.12	9.02±1.11
F value	14.630	11.030	46.950	24.980
P value	<0.001	<0.001	<0.001	<0.001

Table 4. Diagnostic efficiency of quantitative parameters of IVIM-DWI

Parameters	Area under the ROC curve	Sensitivity (%)	Specificity (%)
D value	0.908	74.8	94.9
D* value	0.739	69.4	84.9
ADC value	0.926	77.1	96.8
f value	0.806	79.3	88.6

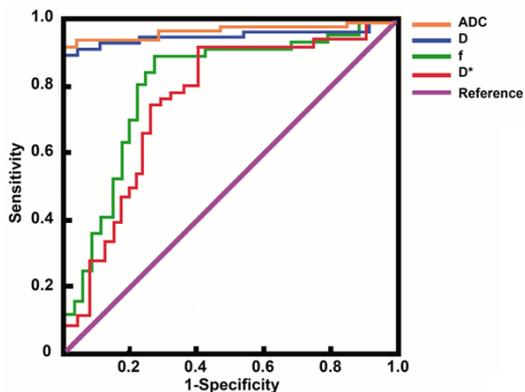


Figure 1. ROC curve of quantitative parameters of IVIM-DWI for diagnosis of prostate cancer.

make it difficult for many patients to accept [14, 15]. Therefore, the ideal detection method for prostate cancer should be less traumatic or non-invasive, less side effects, and a high proportion of patients would benefit. This study mainly explores the diagnostic value of a new

magnetic resonance imaging technique IVIM-DWI for prostate cancer. Apparent diffusion coefficient (ADC value), molecular diffusion coefficient (D value), perfusion-related diffusion coefficient (D* value) and perfusion fraction (f value) were calculated through monoexponential and IVIM model fits and could accurately reflect the diffusion and perfusion features. Quantitative parameters of IVIM-DWI could better reflect the physiological and pathological conditions of the prostate from the perspective of morphology and function. The results of this study showed that compared with those in benign prostatic hyperplasia group, D value, ADC value and f value in prostate cancer group were significantly decreased, and D* value was significantly increased. This is consistent with the results reported by Beyhan et al [16]. Moreover, ROC analysis results showed that the area under the ROC curve of the D value was 0.908 with the sensitivity of 74.8% and the specificity of 94.9%, the area under the ROC curve of the D* value was 0.739 with the sensitivity of 69.4% and the specificity of 84.9%, the area under the ROC curve of f value was 0.806 with the sensitivity of 79.3%, and the specificity of 88.6%, and the area under the ROC curve of ADC value was 0.926 with the sensitivity of 77.1% and the specificity of 96.8%. It was indicated that there was high diagnostic efficiency of quantitative parameters of IVIM-DWI for prostate cancer. Among these parameters,

Diagnostic value of IVIM-DWI in prostate cancer

Table 5. The correlation analysis between quantitative parameters of IVIM-DWI and Gleason scores and PSA concentration

Parameters	Gleason score		PSA concentration	
	Correlation coefficient	P value	Correlation coefficient	P value
D value	-0.706	0.003	-0.694	0.004
D* value	0.548	0.025	0.517	0.031
ADC value	-0.785	0.002	-0.753	0.013
f value	-0.611	0.017	-0.607	0.026

ADC value and D value were more significant. It was confirmed that D value and ADC value could accurately reflect the diffusion movement of water molecules inside and outside the cell, which was in accordance with results reported by previous studies [17, 18].

Gleason score was currently the most commonly used prostate cancer pathology grading system. The higher the Gleason score, the worse the tumor differentiation. Some studies reported that Gleason score was not only correlated with biological behaviors such as tumor invasion, lymph nodes and distant metastasis, but also has important roles in evaluation of prognosis [19, 20]. The results of this study showed that there were significant differences for the following IVIM-DWI quantitative parameters: D value, D* value, ADC value and f value among different Gleason score groups. As the Gleason score increased, the D value, ADC value and f value decreased while D* value increased. Moreover, the D value, ADC value and f value were negatively correlated with Gleason score, while D* value was positively associated with Gleason score. This was basically consistent with previous reports [21, 22]. This may be due to the increase in tumor tissue specificity, the destruction of normal tissue structure, the smaller and denser arrangement of tumor cells, and the restricted diffusion motions of water molecules in the extracellular space with the increase of Gleason score. Another study reported that the degree of diffusion of water molecules in tissues was negatively associated with proliferation of tumor cells [23].

PSA was the most clinically valuable marker for the detection of prostate cancer. It was currently widely used as an indicator for the screening and evaluation of therapeutic effect in prostate cancer [24]. Some studies reported that PSA concentration was positively correlated with the clinical stage of prostate cancer

[25]. The worse grade malignancy and destruction of surrounding tissues by tumors, the higher levels of PSA. The results of this study showed that the IVIM-DWI quantitative parameters D value, ADC value and f value were negatively associated with PSA concentration, and D* value was positively correlated with PSA concentration. This may be due to the decrease of the extracellular space and the increase of blood perfusion in tumor tissues. The results of this study also indirectly indicated that the quantitative parameters of IVIM-DWI may be related with grade malignancy of prostate cancer. This was basically similar to the results reported by Merisaari et al [17, 26].

In summary, quantitative parameters of IVIM-DWI had significant advantages in diagnosis of prostate cancer. For IVIM-DWI quantitative parameters, the decrease of D value, ADC value and f value, and the increase of D* value was helpful for the diagnosis of prostate cancer. And the D value, ADC value and f value were negatively correlated with Gleason score and PSA concentration, while D* value was positively correlated with Gleason score and PSA level, suggesting that IVIM-DWI quantitative parameters were helpful for the assessment of prognosis in prostate cancer patients. There were some limitations in this study: 1. The sample size in this study was small; 2. The accurate selection of ROI was affected to a certain extent; 3. The choice of different b values may have a great influence on quantitative parameters. In the future research, it was need to confirm this finding by increasing the sample size, adopting better mathematical fitting models and improving the stability of parameter measurement.

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Diagnostic value of IVIM-DWI in prostate cancer

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Disclosure of conflict of interest

None.

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Diagnostic value of IVIM-DWI in prostate cancer

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