ROLE OF MULTIPARAMETRIC MAGNETIC RESONANCE IMAGING IN THE EVALUATION OF PROSTATIC PATHOLOGIES ON 3 TESLA MACHINE

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ABSTRACT Background and objectives: Prostate diseases with an overall incidence of 9% are the leading cause affecting millions of males worldwide, with prostate cancer being the primary cause of death in males owing to benign prostatic hypertrophy being the primary cause of morbidity in the older age group. In light of this, we aimed to evaluate the utility of Magnetic Resonance Imaging in evaluating and characterization prostatic pathologies and grading prostatic cancer using PIRADS v2.

Methods: This was a study carried out on 50 patients with the age group ranging from 50 to 90 years with clinical suspicion or ultrasonographically demonstrable prostatic pathology and correlation of multiparametric MRI findings on various sequences with clinical features and histopathological findings and classification into groups of benign and malignant prostatic lesions and according to the PIRADS v2 scoring.

Results: Out of our study group, 4 cases were diagnosed with prostatitis and prostatic abscess, and 46 cases were categorized into PI-RADS, out of which most cases were classified into PI-RADS category V, followed by PI-RADS II and III. These were then evaluated with MR spectroscopy, of which 30 cases showed choline peak, and 16 cases showed citrate peak. The sensitivity and specificity for multiparametric MRI sequences combination detect the carcinoma of the prostate was calculated, and the Positive Predictive Value (PPV) & Negative Predictive Value (NPV) was found as 76% and 92%, respectively.

Conclusion: Based on our findings, we found out that the multiparametric MRI approach gives a wealth of practical information that has dramatically enhanced the detection and characterization of prostatic lesions. We also found out that morphological and functional sequencing improves the sensitivity and specificity of the lesions’ identification and characterization.

KEYWORDS Prostate MRI, PIRADS, MR Spectroscopy, Prostate cancer

Introduction

The prostate gland is a male reproductive organ that produces sperm-feeding and sperm-protecting substances. Prostate diseases, with an overall incidence of 9%, are the leading cause affecting millions of males worldwide. Prostatitis is the infection or inflammation of the prostate gland. Benign prostatic hyperplasia (BPH) is another most common pathology of the prostate gland. Prostate cancer, the primary cause of death in males owing to prostatic disorders, is given special attention. In contrast, benign prostatic hypertrophy is the primary cause of morbidity in an older age group in the world population. Like other types of cancer, prostate cancer responds best to treatment when detected early in the disease’s progression. As a result, better diagnostic procedures are crucial for guiding effective therapy and a better patient outcome [1].

Magnetic resonance imaging (MRI) is a good technique for presenting the prostate’s anatomical details. It is usually used as a staging technique once a transrectal biopsy has confirmed the
diagnosis [2]. In addition, MRI may benefit patients who have had negative Transrectal Ultrasonography (TRUS) guided biopsies. MRI examination is also beneficial prior to TRUS-guided biopsy, particularly in individuals with a high chance of high-grade malignancies [3]. As a result, MRI of the prostate plays various roles in treating prostate cancer, including improving diagnostic accuracy, early staging, characterization of prostatic tissue, and, more recently, advice for focused therapy [4].

Besides conventional anatomical imaging with T1 weighted imaging and T2 weighted imaging sequences, recent improvements use functional and physiologic MR imaging approaches [5]. As part of a multiparametric strategy, these novel methodologies are combined. The tissue microstructure at the tiny, microscopic scale of water self-diffusion (Brownian motion) is used in diffusion-weighted imaging (DWI). The chemical composition of various tissue diseases is estimated using MR spectroscopy (MRS). Contrast-enhanced (CE) MR imaging estimates the distribution of an intravenous gadolinium contrast agent between tissue and the blood pool, allowing researchers to evaluate changes in the microvascular environment caused by tumour angiogenesis [6-8]. All these methodologies necessitate ongoing advancements in imaging unit hardware and software.

Materials and Methods

Study design
Our study was a hospital-based descriptive and analytical prospective study at our tertiary care hospital. This study was carried out on 50 patients aged 50 to 90 years with clinical suspicion or ultrasonographically demonstrable prostatic pathology in the Department of Radiodiagnosis at our institution starting from September 2019, lasting over two years until August 2021. The MRI findings were correlated with clinical features and histopathological findings wherever available. Clearance of the ethical committee of our institute (IESC) was taken prior to the start of the study. The approval number is IESC/PGS/2019/175. Informed consent was taken from all the patients involved in the study.

Inclusion Criteria
Patients in the age group of 50 to 90 years with clinical signs and symptoms suspicious of prostatic pathology and those with USG evidence of prostatic pathology were included in our study.

Exclusion Criteria
Patients falling out of the described age group and patients with contraindications to MRI (E.g., electrically, magnetically or mechanically activated implants like cardiac and auditory claustrophobia) were excluded from our study.

Data Collection
After the patient followed all the inclusion criteria, relevant clinical history was taken, and other local and systemic examination findings were noted. Patients were then subjected to multiparametric MRI of the prostate. Again, relevant laboratory tests were noted, including the serum PSA levels. In addition, USG examination findings were noted for comparison. Histopathological correlation was then done.

Prostate Imaging Reporting and Data System (PI-RADS) - The Prostate

Imaging Reporting and Data System Version 2 (PI-RADS™ v2) [9] is designed to provide global standardization and minimize the variation occurring in the acquisition, interpretation, and reporting of the prostate using the multiparametric magnetic resonance imaging (mp MRI). The overall objective is to improve the outcomes for patients. PI-RADS™ v2 assessment uses a 5-point scale based on the likelihood (probability) that the combination of findings of mp-MRI based on T2W, DWI, and DCE sequences correlates with the presence of a clinically significant cancer for each lesion in the prostate gland.

Assignment of a PI-RADS™ v2 Assessment Category should be based on mp-MRI findings only, and it should not incorporate other factors like the serum prostate-specific antigen (PSA), digital rectal exam, clinical history, or choice of treatment. Biopsy should be considered in the PI-RADS 4 or 5 category, but not for PI-RADS 1 or 2.

For the Peripheral zone (PZ), Diffusion-weighted imaging (DWI) is the primary determining sequence. PI-RADS score for a PZ lesion is based on DWI unless the DWI score is PI-RADS 3. In this scenario, Dynamic contrast enhancement is used to decide between PI-RADS 3 (no focal or early enhancement) or upgrade to PI-RADS 4 (focal and early enhancement present). For the Transitional zone (TZ), T2 weighted imaging is the primary determining sequence. PI-RADS score for a TZ lesion is based on T2W unless the T2W score is PI-RADS 3. In this scenario, DWI is used to decide between PI-RADS 3 (DWI score <5) or upgrade to PI-RADS 4 (DWI score 5). The index (dominant) intraprostatic lesion should be identified. Thus, a smaller lesion with EPE should be defined as the index lesion despite a larger tumour with the identical PI-RADS Assessment Category.

Imaging Protocol

The examination was performed using the Siemens 3T Magnetom Vida MRI Machine with the patient in the supine position and pelvic phased-array coils as the receiver coil. The following sequences were taken and examined in each patient: Localizer images utilizing a Half-Fourier acquisition single-shot turbo spin-echo (HASTE), T2 Weighted Imaging (T2WI) in axial and sagittal planes, T1 Weighted Imaging (T1WI) in the axial plane, Diffusion-Weighted Imaging (DWI) in axial planes, T1 Weighted Dynamic Post-contrast Imaging in axial, coronal and sagittal planes and Magnetic Resonance Spectroscopy images using multivoxel PRESS box in three orthogonal planes.

Statistical Analysis

Statistical analysis was performed by entering the data into Microsoft Excel and evaluating it using the SPSS Statistics software version 17.0 (IBM, Armonk, NY). Using the statistical methods, sensitivity and specificity for individual sequences and the overall combination of these sequences to detect prostate carcinoma were calculated.

Results

A total of 50 male patients with suspected lesions in the prostate were evaluated with multiparametric-MRI for identification and characterization of the lesions. The patients were grouped according to age. The highest incidence was found in the 61-70 age group, accounting for 52% of the total cases, and the least was seen in the 81-90 years age group, which accounted for 2% of the cases. The mean age of the cases was 67 years.

PI-RADS distribution

We classified the final diagnosis on MRI according to the PI-RADS v2. A total of 46 cases were categorized into PI-RADS,
out of which most cases were classified into PI-RADS category V, followed by PI-RADS II and III. This is shown in Table 1.

Extracapsular Extension and Metastases
Twelve cases showed extracapsular extension and extension into adjacent organs (Table 2). Involvement of the seminal vesicles was most seen (n=6). The urinary bladder was also seen to be involved in 6 of the cases. The rectum was seen to be involved in 4 cases. Involvement of the corpus spongiosum of the penis was seen in 1 case. Distant metastases to bones seen as osteoblastic lesions were noted in 5 cases involving pelvic bones and spine mainly. Metastases to the spleen were also noted in 1 case. Seven cases also showed enlarged pelvic lymph nodes (Table 3).

MR Spectroscopy
MR Spectroscopy is one of the multiparametric approaches for prostatic pathology. Total 46 cases were evaluated with MR spectroscopy in which 30 cases showed choline peak and 16 showed citrate peak. One of the cases with a high choline ratio turned out to have a benign cause, and 1 case with no choline peak was later discovered to have malignant aetiology. This is shown in Table 4.

Biopsy
In this study, 49 cases underwent biopsy to confirm the various pathologies, out of which 32 cases turned out to be adenocarcinoma of the prostate, and 13 cases turned out to be benign pathologies. Of the benign pathologies, 13 cases were of benign prostatic hyperplasia and four cases of prostatitis and prostatic abscesses. This is shown in Table 5.

Out of 50 cases, four were diagnosed with prostatitis and prostatic abscess. The prostate was enlarged in size and appeared iso to hyperintense on T2WI, with heterogeneous contrast enhancement and central diffusion restriction on DWI. In this study, initially, 12 cases were diagnosed as BPH (PI-RADS - II) on MRI, out of which 11 turned out to be BPH and 1 case turned out to be adenocarcinoma of the prostate. The prostate showed moderate to severe enlargement in size. On T2WI, mild heterogeneity was noted in the transition zone (either bilaterally or on one side) with well-demarcated BPH nodules with the thinning of the peripheral zone.

Markedly hypointense focus in the transition zone on T2WI is usually a focus of stromal hyperplasia. However, transitional zone cancers also show a markedly hypointense signal (erased charcoal sign) with ill-defined or well-defined margins and an amorphous, lenticular (lens-like) round or oval shape. ADC values were calculated for all prostatic pathologies in which transitional zone cancers had values from 0.93-1.35 x 10^-3 sec/mm² while BPH nodules were from 1.35-1.76 x 10^-3 sec/mm². The lower the ADC values, the higher the probability of prostatic cancer.

In this study, 8 cases were diagnosed as having equivocal chances for having benign and malignant aetiology (PIRADS - III) (Figures 1 and 2 show PIRADS III lesion in a 66-year-old patient), out of which 2 turned out to be BPH, and six turned out to be adenocarcinoma of the prostate. The prostate showed mild to moderate enlargement in size. On T2WI, heterogeneity was noted in the transition zone (either bilaterally or on one side) with few well-demarcated BPH nodules and few nodules with obscured margins with the peripheral zone appearing hyperintense on T2-weighted images. Seven cases were diagnosed with likely chances of having malignant aetiology (PIRADS - IV), out of which seven were adenocarcinoma of the prostate after the biopsy. The prostate showed mild enlargement in size. On T2WI, heterogeneity was noted in the transition zone (either bilaterally or on one side), with suspicious lesions in the peripheral zone appearing hypointense on T2-weighted images. In this study, 18 out of 50 cases were initially diagnosed to be of having highly likely chances of malignant aetiology (PIRADS - V) (Figures 3, 4 and 5 show PIRADS V lesion in an 82-year-old patient) by the multiparametric approach out of which all 18 are turned out to be malignant on biopsy. They typically showed hypointensity on T2WI, enhancement in the post-contrast study, and restriction on DWI with increased choline: citrate ratio on spectroscopy.
Table 1 Table showing categorization of patients corrodng to PI-RADS grading

| PI-RADS | No. of Patients | Percentages |
|---------|----------------|-------------|
| I       | 1              | 2.17%       |
| II      | 12             | 26.08%      |
| III     | 8              | 17.39%      |
| IV      | 7              | 15.21%      |
| V       | 18             | 39.13%      |
| Total   | 46             |             |

Table 2 Table showing number of patients having extra-capsular extension

| Extracapsular extension | No. of patients | Percentages |
|-------------------------|----------------|-------------|
| Present                 | 12             | 24%         |
| Not present             | 38             | 76%         |
| Total                   | 50             |             |

Table 3 Table showing number of patients having Metastases

| Metastases | No. of patients | Percentages |
|------------|----------------|-------------|
| Present    | 7              | 14%         |
| Not present| 43             | 86%         |
| Total      | 50             |             |

Table 4 Table showing number of patients with choline peak and citrate peak on MR spectroscopy.

| MR Spectroscopy     | No. of patients | Percentages |
|---------------------|----------------|-------------|
| Choline peak        | 30             | 60%         |
| Citrate peak        | 16             | 32%         |
| Not done            | 4              | 8%          |
| Total               | 50             |             |

Table 5 Table showing of categorization of patients into benign and malignant based on biopsy.

| Diagnosis on Biopsy | No. of patients | Percentages |
|---------------------|----------------|-------------|
| Malignant           | 32             | 64%         |
| Benign (BPH+Prostatitis) | 17 | 34% |
| Not done            | 1              | 2%          |
| Total               | 50             |             |

Table 6 Sensitivity and specificity of various sequences for prostate carcinoma detection

| Sequence                     | Sensitivity | Specificity |
|------------------------------|-------------|-------------|
| T2Weighted Images            | 82.1        | 87.7        |
| Apparent Diffusion Coefficient (ADC) | 96.9       | 88.6        |
| Diffusion weighted Imaging (DWI) | 90.6       | 85.7        |
| Dynamic Contrast Susceptibility (DCS) | 93.8       | 88.6        |
| MR Spectroscopy (MRS)        | 90.6        | 92.9        |
| Overall (T2 + ADC + DWI + DCS + MRS) | 96.8     | 95.7        |
Pre and Post-contrast T1 fat-saturated images (2A and 2B) showed no abnormal contrast enhancement. MR Spectroscopy (2C) shows a prominent citrate peak. On biopsy, the lesion was found to be adenocarcinoma.

Prostatomegaly with enlarged and heterogeneous transitional zone showing an ill-defined lesion of size 3(CC) x 2.7(T) x 2.2(AP) cm in the right mid and apical aspect of transitional zone appearing hypointense on T2WI (3A, 3B and 3C) with low ADC values (3D) and showing restriction on DWI (3E). It is seen abutting the neurovascular bundle lateral to it with loss of fat planes in between. Loss of fat plane between the right proximal seminal vesicle and lesion with the invasion of the seminal vesicle. Superiorly it is invading the bladder base. Posteriorinferiorly, there is loss of fat plane between the lesion and the anterior rectal wall.

Discussion

Multiparametric MRI is an exciting new method for evaluating pelvic diseases, showing the best soft-tissue resolution. Advantages of MRI over CT included the ability to do multidimensional imaging, which was particularly useful in delineating the extent of diseases, such as anterior spread into the space of Retzius or invasion of the base of the bladder, which is better shown in sagittal scans and its ability to identify the regional enlarged lymph nodes. High-spatial-resolution T2-weighted fast acquisition with refocused echo sequences with a narrow field of view performed using body phased-array coils is commonly used to describe prostate anatomy. However, the prostate has a very low T1-weighted contrast. As a result, T1-weighted pictures make it difficult to distinguish between distinct anatomic zones [10, 11]. We also found that T2-weighted images were the most helpful sequence in identifying and characterizing the lesion. Of all malignant cases, 18 cases of prostatic carcinoma appeared as a hypointense lesion within the hyperintense peripheral zone. Extracapsular extension, lymph nodes and metastases were also seen well in this sequence. In this study, 1 case of prostatitis appeared homogeneous on T2 with signal intensity similar to normal prostate and 12 cases diagnosed as BPH on MRI showed well-defined T2W hypointense nodules. All 11 cases were confirmed as BPH, and 1 case was diagnosed as prostate cancer after the biopsy. Eight cases diagnosed with equivocal chances of benign and malignant aetiology on MRI showed few obscured and well-defined T2W hypointense nodules 2. Cases were diagnosed as BPH, and 6 cases were diagnosed as prostate cancer after the biopsy, 7 cases were diagnosed as having likely chances of ma-
lignant aetiology on MRI showing ill-defined T2W hypointense lesions and all 7 cases were diagnosed as prostate cancer after the biopsy. Post-contrast images were also helpful in the characterization of the lesions. The enhancement was usually seen in the malignant lesions, while the benign lesions were usually isointense to the rest of the enhancing parenchyma.

Diffusion-weighted imaging (DWI) is a type of functional imaging that gives both quantitative and qualitative data at the cellular level, with the added benefit of a quick acquisition time and ease of use. The apparent diffusion coefficient (ADC) number can be calculated using DWI. DWI is used to create ADC maps, which are calculated voxel-by-voxel from numerous DWI sequences [12-14]. As a result of the confined diffusion, prostate tumours show a high signal on raw DWI but a low signal on ADC maps [12-14]. This is demonstrated in the majority of our cases.

On MR Spectroscopy, the resonances for the metabolites of the prostate, such as citrate, creatine, polyamines and choline, appear at different positions in the spectrum and different frequencies (2.6, 3.0, 3.1, and 3.2 ppm, respectively). The resonance peaks for prostate metabolites, such as creatine, polyamines and choline, overlap when MRS is performed at 3 Tesla MRI machines [15]. The concentrations of the various metabolites are associated with the areas beneath these signals, and concentration changes can be utilized to detect carcinoma. The prostate gland produces citrate and polyamines when it is healthy. Citrate and polyamine levels drop dramatically in prostate cancer [15]. Because of increased turnover of the cell membrane, the density of cells, and the metabolism of phospholipid, prostate cancer causes an increase in choline. In cancer, the ratio of choline to citrate rises. Because creatine’s resonant peak is similar to choline’s, the ratio of choline plus creatine (Ch + Cr) to citrate (Ci) is commonly evaluated using clinical spectroscopy.

In most cases of prostatic cancer, we detected elevated choline plus creatine to citrate ratio, which was later verified by biopsy. However, 1 of the cases with a high ratio turned out to have a benign cause. One case with no choline peak was later discovered to have a malignant aetiology. The concomitance of MRS with prostate MRI showed enhanced identification, assessment, and evaluation of the aggressiveness of prostate carcinoma [16], which is comparable to our findings. However, MRS is technically complex, with drawbacks such as extended acquisition times, artefacts from post-biopsy bleeding, and difficulty achieving appropriate shimming and fat and water suppression. Furthermore, manual case-specific adjustments are required to maximize spectroscopic data post-processing, which is sometimes impossible with commercially available spectroscopy software and necessitates proper training.

Clinical Applications: Localization, characterization, tumour volume, lesion aggressiveness, and staging are essential aspects of multiparametric MRI of the prostate. Data from multiparametric MRI examinations can be used for biopsy guidance, assisting in selecting the best therapy plan. The main limitation of our study was a smaller study group. Studies on a larger population and more intricate laboratory correlation can help better understand the pathologies and disease progression.

Conclusion

The multiparametric approach gives a wealth of helpful information that has dramatically enhanced the detection and characterization of prostatic lesions. We also found that morphological and functional sequencing improves the sensitivity and specificity of the lesions’ identification and characterization. However, different functional sequences have their limits, which must be considered, and a combination of these sequences should be examined when describing the lesion. Therefore, T1 and T2 weighted MR imaging combined with Diffusion-weighted and contrast-enhanced MR imaging is suggested as minimum prerequisites for multiparametric MR imaging for clinical evaluation of prostate cancer. DW imaging and MR spectroscopic imaging are both precise functional MR techniques that can be used to improve specificity for various clinical purposes and determine prostate cancer’s aggressiveness. The multiparametric method is also effective for determining the aggressiveness of a lesion, staging, biopsy guiding, and treatment planning. In addition, contrast-enhanced MR imaging can be utilized to identify possible prostate cancer spots with excellent sensitivity.

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Conflict of interest

There are no conflicts of interest to declare by any of the authors of this study.

Author contribution

DRA contributed to the study concept, data collection, interpretation of the data, statistical analysis, and manuscript drafting. PK and SC contributed to data collection, interpretation of the data, and revision of the manuscript. PK, SD, SC, DK, and PL contributed to the data interpretation and manuscript revision. VMK contributed to the study concept, interpretation of the data, and revision of the manuscript. All authors read and approved the final manuscript.

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