Original Research Article

Multi-parametric 3-Tesla MRI evaluation of prostate in cases with negative prostatic biopsy with raised PSA levels - A tertiary care hospital study

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Abstract

The incidence of prostate cancer has been gradually increasing in the world. Checking the serum prostate-specific antigen (PSA) level and a digital rectal examination (DRE) are the gold standards for prostate cancer screening. Prostate gland is divided into four zones, the peripheral zone (PZ), transitional zone and central zone and anterior nonglandular fibromuscular stroma. Prostate is divided into minimum 16 and optionally 27 regions of interest as per European consensus meeting. Until recently, most professionals have been skeptical that magnetic resonance imaging (MRI) could be used on a widespread basis to diagnose or stage prostate cancer with any degree of reliability, and therefore help with making treatment decisions. The aim of the present study was to study diagnostic value of mpMRI of prostate in cases of raised PSA but with negative biopsy. The present study was carried out in the post graduate department of Radiodiagnosis and imaging Govt. Medical College Srinagar over a period of one year from May 2016 to April 2017. All patients with negative prostatic biopsy were evaluated on Siemens 3 tesla MRI scanner. All patients underwent initial T1W scanning to look for any evidence of hemorrhage and patients having hemorrhage due to previous biopsy were also excluded from study or their study was deferred until hemorrhagic artifacts disappear. After proper case selection patients were subjected to detail Multiparametric MRI (mpMRI) for prostate 6-8 weeks period was given from previous biopsy time to MRI study and cases with hemorrhage on T1 weighted sequence were either excluded from study or their study was deferred till resolution of

haemorrhage. The conclusion of the present study was that Mp-MRI prior to repeat biopsies can improve the detection rate of clinically significant PCa and allow for a more accuracy in prostate disease diagnosis.

Key words

mpMRI, Prostate gland, Radiodiagnosis, Hemorrhagic artefacts, Sensitivity and Specificity.

Introduction

The prostate is a walnut-sized gland located between the bladder and the penis. The prostate is just in front of the rectum. The urethra runs through the center of the prostate, from the bladder to the penis, letting urine flow out of the body. The prostate secretes fluid that nourishes and protects sperm. During ejaculation, the prostate squeezes this fluid into the urethra, and it's expelled with sperm as semen.

The incidence of prostate cancer has been gradually increasing in the world. The increase in the aged population, a westernized lifestyle, the development of diagnostic tools, and surveillance programs for early prostate cancer detection may all have contributed to the increased detection rate of prostate cancer.

Checking the serum prostate-specific antigen (PSA) level and a digital rectal examination (DRE) are the gold standards for prostate cancer screening. If repeated PSA levels exceed 4 ng/ml or prostate nodule or asymmetry are found by DRE, transrectal ultrasonography (TRUS)-guided needle biopsy is performed to pathologically confirm the diagnosis [1, 2].

Prostate gland is divided into four zones, the peripheral zone (PZ), transitional zone and central zone and anterior non-glandular fibromuscular stroma. 70-80% of prostate is made of PZ and 70% of cancers arise in this zone [3]. This zonal demarcation of central zone and peripheral zone is not well seen on MRI and are collectively called central gland which is separated by pseudocapsule from peripheral zone [4].

PZ has high signal on T2W images due to high fluid filled ducts and acinar components [5, 6]. As central gland has reduced amount of glandular and smooth muscle it's relatively heterogeneous on T2W images the true capsule is more discernable along posterior and posterolateral aspect this capsule has clinical significance the seminal vesicles are seen as elongated structures posterior to prostate with hypo and hyperintense signal of T1W and T2W images respectively. Medial to seminal vesicles vas deferens is seen with low T1 and T2W signal. Prostate is divided into minimum 16 and optionally 27 regions of interest as per European consensus meeting and each region is assigned a score of 1-5 based on PIRADS score. Clinically significant disease is defined when a lesion with volume ≥ 0.5 cm^3 and or Gleason's score of $\geq$ 4+3 [7].

Until recently, most professionals have been skeptical that magnetic resonance imaging (MRI) could be used on a widespread basis to diagnose or stage prostate cancer with any degree of reliability, and therefore help with making treatment decisions. MRI technology has substantially improved in the past few years, and some experts believe it may be time to reevaluate its use in guiding treatment decisions. A new generation of MRI devices and additional technological advances (contrast enhancement and special processing) are being used together - in select imaging centers - to generate amazingly clear images of the prostate.

Men with a persistent suspicion of PCa with one or more negative SB represent a diagnostic dilemma for urologists. Prostate multiparametric MRI (mpMRI) has been useful in this population by identifying suspicious prostate lesions, often

in areas under-sampled by the SB. Currently the recommended mpMRI of the prostate consists of T1-weighted, high resolution T2-weighted images and at least 2 functional MRI techniques [8, 9].

The aim of the present study was to study diagnostic value of mpMRI of prostate in cases of raised PSA but with negative biopsy.

Materials and methods

The present study was carried out in the post graduate department of Radiodiagnosis and Imaging Govt. Medical College, Srinagar over a period of one year from May 2016 to April 2017. The study was done by a prospective data collection of all patients visiting Department of Radiodiagnosis. Before the examination of the study population the aim of the study was explained to the participants. After their understanding and positive consent the subjects were included in the study. Informed consent of all patients was taken and before examination all patients were explained the procedure and patients having any contraindication to MRI were excluded from the study like history of metallic stents, pacemakers, intracochlear devices, deranged kidney function tests etc.

All possible pros and cons of the study were explained to the population and it was explained to them that all the data and information collected from them during the course of the study will be kept safe and confidentiality of such shall be maintained.

For the purpose of this study a convenience sampling of the available samples was used. In the selected samples we studied patients as per PI-RADS version2 [10] which is a 5 point scale as follows;

- PI-RADS 1 –very low (clinically significant cancer is highly unlikely to be present)
- PI-RADS 2 – low (clinically significant cancer is unlikely to be present)
- PI-RADS 3 –intermediate (the presence of clinically significant cancer is equivocal)
- PI-RADS 4 –high (clinically significant cancer is likely to be present)
- PI-RADS 5 –very high (clinically significant cancer is highly likely to be present). For statistical simplification we categorized PIRADS 1-3 as normal and PIRADS 3-5 as suspicious.

MR spectroscopy was excluded in the study because we categorized patient as per PIRADS version 2 which does not incorporate MR spectroscopy in it. In addition there have been many large clinical trials which suggested that MRS provided little additional information compared with T2w imaging [11].

All patients with negative prostatic biopsy were evaluated on Siemens 3 tesla MRI scanner. No endorectal coil was used in our study and all patients were given 2 mg of buscopan (hyosine butylbromide) injection before the start of study to avoid bowel motion artifacts. Gadolinium was given in dynamic phasic manner with 0.1-0.2 mmole per kg body weight. Field of view was selected which included base to apex of prostate and seminal vesicles. Before starting study in the selected cases a gap of 8 weeks was given from the period of previous biopsy to avoid any misinterpretation in mpMRI reporting.

All patients underwent initial T1W scanning to look for any evidence of hemorrhage and patients having hemorrhage due to previous biopsy were also excluded from study or their study was deferred until hemorrhagic artifacts disappear. One T2W imaging was used in coronal axial and sagittal planes and two functional images like diffusion imaging and dynamic contrast enhanced images in axial and multiple orthogonal planes respectively. Axial high resolution T2w images were taken with repetition time of 3710 msec, echotime (TE) 113 msec, slice thickness 3 mm, pixel size 0.4x0.4

mm, fov of 230 mm and acquisition time (TA)4 mints 30 seconds.

Axial diffusion weighted imaging was also done in each patient with b value of 0,500,1000,1500 and 2000 s/mm2 with following imaging parameters: TR 4700 msec, TE 93 msec slice thickness 3mm FOV 170 mm and TA 6 mints and 40 seconds.

In dynamic contrast MRI gadolinium based contrast agent was given with a dose of 0.1-0.2 mml/kg with an injection rate of 2.5cc/sec in a dynamic phase manner.TR 4.22 msec, TE 1.3 msec, slice thickness 3.5 mm FOV 220 and TA 4 mints 45 seconds.

After proper case selection patients were subjected to detailed Multiparametric MRI for prostate .6-8 weeks period was give from previous biopsy time to MRI study and cases with hemorrhage on T1 weighted sequence were either excluded from study or their study was deferred till resolution of haemorrhage. Each patient was scored 1-5 points for TW2, and DWI as per the PIRADS version 2 scoring system. For statistical simplification we categorised PIRADS 1-3 as normal and PIRADS 3-5 as suspicious. DCE was considered positive or negative depending upon the presence or absence of early arterial enhancement pattern.

For analysis, only those variables were considered about which information was present in more than 95% of charts. We used the chi-square or Fisher tests to evaluate categorical variables. Numerical variables are presented as mean ± standard deviation. We used the Student t test to compare means. We considered $p < 0.05$ as statistically significant. We also calculated the odds ratio when appropriate (**Figure – 1 to 3**).

Figure – 1: Case of prostatic carcinoma localized in ventral prostate more than 2 cm away from rectal wall, missed by transrectal ultrasound and guided biopsy. The lesion is hypointense on T2w images (A) and shows bright focus on b2000 images (B) with diffusion restriction on ADC (C) with brisk enhancement after gadolinium injection.

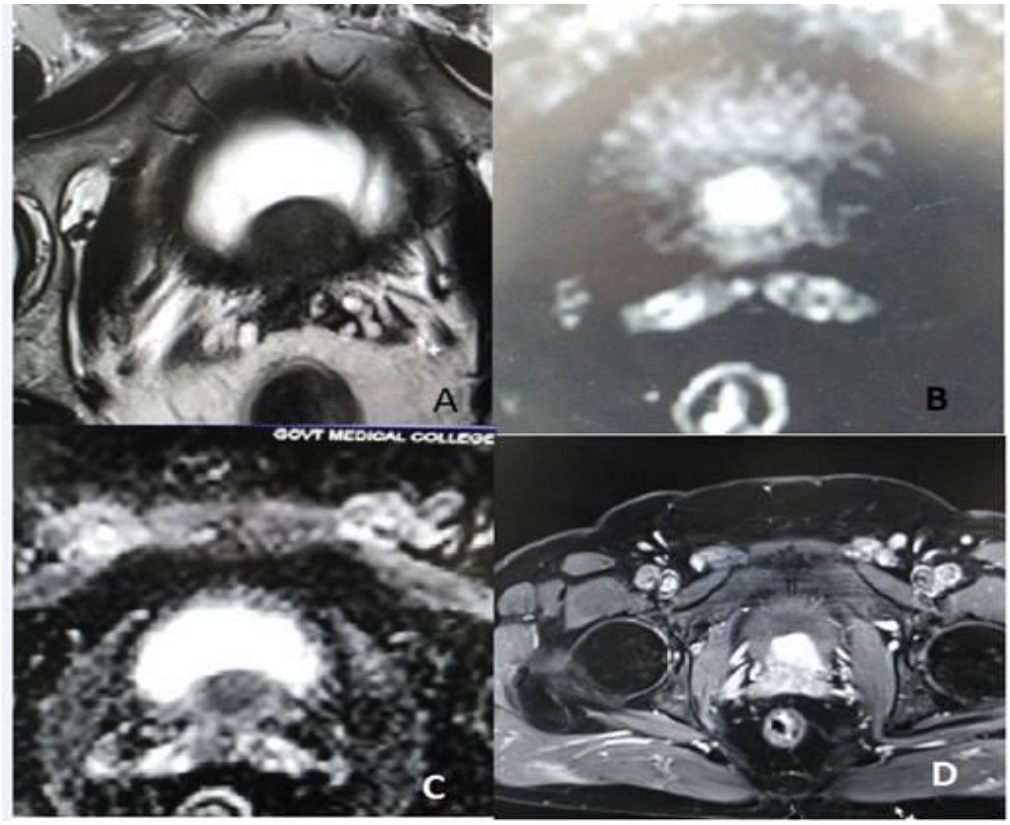


Figure – 2: Case of prostatic carcinoma localized in left peripheral zone. On T2w images (A) there were two hypointense lesions in prostate larger one in central gland and another in peripheral zone. Both the lesions were bright on b2000 images (B) however only peripheral zone lesion revealed diffusion restriction (C).

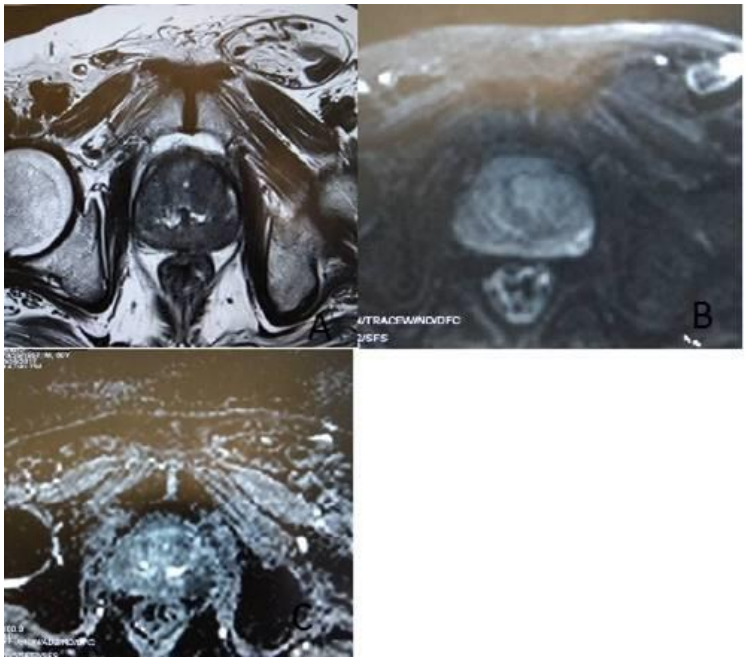
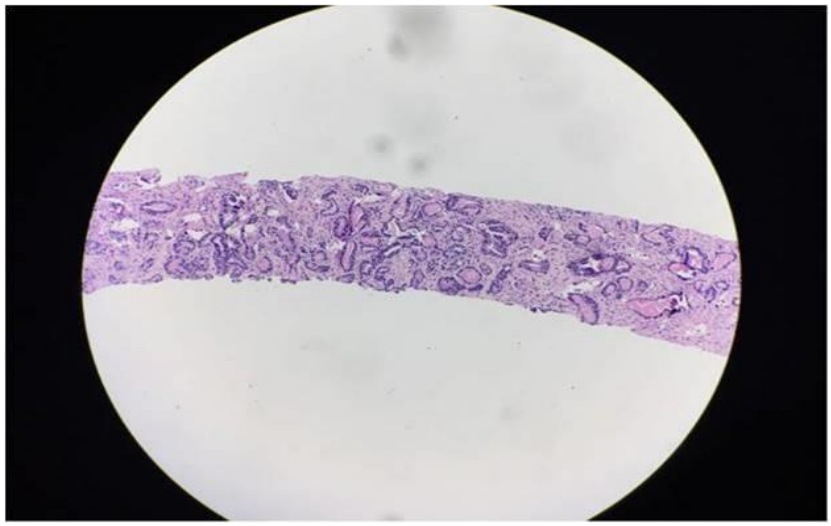


Figure - 3: One core of prostatic carcinoma (3+3 Gleason's score).



Results

The present study was carried out in the post graduate department of Radiodiagnosis and imaging Govt. Medical College, Srinagar over a period of one year from May 2016 to April 2017, the study was carried out on 36 patients with one or more negative prostatic biopsies with raised PSA levels (>4 ng/ml) who were referred to our department of Radiodiagnosis and imaging from department of urology.

Table - 1 presents the T2w imaging wherein it differentiates the Suspicious of malignancy and Normal. As per Table – 1, the imaging process showed a Sensitivity of 53.33%, Specificity 80.95%, Positive predictive value of 66.6%, Negative predictive value of 70.8% and an accuracy of 69.4%. A total of 36 cases were examined of which 15 were suspicious of malignancy and rest 21 were normal.

Table - 1: T2w imaging.

	Suspicious of malignancy	**Normal**	**Total**
Suspicious of malignancy	8	4	12
Normal	7	17	24
	15 (disease)	21 (non-diseased)	36
Sensitivity 53.33%, Specificity 80.95%,PPV 66.6 %, NPV 70.8% and Accuracy 69.4%			

Table - 2: Diffusion imaging.

	Suspicious of malignancy	**Normal**	**Total**
Suspicious of malignancy	9	5	14
Normal	2	20	22
	11 (disease)	25 (non-diseased)	36
Sensitivity 81.82%, Specificity 80%, PPV 64.2%, NPV 90.91% and Accuracy 80.56%			

Table - 3: Dynamic contrast enhanced MRI

	Suspicious of malignancy	**Normal**	**Total**
Suspicious of malignancy	10	6	16
Normal	1	19	20
	11(disease)	25 (non-diseased)	36
Sensitivity 90.9 %, Specificity 76.0%, PPV 62.5%, NPV 95% and Accuracy 80.56%			

Table - 4: Overall mpMRI.

	Suspicious of malignancy	**Normal**	**Total**
Suspicious of malignancy	10	6	16
Normal	1	19	20
	11(disease)	25 (non-diseased)	36
Sensitivity 90.9 %, Specificity 76.0%, PPV 62.5%, NPV 95% and Accuracy 80.56%			

Table - 2 presents the Diffusion imaging which shows that out of the 36 patients screened 11 were found to be Suspicious of malignancy and rest 25 were deemed to be normal. The table shows that the imaging process showed a Sensitivity of 81.82%, Specificity 80%, Positive predictive value of 64.2%, Negative predictive value of 90.91% and an accuracy of 80.56%.

Table - 3 presents the results of the Dynamic contrast enhanced MRI which shows that out of the 36 patients screened 11 were found to be Suspicious of malignancy and rest 25 were found to be normal.

Table - 4 presents the results of the Overall mpMRI which shows that out of the 36 patients screened 11 were found to be Suspicious of malignancy and rest 25 were found to be normal. As per Table – 4, the imaging process showed a Sensitivity of 90.9%, Specificity 76.0%, Positive predictive value of 62.5%, Negative predictive value of 95% and an accuracy of 80.56%.

Discussion

mpMRI is an evolving tool for prostate imaging which noninvasively decreases the risks associated with repeated prostatic biopsy. It not only helps for targeted biopsy but also reduces complication rate. The present study was based on 36 properly selected patients who were referred to the department of Radiodiagnosis and imaging GMC hospital Srinagar Kashmir after negative repetitive 12 core biopsies.

The current diagnostic approach with PSA testing and digital rectal examination followed

by transrectal ultrasound biopsies (TRUS-bx) lack in both sensitivity and specificity in PCa detection and offers limited information about the aggressiveness and stage of the cancer. Scientific work supports the rapidly growing use of multiparametric magnetic resonance imaging (mp-MRI) as the most sensitive and specific imaging tool for detection, lesion characterisation and staging of PCa.

In our experience and in the experience of others the mpMRI is an essential problem solving tool in the radiologists armamentarium [12]. On T2W imaging alone the sensitivity and specificity reported by us is 53.33% and 80.95% with positive predictive value of 66.6 %, negative predictive value of 70.8% and accuracy of 69.4%.

The sensitivity and specificity alone with T2 W imaging shown by Kim et al was 25% and 57% respectively while as it was 62% and 91%, respectively for combined T2W AND DWI [13]. In our study the sensitivity and specificity though more than as reported by Kim, et al. [13] however, it is almost same as reported by Haider, et al. [14] DWI alone has a sensitivity of 81.8%, specificity of 80%, PPV 64.2% and NPV of 90.9%.

Earlier studies showed b values of 1000 s/mm^2 but in our setting at 3 tesla scanner values of 2000 s/mm^2 were obtained in which suppression of background normal prostatic tissues and hyperintense signal of cancerous areas was seen. Same was shown by other people working on 3 tesla scanner. Diffusion weighted imaging actually is based on principal of Brownian motion of molecules in tissues [15]. There is no need of any specialized hardware and it has got an advantage of short acquisition with improved specificity.

In our study, the sensitivity and specificity of DCE is 90.90% and 76% with positive predictive value of 62.5% and negative predictive value of 95%. Accuracy is 80.55%.As reported by Jackson, et al. the sensitivity and specificity of DCE-MRI was 50% and 85% respectively and is higher than t2w imaging alone which is 21% and 81% respectively [16].

With DCE –MRI the localization accuracy as reported by other authors is 72-91% when compared with morphological T2W MR imaging with which it is 69-72% [17, 18]. In our study, the accuracy of t2w imaging is same as reported by other authors.

In our study, the overall mpMRI Sensitivity 90.9%, Specificity 76.0%, PPV 62.5%, NPV 95% and Accuracy 80.56%. Study done by Yuen, et al. shows sensitivity of 100%, specificity of 70.6% and PPV OF 58.3% [19]. The NPV of mpMRI shown by Rooji, et al. is 65-95% which is as almost same as of ours [20]. The accuracy of mpMRI in our study is 80.56 % which is better than as reported by Hoeks, et al. and lesser in comparison to delphine etal which have been reported to around 88% [21, 22]. The lower accuracy of mpMRI in Hoeks study could be due to use of lower b value of <1000s/mm in their study. In our study we used higher b-value of 2000 s/mm which resulted in higher tumor detection in peripheral zone, there are studies which have shown increased detection rate of prostatic carcinoma by increasing b value [23, 24].

Conclusion

The conclusion of the present study was that Mp-MRI prior to repeat biopsies can improve the detection rate of clinically significant PCa and allow for a more accuracy in prostate disease diagnosis.

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