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Original Article

Role of Diffusion-Weighted Imaging in the diagnosis of Prostatic Cancer.

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Abstract

Background: Magnetic Resonance Imaging (MRI) plays a vital role in diagnosing prostatic cancer routinely done before biopsy for the lesion's extent and defining the correct path for ultrasound-guided prostate biopsy. Diffusion-Weighted Imaging (DWI) is a non-invasive MRI sequence that shows improved sensitivity and specificity in the same setting with no additional cost. The study aims to evaluate the diagnostic accuracy (DA) of DWI in the detection of prostatic cancer.

Methodology: A cross-sectional study was conducted at the radiology department of Dr. Ziauddin University Hospital between 15/ 04 /2016 to 15/ 4 /2017. A total of 201 patients who were clinically suspected of having prostatic tumors were in this study's inclusion criteria. MRI, including DWI, was done. The final diagnosis was based on an analysis of the histopathology report.

Results: Out of 201 males with clinical suspicious of prostatic cancer, 160 were diagnosed with prostatic cancer on histopathology. Of these, 150 were positive on DWI. The sensitivity of diffusion-weighted MRI was found to be 93.7 %, 75.60 % specificity, and 90.0 % DA for the diagnosis of prostatic cancer.

Conclusion: Diffusion-weighted sequence in MRI examination has a vital role in diagnosing prostatic cancer and should be considered a routine pre-biopsy investigation along with MRI in clinically suspected cases of prostate cancer.

Keywords

Magnetic Resonance Imaging, Diffusion-Weighted Sequence, Prostatic Cancer, Histopathology.

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Introduction

According to the 2012 American Cancer Society statistics, the most common cause of a new cancer diagnosis is prostate cancer and a frequent cancer death[1,2]. The detection and further evaluation of prostatic tumors depend upon serum PSA levels, clinical staging, and pathological findings of surgery[3]. The patients with symptoms and elevated prostatic specific antigen do not necessarily have prostate cancer[4]. Due to technical limitations, trans-rectal ultrasound suffers from poor accuracy[5]. It has been reported that trans-rectal ultrasound-guided biopsies can miss up to 30 % of the tumor.

In comparison with radical prostatectomy, biopsy results had an NPV and PPV of 36 % and 83 %, respectively[6]. Tumors located anteriorly can be easily missed by TRUS biopsy until they become large and possess a size of approximately 15–20 mm, leading to delayed diagnosis. According to the previous studies, TRUS biopsy has underestimated the Gleason score of prostatic cancer on histopathology, which results in inaccurate diagnosis and inappropriate further management. Therefore, some independent statements are published by the United States and the Canadian Task Force on Preventive Health Care, arguing that the risks of serum prostate-specific antigen tests exceed the benefits[7].

As it is already known that MRI before biopsy gives the best tumor assessment and defines the correct path of ultrasound-guided biopsy[3]. However, MRI has good sensitivity but poor specificity[8-10]. Current studies compare magnetic resonance imaging (MRI) results and histopathology and reported sensitivity in the detection of prostatic cancer between 37 % and 96 %, with differences because of different types of cancer, excluding the transition zone cancers, and criteria used for positive findings[11]. These studies show that specificity ranged from 21 % to 67 %.

DWI is an additional MRI sequence done in the same setting with no additional cost. It requires less time as compared to spin-echo imaging. DWI is a very useful investigation to evaluate diagnosis, staging, treatment response, and recurrence of prostatic cancer[12]. DWI works on a principle to determine the diffusion rate of water molecules, different in different tissues depending upon cellularity. The rate of water diffusion in normal prostate tissue is greater than cancer tissue because of decreased water molecules' diffusion in tightly packed cancerous cells. In T2W imaging peripheral zone of the prostate gland gives high signal intensity, while prostatic cancer appears as a region of decreased signal intensity. DWI is a T2 weighted sequence, but, in contrast to typical T2W imaging, tumor cells frequently demonstrate increased signal intensity on standard DWI scans; hence it is difficult to appreciate the tumor within the normal high peripheral zone. To decrease this effect, the apparent diffusion coefficient is used. Prostate cancer appears as an area of high signal on DWI images and shows decreased signal intensity on apparent diffusion coefficient[13].

According to recent studies, DWI, when used with T2 weighted magnetic resonance imaging, improves sensitivity and specificity[14-16]. As per our knowledge, no such data that focuses on DWI's role in the diagnosis of prostatic cancer is available in our population. Hence, by conducting this study, we would know the role of DWI in diagnosing prostatic cancer in our population, as stated in international literature. Thus, adding DWI reduces morbidity and mortality by increasing sensitivity and will offer the patients a better prognosis.

Methodology

This cross-sectional study was conducted at Dr. Ziauddin University Hospital, Karachi, from 15/ 04 /2016 to 15/ 04 /2017 for one year. After approval from the institutional ethical review committee, written informed consent was obtained from the patient referred to the radiology department to request a pelvis MRI to exclude prostatic cancer. The total number of patients was 201 and the sampling was done by a non-probability consecutive method. The sample size was calculated with the help of disease prevalence from literature[17] by the statistics department.

We included suspicious cases having age ranging between 50 and 75 years. Patients who were already diagnosed with prostatic cancer ad those < 50 years of age were excluded as most of the cases of prostate cancer are observed among individuals aged over 65 years, and an estimated incidence of only 0.1% is present among those aged under 50 years. The presence of one or more of the following conditions are considered as suspicious cases of prostatic cancer:

1. Patients having heterogeneous areas on Trans-rectal ultrasound.
2. Patients with hard or nodular prostate on digital rectal examination.
3. Patients with PSA > 4 ngm/ml.

MRI was performed using 1.5 TMR units Magnetrons Harmony by (SIEMENS) using the prostate surface coil. Axial along with coronal and sagittal thin sections, high-resolution T2 weighted images of the pelvis were obtained using these parameters: Repetition time range 5000-7000 ms, time to echo 100 ms, the field of view 20 cms, slice thickness 3 mm, intersection gap of 1 mm, and matrix 256 x 256. Based on T2 W, diffusion restriction images were obtained by applying a single-shot echo planer imaging sequence in axial orientation to include the whole pelvis, using these parameters: Repetition time: 4000 -5000, time to echo 84 ms, the field of view; 30 cm, a slice thickness of 4 mm, intersection gap of 1 mm, matrix 256 x 256 and b value 50-800 s/mm^2. ADC mapping will be generated from the DWI sequence in each pixel of each slice, and the presence of increased signal intensity on DWI as compare to adjacent tissues was labeled as prostatic cancer. This information, along with age, duration of symptoms, and weight of patient and size of the lesion, were recorded in a pre-deigned Performa.

The statistical analysis was done using SPSS version 17.0. Mean ± SD for age, duration of symptoms, the patient's weight, and the size of the lesion were computed. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), DA of DWI (MRI) were calculated. The effect modifiers like age, duration of symptoms, and weight of patient and size of the lesion were addressed through stratification. 2x2 table was used to calculate sensitivity, specificity, NPV, PPV, and DA.

Results

During one year of study from April 2016 to April 2017, 201 patients turned up for MRI pelvis with clinical suspicion of prostatic cancer. The duration of symptoms in all patients was between 3 months to 1 year. Most of the patients diagnosed with prostatic cancer were in between 61-65 years (n=55), followed by 66 - 70 years (n=52). The lowest number of patients were in the group of 50-55 years (n=6). The range of the weight of patients who came with suspicion of prostatic cancer was between 50-110 kg. Patients diagnosed with prostatic cancer mainly lied in the weight range of 80-90 kg (n=60), followed by 90-100 kg (n=55).

Table 1: Demographic characteristics of the study population

Variables		n=201
Age (years)		63.4±4
	< 65 years	112(55.7)
	> 65 years	89(44.3)
Duration of symptoms		5.5±0.6
	<3 months	60(29.85)
	3-6 months	70(34.82)
	>6 months	71(35.32)
Weight (kg)		89±5
	< 80 kg	70(34.8)
	> 80 kg	131(65.2)

Size of lesion	2.8±0.3

*Values are given as mean ± SD or n(%)

Out of the patients with positive prostate cancer, the diagnostic accuracy of DWI was directly proportional to the size of the lesion. The smallest lesion, which was detected as true positive, was 4 mm.

Table 2: Diagnostic accuracy w.r.t. to the size of the lesion

Size of the lesion (cm)	(n)	TP	TN	FP	FN	DA(%)
0.0-0.1	41	26	10	1	4	86.66
1.1-2.0	45	28	12	2	3	88.88
2.1-3.0	55	42	8	3	2	95
3.1-4.0	50	44	1	4	1	97
4.1-5.0	10	10	-	-	-	100

*TP-True Positive; TN-True Negative; FP-False Positive; FN-False Negative; DA-Diagnostic accuracy

Histopathology confirmed the diagnosis of prostatic cancer in 160 patients (79.6 %), and the remaining 41 patients (20.4 %) were found out to be disease negative. DWI correctly diagnosed 150 patients as true positive, while 31 patients were true negative.

Table 3: Comparison of Diffusion-Weighted Imaging and Histopathology results

Diffusion-weighted MRI	Histopathology	
	Positive	Negative
Positive	150	10
Negative	10	31

In the diagnosis of prostatic cancer, the sensitivity of DWI was found out to be 93.75 % and specificity of 75.60 %, with a gold standard of histopathology. The positive predictive value was 93.75 %, and the negative predictive value was 75.60 %. DWI's diagnostic accuracy in diagnosing prostatic cancer was found out to be 90.0 % with a gold standard of histopathology.

Table 4: Validity indicators of Diffusion-Weighted Imaging (MRI) Results

Validity indicators	Percentage (%)
Sensitivity	93.8
Specificity	75.6
Positive Predictive Value	93.8
Negative Predictive Value	75.6
Diagnostic Accuracy	90.0

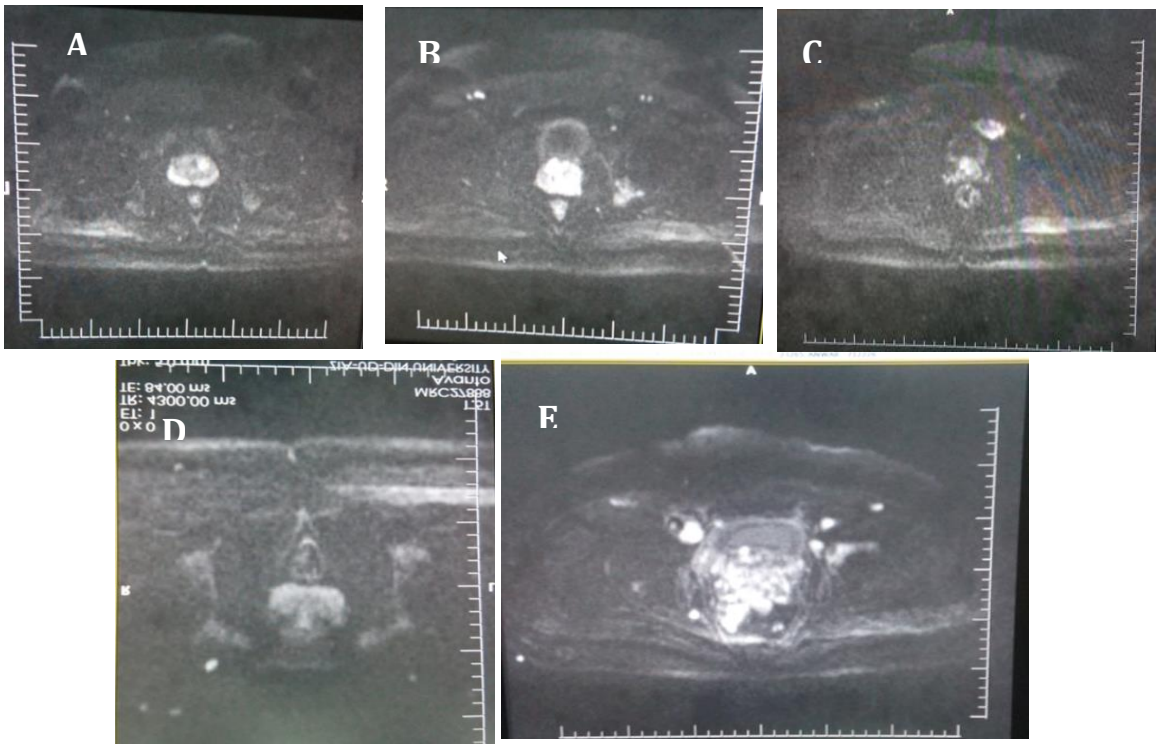

Figure 1(A): 61 years old male presented with hematuria and raised PSA levels (11ng/ml). Axial DWI image of the prostate shows a hyperintense lesion in the right lobe of the prostate gland, it was reported as a malignant neoplastic lesion. In histopathology, it was confirmed as adenocarcinoma (B): 65 years old male presented with urinary obstruction and hematuria. On DRE, there was hard and nodular prostate. Axial DWI image of the prostate showed a hyperintense lesion in the left lobe, crossing along the midline and reaching up to the right lobe. Findings were consistent with the malignant neoplastic lesion, and in histopathology, it turned out adenocarcinoma of the prostate. (C) 60 years old male presented with urinary incontinence and increased PSA levels (10 ng/ml). Axial DWI image of the prostate shows a hyperintense lesion in the central zone, and histopathology confirmed it as adenocarcinoma. (D): 55 years old male presented with hematuria and increased PSA levels (6ng/ml). DRE shows hard prostate gland parenchyma. Axial DWI image of the prostate gland shows a normal prostate gland; no lesion was identified in it. Histopathology also shows normal prostate parenchyma. (E) 56 years old male came with hematuria and burning micturition. PSA levels were raised (10ng/ml). Axial DWI image of the prostate gland shows a hyperintense lesion involving the peripheral zone of the prostate. It was reported as a malignant neoplastic lesion, but histopathology shows inflammatory cells representing prostatitis.

Discussion

Digital rectal examination, along with serum prostate-specific antigen levels and ultrasound-guided trans-rectal prostate biopsy, is used in the detection of prostate cancer till now[18]. PSA has low specificity (36 %) as other benign conditions like benign prostatic hyperplasia, prostatitis, and urinary tract infections can also cause elevated PSA. Therefore, raised PSA levels cannot be translated as a tumor. Similarly, a normal PSA value cannot exclude a tumor[19,20]. TRUS guided prostatic biopsy is non-targeted and directed towards the peripheral gland, which results in false-negative results of some tumors, particularly those in the anterior prostate. Besides this, TRUS biopsy has an NPV of 70–80 %. Prostate cancer may still present in approximately 20–30 % of patients with negative biopsy[21].

As it is already known that pre-biopsy MRI gives the best clinical assessment as well as provides the correct path for targeting biopsy[3]. DWI is an additional MRI sequence that doesn't require extra preparation, no additional cost, and takes much less time than other sequences. The signals of diffusion restriction images develop from the movement of water molecules across the cells[22]. Tumors have increase vascularity as well as cellularity, which are responsible for increased signal generation on DWI sequence[23]. DWI is an easily available technique, and it is one of the most useful functional imaging sequences. Functional imaging (DWI, DCE, and MRSI), particularly DWI, can differentiate tumors from benign conditions, including inflammation (abscess), fibrosis, scar tissue, hemorrhage or post-radiotherapy. Thus, for the detection of tumors in the peripheral zone and in the transition zone, DWI is considered an important sequence[24]. As demonstrated in previous studies, it is the most useful MP-MRI sequences for the detection of prostate cancer[25-29].

In our study, most of the cases diagnosed as prostatic cancer were in between 61 to 65 years of age. This is similar to a previous study conducted by Ganesh et al. (2001), which showed that the average age of prostatic cancer cases was 64 years. We found an increased incidence of prostatic cancer in patients having increase body weight (80-90 kg). This is similar to the previous literature[30-32]. Results suggest that larger suspicious lesions on DWI have more propensity of having prostatic cancer.

In the present study, the sensitivity and specificity of DWI were found to be 93.75 % and 75.60 %, respectively, in diagnosing prostatic cancer, taking histopathology as a gold standard. The positive and negative predictive values were found out to be 93.75 % and 75.60 %, respectively, while the DA was calculated as 90.0 %. Other studies support these findings as well[30-32]. A study by AbdelMaboud et al. (2014) showed 84 % sensitivity, 62 % specificity, and 78% DA of DWI in diagnosing prostatic cancer. We have reported better DA of diffusion-weighted MRI in diagnosing prostatic cancer[33].

Conclusion

DWI is an additional MRI sequence that needs no extra preparation, no additional cost, and takes much less time than other sequences; however, it has a vital role in detecting prostatic cancer. In patients with clinical signs and symptoms, DWI's DA in the detection of prostatic cancer is very close to histopathological findings. Diffusion-weighted MRI performed in patients with suspected prostatic cancer improves patient's survival by providing more accurate diagnosis without missing lesions, which reduces mortality and morbidity—taking into account the above benefits and high sensitivity, specificity, and DA of this examination. Diffusion-weighted MRI should be considered as a routine pre-biopsy examination in the detection of prostatic cancer.

Conflicts of Interest

None.

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