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Role of Multi-Parametric Magnetic Resonance Imaging (MRI) in Assessment of Malignant Prostatic Lesions

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ABSTRACT

Background: carcinoma of the prostate is an important health problem. It is the one of the most frequently diagnosed solid malignant tumor among men. Multi-parametric MRI of the prostate has been increasingly used as an imaging technique through the last years. **Objective:** our study aimed to evaluate the sensitivity of multiparametric magnetic resonance (MR) imaging in detection of cancer prostate, using the Prostate Imaging Reporting and Data System (PI-RADS) version 2.0. **Patients and Methods:** thirty patients were enrolled in the study. All patients with elevated PSA values greater than 4 ng/ml underwent sextant TRUS guided biopsies. MRI examination was done either prior to the TRUS biopsy or at least 3 weeks after the TRUS biopsy.

Results: the application of PI-RADS version 2 has significantly improved the diagnostic performance in detection of clinically significant cancer. Considering PIRADS score greater than 3 as a strong indicator for malignancy, the sensitivity of PI-RADS version 2 was 80% for detection of malignant lesions in general (significant and insignificant). Moreover, our study revealed an 88% sensitivity and 33% specificity of mp-MRI in detection of clinically significant cancer prostate (with PIRADS score 4 or more for clinically significant caner that have a Gleason score 7 or more, or extraprostatic extension), with a significant p value <0. 001.

Conclusion: as a preoperative imaging tool, use of PI-RADS version 2 helps to diagnose clinically significant prostate cancer, considering PI-RADS scores of 4 and 5 to be associated with the presence of clinically significant cancer.

Keywords: MRI, Malignant Prostatic Lesions, PI-RADS.

INTRODUCTION

Prostate carcinoma is the second most frequent cause of cancer-related death in men. The increase in the number of the aged, as well as the advent and the ever more frequent use of the prostate-specific antigen serum test for detection, has resulted in an increase in prostate cancer incidence [(1)].

The major goal for prostate cancer imaging in the upcoming years is more accurate disease characterization through gathering more accurate anatomic, functional, and molecular imaging information [(2)].

Localization of prostate cancer is an important given in the emergence of disease- targeted therapies, such as intensity- modulated radiation therapy, interstitial brachytherapy, and cryosurgery, as a part of patient care. Identifying the tumor location within the prostate can help directing maximal therapy to the largest focus of the tumor while minimizing damage to the surrounding healthy structures, such as the neurovascular bundles, the rectal wall, and the neck of the bladder [(3)].

These modalities are ultrasound based (including color Doppler Ultrasonography, ultrasound contrast agents, and harmonic ultrasound imaging), MR based including (dynamic MR contrast imaging, MR spectroscopy and Diffusion weighted MR imaging) [(4)].

Magnetic resonance (MR) imaging has shown great promise as a noninvasive diagnostic tool in the evaluation and management of prostate cancer. By aiding in the detection, localization, and staging of prostate cancer, multiplanar T2-weighted endorectal MR imaging can facilitate more appropriate treatment selection and planning. However, for distinguishing prostate cancer from nonmalignant tissue, T2-weighted MR imaging has high sensitivity but low specificity. To further improve the specificity and sensitivity of MR imaging, functional MR imaging techniques such as three dimensional (3D) hydrogen 1 (1H) MR spectroscopic imaging, dynamic contrast material enhanced MR imaging, and diffusion-weighted imaging have been proposed [(5)].

The implementation of multiparametric magnetic resonance imaging (mpMRI) into a screening program may reduce the risk of overdetection of non-significant PC and improve the early detection of clinically significant PC. A mpMRI consists of T2-weighted images supplemented with diffusion-weighted imaging, dynamic contrast enhanced imaging, and/or magnetic resonance spectroscopic imaging and is preferably performed and reported according to the uniform quality standards of the Prostate Imaging Reporting and Data System (PIRADS). International guidelines currently recommend mpMRI in patients with persistently rising PSA and previous negative biopsies, but mpMRI may also be used before first biopsy to improve the biopsy yield by targeting suspicious lesions or to assist in the selection of low-risk patients in whom consideration could be given for surveillance [(1)].

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To evaluate the prostatic lesions more accurately, the PI-RADS (Prostate Imaging Reporting And Data System) -which is a systematic and schematic way for appraisal of the prostate- has been developed and is being widely used. The system has been modified to be PI-RADS 2 seeking for more accurate interpretation, depending on 4 sequences mainly : T2 weighted PZ, T2 TZ, DWI, DCE [(6)].

AIM OF THE WORK

Our study aims to evaluate the sensitivity of multiparametric magnetic resonance (MR) imaging in detection of cancer prostate, using the Prostate Imaging Reporting and Data System (PI-RADS) version 2.0.

PATIENTS AND METHODS

This prospective study was approved by the Local Ethics Committee, and written informed consent was obtained from all patients for use of their imaging and histopathologic data in future research studies.

The study was approved by the Ethics Board of Al-Azhar University and an informed written consent was taken from each participant in the study.

Thirty patients patients were enrolled in the study. All patients with elevated PSA values greater than 4 ng/ml underwent sextant TRUS guided biopsies. MRI examination was done either prior to the TRUS biopsy or at least 3 weeks after the TRUS biopsy.

Inclusion criteria:

- Histopathologically (biopsy) proven prostate cancer.
- No age predilection.

Exclusion criteria:

- Patients having contraindication to MRI.
- Histopathologically proven cases of benign lesions.

Histopathological analysis: The histology was reviewed by an experienced pathologist.

MRI imaging:

Conventional MRI and DWIs were performed using Philips achieva XR 1.5-T system using a torso XL 16 channels phased array coil. Before doing scanning, each patient received an intramuscular injection of 20 mg of butyl scopolamine to suppress bowel peristalsis. T2-weighted turbo spin-echo images were acquired in three orthogonal planes (axial, sagittal, and coronal).

The T2-weighted imaging parameters were as follows:

TR range/TE range, 2,690–3,800/80–90; slice thickness, 3 mm; interslice gap, 0.3–1mm; 512×304 matrix; field of view (FOV), 20 cm; number of signals acquired (NSA), 4; sensitivity-encoding (SENSE) factor, 2; voxel size, 0.35 × 0.59 × 3 mm; slice number,36; and acquisition time of each plane, 6 minutes.

Turbo Spin Echo (TSE) technique is used as well.

Diffusion study:

DW images were acquired in the axial plane using the single-shot echo-planar imaging technique. The scanning parameters were as follows: 2,740–2,750/83–85; slice thickness, 3 mm; inter-slice gap, 1 mm; matrix, 112 × 110; FOV, 20 cm;SENSE factor, 2; and NSA, 6. Diffusion-encoding gradients were applied using three b values of 0 ,600 and 800 s/mm along the three orthogonal directions of motion-probing gradients. ADC maps were automatically constructed on a pixel by-pixel basis. The acquisition time of DWI was within 3 minutes.

Dynamic Contrast Enhanced (DCE):

An intravenous contrast (gadolinium) bolus is injected and rapid repeated T1W images are obtained. Images are obtained sequentially every 5 seconds for up to 5 minutes to detect early enhancement. The dose is 0.1 mmol\kg body weight.

Statistical Analysis

Data were coded and entered using the statistic analytical too of Microsoft Excel 2016 as well as statistical package SPSS (Statistical Package for the Social Sciences) version 23. Data were summarized using mean, standard deviation, median, minimum and maximum in quantitative data and using frequency (count) and relative frequency (percentage) for categorical data.

RESULTS

The 30 patients enrolled in this study were ranging from 64to 85 years with mean age of 75.86years. The total PSA waselevated ranging from 7.6 to 905.5 in all patients.

Table (1): Demonstrating the PSA and age of the patients.

	Mean	Standard Deviation	Median	Minimum	Maximum
PSA	100.1	168.05	35.7	7.6	905.5
Age	73.4	7.14	75.00	64.00	85.00

Regarding the histopathological type of the diagnosed prostate cancer patients, all had adenocarcinoma. In terms of Gleason scores, 2 of the cases have Gleason score (3+3),5 have Gleason score (3+4),4 have Gleason score(4+3), 17 have Gleason score (4+4), and 2 cases have Gleason score (5+4).

Figure (1): chart demonstrating Gleason score representation among patients.

Multi-parametric MRI revealed that 53.4% of the malignant lesions are situated in the peripheral zone (16 cases), 13.3% in the transitional zone (4 cases), 6.6% in the central zone (2 cases), while 26.6% are of infiltrative nature and occupying peripheral, central and or transitional zones (8 cases), with no definite radiological clue that pinpoints the exact anatomical \ zonal source of the lesion.

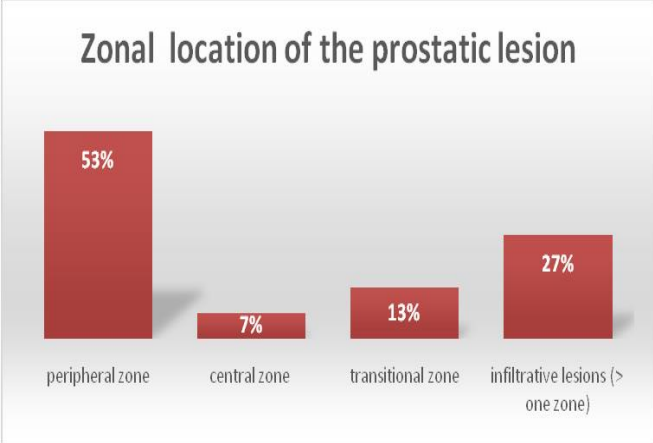

Figure (2): Chart demonstrating the site of the prostate cancer.

In terms of clinical significance, 73.3 % of the prostate specimens of our study are of clinically significant cancer (Gleason Score 7 or more).

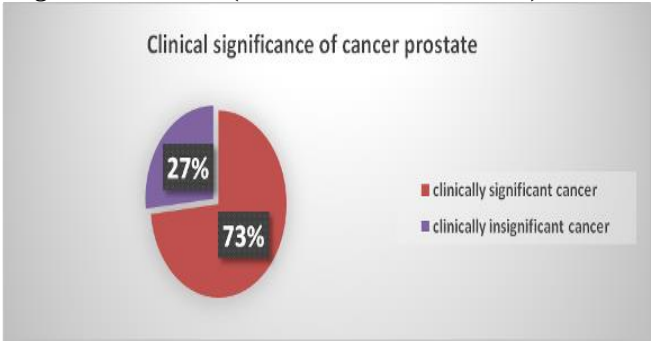

Figure (3): Pie chart demonstrating percentage of clinically significant cancer

It is noteworthy that combined sequences in the mp-MRI protocol have higher sensitivities regarding detection of cancer prostate.

In our study, adding DCE or DWI to T2WIs has raised the relative sensitivity to 83.3%.

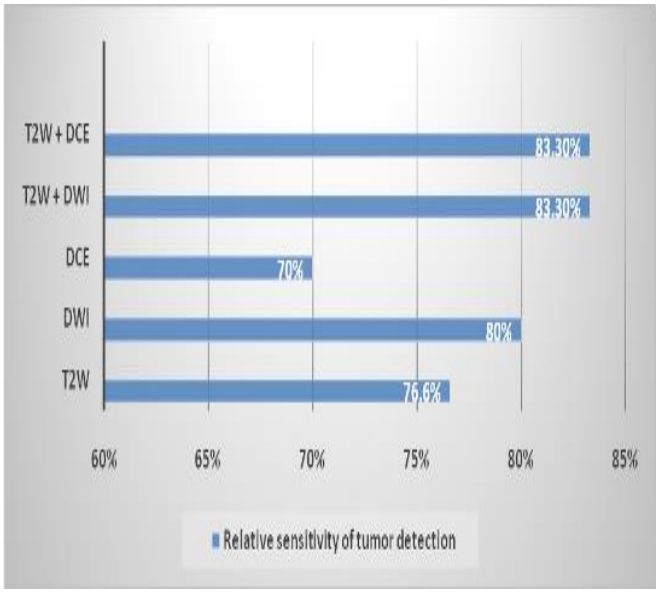

Figure (4): Chart demonstrating the relative sensitivity of tumor detection in T2, DWI and DCE MRI

In our study, multiparametric MRI detected seminal vesicle invasion or extraprostatic / extracapsular extension in 36.6% of cases. Such finding is sufficient to make the PI-RADS score directly jump to 5 regardless the descriptive features and measurements in different sequences.

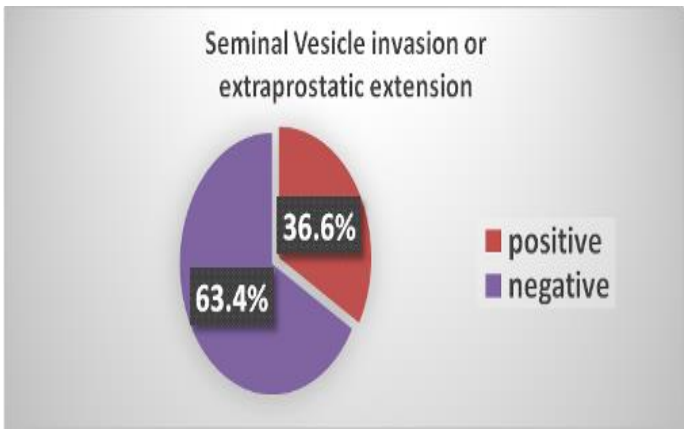

Figure (5): Pie chart demonstrating percentage of extra-prostatic extension

Applying the PIRADS V2 scoring system, the vast majority of cases scored PIRADS score 4 and 5 (14 cases for PIRADS 4 and 8 cases for PIRADS 5). While less than the third of cases score 2 and 3 (4 cases for PIRADS 2 and 3 cases for PIRADS 3).

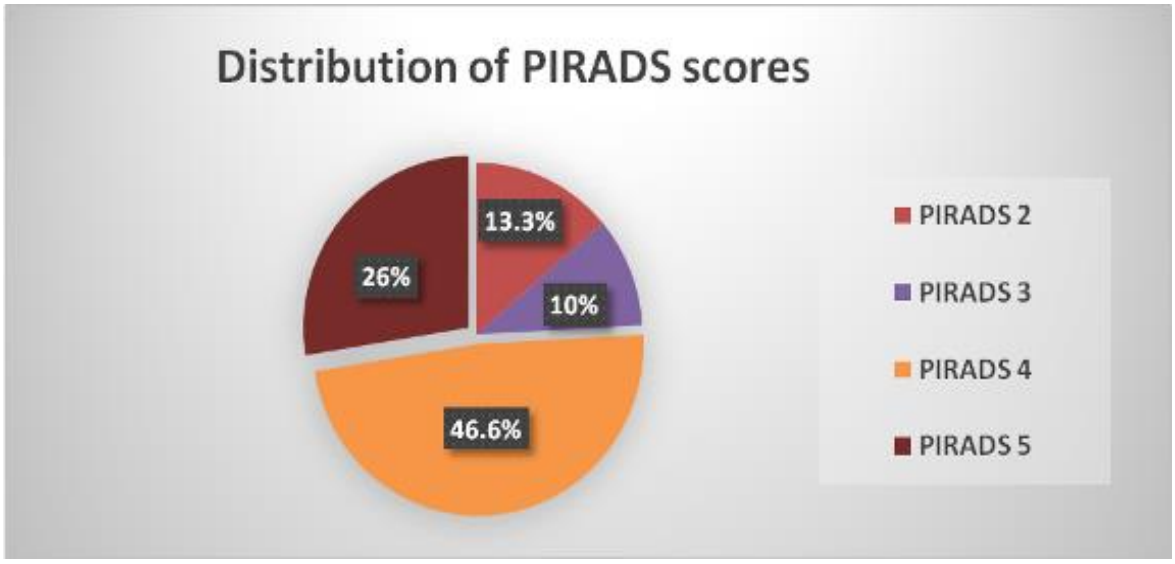

Figure (6): Pie chart demonstrating distribution of PIRADS scores percentage wise.

Regarding TNM staging of the lesions of our study, and depending only on the images gathered form mp-MRI study of prostate without performing further studies, 5 cases (16.6%) were reported that the lesion was infiltrating the urinary bladder base or encroaching recta wall (stage T4). 5 cases (16.6%) showed evidence of extracapsular extension (stage T3a), while other 3 cases (10%) depicted seminal vesicle invasion (stage T3b). 5 cases (16.6%) had regional lymph node metastasis (stage N1). 11 cases (36.6%) had bone metastasis (stage M1b).

In our study, application of PIRADS version 2 has revealed that the sensitivity of multi-parametric MRI in detection of malignant lesions in general (significant and insignificant) is 80%. While it is 88% for detection of clinically significant cancer prostate (with PIRADS score 4 or more for clinically significant caner that have a Gleason score 7 or more, or extraprostatic extension), with a significant *p value* < 0. 001.

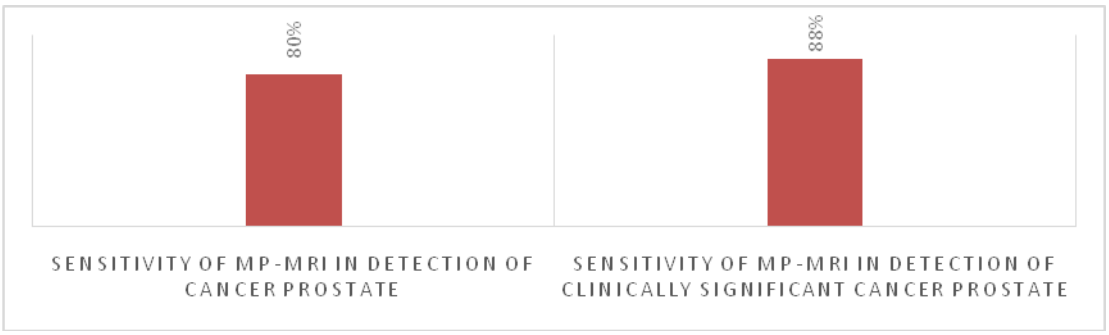

Figure (7): Bar chart demonstrating the sensitivity of mp-MRI in detection of cancer prostate

According to the statistical data of our study, multiparametric MRI of prostate -with applying the scoring system of PIRADS version 2- has shown a 79.1% sensitivity in detection of clinically significant cancer, as well as 33% specificity, 82.6% positive
predictive value, 28.5% negative predictive value, and 70% accuracy.

CASES

Case I

A 67 years old male patient with total PSA 274.3 ng/ml.

Histopathology: Adenocarcinoma GS 9.

MRI findings:

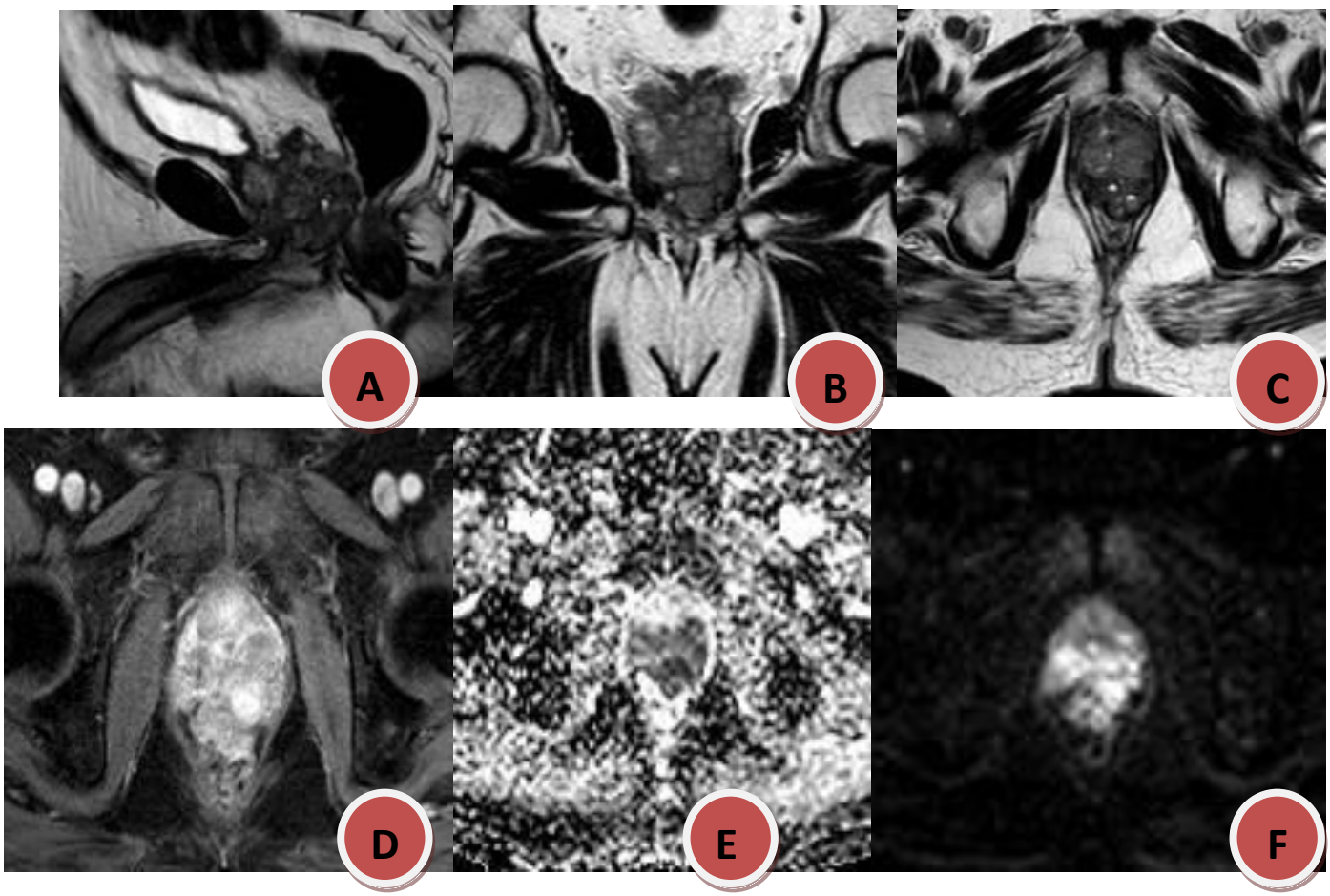

Figure (8): Enlarged prostate with nodular pattern. The left peripheral zone shows a heterogenous, mainly hypointense focus/mass with posterior extraprostatic extension/invasive behavior as seen in A (axial T2W), B (coronal T2W) and C (sagittal T2W). DWIs revealed restricted diffusion, bright signal (D), and dark ADC (E). Post-contrast study shows a focal extra-enhancement of the left peripheral zone nodule. According to the previous data, the case is of PIRADS 5.

Case II

A 74 years old male patient with total PSA 73ng/ml.

Histopathology: Adenocarcinoma GS 8.

MRI findings:

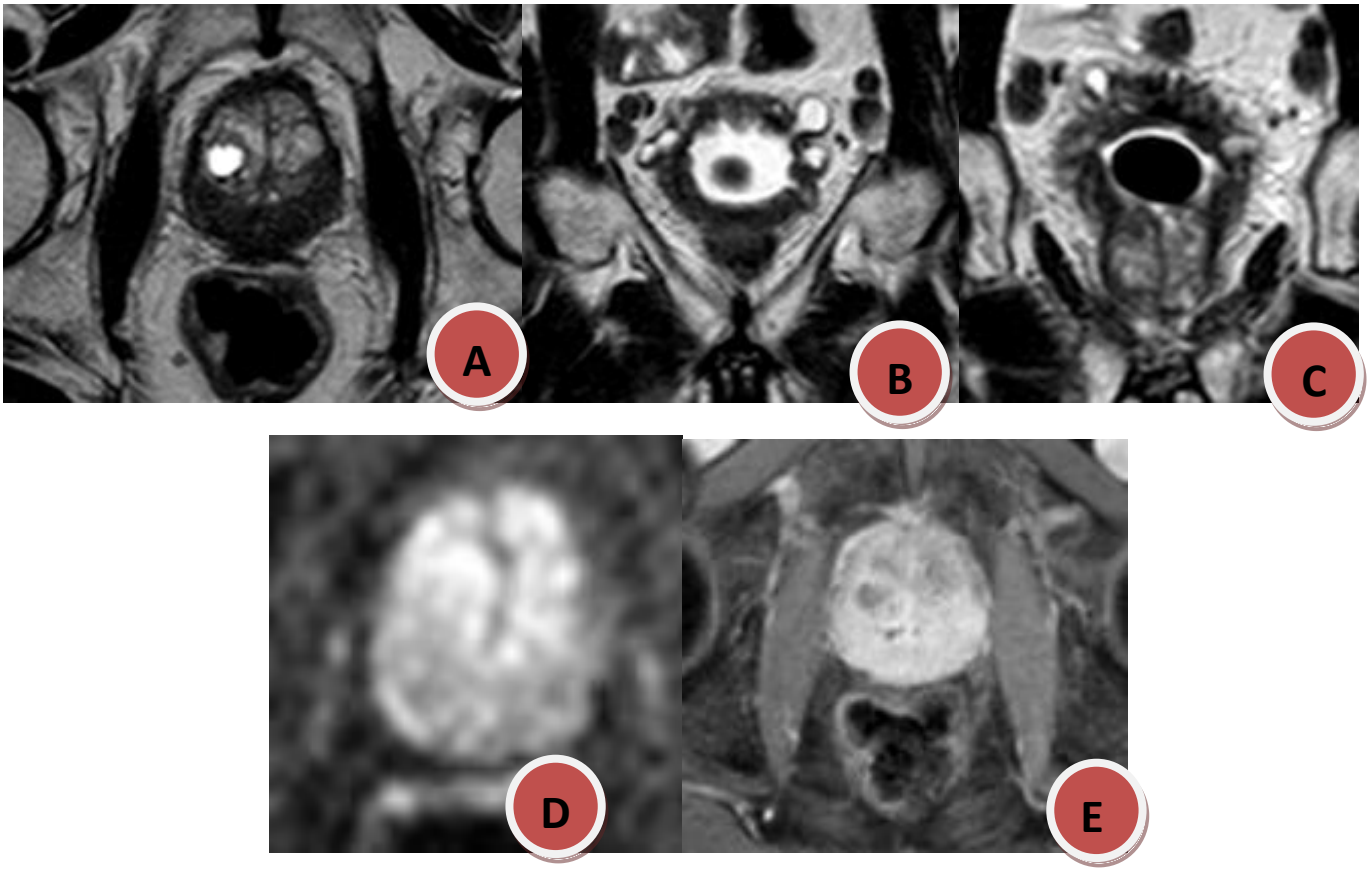

Figure (9): The prostate is enlarged in size with heterogenous central zone showing heterogenous signal intensity especially in the T2WIs (A). It is indenting the urinary bladder base. The peripheral zone is of low T2 signal intensity and relatively compressed by the hypertrophied central zone. No definite well defined focal areas of abnormal signal intensities could be detected throughout the different sequences or even in the post-contrast phase (E). Intact appearance of the seminal vesicles with preserved semino-vesical angles. A large low signal intensity urinary bladder stone is noted (C). The urinary bladder shows multiple diverticular outpouching (B). Normal marrow texture of the examined skeleton. According to the previous data, the case is of PIRADS 2, which contradicts the pathology results (Gleason Score 8).

DISCUSSION

The collected 30 pathology specimens were sampled by means of transrectal US guided biopsy. In terms of the histopathological examination, all specimens were adenocarcinoma, 2 have a Gleason score equal to 6 and 28 have a Gleason score (GS) greater than or equal to 7 (9 cases GS 7, 16 cases GS 8, and 1 case GS 9). The median of Gleason score is 8. Percentage of patients with clinically significant cancer (Gleason Score 7 or more, or extraprostaic extension) is 73%. The proportion of clinically insignificant cancer patients in our study is as modest as 27%. According to **Foster *et al.*** [4], the proportion of prostate cancer diagnoses with a Gleason score ≤ 6 has continued to steadily decline over the last years. This is primarily due to increasingly rare occurrence of a Gleason score ≤ 5 at diagnosis (1.5% of all known Gleason scores).

In our study, multi-parametric MRI revealed that 53.4% of the malignant lesions are situated in the peripheral zone (16 cases), 13.3% in the transitional zone (4 cases), 6.6% in the central zone (2 cases), while 26.6% are of infiltrative nature and occupying peripheral, central and or transitional zones (8 cases), with no definite radiological clue that pinpoints the exact anatomical \ zonal source of the lesion. Our results are close to those of **Erbersdobler *et al.*** [7]**,** who examined the post prostatectomy specimens of 104 cases of cancer prostate, and found that in 57.6% of cases the lesion occupied the peripheral zone, 6.7% the central zone and 20.4% the transitional zone. While in 15.3% of cases, the lesion couldn't be assigned to a definite zone. It is expected that Erbersdobler's results are more representative than ours, as his study involved a wider sample volume (104 cases). Moreover, his study dealt with post prostatectomy surgical specimens, which are more accurate than ultrasound guided biopsy specimens of our study.

T2-weighted imaging (T2WI) has a high spatial resolution, enabling it to highlight the zonal anatomy of the prostate gland. Our study revealed that the T2 detectability of malignant prostatic lesions is 76.6%. All the detected lesions appeared as hypointense ill-defined lesions. 23.4% of the lesions were missed by T2WIs. These results lie within the range of T2WIs sensitivities reported by **DeVisschere *et al.*** [1]**,** which range from 57% to 88%.

Hung *et al.* [8] claimed that failure of detection of malignant prostatic lesions could be due to small size, as MRI is limited in detection of cancers < 5 mm, and shows high sensitivity in detection of cancers > 10 mm. Moreover, **Hung** linked between undetectability and low grade cancers, as 75.2% of the undetected cases in their study were of Gleason score 6 or less. While in our study, 42.8% of the undetected cases are low grade cancers (3 cases out of 7).

DWIs aid in distinguishing benign from malignant tissues by measuring restriction of diffusion. In our study, 80% of lesions showed restricted diffusion. In agreement with our study, **Anwar *et al.*** [9] found that DWI sensitivity in detection of cancer prostate is 84%. On the other hand, **Rosenkrantz *et al.*** [10] found a lesser sensitivity (64.7 %) of DWIs in detection of prostatic malignant lesions, making DWIs solely less sensitive than T2WIs in detection of malignant prostatic lesions. Such conclusion contradicts our study, putting in consideration that Rosenkrantz's study sample volume is more representative than ours as well as • Anwar's study (49, 30 and 28 patients respectively). **Rosenkrantz *et al.*** [10] recommends computed DWI with b = 2000 more than the widely used acquired DWI with b = 1000, as it is more sensitive in detection of malignant lesions and more discriminative between malignant lesions and other pathologies.

In terms of dynamic contrast enhanced study, our study revealed a 70% sensitivity in detection of malignant lesions, by observing the odd pattern of enhancement (i.e increased or decreased enhancement in comparison with the background prostate without appraisal of wash-in and wash-out curves). In agreement with our study, **Starobinets *et al.*** [11] found that DCE sensitivity is 74%. **Starobinets** stated that although DCE MRI is less integral to PIRADS evaluation than in the past, it is still an important part of the mpMRI-based prostate examination.

Regarding relative sensitivity, there is a common consensus that combining T2WIs with other functional sequences (DWIs and\or DCE) increase the sensitivity of MRI in detection of cancer prostate. In our study, combined (T2WIs + DWIs) and (T2WIs + DCE) have shown synergistic effect with a resulting sensitivity 83.3% for both combined sequences. In the same context, **Cornud *et al.*** [12] found that such combinations improved the sensitivity of MRI in detection of malignant lesions from 63% for T2WIs alone, to 81% and 79% for (T2WIs + DWIs) and (T2WIs + DCE) respectively.

Regarding TNM staging of the lesions of our study, 5 cases (16.6%) were reported that the lesion was infiltrating the urinary bladder base or encroaching recta wall (stage T4). 5 cases (16.6%) showed evidence of extracapsular extension (stage T3a), while other 3 cases (10%) depicted seminal vesicle invasion (stage T3b). 5 cases (16.6%) had regional lymph node metastasis (stage N1). 11 cases (36.6%) had bone metastasis (stage M1b). Hence, our results suggest that skeletal metastasis is the most common form of extraprostatic spread of cancer prostate. In agreement with that, **Hernandez *et al.*** [13] found that 18% of cancer prostate patients get skeletal metastasis, and 4.7% of them get lymph node metastasis. It is noteworthy that the results of TNM staging in our study are limited as they depend only on the images gathered from mp-MRI study of prostate and pelvis without performing further more comprehensive

studies regarding detection of metastasis (whole body CT / MRI or PET scan).

Applying the imaging criteria of PIRADS version 2.0 scoring system, the vast majority of cases scored PIRADS score 4 and 5, 14 cases (46%) for PIRADS 4 and 8 cases (26%) for PIRADS 5. While less than the third of cases score 2 and 3, 4 cases (13%) for PIRADS 2 and 3 cases (10%) for PIRADS 3. This finding is compatible with the PIRADS score distribution reached by **Park *et al***. [(14)] In the study, 12% were scored as PIRADS score 2, 16% score 3, 47% score 4 and 25% score 5.

In our study, the application of PI-RADS version 2 has significantly improved the diagnostic performance in detection of clinically significant cancer. Considering PIRADS score greater than 3 as a strong indicator for malignancy, the sensitivity of PI-RADS version 2 was 80% for detection of malignant lesions in general (significant and insignificant). Moreover, our study revealed an 88% sensitivity and 33% specificity of mp-MRI in detection of clinically significant cancer prostate (with PIRADS score 4 or more for clinically significant caner that have a Gleason score 7 or more, or extraprostatic extension), with a significant *p value* < 0. 001. Such results are reasonable and acceptable if compared to the results of **Hashim *et al.*** [(15)] study, which revealed a sensitivity and specificity of 93% and 41% respectively. In contrary, **Tan *et al.*** [(16)] found that mp-MRI is more specific in detection of clinically significant prostate cancer, with a 60% specificity. The difference in sample sizes should be considered, as the sample sizes of **Hashim *et al.*** [(15)] and **Tan *et al.*** [(16)] are more representative (740 and 215 respectively). Furthermore, it is noteworthy that **Tan *et al.*** [(16)] used the former version of PIRADS, while **Hashim *et al.*** [(15)] used the recent refined version PIRADS 2.

In conclusion, as a preoperative imaging tool, use of PI-RADS version 2 helps to diagnose clinically significant prostate cancer, considering PI-RADS scores of 4 and 5 to be associated with the presence of clinically significant cancer.

CONCLUSION

This study suggests that mpMRI could help in deferring or omitting requests for invasive prostate biopsies in cases of clinically insignificant cancers, and adopting PIRADS scores 4 and 5 to be considered as a strong indicator for clinically significant cancer.

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