Submitted: 01 August, 2023 Accepted: 04 January, 2024 Published: 30 March, 2024 DOI:10.22514/jomh.2024.041

ORIGINAL RESEARCH

JOMH Journal of Men's Health

Clinical significance of MRI-DWI and PWI scans in identifying benign prostatic hyperplasia and prostate cancer

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Abstract

To investigate the importance of magnetic resonance diffusion-weighted imaging (DWI) and perfusion-weighted imaging (PWI) for distinguishing between prostate cancer (PCa) and prostate hyperplasia (BPH). A total of 78 patients with prostate disorders and 20 individuals without prostate disorders (control group) treated between June 2020 and June 2023 were examined. Among them, 30 were pathologically diagnosed with BPH and 48 with PCa. (Magnetic Resonance Imaging-diffusion weighted imaging) MRI-DWI and PWI parameters, specifically the apparent diffusion coefficient (ADC), maximum slope of perfusion curve (SSmax) and quasi-T2 relaxation rate (ΔR_2*peak), were compared among the three groups. Microvessel density (MVD) of vascular endothelial growth factor (VEGF) and PCa were quantified through immunohistochemistry. No statistically significant differences were observed in ADC values within the transition zone of the prostate among the control group, BPH and PCa patients ($p > 0.05$), while significant differences in ADC values were observed within the peripheral zone of the three groups ($p < 0.05$). The ADC and T2 values of BPH lesions were significantly higher than those of PCa tissue ($p < 0.05$). Moreover, SSmax and ΔR_2*peak values were significantly different in BPH lesions ($p < 0.05$). MVD levels were significantly lower in BPH lesions compared to PCa lesions, and the positive expression rate of VEGF was also significantly lower in BPH lesions ($p < 0.05$). Correlation analysis revealed a positive association between SSmax and ΔR_2*peak levels in PCa lesions and their MVD and VEGF levels ($p < 0.05$). Both MRI-PWI and DWI imaging demonstrate substantial value in distinguishing between PCa and BPH. Furthermore, a significant correlation was observed between PWI scan parameters, such as SSmax, ΔR_2*peak and VEGF and MVD levels in tumor tissues, offering a promising non-invasive option for assessing tumor neovascularization.

Keywords

Prostate cancer; Magnetic resonance perfusion-weighted imaging; Diffusion-weighted imaging; Tumor angiogenesis

1. Introduction

Prostate cancer (PCa), second only to lung cancer, is the most prevalent cancer among males. In China, the incidence of PCa has been increasing in recent years, primarily due to factors such as aging, environmental pollution, and psychological stress [1–3]. Accurate diagnosis of PCa is a crucial prerequisite for effective treatment and better patient outcomes. Conventional PCa diagnostic methods have limitations in terms of sensitivity and specificity. With the introduction of MRI and its continuous development of functional techniques, more and more functional imaging techniques are being used in clinical practice. Notably, diffusion-weighted imaging (DWI) can depict water molecule diffusion within tissues, while perfusion-weighted imaging (PWI) can reveal microvessel distribution and tissue blood perfusion, both offering valuable insights into the identification of malignant tumors [4–6]. Moreover, malignant tumor growth and metastasis are closely linked to internal neovascularization, which is typically evaluated through immunohistochemistry to assess VEGF and MVD using tissue sections [7–10]. Therefore, finding a non-invasive and efficient method to assess angiogenesis is crucial for malignant tumors. Based on these considerations, this study investigates the utility of MRI-PWI and DWI imaging in distinguishing between BPH and PCa, as well as their capacity to reflect intratumor angiogenesis.

2. Study participants and methods

2.1 Research participants

Between June 2020 and June 2022, a total of 78 patients suspected of having prostate diseases, with confirmed pathological examination data obtained through surgery or prostate puncture biopsy, were enrolled as study participants from our hospital. Among these 78 patients, pathological examination suggested 30 cases of prostate hyperplasia and 48 cases of PCa. Additionally, a control group consisting of 20 healthy volunteers of the same age, without urological diseases, was selected.

The control group had an age range of 50 to 80 years, with a mean age of (62.45 $\pm$ 12.15) years and PSA levels below 4 ng/mL (within the normal range). Patients with prostatic hyperplasia had an age range of 52 to 79 years, with a mean age of (61.85 $\pm$ 11.78) years and PSA levels below 4 ng/mL (normal). Patients diagnosed with PCa had an age range of 53 to 80 years, with a mean age of (63.11 $\pm$ 12.58) years and PSA levels ranging from 6.57 to 194.55 ng/mL, with a mean of (79.45 $\pm$ 13.25) ng/mL. There were no statistically significant differences in age when comparing the three groups ($F = 0.089$, $p = 0.915$).

The study inclusion criteria were as follows: patients had to undergo a complete MRI routine examination, MRI-PWI and MRI-DWI scanning, with high-quality imaging (clear and artifact-free) suitable for clinical analysis. Patients with prostate lesions also needed to obtain a confirmed pathological diagnosis within 6 months following the examination.

Cases that were excluded comprised those who could not cooperate to complete the study and those with incomplete imaging data.

2.2 Sample size calculation

In this study, with a bilateral significance level (α) of 0.05 and a statistical power ($1 - \beta$) of 0.75, combined with preliminary experimentation and findings from previous literature, we assumed that the difference (δ) between the overall means of each group for each measurement was equal to the overall standard deviation (S). According to the formula $N = \frac{4(t_\alpha + t_\beta)s^2}{\delta^2}$, N = 86 was initially calculated. However, considering a 20% loss to follow-up rate and the practical circumstances in the hospital, a final total of 98 participants were included in the study.

2.3 Imaging methods

2.3.1 Examination instrument

The Siemens Symphony 1.5T superconducting magnetic resonance imaging machine (GE, Boston, MA, USA) was utilized in this study, and the contrast agent employed was gadopentetate dextran (Gd-DTPA- BioPAL, Inc., MA, USA).

2.3.2 Imaging method

(1) Firstly, a routine MRI scan was performed.

A standard MRI scan was initially conducted, and the scanning sequences and related parameter settings are outlined in Table 1.

(2) MRI diffusion-weighted imaging:

MRI diffusion-weighted imaging was performed using a single excitation Spin Echo- Echo Planar Imaging (SE-EPI) sequence with fat suppression. The parameter settings were as follows: Time-resolved (TR) = 170 ms, Echo Time (TE) = 94 ms, Flip Angle = 90°, Field of View (FOV) = 250 $\times$ 250 mm, matrix = 128 $\times$ 128, layer thickness = 4 mm, spacing = 1 mm. A total of 9 layers were acquired. Different diffusion gradient factors were applied before and after the 180° pulses of the SE sequence, resulting in varying b-values of 0 s/mm^2, 300 s/mm^2 and 1400 s/mm^2, respectively. Subsequently, ADC maps were generated through computer processing.

(3) MRI perfusion-weighted imaging:

For MRI perfusion-weighted imaging (PWI), the optimal levels within both the peripheral and transition zones of the prostate were chosen. The pulse sequence employed was Echo Planar Imaging-Free Induction Decay (EPI-FID), and the parameters were configured as follows: TR = 120 ms, TE = 47 ms, Flip Angle = 90°, FOV = 250 $\times$ 250 mm, matrix = 128 $\times$ 128, echo train length (ETL) = 128, layer thickness = 4 mm, and interval = 1 mm. The EPI-FID sequence was executed for a total of 60 consecutive scans. Contrast agent injection through the elbow vein was initiated at the onset of the 5th scan, resulting in a collection of 60 frames over a duration of 120 seconds. The same layer was consistently selected, and the dynamic signal intensity-time (SI-T) curve was constructed using the Mean Curve method.

(4) Image analysis

ROI selection should align with the scanning or enhancement sequences and the level at which the lesions are visible. In normal prostate tissue, ROIs should be randomly chosen from both the peripheral zone (PZ) and central gland (CG), with each ROI selected three times for subsequent averaging. For patients with BPH and PCa, ROIs should preferably be located in areas exhibiting substantial signal differences between internal and external regions. These ROIs should avoid regions with visible cystic necrosis, necrosis or hemorrhage, and should avoid blood vessels and tissue edges as much as possible. Each ROI should cover an area of approximately 2 mm^2, and each ROI should be measured three times to compute the average value. Consistently-sized ROIs should be positioned at identical locations on the same image-level for images acquired using different b-values and perfusion images. Several parameters, including the maximum linear slope (SSmax) and quasi-T2 relaxation rate (ΔR_2*peak), were calculated based on the relevant formulas for different b-values at ADC values. For SSmax calculation, the formula used was:

SSmax = [(SIend $-$ SIpiror)/(SIbaseline $\times$ T)] $\times$ 100(%/s), where SS denotes the maximum linear slope, SIend and SIprior represent the signal intensity of two adjacent points with the most significant difference in the signal intensity-time curve for each pixel, SIbaseline is the average signal intensity of the same pixel before enhancement, and T represents the temporal resolution.

For ΔR_2*peak calculation, the formula used was:

ΔR_2*peak = {$-$ln[SI(peak)/SI(0)]}/TE, where SI(peak) corresponds to the signal intensity at the peak time (t), SI(0) represents the signal intensity before enhancement, TE denotes the echo time, and ΔR_2*peak is directly proportional to the concentration of contrast agent in the tissue.

TABLE 1. Conventional MRI scan parameter settings.

Scan Sequence	TR (ms)	TE (ms)	Flip Angle (°)	ETL	FOV (mm)	Matrix	Layer thickness (mm)	Spacing (mm)
Axial SE Sequence	450	14	--	--	--	--	--	--
Axial TSE sequence	4000	100	150	13	--	--	--	--
T2WI + fat suppression	4230	100	150	13	--	--	--	--
Coronal TSE	4000	100	150	13	--	--	--	--
Sagittal TSE sequence	4000	100	150	15	250 × 250	256 × 256	4	1

Note: TR: repeat time, time-resolved; TE: echo time; ETL: echo train length; FOV: field of view; T2WI: T2 Weighted Image; TSE: Turbo Spin Echo Sequence.

2.4 Detection of VEGF and MVD levels in focal tissues

The MRI images were meticulously examined, and the selection of sampling levels was determined in accordance with the respective scale. Tissue samples were acquired from the lesion tissues of patients with BPH and PCa, and the expression levels of VEGF and MVD in these tissues were assessed using immunohistochemistry. (1) MVD was determined through CD34 staining, and the average number of Microvessels (MVs) was calculated under a magnification of 400×, following Weidner's counting method. (2) VEGF staining was conducted using VEGF reagent, and the degree of VEGF staining was categorized into four levels based on Mattern's semi-quantitative counting method under 400× magnification. Specifically, (−) and (+) designations were regarded as VEGF negative, while (++) and (++++) were interpreted as VEGF positive.

2.5 Method of matching MRI lesions with lesions on large pathologic sections

Comprehensive evaluations were conducted by experienced radiologists and pathologists. For pathology slides related to PCa, pathologists delineated the boundaries of lesions and marked areas where cancer had spread. Radiologists independently assessed the MR images for each case using prostate imaging-reporting and data system version (PI-RASD) v2.1 to identify lesions with PI-RADS scores $\geq$3. Subsequently, pathologists performed a second interpretation of PI-RADS v2.1 on the same cases. In instances where disparities occurred between the two interpretations, consensus was reached through discussions. To ensure alignment between the pathology and MRI sections, tissue matching was conducted. A lesion was considered "false-positive" if it was identified by MRI but did not correspond to the same location on the pathology macroscopic section. Conversely, a lesion was classified as "false-negative" if it was labeled on the pathology section but did not appear in the corresponding position on the MRI.

2.6 Statistical data

SPSS 19.0 statistical software (BMI Corporation, Chicago, IL, USA) was used to process the data. Measurement data are expressed as ($\bar{x} \pm s$), *t*-test was used for comparison between two groups, and *F*-test was used for comparison between multiple groups. Count data are expressed as examples, and the χ^2 test was used for comparison between two groups. Spearman's correlation coefficient was used to analyze correlations, and the differences were considered statistically significant at $p < 0.05$.

3. Results

3.1 Comparison of ADC values among the three groups

No statistically significant difference in ADC values within the central zone of the prostate was observed among the three groups ($p > 0.05$). However, when comparing ADC values within the peripheral zone among the three groups, a statistically significant difference was observed ($p < 0.05$).

Among the 48 patients diagnosed with PCa, 36 lesions were situated in the peripheral zone, while 12 lesions were located in the central zone. Within the group of 48 PCa patients, 28 cases were categorized with an MRI staging of $\leq$ stage B and these lesions were contained within the prostatic membrane. Additionally, 13 cases were classified as stage C, indicating they had extended beyond the peripheral membrane but had not exhibited distant metastasis. Seven cases were identified as having distant metastasis (Table 2).

TABLE 2. ADC value ratio of the three groups (mm^2/s).

Grouping	n	Peripheral zone	Central zone
Control group	20	2.69 ± 0.43	1.84 ± 0.28
BPH	30	2.01 ± 0.35	1.79 ± 0.31
PCa	48	0.28 ± 0.04	1.81 ± 0.29
F		499.644	0.245
p		<0.001	0.783

BPH: prostate hyperplasia; PCa: prostate cancer.

3.2 Comparison of T2 and ADC values between BPH and PCa patients

ADC values and T2 values of BPH lesions were higher than those of PCa tissues, and the differences were statistically significant ($p < 0.05$) (Table 3).

TABLE 3. Comparison of T2 values and ADC values between BPH and PCa patients.

Grouping	n	ADC value	T2 value
BPH	30	2.01 ± 0.35	171.43 ± 11.99
PCa	48	0.28 ± 0.04	120.58 ± 12.78
t		34.023	17.501
p		<0.001	<0.001

ADC: apparent diffusion coefficient; BPH: prostate hyperplasia; PCa: prostate cancer.

3.3 Comparison of SSmax and ΔR_2*peak levels between BPH and PCa patients

The SSmax values and ΔR_2*peak values of BPH lesions were lower than those of PCa lesions, and the differences were statistically significant ($p < 0.05$) (Table 4).

TABLE 4. Comparison of SSmax and ΔR_2*peak levels between BPH and PCa patients.

Grouping	n	SSmax (%)	ΔR_2*peak ($\times 10^{-2}$)
BPH	30	35.15 ± 3.79	1.43 ± 0.39
PCa	48	61.27 ± 6.54	3.15 ± 0.65
F		19.861	13.078
p		<0.001	<0.001

SSmax: maximum slope of perfusion curve; BPH: prostate hyperplasia; PCa: prostate cancer.

3.4 Comparison of MVD and VEGF expression in BPH and PCa lesions

MVD levels were significantly lower in BPH lesions than in PCa lesions, and the VEGF positive expression rate was also significantly lower than in PCa lesions ($p < 0.05$) (Table 5).

TABLE 5. Comparison of MVD and VEGF expression in the tissue of BPH and PCa lesions.

Grouping	n	MVD	VEGF Positive
BPH	30	20.14 ± 7.15	27
PCa	48	58.48 ± 10.86	2
t/χ^2		17.134	58.234
p		<0.001	<0.001

MVD: Microvessel density; VEGF: vascular endothelial growth factor; BPH: prostate hyperplasia; PCa: prostate cancer.

3.5 Correlation analysis between SSmax, ΔR_2*peak levels and MVD and VEGF in PCa lesions

Correlation analysis suggested that SSmax and ΔR_2*peak levels of PCa lesions were positively correlated with their MVD and VEGF levels ($p < 0.05$) (Table 6).

TABLE 6. Correlation analysis between SSmax, ΔR_2*peak levels, and MVD and VEGF in PCa lesions.

Parameters	MVD		VEGF	
	r	*p*	*r*	*p*
SSmax	0.674	<0.001	0.726	<0.001
ΔR_2*peak	0.622	<0.001	0.639	<0.001

MVD: Microvessel density; VEGF: vascular endothelial growth factor; SSmax: maximum slope of perfusion curve.

4. Discussion

DWI is currently the only imaging technique that can measure the diffusive motion of water in living tissues [11–13]. Malignant lesions are characterized by a high density of closely packed tumor epithelial cells, exceeding that observed in normal tissues. Together with the incessant proliferation of tumor cells, this results in the extrusion and deformation of the extracellular space. Consequently, the movement of water molecules within the tumor becomes restricted, leading to a decrease in ADC values during DWI scans [14–16]. This phenomenon serves as the pathological foundation for the diagnostic utility of DWI in the identification of malignant tumors.

PWI serves as an imaging modality capable of capturing intratissue hemodynamics by detecting signal changes from magnetic susceptibility alterations due to the entry of contrast agents into capillaries [17, 18]. PWI offers real-time and dynamic insights, facilitating the semi-quantitative evaluation of hemodynamics. During the initial passage of the contrast agent, a substantial concentration gradient disparity exists between intra- and extravascular regions, making the signal highly effective in depicting tissue perfusion, which is unmatched by other imaging modalities [19, 20].

In PCa patients, the ADC value within the peripheral zone of the prostate was notably lower than that in the control group, with the control group exhibiting nearly ten times higher values than PCa patients. This observation may be attributed to several factors, including incomplete neovascular endothelium within PCa tissues, increased blood supply, and enhanced water molecule diffusion, all of which collectively contribute to the lower ADC values in the peripheral zone [21–23]. Furthermore, when compared to patients with BPH, PCa patients also demonstrated lower ADC values in the peripheral prostate region, and this can be linked to PCa lesions characterized by low DWI signal and T2 shortening, as well as the presence of both T2 shortening and diffusion enhancement, both of which result in a decrease in DWI signal [24, 25].

PCa tissues exhibit abundant internal neovascularization and heightened blood perfusion. SSmax values and ΔR_2*peak values serve as common parameters in PWI, effectively portraying tissue characteristics [26–28]. In this study, we observed lower SSmax values and ΔR_2*peak values in PCa lesions, which highlights the potential of these parameters in providing insights into the nature of prostate lesions.

Intra-tumor angiogenesis is recognized as a critical factor influencing tumor growth and metastasis. Currently, VEGF and MVD are the commonly used indicators to assess neovas-

cularization in tumors. VEGF, in particular, plays an active role in promoting angiogenesis. Its ability to enhance vascular permeability facilitates tumor entry into the vascular system and promotes metastasis [29]. Conversely, MVD serves as a quantitative measure reflecting microvascular density [30]. In this study, we observed that the expression of VEGF and MVD in PCa tissues was significantly higher compared to that in BPH tissues. Furthermore, our analysis revealed a positive correlation between the SSmax and ΔR_2*peak levels of PCa lesions and their respective MVD and VEGF levels, suggesting that MRI-PWI scan parameters, specifically SSmax and ΔR_2*peak levels, hold promise in depicting the neovascularization status within PCa lesions and may serve as non-invasive tools for evaluating tumor neovascularization. These scan parameters offer valuable insights for assessing tumor growth, distant metastasis and prognosis, providing a valuable reference for devising clinical treatment strategies for patients.

5. Conclusions

In conclusion, MRI-PWI and DWI imaging showed good clinical implications in differentiating PCa from BPH. In addition, a significant correlation was observed between the parameters SSmax and ΔR_2*peak and the levels of VEGF and MVD in tumor tissues, which is expected to be a non-invasive assessment option for tumor neovascularization.

AVAILABILITY OF DATA AND MATERIALS

The authors declare that all data supporting the findings of this study are available within the paper and any raw data can be obtained from the corresponding author upon request.

AUTHOR CONTRIBUTIONS

QF and PJ—designed the study and carried it out; supervised the data collection, analyzed the data, interpreted the data, prepared the manuscript for publication, and reviewed the draft of the manuscript. All authors have read and approved the manuscript.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Ethical approval was obtained from the ethical committee board of Yiwu Central Hospital (Approval No. K2022-IRB-042). Written informed consent was obtained from a legally authorized representative for anonymized patient information to be published in this article.

ACKNOWLEDGMENT

Not applicable.

FUNDING

This research was funded by the Public welfare technology project of Jinhua City, Zhejiang Province (Grant No. 2022-4-341).

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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How to cite this article: Quan Fang, Ping Jin. Clinical significance of MRI-DWI and PWI scans in identifying benign prostatic hyperplasia and prostate cancer. Journal of Men's Health. 2024; 20(3): 83-88. doi: 10.22514/jomh.2024.041.