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Role of MRI in staging of prostatic cancer based on PIRADS classification version 2

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***Abstract*---**Prostate cancer is the second most common cancer in men worldwide. Two thirds of prostate cancer cases are diagnosed in the more developed regions of the world. The aim of this study was to evaluate the role of MRI imaging in staging of prostate cancer based on Prostate Imaging Reporting and Data System (PI-RADS) version 2. Thirty male patients were included in our study. They were referred to the department of Radiology, Minia Oncology Center with clinical and pathological diagnosis of prostatic carcinoma during the period extended from January 2019 to January 2021. There was a statistically significant difference between PIRADs 4 and PIRADs 5 lesions as regard patients' PSA, with higher values among PIRADs 5 cases. There was a statistically highly significant difference between PIRADs 4 and PIRADs 5 lesions as regard patients' Gleason score, with higher values among PIRADs 5 cases. MRI examination of the prostate gland has a high specificity and sensitivity in primary diagnosis or staging over clinical assessment alone (PSA level and DRE), and other modalities like ultrasound.

***Keywords*---**prostate cancer, ultrasound, ADC value, PIRADs.

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Introduction

Prostate cancer is the second most common cancer in men worldwide. Two thirds of prostate cancer cases are diagnosed in the more developed regions of the world. The incidence varies over a broad range among different countries probably as a result of a difference in the use of diagnostic screening tests as well as the number of men screened (1). Mortality of prostate cancer is difficult to measure due to the mortality of concomitant cardiovascular diseases and other cancers which share similar risk factors and therefore act as confounders (2). According to the European Randomized Study of Screening for Prostate Cancer (ERSPC), screening for prostate cancer is controversial. Prostate cancer screening is based on digital rectal examination (DRE) and prostate-specific antigen (PSA) level testing in the blood serum (3).

When PSA is highly sensitive but not specific for prostate cancer, benign pathologies such as benign prostatic hyperplasia can raise PSA levels and normal PSA levels cannot exclude prostate cancer (4). Magnetic Resonance Imaging (MRI) has been used for noninvasive assessment of the prostate gland and surrounding structures since the 1980s. Initially, prostate MRI was based solely on morphologic assessment using T1-weighted (T1W) and T2-weighted (T2W) pulse sequences, and its role was primarily for locoregional staging in patients with biopsy proven prostate cancer (5). Advances in technology (both in software and hardware) have led to the development of multiparametric MRI (mpMRI), which combines anatomic T2W with functional and physiologic assessment, including diffusion-weighted imaging (DWI) and its derivative apparent-diffusion coefficient (ADC) maps, dynamic contrast-enhanced (DCE) MRI, and sometimes other techniques such as in-vivo MR proton spectroscopy (5).

MRI became the method of choice for detection and staging of prostate cancer. Prostate Imaging Reporting and Data System (PI-RADS) were published by the European Society of Urogenital Radiology (ESUR): PI-RADS™ version 1. This first guideline paper was based on different sequences of mpMRI (6). These guidelines have been updated recently by the American College of Radiology (ACR) and ESUR to the PI-RADS v2. In this version spectroscopy was omitted and DCE-MRI was attributed a minor role in contrast to version 1. The objectives of these guidelines were to promote global standardization of prostate imaging, to improve detection, localization, characterization, risk stratification of prostate cancer in treatment as well as to improve communication with referring urologists (7). The aim of this study was to evaluate the role of MRI imaging in staging of prostate cancer based on Prostate Imaging Reporting and Data System (PI-RADS) version 2.

Patients and Methods

Thirty male patients were included in our study. They were referred to the department of Radiology, Minia Oncology Center with clinical diagnosis of prostatic carcinoma during the period extended from January 2019 to January 2021. Approval of the local ethical committee to perform the study was obtained. A written informed consent was taken from all patients after full explanation of the technique and the aim of the current study.

- Inclusion Criteria: The inclusion criteria for the study were established diagnosis of prostate cancer based on laboratory, radiological and/or histopathological evaluation.
- Exclusion Criteria: Patients contraindicated for MRI Imaging such as:
  - Claustrophobic in closed magnets (high-field open magnet provides high-resolution imaging as an alternative for claustrophobic patients).
  - Long examination times, which may be associated with patient motion,.
  - Contraindicated in patients with many types of implanted mechanical devices, such as pacemakers, patients with metal in orbits, intracranial aneurysm clips and Orthopedics appliances (plates, screws, prosthetic implants, etc.).
  - Patients with severe renal disease (eGFR <30 mL/min/1.73 m2), or acutely deteriorating renal function, who will be at risk of nephrogenic systemic fibrosis.

Sample Size: 30 patients with clinically and pathologically diagnosed prostatic carcinoma

Procedures: Full history taking and clinical examination including digital rectal exam (DRE) findings, medications by referring clinician including family history of similar or other oncology-related conditions. Review and recording of all previous relevant investigations such as recent serum prostate specific antigen (PSA) level, date and results of prostate biopsy (including number of cores, locations and Gleason scores of positive biopsies). All patients underwent MRI with diffusion - weighted sequence

MRI examination:
Examination time: 30 minutes.
Equipment and coils: MRI of the prostate was performed according to the PI-RADS™ v2 guidelines without an endorectal coil. The examination was performed by using 1.5 T machine GE (SIGNA Explorer) MRI machine by using phased array body coil. The improved SNR allows an increase in matrix, decrease in slice thickness, and decrease in FOV, all of which result in improved resolution.
Patient Positioning: The patient was positioned in a supine position with head pointing toward the magnet (headfirst supine). Position the patient over the spine coil and place the body coil over the abdomen and pelvis (nipple down to three inches below symphysis pubis).

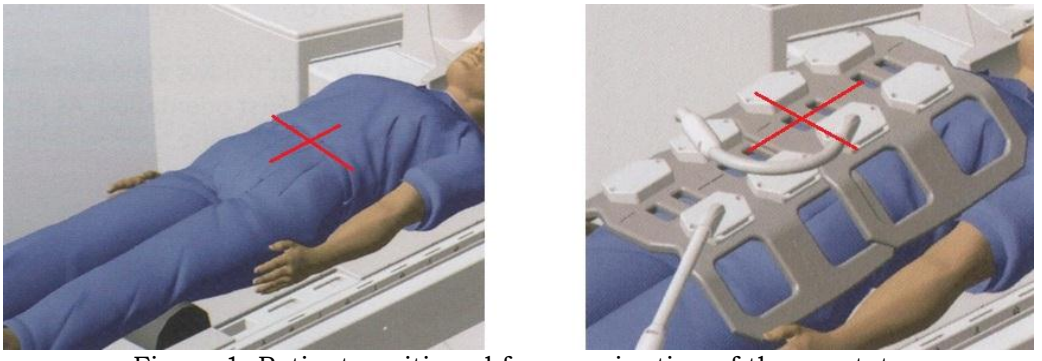

Figure 1. Patient positioned for examination of the prostate

MRI imaging planes and protocol

1-Localizer images: Localizer images used to obtain the three imaging planes True FISP localizer must be taken initially to localize and plane the sequences. These are fast single shots localizer with less than 25 s acquisition time which are excellent for localizing abdominal and pelvic structures.

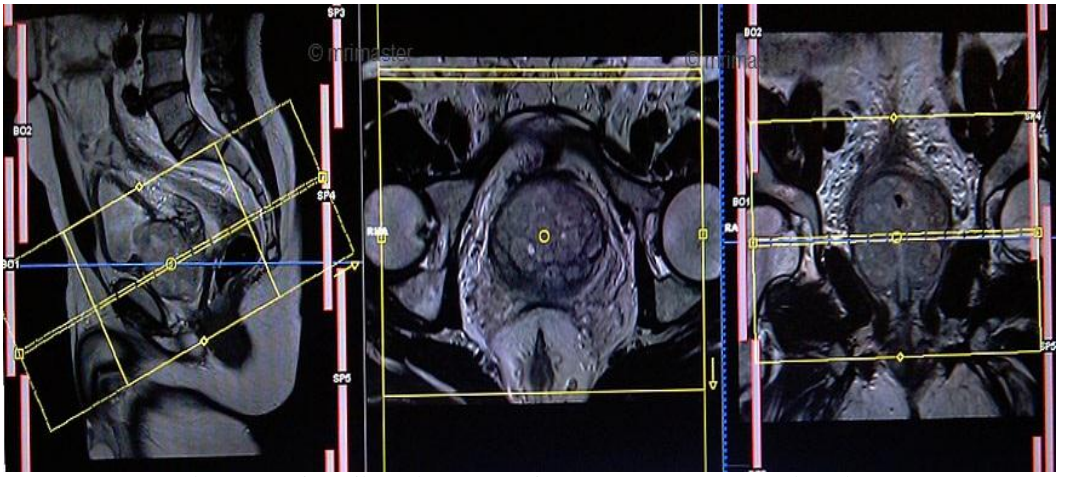

Figure 2. localizer images of prostate MRI examination

Examination protocol

Planes and sequences: The examinations were done by taking different planes at different pulse sequences: Axial and sagittal & 3D coronal planes. high-resolution T2w sequence was performed with field of view (FoV) = 220 mm. Axial DWI sequence with b-values of 0, 500, 1000, 1500 and 2000 s/mm2 and with FoV = 160 mm. Axial DCE-MRI sequence with a standard, preferable macrocyclic, gadolinium based contrast agent was administered with a dose of 0.1mml/kg. With FoV = 220 mm. A pre contrast T1w sequence obtained to exclude haemorrhage, from the aortic bifurcation to the pubic symphysis with FoV = 400 mm. Finally, though not part of the PI-RADS™ v2 guidelines, the entire pelvis should be scanned after contrast medium administration with an isotropic T1w fat saturated sequence with a voxel size of 1.2 mm for lymph node involvement, bone metastases and other findings. Especially DWI sequences of the entire pelvis in combination with 3D T2w sequences.

Images parameters

Image analysis is based on DWI, DCE-MRI and on T2w sequences. Pattern recognition on these sequences is primarily defined by the criteria of the PI-RADS™ v2 guidelines and findings will be described according PI-RADS™ v2 guidelines. Before starting image interpretation, the quality of the images has to be assured. Artifacts like metal implants (e.g. hip prosthesis), air in the rectum and patient movements can compromise the diagnostic value of images. When DWI or DCE-MRI are inadequate, PI-RADS™ v2 guidelines advise to use substitute sequences. Peripheral zone and transition zone are assessed separately

due to the fact that 70-75 % of prostate cancers arise in the peripheral zone; we recommend starting viewing functional images first.

In the peripheral zone the dominant sequence is DWI. Suspicious lesions typically have a hyperintense signal intensity on high b-value DW images and a hypointense signal intensity on the corresponding ADC maps. In case a lesion on DWI reveals PI-RADS assessment category 3, the lesion is further assessed on DCE-MRI as positive or negative. If DCE-MRI is positive, findings are detected in a lesion corresponding PI-RADS assessment category 3 on DWI in the peripheral zone, the PI-RADS assessment category is uprated from 3 to 4. Otherwise, if DCE-MRI is negative for a lesion in the peripheral zone with PIRADS assessment category 3 the lesion remains 3. In the transition zone T2w is the dominant sequence. Suspicious lesions have a heterogeneous signal intensity with obscured margins, lenticular or non-circumscribed homogeneous moderately hypo intense signal intensity on T2w images. Data Management and Analysis: The collected data was revised, coded, tabulated and introduced to a PC using Statistical package for Social Science (SPSS). Data was presented and suitable analysis was done according to the type of data obtained for each parameter.

Results

This study included 30 males referred to Radiology Department Minia Oncology Center with clinical diagnosed and pathologically proved is of prostatic carcinoma. The patients were divided into two groups according to their histo pathological examination (Results of prostatic biopsy). Group I included patients with prostatic carcinoma with Gleason score of 7 or less. Group II included patients with prostatic carcinoma with Gleason score of more than 7. By applying the PI-RADS score v2 system with using of Multiple MR imaging techniques to all patients according to PIRADS version II guidelines, patients with pathologically proved of prostatic cancer are (PIRADs score 4 or PIRADs score 5 of prostate cancer),14 patients of PIRADs score 4 and 16 patients of PIRADs score 5 of prostatic cancer. The largest affected age group is 60-70 yrs, due to age related increased risk of prostatic cancer & BPH. Figure (3)

The table shows that the mean PSA, Gleason score and ADC value among cases were 337.50± 523.56, 7.37± 1.16 and 0.94± 0.26 respectively with a median of 113.5, 7 and 1.5 respectively. Cases with Poorly differentiated Tumor, PIRADs 5, positive locoregional LNs, Extra prostatic extension , Central zone tumor , and larger than 15 mm tumour represented 30% ,70%, 53.3% , 36.7% and 70% of cases respectively. Table (1). There was a statistically significant difference between PIRADs 4 and PIRADs 5 lesions as regard patients' PSA, with higher values among PIRADs 5 cases. Table (2). There was a statistically highly significant difference between PIRADs 4 and PIRADs 5 lesions as regard patients' Gleason score, with higher values among PIRADs 5 cases. Table (3). There was a statistically highly significant difference between PIRADs 4 and PIRADs 5 lesions as regard patients' ADC values, with higher values among PIRADs 5 cases (1.22± 0.23 vs. 0.81± 0.15). Table (4)

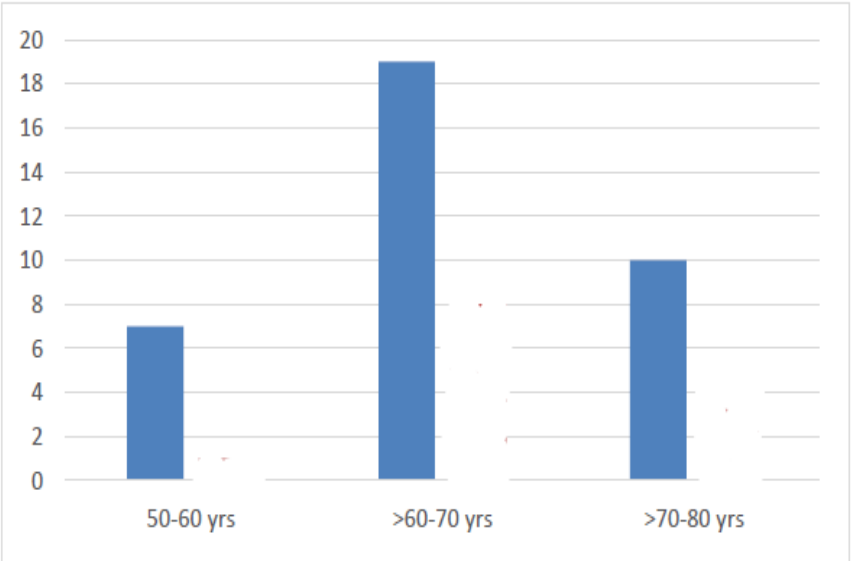

Figure 3. Age status of patients

Table 1
Clinical, laboratory & pathological assessment of all patients

		Mean	±SD	Minimum	Maximum	Median(IQR*
PSA level		337.50	523.56	20.00	2100.00	113.5(65-300)
Gleason score		7.37	1.16	6.00	10.00	7(6-8)
ADC value		0.94	0.26	0.60	1.50	0.9(0.8-1.1)
Pathology	Undifferentiated	5	16.7%			
	Poorly differentiated	9	30.0%			
	Moderately differentiated	9	30.0%			
	Well differentiated	7	23.3%			
PIRADs	4	9	30.0%			
	5	21	70.0%			
Locoregional LNs	No	14	46.7%			
	Yes	16	53.3%			
Extra prostatic extension	No	14	46.7%			
	Yes	16	53.3%			
Site	Peripheral zone	19	63.3%			
	Central zone	11	36.7%			
Size	Less than 15 mm	9	30.0%			
	More than 15 mm	21	70.0%			

*Interquartile range

Table 2
Comparison between PIRADs 4 and PIRADs 5 lesions according to PSA level

PIRADs										P	Sig
4					5						
Mean	±SD	Median	IQR*		Mean	±SDD	Median	IQR*			
80.56	43.46	80	50	100	447.62	595.2	200	70	568	0.028**	HS

*Interquartile range
** Mann Whitney test

Table 3
Comparison between PIRADs 4 and PIRADs 5 lesions according to Gleason scores

	PIRADs				P	Sig
	PIRADs 4		PIRADs 5			
	Mean	±SD	Mean	±SD		
Gleason score	6.56	0.73	7.71	1.15	0.009*	HS

*student t test

Table 4
Comparison between PIRADs 4 and PIRADs 5 lesions according to ADC values

	PIRADs				P	Sig
	4		5			
	Mean	±SD	Mean	±SD		
ADC value	1.22	.23	0.81	0.15	0.001	HS

*student t test

Table 5
Comparison between PIRADs 4 and PIRADs 5 lesions according to Pathology, Locoregional LNs, Extra prostatic extension, tumor site and size

		PIRADs				P**	Sig
		4		5			
		N	%	N	%		
Pathology	Undifferentiated	0	0.0%	5	23.8%	0.001	HS
	Poorly differentiated	0	0.0%	9	42.9%		
	Moderately differentiated	3	33.3%	6	28.6%		
	Well differentiated	6	66.7%	1	4.8%		
Locoregional LNs	No	9	100.0%	5	23.8%	0.001	HS
	Yes	0	0.0%	16	76.2%		
Extra prostatic extension	No	9	100.0%	5	23.8%	0.001	HS
	Yes	0	0.0%	16	76.2%		
Site	Peripheral zone	5	55.6%	14	66.7%	0.687	NS

	Central zone	4	44.4%	7	33.3%		
Size	Less than 15 mm	9	100.0%	0	0.0%	0.001	HS
	More than 15 mm	0	0.0%	21	100.0%		

Case (1)

75-year-old male patient, Complaint: urgency & Suspicious DRE, laboratory data: Elevated PSA level 25 ng/ml. MRI findings: Peripheral zone: T2W: well circumscribed hypo-intense nodule seen at the postero-lateral segment of the peripheral zone at the left side measures about 15 mm, ADC shows marked diffusion restriction, ADC value 0.9 X 10-3 mm2/sec. Intact Central gland: intact prostatic capsule with no definite contour bulge, intact NVB, no nodal enlargement, intact both seminal vesicles and intact recto-prostatic angle. TRUS guided biopsy: adenocarcinoma, Gleason score 4+3. Classification: final PI-RADS score of the prostate = 4 and TNM staging: T2aN0Mx

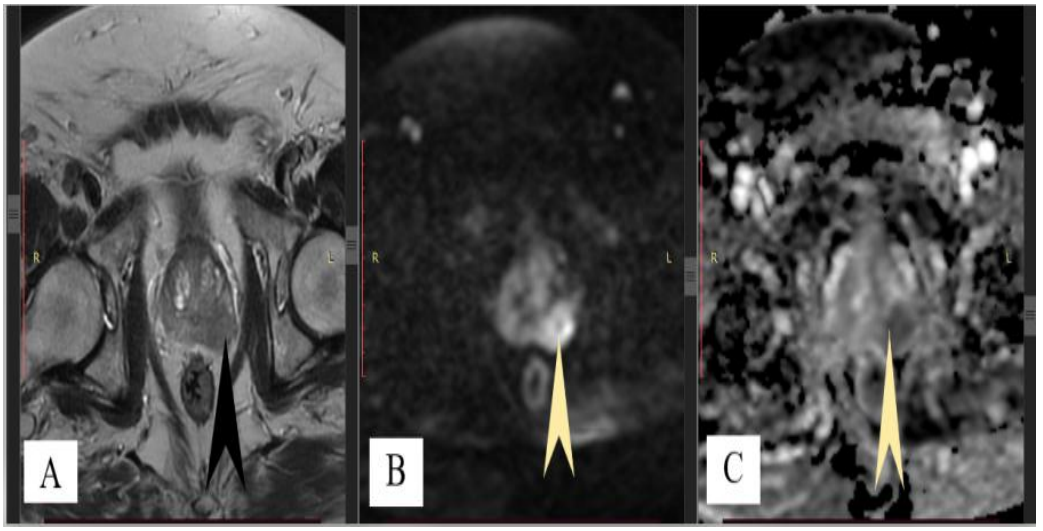

Figure 5. A) axial T2, show hypo-intense lesion at the left postero-lateral lateral segment of the peripheral zone with no definite capsular bulge (Black arrow). B&C) axial D1W & ADC shows diffusion restriction correlated with T2 hypo-intensity (Yellow arrows)

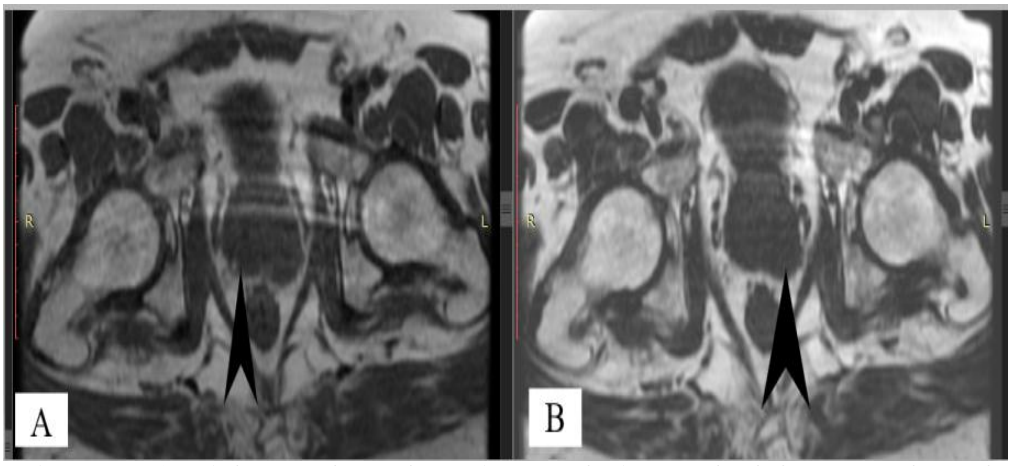

Figure 6. A) axial T1W shows hypo-intense lesion at the left postero-lateral segment of the peripheral zone with no definite capsular bulge (Black arrow). B) axial T1W with contrast show faint enhancement (Black arrow)

Case (2)

66-year-old male patient, complaint: Burning micturition, laboratory data: Elevated PSA level 30 ng/ml. MRI findings: Peripheral zone: T2W: non-circumscribed hypo-intense nodule seen at the basal segment of the peripheral zone at the left side measures about 14 mm, ADC shows focal diffusion restriction less than 1.5cm, ADC value 1.1 X 10-3 mm2/sec. Intact Central gland: intact prostatic capsule with no definite contour bulge, intact NVB, no nodal enlargement, intact both seminal vesicles and intact recto-prostatic angle. TRUS guided biopsy: Adenocarcinoma, Gleason score 3+3. Classification: final PI-RADS score of the prostate = 4 and TNM staging: T2aN0Mx

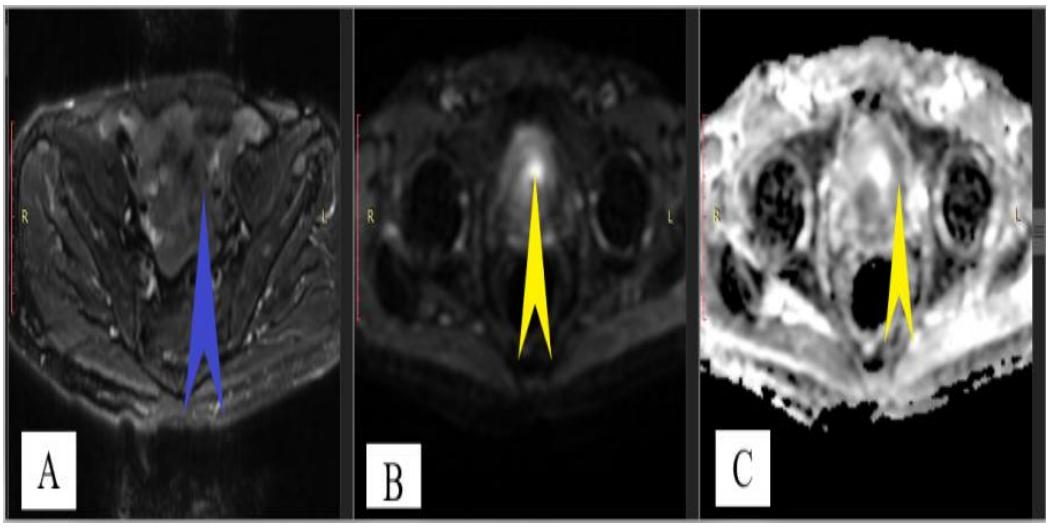

Figure 7. A) axial T2W, shows hypo-intense lesion at the basal segment of the peripheral zone at the left side with no definite capsular bulge (Blue arrow). B&C) axial D1W & ADC shows diffusion restriction correlated with T2 hypo-intensity (Yellow arrows)

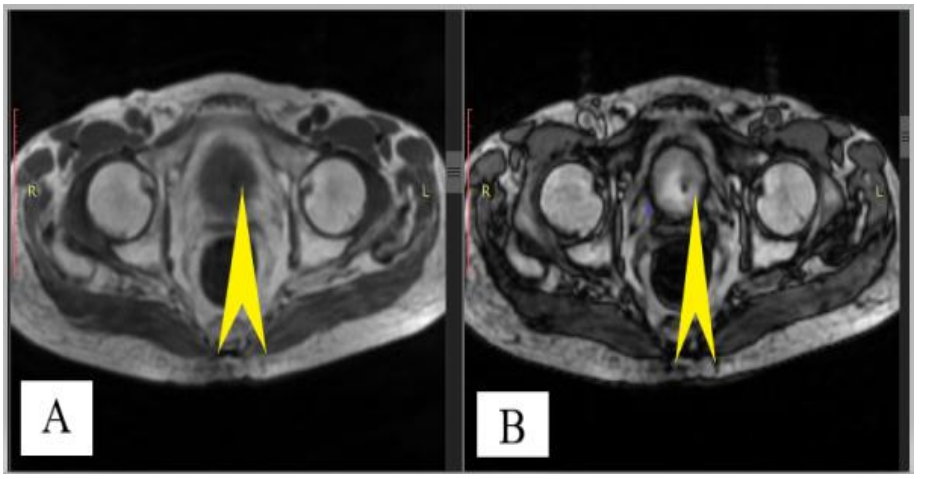

Figure 8. A) axial T1W shows hypo-intense lesion at the basal segment of the peripheral zone at the left side with no definite capsular bulge, B&C) axial T1W with contrast show faint enhancement (Yellow arrows)

Case (3)

66-year-old male patient. Complaint: urgency & Suspicious DRE. Laboratory data: Elevated PSA level 125 ng/ml.MRI findings: Peripheral zone: T2W: Large sized hypo intense lesions seen at the basal segment of the peripheral zone at the left side with capsular bulge, measures about 5 x 5 cm. ADC shows focal marked diffusion restriction, ADC value 0.9 X 10-3 mm2/sec. Intact Central gland. Infiltration & bulging of the prostatic capsule. Infiltration NVB. Multiple loco regional LNs enlargements. Infiltration of the seminal vesicle at the left side. Intact recto-prostatic angle.TRUS guided biopsy: Adenocarcinoma, Gleason score 5+5. Classification: Final PI-RADS score of the prostate =5. TNM staging : T3aN3Mx

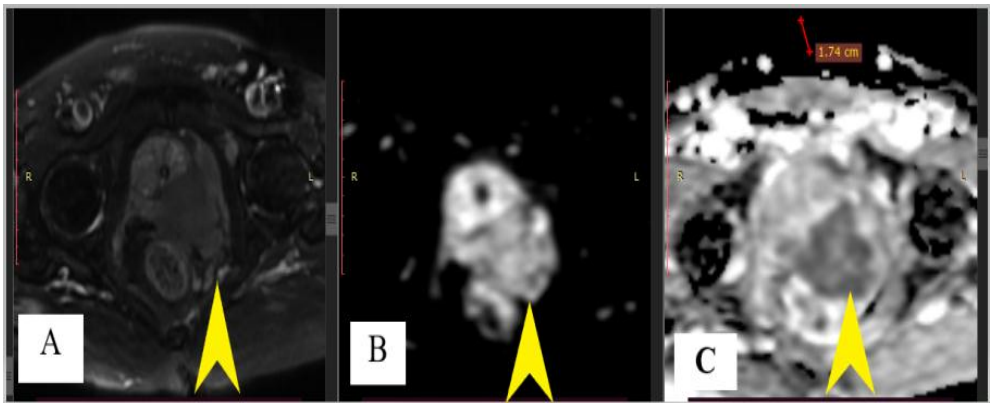

Figure 9. A) axial T2 FS, shows large sized hypo-intense lesion at the basal segment of the peripheral zone at the left side with definite capsular bulge and enlarged loco regional LNs at both sides (Yellow arrow). B&C) axial D1W & ADC show marked restriction correlated with T2 hypo-intensity (Yellow arrows).

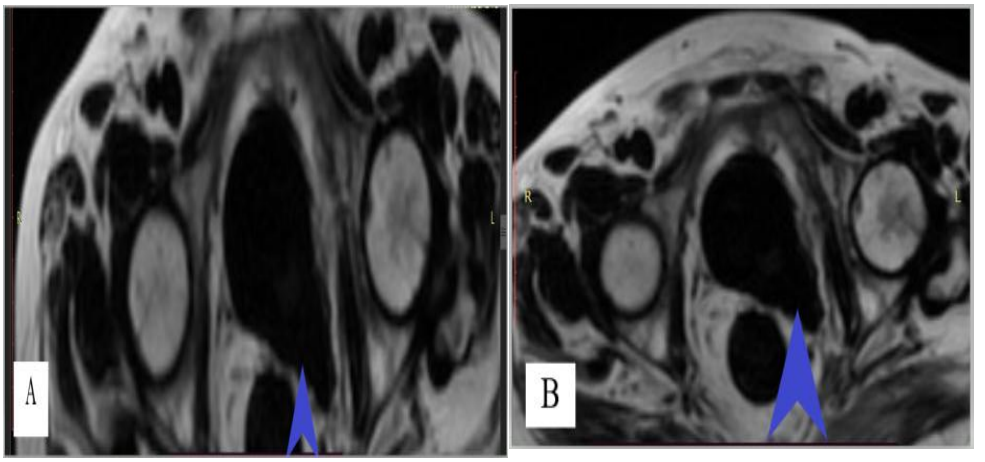

Figure 10. A) axial T1W shows large sized hypo-intense lesion at the basal segment of the peripheral zone at the left side with definite capsular bulge (Blue arrow). B) axial T1W with contrast shows faint enhancement of the lesion (Blue arrow)

Discussion

In initial version of PI-RADS, the use of dedicated software programs and workstations to analyze the enhancement curve types of tumor was mandatory, which might be one of limitations to its wide application (6). There was substantial effort to improve PI-RADS compared with other imaging scoring systems. In some studies, the Likert scale, which is a relatively subjective and convenient method that relies on a five-point scale, demonstrated comparable feasibility and reproducibility for detecting prostate cancer (8). This study including 30 male patients had established diagnosis of prostate cancer based on laboratory, radiological and/or histopathological evaluation. The commonest age group (>60-80yrs). This mean that prostatic carcinoma is a common finding among elder patient presented with urological symptoms related to prostate gland. The importance of the clinical and laboratory assessment is being the first line in assessment of the prostatic carcinoma. Digital rectal examination (DRE), trans rectal ultrasound, total PSA are used for assessment of prostatic carcinoma (9).

Our study aiming For comparing the PSA level, Gleason score; surgical Gleason score, Pathology, ADC value and presence of extra capsular extension, seminal vesicle invasion, or clinically significant prostate cancer between PI-RADS score of 4 and PI-RADS score of 5. In our study, the use of PI-RADS version 2 allowed for acceptable diagnostic performance in predicting clinically significant prostate cancer. With PIRADS score of 4 or greater as a threshold, the sensitivity and specificity of PI-RADS version 2 were 77.0% and 73.8% for reader 1 and 77.3% and 71.4% for reader 2, respectively. In a recent meta-analysis study done by Hamoen et al., (10) the sensitivity and specificity of PI-RADS version 1 were reported to be 0.84 (95% CI: 0.76, 0.89) and 0.75 (95% CI: 0.66, 0.83) for clinically significant cancer detection, respectively.

In our study, the use of PI-RADS version 2 allowed for diagnosing prostate cancer with Gleason score of 7 or greater, the sensitivity of PI-RADS version 2 were 84.2% for reader 1 and 82.5% for reader 2, which is similar to those in the previous reports using PI-RADS version 1 (sensitivity, 77.3%–95.5%) or the Likert scale (sensitivity, 63.6%– 82.6%). In a study done by Roethke et al., (11) similar specificity and slightly lower sensitivity, for the PI-RADS version 2 were reported. In our study, cases with Poorly differentiated Tumor, PIRADs 5, positive locoregional LNs, Extra prostatic extension , Central zone tumor, and tumors larger than 15 mm represented 30% ,70%, 53.3% , 36.7% and 70% of cases respectively. Cases with Well differentiated Tumor, negative locoregional LNs, negative Extra prostatic extension , Central zone tumor , and tumors lesser than 15 mm represented 66.7% ,100% , 100%, 44.4% and 100% of cases respectively. Cases with Poorly differentiated Tumor, positive loco regional LNs, positive extra prostatic extension, Central zone tumor, and tumors larger than 15 mm represented 44.2, 76.2%, 76.2%, 33.3% and 100% of cases respectively.

The DW and DCE imaging had been reported to reflect the tumor aggressiveness in prostate cancer. A lower ADC or earlier enhancement is related to the more aggressive nature of prostate cancer according to pathologic findings (12). Moreover, large, apparently visible cancers on multiparametric MR images are more likely to be clinically significant cancer (ie, high Gleason score, tumor volume 0.5 cm3, or positive extracapsular extension or seminal vesicle invasion) (13). So, multiparametric MR imaging has a great advantage in detecting anteriorly located prostate cancer that is usually missed with systematic biopsy. Hence, the use of PI-RADS with multiparametric MR imaging may enable detection of clinically significant prostate cancer that could otherwise be underestimated with biopsy results (14).

In our study, patients are divided into groups as regarding their PIRADs score (4 or 5), 11 patients with PIRADS score 4 and 19 patients with PIRADs score 5 lesions. In our study patient population, seminal vesicles and neruo-vascular bundles were the most common forms of extra-capsular extensions. TNM staging is a clinical staging system of cancer. In pre-treatment assessment of prostate cancer, MRI can estimate the tumor size, loco-regional lymph node assessment. In our study TNM staging has positive correlation with PI-RADS score, patient with a high PIRADS score, aslo had high TNM staging. There is correlation between the (N=nodal & M=metastasis). Increasing tumor size will increase the incidence of invasion to the adjacent structures with subsequent increasing the incidence of nodal involvement as well as distant metastasis; nevertheless some patients with lesiond confined to the prostate gland had nodal or even osseous involvement (15).

MRI is the best modality compared to TRUS & TRUS guided biopsy in assessment of the loco-regional nodal and osseous involvement if extended protocol of distant metastasis is used (15). Regarding the relation between total PSA level and nodal and osseous involvement in our study, 15 patients of total 16 patients with nodal involvement had elevated total PSA level above 100ng/ml with sensitivity of 87.5%, 2 patients of total 3 patients with osseous involvement had elevated PSA above 500ng/ml with sensitivity of 66.6%. ADC value is a non-subjective method to evaluate the prostatic lesions. ADC value of the malignant lesions is seen to be

below 1 x 10-3 mm2/sec as cut-off value. The main ADC value for malignant central gland lesions was 0.79 x10-3 mm2/sec, for malignant peripheral zone lesions was 0.64 x10-3cm/s).

Trying to predict the aggressiveness of prostatic carcinoma using diffusion MRI as regarding the relation between as ADC values and Gleason score was done, there was negative correlation between ADC value and Gleason score. This was due to the methods of calculation of Gleason score and ADC value. The use of MRI guided biopsy may be helpful to solve this issue for accurate correlation between ADC values and histopathological results (15). Finally, MRI of the prostate gland has an important role in evaluation of prostatic carcinoma, in patients with elevated PSA & suspicious DRE, MRI will help in lesion localization & preparation of patients for targeted biopsy.

Conclusion

MRI examination of the prostate gland has a high specificity and sensitivity in primary diagnosis or staging over clinical assessment alone (PSA level and DRE), and other modalities like ultrasound. mp-MRI is considered the best anatomical and functional imaging modality that is used for detection and characterization of prostate tumors and for clinical staging of patients with prostate cancer, including (T1, T2 and DWI & ADC). The Prostate Image reporting of prostate MRI adheres strictly to PIRADS™ v2 guidelines which aimed at standardizing the acquisition, interpretation and reporting of prostate MRI. ADC value is used differentiation between benign and malignant lesions, main ADC value of the malignant lesions below 1x10- 3cm/s.

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