Section: Urology

Original Research Article

EFFICACY OF MULTI-PARAMETRIC MRI IN CORRELATION WITH GLEASON SCORING IN DIAGNOSING CARCINOMA OF PROSTATE

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Abstract

Background: The gold standard approach for identifying prostate cancer is still histologic evaluation of a biopsy specimen followed by Gleason score. Despite being a non-invasive technology, the use of multi-parametric MRI to diagnose the same illness is still controversial. The purpose of this study was to compare the effectiveness of multi-parametric MRI with Gleason scores of TRUS biopsies. **Materials & Methods:** Prospective observational study was conducted in the department of Urology at Madras Medical College, Chennai. It comprised instances with signs of obstructive lower urinary tract obstruction. Cases aged 50 to 78 were included in the study, with PSA levels ranging from 4 to 10 ng/ml and a normal digital rectal examination without any other co morbidities. Twenty-five patients were included in the study. mp-MRI and TRUS biopsies were performed on all of the cases. SPSS 17 was used to analyse the data. **Results:** Pre-biopsy multiparametric MRI can serve as a significant diagnostic study, assisting in guided and targeted biopsy, as well as defining the extent and intensity of prostate cancer at an early and non-invasive stage. Furthermore, multiparametric MRI can minimise the number of negative biopsies in patients with PSA levels in the grey zone between 4 and 10 ng/ml and a normal DRE, reducing patient suffering and wasteful cost. **Conclusion:** For cases with grey zone PSA and normal DRE, multiparametric MRI of the prostate is a valuable, non-invasive, and doable option for identifying carcinoma prostate with high sensitivity and specificity.

INTRODUCTION

Prostate cancer is one of the prominent reasons of cancer mortality among older men. Men's non-cutaneous cancer is the most common.[1] Prostate cancer is becoming more common, partially due to increased use of prostate-specific antigen (PSA) screening tests and partly due to increased life expectancy.[2] Because most malignant cells of prostate are slow-growing and indolent rather than aggressive, they rarely cause symptoms until they are advanced. As a result, early detection of carcinoma of prostate can improve treatment outcomes while also assisting in the selection of different therapy alternatives. PSA, digital rectal examination (DRE) and transrectal ultrasonography guided biopsy have all been used in the past (TRUS). Prostate cancer can only be confirmed with a biopsy, which is usually a 12-core TRUS biopsy. All of these strategies, however, have their own set of limits and drawbacks. PSA assay levels are insensitive and specific, and DRE is a crude procedure with a low accuracy rate and substantial inter-observer variability. TRUS biopsy has been demonstrated in studies to miss up to 20% of prostate malignancies due to under sampling of the anterior prostate, apex, and midline, resulting in a high rate of false negatives.[3] Furthermore, identifying prostate cancer in patients with a PSA level of 4 to 10 ng/ml and a normal digital rectal examination continues to remain difficult. Furthermore, around 70% of initial biopsies conducted in men with elevated PSA levels are negative for prostate cancer, resulting in an increase in the number of negative biopsies and increased screening expenses.[4] Because of the limitations of currently available techniques, researchers have turned to radiologic imaging techniques such as magnetic resonance imaging (MRI) as a diagnostic instrument. In particular, multi-parametric MRI (mp-

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MRI) has received a lot of attention in recent years, which builds on the regular pros of MRI.

mp-MRI combines T1 and T2 weighted anatomical imaging with two functional methods: diffusion-weighted imaging (DWI) and dynamic contrast enhanced imaging (DCE) with or without MR spectroscopy. Apart from assisting in the pre-biopsy diagnosis of cancer of the prostate, mp-MRI also aids in the guidance of biopsy, whether it is a real-time MRI-guided biopsy, a cognitive TRUS guided biopsy, or a fusion biopsy with MRI and TRUS, as well as characterising the extent of disease involvement, which can aid in minimally invasive procedures. It also aids in the prediction of therapy outcomes and the selection of appropriate treatment alternatives. Furthermore, DWI, DCE, and MR spectroscopy hold the promise in terms of better characterisation of lesions and cancer aggressiveness assessment in relation to low, middle, and high Gleason scores. Furthermore, mp-MRI can minimise the number of negative biopsies in men with high PSA levels, as well as increase surgical margin rates, lowering the risk of cancer recurrence and negating the requirement of adjuvant radiotherapy.[5] Even today, the histologic examination of a biopsy specimen and application of Gleason scoring for grading the two most common cell patterns from 1 (lowest) to 5 (highest) and adding them to yield a score with a maximum of 10 are considered adverse to prostate cancer. Scores above 7 are considered averse to prostate cancer.[6] With this in mind, the goal of this study was to determine the usefulness of multi-parametric MRI in detecting prostate cancer in males with PSA levels between 4 and 10 ng/ml and a normal digital rectal examination in comparison to Gleason scores of biopsies.

MATERIALS AND METHODS

Study settings and design

This prospective observational study was undertaken in the department of Urology at Madras Medical College, Rajiv Gandhi Government General Hospital, Chennai, between September 2014 and April 2016. The study was approved by Institutional Ethical Committee with the reference number 14112015 by Madaras Medical College, Chennai, Tamil Nadu. It included cases reported with obstructive lower urinary tract symptoms. The study comprised cases aged 50 to 78, with PSA values between 4 and 10 ng/ml and a normal digital rectal examination (DRE) without any other co morbidities. The study excluded cases with urinary tract infections, bleeding problems, claustrophobia, AUR, Prostatitis, and implants. Study procedure was explained each patient and informed consent was obtained. The study covered a total of twenty-five patients. The multi-parametric MRI sequences used on all 25 patients included T1 and T2 weighted anatomical imaging, functional imaging employing diffusion weighted MRI and DCE, and MR spectroscopy. SEIMENS 3.0 Tesla with phased array body coil was employed in this study. The 2D T2w-MRI, DW-MRI, DCE-MRI, and MRSI multiparametric MR imaging protocols were used. Axial, sagittal, and coronal T2WI images were captured in three orthogonal planes using the T2w turbo spin echo procedure. The signal intensities of the lateral lobes, median lobe, and peri- urethral glandular region of the prostate gland were investigated. The study used the prostate imaging-reporting and data system (PI-RADS).[7]

Procedure

TRUS scans were performed on all twenty-five patients using a 7 Mhz Aloka machine with the rectal probe in the left lateral position. The entire zonal anatomy of the prostate was investigated, and 13 core sextant biopsies were collected. Each biopsy specimen was tagged and sent for histological investigation according to the orientation of the biopsy site. One dosage of ciprofloxacin 500 mg was given to each patient half an hour before the TRUS biopsy. Prior to the biopsy, all of the patients had a low rectal enema. Following the operation, no unexpected complications occurred in any of the patients.

Statistical Analysis

The data was expressed in number and percentage. Statistical Package for Social Sciences (SPSS software version 17) was used for statistical analysis.

RESULTS

The patients in this study ranged in age from 51 to 81 years old, with an average age of 66.76 7.8 years. Out of the 25 patients who had a TRUS biopsy, around 8 of them had a Gleason score of 6

or higher, indicating malignancy. Only two of the eight patients had a Gleason total score of 6, whereas the others had 7 or higher. In comparison to the TRUS biopsy, the multi-parametric MRI-based PIRADS score had a sensitivity of roughly 100% with a 95% confidence interval of 63.06 percent and 100% and a specificity of 94.12 percent with a 95% confidence interval of 71.31 percent and 99.85 percent. Because multi-parametric MRI has a better sensitivity, it can be claimed that it is an excellent screening technique for patients in the grey zone between PSA 4 and 10ng/ml, and TRUS biopsy can be used for those with a higher PIRADS score in the multi-parametric MRI. Multi-parametric MRI has a high specificity, meaning that it has the ability to eliminate patients who would otherwise undergo TRUS biopsy for a negative result. As a result, employing multi-parametric MRI, undesirable and unneeded biopsies can be avoided, decreasing patient discomfort and wasteful health-care costs. Furthermore, the positive predictive value was 88.89 percent with a 95% confidence interval of 51.75 percent to 99.72 percent, while the negative predictive value was 100 percent with a 95% confidence interval of 79.41 percent to 100 percent.

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Multi-parametric MRI's high negative predictive value shows that it can accurately rule out individuals with PSA levels between 4 and 10ng/ml for TRUS biopsy. As a result, the post-test likelihood of a patient with negative multi- parametric MRI results having a malignant lesion is nil. The ability of a diagnostic test, in this case it is multi-parametric MRI, to properly classify individuals with disease and exclude those without disease is known as its accuracy. Multi- parametric MRI had a 96 percent accuracy rate, with a 95 percent confidence interval of 73.21 percent to 100 percent. As a result, multi-parametric MRI inpatients play an important role in deciding whether or not to have TRUS biopsy, particularly in the grey zone between PSA 4 and 10ng/ml.

Among eight cases with malignancy, Gleason score was reported as score 8 in 3 (37.5%), score 7 in 3 (37.5%) and score 6 in 2 (25%) cases. According to the PIRADS score based on multiparametric MRI, roughly 24 percent of the cases had highly suspected malignancy, about 12 percent had a probably malignant lesion, and 16 percent had ambiguous lesions. The other patients all had benign lesions. The issue with these ambiguous lesions is that without surgical excision of the prostate, a clear diagnosis cannot be obtained even with TRUS biopsy.

PIRADS score and Gleason score, as well as PIRADS score and PSA levels, had a positive linear connection, indicating that an increase in PIRADS score corresponded to a rise in Gleason score and PSA levels. Although the positive linear correlation between PIRADS score and Gleason score was not statistically significant, it does suggest that among patients who tested positive for malignancy in TRUS biopsy, the higher the Gleason sum score, the higher the PIRADS score, and thus the role of multiparametric-MRI in determining the extent and aggressiveness of the malignancy is revealed. This is an extra benefit, particularly in the case of pre-biopsy MRI, because it may aid in focused biopsy and therapy, reducing recurrence and providing better guidance for complete surgical clearance.

The positive linear correlation between PIRADS score and PSA levels, on the other hand, was statistically significant ($p<0.05$), indicating that the higher the PSA levels, the higher the PIRADS score, and the higher the risk of malignancy, even among patients in the grey zone between PSA 4 and 10ng/ml, even though the optimal PSA cut-off cannot be determined.

In this study mean PSA was reported as 6.51.83 ng/ml, mean Choline/Creatinine ratio as 0.98±0.47, mean ADC value as 1.52±0.45 and total PIRADS score was 11.0±5.5. Patients with TRUS-diagnosed malignancy had a greater mean choline-creatine/citrate ratio (1.5875± 0.188) than those with a negative TRUS biopsy (0.6953± 0.213), and this difference was found significant ($p<0.001$). Patients with TRUS-diagnosed malignancy had a lower mean ADC value (1.0013±0.103) than those who had a negative TRUS biopsy (1.7706±0.307), and this difference was statistically significant ($p<0.001$). The mean total PIRADS score among patients who had a positive TRUS biopsy was (18.25± 2.121), but the mean PIRADS score among patients who had a negative TRUS biopsy was just (7.59± 2.210), indicating a strong separation between malignant and benign lesions.

Table 1: Proportion of malignancy and benign lesion based on mp-MRI and TRUS biopsy

Multi-parametricMRI	TRUS Biopsy		Total (%)
	Malignancy (%)	Benign (%)	
Malignancy	8 (32)	1 (04)	9 (36)
Benign	0	16 (64)	16 (64)
Total	8 (32)	17 (68)	25

Table 2: Diagnostic efficacy of mp-MRI

Parameter	Value	95% CI
Sensitivity	100%	63.06% - 100%
Specificity	94.12%	71.31% - 99.85%
Positive Predictive Value	88.89%	51.75% - 99.72%
Negative Predictive Value	100%	79.41% - 100%
Diagnostic Accuracy	96%	73.21% - 100%

Table 3: Mean difference of different variables in benign and malignant lesion

Variable	Adenocarcinoma Prostate (N=8)	Benign Prostatic hyperplasia (N=17)	Student t test p value
Choline-creatine /citrate ratio	1.5875± 0.188	0.6953±0.213	<0.001*
ADC value	1.0013±0.103	1.7706±0.307	<0.001*
Total PIRADS score	18.25± 2.121	7.59 ± 2.210	<0.001*

*Significant

Table 4: Correlation between PIRADS score and different variables

Variable	N	Correlation	p value
PIRADS score vs Age	25	-0.480	0.270
PIRADS score vs Gleason score	8	0.383	0.349
PIRADS score vs PSA	25	0.556	0.004*

*Significant

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DISCUSSION

In the recent decade, the usefulness of PSA as a screening technique for early detection of prostate cancer has been questioned. When compared to detection without PSA, it has been proven that using PSA boosts prostate cancer detection rates and leads to the diagnosis of prostate tumours that are more likely to be contained. Population-based statistics, observational research, and randomised screening trials have all confirmed this. The choice of a PSA threshold or cut point over which further examination in the form of a prostate biopsy using TRUS would be recommended to rule out prostate cancer is debatable90-92. The debate is whether using higher PSA thresholds increases not only unwarranted biopsies as well as the proportion of biopsies that identify clinically insignificant disease that would not have been detected in the absence of screening, whereas using lower PSA thresholds increases not only unnecessary biopsies as well as the proportion of biopsies that identify clinically insignificant disease that would not have been detected in the absence of screening. Most clinicians agree that a PSA level of 4.0 ng/mL for males over 50 years of age strikes a good balance between these costs.

The mean total PIRADS score among patients who had a positive TRUS biopsy was (18.25± 2.121), but the mean PIRADS score among patients who had a negative TRUS biopsy was just (7.59± 2.210), indicating a strong separation between malignant and benign lesions. TRUS is not indicated as a first-line screening test for early prostate cancer because of its low predictive value, according to studies.[8,9] TRUS' inability to detect early prostate cancer has been validated in several studies.[10,11] It's a difficult effort to minimise unneeded TRUS biopsies while still finding cancer in cases with grey zone PSA. TRUS biopsies have a poor sensitivity of 60%, a PPV of only 25%, and a false-negative rate estimated to be as high as 15–34 percent, according to numerous studies.95, 96. Combining MRI with TRUS-guided biopsy could help to take biopsy from the suspect area, improving detection rate, and avoid biopsy in those who have no worrisome lesions, avoiding all dangers associated with an invasive biopsy. The research investigations prospectively investigating the significance of MRI in men with a PSA level of less than 10 ng/mL, who have the lowest cancer detection rate and the greatest false-negative rate on TRUS biopsy, reported a cancer detection rate nearly three times better and an NPV approaching 100% 97,98. This study likewise found a similar negative predictive value.

The findings of this study are similar to those of Delongchamps NB et al,[12] who found that tumour size was correctly anticipated in 77% of cases and that about 80% of bilateral cancers were detected, and that multi-parametric MRI could be used to rule out bilateral involvement and has a good prognostic value. De Rooij M et al,[13] found similar results in a meta-analysis of studies looking at the accuracy of multiparametric MRI in prostate cancer detection, with a specificity of 88 percent and a sensitivity of 74 percent. Furthermore, in the study mentioned above, the negative predictive value ranged from 66% to 81 percent. The sensitivity and specificity of multiparametric MRI found in this investigation were higher than those found by Citak E et al,[14] who used linear discriminant analysis (LDA) and support vector machines to predict the final Gleason score based on pre-operative multiparametric MRI (3 Tesla). Prior to Gleason classification, a typical principal component analysis yielded sensitivity of 51.19 percent and 64.37 percent, respectively, with specificities of 72.7 percent and 39.9 percent for LDA and SVM. They found that the SVM classifier had somewhat higher sensitivity but lower specificity than the LDA classifier.

The diagnostic accuracy and cost-effectiveness of MR spectroscopy and improved MRI techniques (DCE and DWI) for localising prostate anomalies for biopsy were reviewed and evaluated by Mowatt G et al [15]. MRSI had the best sensitivity, at 92 percent, whereas TRUS imaging had the highest specificity, at 81 percent. The new investigation found similar results with good sensitivity and specificity. They concluded that MRSI outperformed T2-MRI in terms of sensitivity and specificity. According to Ageeli W et al [16], mp-MRI with PI-RADS classification can accurately predict Gleason score of clinically relevant prostate cancer. The PI-RADS grading method had a slight connection with thicker lesions on ultrasonography. USWE could be used to target prostate cancer suspects. Boschheidgen M et al,[17] stated that mp-MRI provides useful pre-biopsy information about prostate carcinoma aggressiveness. The best prediction of the biopsy ISUP grade group was obtained using a mix of quantitative and qualitative factors, which may improve clinical route and treatment planning by providing information beyond the PI-RADS assessment category. In cases of negative or post-biopsy low-grade prostate carcinoma, an early re-biopsy appears to be necessary due to the high prevalence of higher grade prostate carcinoma. Mayer R et al,[18] found that prostate cancer with a spherical form has a higher Gleason score. This new discovery is related to lung and breast adenocarcinomas, but not to other primary tumour forms. Multi-parametric MRI analysis can non-invasively evaluate the morphology of a prostate tumour and provide essential information for prognosis and disease management. Unlike eccentricity measured by histology of whole mount prostatectomy, MP-MRI eccentricity of smaller tumours correlates strongly with Gleason score. Also in another study Mayer R et al,[19] reported that prostate tumour eccentricity, as evaluated by histology or MRI, predicted Gleason score more reliably than prostate tumour volume. In contrast to MRI, combining tumour eccentricity with volume

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from histology-based analysis improved Gleason score prediction.

Based on these findings, it is safe to use multi-parametric MRI which has high sensitivity and specificity, as well as better predictive values, and that pre-biopsy multiparametric MRI can serve as not only a screening tool, but also a valuable diagnostic investigation, assisting in guided and targeted biopsy, as well as characterising the extent and aggressiveness of prostate cancer at an early and non-invasive stage. Furthermore, using multiparametric MRI for patients with PSA levels in the grey zone between 4 and 10 ng/ml and a normal DRE can reduce the number of negative biopsies, minimising patient distress and unnecessary cost. It proves that multi-parametric MRI has an important role to play not only in prostate cancer screening but also in diagnosis, treatment, and prognosis.

CONCLUSION

Based on the findings of this study, it can be concluded that multiparametric MRI of the prostate for patients with grey zone PSA and normal DRE is a valuable, non-invasive, and feasible option for detecting carcinoma prostate with high sensitivity and specificity, as well as high predictive values, and can assist in identifying patients who require biopsy, as well as targeted biopsy and characterising the extent and aggressiveness of the prostate cancer.

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Conflict of interest

There are no conflicts of interest.

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