Original Article

False-positive magnetic resonance imaging prostate cancer correlates and clinical implications

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Abstract

Background: False-positive (FP) multiparametric magnetic resonance imaging (MPMRI) obscures and swift needless biopsies in men with a high prostate-specific antigen.

Materials and Methods: This was a retrospective study, in which all patients who had been exposed to consecutive MP-MRI of the prostate combined with transrectal ultrasound-guided-magnetic resonance imaging fusion-guided prostate biopsy between 2017 and 2020 were involved in the study. The FP was measured as the number of biopsies that did not encompass prostate cancer divided by the whole number of biopsies.

Results: The percentage of FP cases was 51.1%, the highest percentage was found in Prostate Imaging–Reporting and Data System (PI-RADs) 3 (37.7%) and the lowest was detected in PI-RAD 5 (14.5%). Those with FP biopsies are younger, and their total prostate antigen (PSA) and PSA density (PSAD) are significantly lesser. The area under the curve PSAD, age, and total PSA are 0.76, 0.74, and 0.69, respectively. An optimum PSAD value of 0.135 was chosen as a cutoff because it showed the highest sum of sensitivity and specificity, 68% and 69%, respectively.

Conclusion: FP results of mpMRI were detected in more than half of our sample, more than one-third were presented in Pi-RAD3, improved imaging techniques to decrease FP rates are highly needed.

Keywords: PIRADs, prostate cancer, transrectal ultrasound-guided biopsy- magnetic resonance imaging fusion-guided prostate biopsy

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INTRODUCTION

Prostate cancer diagnosis differs from the diagnosis of other solid organ cancers, where imaging is utilized to distinguish those patients who require a biopsy. The pathway to the establishment of prostate cancer gives a transrectal ultrasound-guided biopsy (TRUS biopsy) in men who have raised serum levels of prostate antigen (PSA). As a result, numerous men without cancer experience false-positive (FP) biopsies, clinically immaterial cancers are regularly identified, and clinically critical cancers are in some cases missed.[1,2] TRUS biopsy is additionally related to critical dismalness and can cause life-threatening sepsis.[3] A method utilizing imaging as a triage test to choose which men with lifted PSA go for biopsy seems both diminish

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unnecessary biopsies and make strides in symptomatic precision.

Multiparametric-magnetic resonance imaging (MP-MRI) gives data not as it were around tissue life systems but moreover around tissue characteristics; for instance prostate volume, cell structure, and vascular structure.[4,5]

A number of translation mistakes and specialized issues can happen in MP-MRI the prostate. Disappointment to recognize and rectify these mistakes in patients may result in imperfect treatment. FP analysis of ranges of potential cancer on MP-MRI leads to clinical instability and regularly numerous superfluous biopsies or, in certain cases, surgical treatment of low-grade, low-volume infection. In expansion, disappointment to distinguish clinically critical cancer in men being considered for treatment may lead to imperfect quiet results.[6] Prostate cancer incidence is much lower in our region in comparison to European countries and USA, the finding of our previous study revealed an incidence rate of 0.24% among our cohort.[7] Transrectal ultrasound-guided-(TRUS)-MRI fusion-guided prostate biopsy was first introduced in our region in 2015. The current work was conducted to determine the rate of FP prostate cancer MRI images and to investigate the characteristics and predictors of the FP MRI discoveries in our low cancer predominance region.

MATERIALS AND METHODS

Patients

All patients in the current retrospective study ($n = 320$) who had been exposed to consecutive MP-MRI of the prostate combined with TRUS-MRI fusion-guided prostate biopsy between 2017 and 2020 in King Khalid University Hospital and King Faisal Specialist Hospital and Research Centre in Riyadh were encompassed in the study.

Magnetic resonance imaging securing and analysis

Patients experienced (mpMRI) of the prostate on a 3 Tesla Magnet Skyra framework (Siemens A. G., Erlangen, Germany) utilizing an outside multichannel body staged cluster coil. The MRI examination was performed as takes after (i) hub and coronal T2W quick turn to resound groupings (TSE, ETL 25), 3-mm thick cuts, TR/TE: 5540/107; (ii) pivotal dissemination-weighted (DWI) tall determination arrangement, readout sectioned echo-planar imaging (RESOLVE), 3-mm thick cuts and apparent diffusion coefficient (ADC) maps (with quantitative ADC assessment), TR/TE: 5250/62; (iii) hub T1-weighted 3D angle resound grouping for dynamic contrast-enhanced magnetic resonance imaging (DCE-MRI), 3.5-mm thick cuts, 1922 lattice, TR/TE/FA: 4.9/6.7/150, 10 s time determination, 40 time focuses, bolus infusion of 0.1 mM/kg gadolinium-tetraazacyclododecanetetraacetic acid; and (iv) pivotal T1-weighted fat-suppressed arrangement for late postcontrast imaging of the pelvis and hub, 3.5-mm thick cuts, slope resound arrangement, TR/TE: 3.5/1.5, FOV = 240 mm.

A prepared radiologist was dependable for detailing and translating the MRI discoveries. Discoveries were based on a combination of parameters in need arrange: morphology on T2W pictures, DWI ([ADC] maps), DCE-MRI, CSI, and suspicious return-on-investments (ROIs) molded on pivotal T2W cuts for consequent handling on a biopsy US machine. Elucidation criteria for parameter inspiration were in arrangement with the suggestions of the European Society of Urogenital Radiology within the Prostate Imaging Announcing and Information Framework prostate imaging reporting and data system (PI-RADS). ROIs were delineated and scored 1–5 employing a scoring framework built up earlier to the portrayal of PI-RADS.

Transrectal ultrasound-guided-magnetic resonance imaging fusion-guided prostate biopsy

The biopsy was done with an 18G biopsy needle beneath nearby anesthesia. ROIs distinguished on MRI were electronically stacked into the Artemis/profuse framework and program (Eigen, CA, USA). An efficient 12-core strategy was done in each understanding after taking at slightest 2–3 up to six centers from the target injury, putting into consideration the diameters and the estimate of each lesion.

Histopathology

All biopsies were analyzed based on the Worldwide Society of Urological Pathology (ISUP) 2014 proposals.[8] The biopsy comes about that contained cancer (Gleason ≥3 + 3) were classified as genuine positives, whereas those which did not have cancer were considered untrue positives.

Statistical analysis

The FP was calculated as the number of biopsied injuries that did not have prostate cancer partitioned by all biopsies. The *t*-test was utilized to test the association between continuous variables. Values of $P > 0.05$ (two-sided) were considered measurably significant. Logistic regression analysis was used to predict the factors that could be associated with FP cases significantly.

RESULTS

The total number of suspicious MRI cases subjected to biopsy was 320, 9 cases were excluded from the final

analysis as MRI lesions were unidentified (no PI-RADs scores were assigned). The percentage of MRI-positive cases who were diagnosed as biopsy negative (FP cases) was 51.1%, (195 cases).

The distribution of FP cases across PI-RADS is presented in Figure 1. The highest percentage was found in PI-RAD 3 (37.7%) and the lowest was detected in PI-RAD 5 (14.5%).

Table 1 shows the correlates of FP biopsy cases, where men with negative biopsy tend to be significantly younger, PSA and PSA density (PSAD) were essentially lower within the FP cases than those analyzed with cancer. Prostate volume is insignificantly larger in FP cases, $t = 0.9$, $P = 0.35$. Men who have had a past biopsy were more likely to have a FP MRI perusing (70.2% vs. 55.1%, $P = 0.04$). The majority of FP cases (87%) had negative DRE findings.

Men with younger age, lower total PSA, and lower PSAD were detected to be correlated independently with FP MRI findings in the logistic regression analysis model [Table 2].

The zonal location presented no significant difference between FP and true-positive cases. The percentage of lower urinary tract infection cases in the sample was 40%, 30% was seen among cases with PI-RAD 5 and 20% was seen among cases with PI-RAD 3 and 4.

Figure 2 of the Receiver operating characteristic (ROC) shows that the area under the curve PSA density, age, and Total PSA is 0.76, 0.74 and 0.69 respectively. An optimum PSA density value of 0.135 was chosen as a cutoff because it showed the highest sum of sensitivity and specificity, 68 and 69%, respectively.

DISCUSSION

The FP rate among our sample was 51.1%, more than one-third (37.3%) was associated with PI-RAD 3, followed by PI-RAD 2 (27.7%). The accuracy of prostate MRI continues to be plagued by FP abnormalities. Jyoti *et al*.[9] recently published their findings from in-gantry MRI biopsies, where PI-RADS 3 and 4 lesions with inflammation accounted for 97% of FP lesions, mostly in the transition zone.

Several authors have reported different FP rates, Rourke *et al*. found that patients with an MRI targetable lesion had an FP incidence of 70.5% (43/61).[10] The least figure of FP cases was reported from Australia which was nearly the same as our reported figures (52%).[11]

Nearly 15% of the FP cases are seen in PI-RAD 5 in our study, a higher figure (18%) reported by Sheridan *et al*.,[12] which was ascribed to benign prostatic hyperplasia nodule.

Table 1: Distribution of cases across correlated parameters

Factor	Mean±SD	*t*-test	*P*
Age			
+ve biopsy	70.2±8.8	5.3	0.000
−ve biopsy	63.1±7		
PSA			
+ve biopsy	29.4±8.7	2.2	0.02
−ve biopsy	8.2±7.1		
PSA density			
+ve biopsy	0.24±0.19	4.2	0.000
−ve biopsy	0.13±1.3		
Prostate volume			
+ve biopsy	60.2±35.7	0.9	0.3
−ve biopsy	65.4±30.2		

SD: Standard deviation, PSA: Prostate-specific antigen

Table 2: Logistic regression and determinants of false-positive cases

Variable	OR	*P*	95% CI
Age	0.9	0.000	0.85–0.95
Total PSA	0.95	0.05	0.9–0.99
PSA density	0.02	0.01	0.01–0.013

OR: Odds ratio, CI: Confidence interval, PSA: Prostate-specific antigen

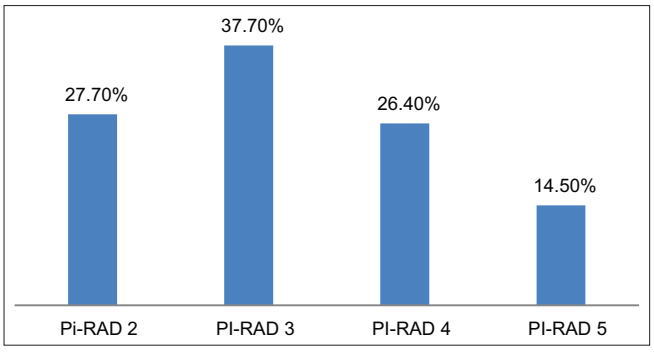

Figure 1: Distribution of false positive (biopsy negative cases) by PI-RADS. PI-RADS: Prostate imaging reporting and data system

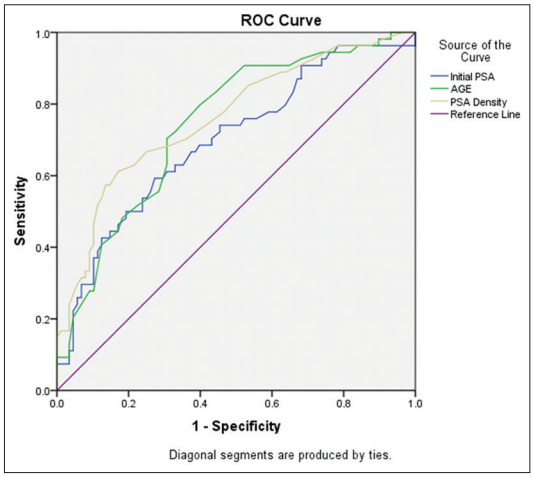

Figure 2: ROC curve for positive biopsy cases

PI-RADS 5 lesions recognized during clinical clarification are frequently linked to an increased risk of clinically serious prostate cancer. Lower prostate-specific antigen density and apex or base position were strongly associated with a benign pathologic outcome, which was most usually attributable to a benign prostatic hyperplasia nodule. They indicated that integration of such clinical findings may progress the clarification of high-risk lesions recognized with mpMRI.[12]

The FP rate for MRI-fusion biopsies can be high and the result of several factors including: MRI quality, radiology read, importing/segmentation of images, biopsy accuracy, in addition to prostate inflammation which is a common clinical problem that is often treated conservatively without the use of imaging or surgery. When such prostatitis patients are imaged, it can imitate PCa at MP-MRI, displaying low SI on T2WI, restricted diffusion, and augmentation patterns, which overlay, with PCa.[10,13]

The experience of radiologists has a significant influence on the rate of FP results of MRI prostate, Stolk *et al*.confirmed that results, where they found that the radiologist's lack of expertise is connected with an FP reading substantially and independently, whereas zonal location is not.[14] In the same context, the studies of Sonn.[15] and Pickersgill *et al*.[16] observed substantial inconsistency in PIRADS score task and significant cancer vintage among radiologists.

PSAD, age, and total PSA were found to be significant predictors for FP results. In accordance with our results, Rourke *et al*.[10] showed that the PSAD was significantly lesser in the FP cases than in cancer cases (median, 0.08 vs. 0.14; $P = 0.02$). Men who had previously had a biopsy were more likely to have had the wrong positive MRI value (90.5% vs. 63.6%, $P = 0.04$). (90.5% vs. 63.6%, $P = 0.04$).

There is rising agreement among radiologists that combining PSAD and prostate MRI is the correct tactic in helping to decide which men with high PSA should be biopsied. The latest study recommended that the enhancement in accuracy for recognition of clinically significant cancer by combining PSAD and PI-RADS scores was verified in men who did not have a prior diagnosis of prostate cancer. The area under the curve (AUC) increased significantly when PSAD was added to PI-RADS in the initial diagnosis group (difference in AUC = 0.031).[17] The study of Sasaki on Japanese males utilizing the receiver-operating characteristic analysis revealed that both the PSAD and serum total PSA were the most useful predictors of prostate cancer. An optimum PSAD value of 0.18 was chosen as a cutoff because it showed the highest sum of sensitivity and specificity, 92% and 54%, respectively.[18]

Two meta-analyses concluded that MP-MRI has a high negative predictive value for the detection of CS cancers,[19,20] and it has been looked at obviously that MP-MRI can evaluate review of PCa compared to histopathology comes about with a sensible degree of exactness.[21] However, due to the lack of robust identification imaging features, publications dealing with the pitfalls of prostate MRI usually contain only benign examples. Illnesses or FPs are related to more technical problems.

In clinical practice, patient risk stratification is utilized to diminish needless biopsies (and thus the need for MR imaging). Clinical variables such as serum PSA levels, rectal examination findings, prostate volume estimates, age, and family history are used to make clinical biopsy decisions. Although the decision to biopsy is grounded on personal preferences, there is a need to weigh the risks (over diagnosis, biopsy related) and benefits (diagnosis and therapy of significant disease). MRI interpretations and the following need for biopsy should be appraised in the context of patient care priorities by multidisciplinary teams. In general, there is an urgent necessity to decrease over-diagnosis in biopsy-naive men, particularly in lower-risk men. The clinical significance of lesions detected by MTI is highly dependent on urologic preferences, which radiologists working in multidisciplinary teams should be alert of.[22,23]

Although noncancer causes of positive MRI decrease as the PI-RADS score increases, it is risky to assume that all PI-RADS 5 lesions are significant cancers; biopsy is always required for confirmation.

The clinical utility of prostate MRI is affected by disease prevalence. When the risk of clinically significant prostate cancer is very high, the benefit of a positive MRI decreases in comparison to a lower but elevated risk. According to the Prospective Assessment of Image Registration in the Diagnosis of Prostate Cancer study,[24] when the risk of clinically significant prostate cancer is very high, the benefits of MRI positives are diminished compared to the low risk but increased risk. Men with lower risk profiles will have a higher FP rate, and the low specificity of MRI will result in a higher number of FPs. This could result in a needless upsurge in biopsy rates, which would have an adverse influence on the benefit-to-harms ratio.[25]

CONCLUSION

FP results of mpMRI are detected in more than half of our sample, which could be predicted through levels of total serum PSA, PSAD, and patients' age. It is clear that

improved imaging technology is urgently needed to reduce FP rates.

Limitations of the study

Our study had some limitations. First, because of its retrospective design, MRI protocols were heterogeneous (i.e., different magnetic field strengths and slightly varying MRI sequence settings). Second, the sample size is comparatively small; however, the incidence of cancer in our region is very low, which is practically reflecting the real situation in the region. Third, this study consists of patients who have previously undergone a biopsy (negative or with cancer but under active surveillance) and may reduce the future generalizability of the results. It is expected that more patients who have not undergone biopsy will undergo MPMRI and targeted biopsy in the future. Finally, as we got our results from two different institutions, nonuniformity in the MRI reading of prostate lesions likely leads to additional disparity, and increasing the inter-observer variability. Therefore, artificial intelligence with deep learning of images can be used in conjunction with other improvement processes providing more accurate alerts to assist radiologists with FP MRI lesions.

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Conflicts of interest

There are no conflicts of interest.

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