ORIGINAL RESEARCH ARTICLE

Role of Dynamic Contrast Enhanced Magnetic Resonance Imaging for Evaluation of Prostate Cancer

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A B S T R A C T

Introduction: To study the sensitivity and specificity of Dynamic contrast-enhanced magnetic resonance imaging (DCE-MRI) in the detection and characterization of prostate in prostate cancer, to obtain histopathological diagnosis and correlate with the imaging findings.

Material and Methods: The study was conducted over a period of 27 months from June 2017 and 30 patients who were clinically suspected to have prostate cancer underwent MRI at our hospital using Siemens Magnetom Avanto 1.5 Tesla machine with a body phase array coil. Multiphasic scanning using T1W, T2W, DWI and dynamic contrast image acquisitions were performed. Dynamic curves were obtained at the areas of interest. Trucut biopsy was performed for all cases to obtain histological diagnosis.

Results: All the patients presenting to us were elderly males with age above 50 years. The maximum number of patients belonged to age group of 61 to 70 years. The most common presenting complaint of these patients was lower urinary tract symptoms like poor stream and hesitancy, which was noted in 80% of patients. PSA levels in our study ranged from 0.02 ng/ml to 26.5 ng/ml and 42.8% of the patients in the range ≤ 10ng/ml had prostate cancer and 73.9% of the patients with PSA > 10ng/ml had prostate cancer. Digital rectal examination (DRE) was suggestive of malignancy in 18 cases and was found to be normal in 12 cases and amongst the patients with normal DRE, 6 cases had prostate cancer on imaging. Out of 20 patients with prostate cancer, DCE – I could accurately detect lesions in 16 patients with sensitivity and specificity of 80% and 70% respectively. Other conventional sequences were also slightly better in detection of prostate cancer and accurately detected lesions in 15 patients with sensitivity and specificity of 75% and 80% respectively. The addition of DCE data to conventional sequences increased the sensitivity to 90% and specificity to 85%.

Conclusion: MRI maintains a critical role in detection, localization and staging of prostate cancer. Newer modalities like DCE-MRI should be used in conjunction with conventional MRI sequences as it increases sensitivity, specificity and diagnostic accuracy. DCE-MRI with PIRADS category of lesions may help differentiating between low risk and high risk prostate cancer patients.

Keywords: Magnetic Resonance Imaging, DCE-MRI, DRE, PSA, T2W, PIRAD

INTRODUCTION

Prostate cancer is the second most malignancy in men worldwide. In India, it is the seventh most common malignancy in men.[1] The clinical management of prostate cancer continues to be one of the most controversial areas, with no consensus on need for cancer screening, choice of diagnostic tests for pre-treatment evaluation, and need for and appropriateness of treatment for any stage of disease.[2] Several major obstacles prevents the optimal clinical management of prostate cancer. The first main obstacle that is related to early detection is the inability of screening tests to differentiate the subclinical disease from clinically significant prostate cancer. The second obstacle, related to treatment planning, is the limitation of currently available tumour prognostic factors in differentiating indolent from aggressive disease.

Although number of tumour prognostic factors such as tumour volume, grade and stage, can generally predict disease at either end of spectrum, most cancers fall into an intermediate range, where it is difficult to distinguish those cancers that are likely to progress than those that can be observed. Patients with prostate cancer are treated with a risk adjusted patient specific method that is designed to improve the control of cancer while reducing the risk of treatment related complications. There is a growing demand for further

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individualization of treatment plans, which necessitates the accurate characterization of the location and extent of prostate cancer.[3]

When palpable, prostate cancer is usually appreciated as induration of prostate on digital rectal examination (DRE). The subjectivity of DRE is well described and significant under-staging and, to a lesser extent, over-staging is observed when correlated with step sectioned radical prostatectomy specimens.[4] Another parameter used for evaluation of prostate cancer is prostate specific antigen (PSA). Tumour grade may also impact upon the amount of PSA production in an individual patient. It has also been hypothesized that the amount and type of benign prostatic hyperplastic tissue in a given patient is an extra variable that can alter an individual's PSA level. Catalona et al[5,6] demonstrated that men with serum PSA levels exceeding 2.5 ng/ml have a >20% chance of having prostate cancer detected by needle biopsy, whereas men with PSA level >10 ng/ml have more than 50% chance of having prostate cancer on needle biopsy.

The use of ultrasound for evaluation of prostate cancer has been widely publicized. Transrectal ultrasound (TRUS) has been reported previously as a technique to evaluate rectal pathology. In 1963, Takahashi and Ouchi were the first to describe the use of TRUS to evaluate the prostate.[7] By placing the transducer in the rectum close to the prostate gland, it is possible to use high resolution transducer with sharply focused near field to image prostate.[8] TRUS has a limitation in diagnosis of early case. Sometimes, a malignant lesion can appear either hypoechoic or hyperechoic, which adds to its limitation.

Magnetic resonance imaging (MRI) has become primary technique throughout the body in routine diagnosis of many disease processes. MRI has a particular advantage as it is non-invasive, non-ionising and has an excellent tissue resolution. As other parts of the body, MRI can be used to identify prostate cancer both locally and regionally. MR in prostate imaging began with conventional T1 and T2 weighted sequences.[9,10] The T2 weighted images are assessed as it demonstrates the internal anatomy of prostate gland well. The peripheral zone shows higher signal intensity than either the central and transition zone on T2 weighted images and is visualised well on coronal, sagittal and transverse planes. The central zone is of low signal intensity and is seen well on coronal and sagittal planes.[11] The low-intensity transition zone is blended with the periurethral glands and pre-prostatic sphincter. The transition zone is of homogenous low signal intensity in young men but varied in size and signal intensity in older men.[9] Anterior fibromuscular stroma has low signal intensity on T2 weighted images. Prostate cancer in the peripheral zone appears as an area of low signal intensity that is easily differentiated from high-signal intensity normal tissue. T2 weighted images has significant limitations for representing cancer in the transitional and central zones, because both cancer and normal tissues both have low signal intensity on T2 weighted images.

The European Society of Urogenital Radiology (ESUR) has established a standardized guideline for the interpretation and reporting prostate MRI, Prostate Imaging-Reporting and Data System version 1 (PIRADS).[12,13] Few studies showed that the use of MR spectroscopy and DCE sequences may not contribute to any significance in interpretation of prostate cancer, therefore PIRADS version 2 was introduced. This helps in improving the detection, localization, characterisation and risk factors in patients suspected of prostate cancer.[14] DWI is performed as an indicator of tumour cellularity and aggressiveness.[15] DWI helps mainly in determining the final assessment category. So, a DWI score of 3 indicates a clinically significant prostate cancer.[16,17,18] DCE-MRI helps in interpretation of T2W and DWI in detection of prostate cancer and surveillance status post-surgery or radiotherapy.[19,20] It helps in differentiating the tumour vasculature from routine blood vessel network in the prostate.[21] Our study is performed to evaluate the effectiveness of DCE-MRI in assessing prostate cancer and to correlate with histopathological diagnosis.

MATERIAL AND METHODS

Study population

The study was conducted over a period of 27 months from June 2017. 30 patients clinically suspected to have prostate cancer on the basis of lower urinary tract symptoms (hematuria, hemospermia, urgency, frequency and nocturia) with raised serum PSA levels of more than 4 ng/ml or with a hard / nodular prostate on digital rectal examination were selected and subjected to MR imaging of prostate after taking an informed consent. Any patient with documented prior treatment for prostate cancer were excluded from the study.

MRI protocol

The 30 patients were examined by MRI using SIEMENS MAGNETOM AVANTO MR Machine with a 1.5 Tesla scanner. T1 and T2 weighted images were taken in axial, coronal and sagittal planes. Diffusion weighted data was acquired using single shot EPI sequences at b value of 0 and 1000. Dynamic images were taken in the axial plane.

Image analysis

T1 and T2 weighted sequences were reviewed in all three planes and the dynamic imaging was performed in axial planes. Any irregular hypointense focal lesions on T2 weighted sequence without any hyperintensity on T1 weighted sequence and showing enhancement in dynamic images was considered suggestive of prostate cancer. Extracapsular extension was diagnosed if there was capsular irregularity, capsular bulge or obliteration of rectoprostatic angle on T2 weighted images or asymmetry of neurovascular bundle on T1 weighted images.

Seminal vesicle invasion was diagnosed on T2 weighted images if there was evidence of hypointensity in either of the seminal vesicles. Prostate cancer was diagnosed on dynamic enhanced contrast images as bright lesions, as these lesions showed intense enhancement of the involved tissue. The dynamic curves were then automatically calculated by placing the ROI well within the confines of the lesion. Tissue with type 3 dynamic curves was considered malignant. For combined data of T2 W + DWI + DCE, prostate cancer was considered positive if either the images was positive. All the 30 patients underwent transrectal TRUCUT 10

core prostatic biopsy. The patients diagnosed as prostate cancer on biopsy was operated or given appropriate treatment depending on individual cause. Imaging diagnosis in all cases was compared with histopathological diagnosis.

STATISTICAL ANALYSIS

MR imaging and TRUCUT biopsy findings were compared and statistical analysis was performed, with $p \leq 0.05$ indicating a statistically significant difference. With use of 2 x 2 contingency table, descriptive statistics (accuracy, sensitivity, specificity, PPV and NPV) was performed for detection of prostate cancer for T2W, DWI with DCE-MRI. Fisher's Exact test was used to compare the sensitivity and specificity of MRI sequences.

RESULTS

The thirty study participants in the current study were recruited with an inclusion criteria of individuals aged 50 years and above. The mean age of the participants was 67.13±7.97 with majority of them belonging to the age group of 61-70 years. The least number of participants belonged to the age group 81-90 years.

The most common clinical manifestation observed was prostatism (73.3%), wherein the patients exhibited signs of urinary tract infection like burning sensation while urinating, frequent need to urinate, blood in urine and semen and poor stream and hesitancy. 26.7% patients presented with a history of hematuria.

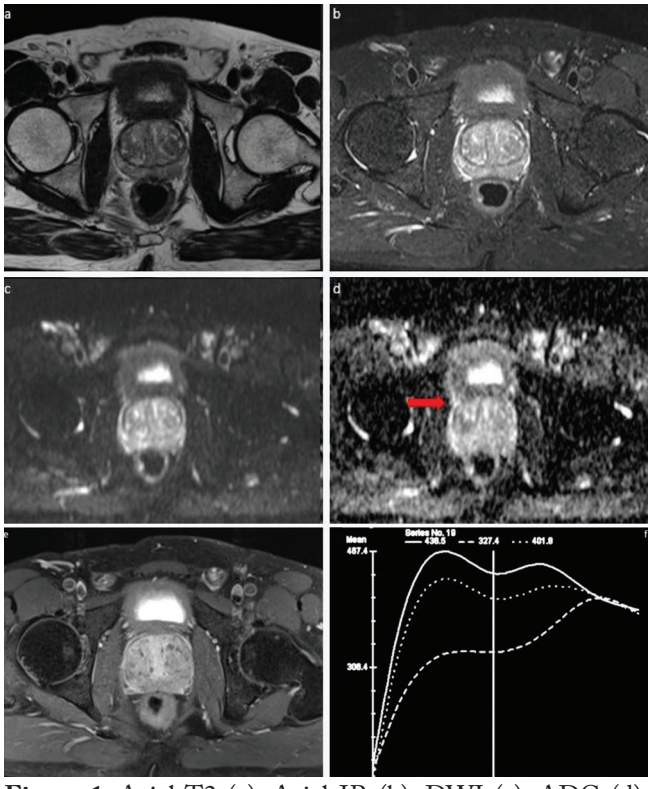

Figure-1: Axial T2 (a), Axial IR (b), DWI (c), ADC (d), Axial T1 post contrast (e) and DCE (f) images showing an ill-defined hypointense lesion in transition zone on right side showing early enhancement on dynamic contrast study. This is a PIRADS IV lesion.

In the present study, digital rectal examination of the prostate gland was performed. It was found that 63.3% patients exhibited a prostate gland of hard consistency followed by soft to firm consistency among 23.3% patients.

Serum prostatic specific antigen level and digital rectal examination were evaluated as screening test in our study. In the present study, the reference value of PSA was considered as > 10 ng/ml. It was found that the mean prostate specific antigen (PSA) level among the study participants was 7.09±6.43 with a range of 0.02 ng/ml to 26.5 ng/ml. 7 of 30 patients had a PSA level above 10 ng/ml and 1 among them had prostate cancer. 13 proven cases had a PSA level < 10 ng/ml, which would have been undetected if only PSA level was taken as reference to detect the cases.

In our study, digital rectal examination was suggestive of malignancy in 23 cases and was normal in 8 cases. Amongst the patients with normal DRE, 3 cases of prostate carcinoma

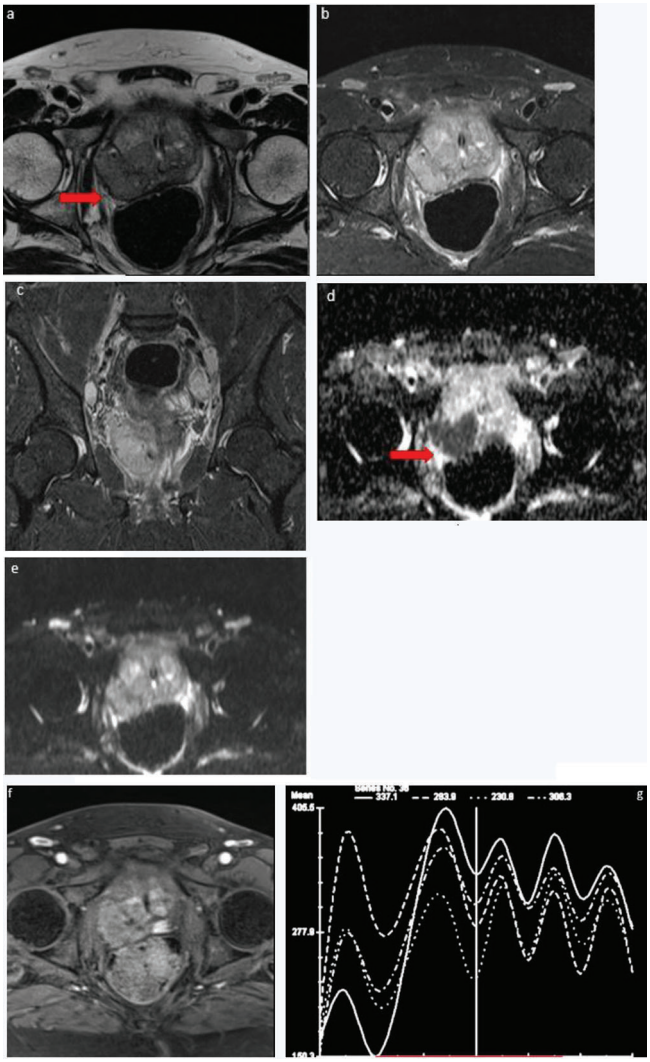

Figure-2: Axial T2 (a), Axial and coronal IR (b,c), DWI (d), ADC (e), Axial T1 post contrast (f) and DCE (g) images showing prostatomegaly with T2 hypointense lesions involving the transition and peripheral zones, showing diffusion restricton and dynamic contrast enhancement (Type III curve). Subtle extracapsular extension noted on right side. This is a PIRADS V lesion.

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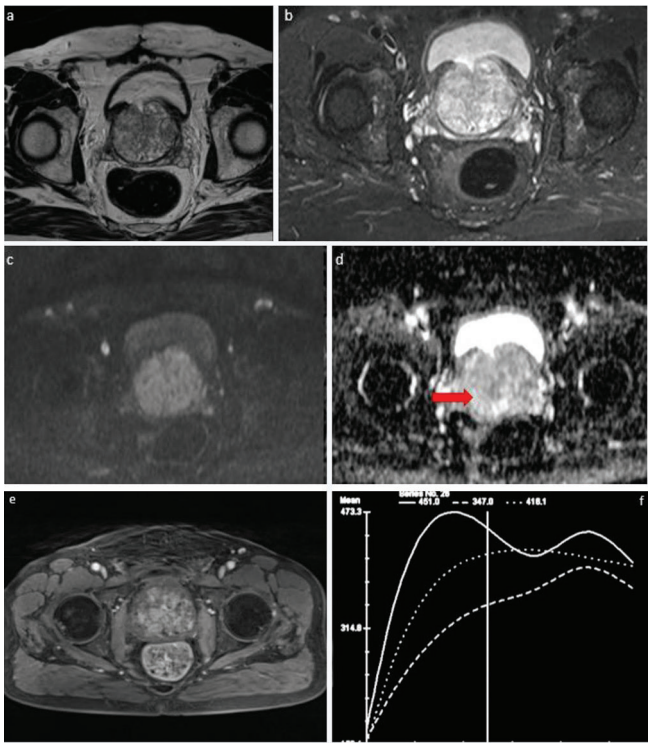

Figure-3: Axial T2 (a), Axial IR (b), DWI (c), ADC (d), Axial T1 post contrast (e) and DCE (f) images showing prostatomegaly with nodular wedge shaped T2 hypointense lesion in posterior transitional zone (arrow), showing subtle diffusion restriction and dynamic contrast enhancement. This is a PIRADS II lesion.

were found and would have been missed if only DRE was used as a screening test to guide biopsy. On combining DRE and PSA levels together, only 3 prostate cancer would have been missed.

In the present study, the analysis of T1 W and T2 W images were conducted on the parameters like presence of lesion, extracapsular extension, seminal vesicle invasion, urinary bladder / rectal invasion, neurovascular invasion and metastasis. It was found that unilateral lesions were prevalent on right more than left side of the prostate. However, invasion to surrounding structures were minimally observed. Extra capsular extension and urinary bladder / rectal invasion were seen among only 3.3% patients, seminal invasion was observed amongst 6.7% whereas neurovascular invasion and lymph node metastasis was present among 13.3% of the patients.

On subjecting the patient samples to PIRADS evaluation, amongst the 30 patients, 36.7% exhibited stage V prostate cancer followed by type IV in 20% cases. In comparison, the PIRADS detection positively detected all the 14 cases that was confirmed through histopathological analysis. Thus, sensitivity of PIRADS in detection of prostate cancer was proved to be 100%. However, the PIRADS detection led to the false positive detection of 3 subjects who were proved negative in histopathological analysis. Thus, the specificity of PIRADS in detecting the true negative cases was comparatively less yielding a score of 81.25%. The positive predictive value was 82.4% and the negative predictive value was 100%.

DISCUSSION

The present study was conducted among 30 outpatients reporting to our hospital who were suspected with prostate cancer based on clinical findings, raised PSA > 4 ng/ml or abnormal digital rectal examination. The parameters evaluated were localization and staging of prostate cancer, DCE-MRI sequences, PIRADS and dynamic curve characteristics.

Majority of the study participants belonged to the age group of 61-70 years. Most of these patients presented with features of prostatism and urinary tract infection. The findings were similar to a study conducted by Gavin et al[22] wherein prostate cancer patients above 60 years of age presented with urinary tract problems. Digital rectal examination was performed, where it was found that 63.3% of patients had prostate gland of hard consistency.

Along with DRE, serum prostatic specific antigen level was also evaluated as part of the screening test. In general, PSA levels greater 4 ng/ml are usually considered suspicious of prostate cancer. As levels increase above 10 ng/ml, the probability of cancer increased dramatically. Therefore, for this study, the reference value of PSA was considered as > 10 ng/ml. A study by Vani et al[23] showed that individuals with PSA > 10 ng/ml had 18 times more chance of being biopsy positive in comparison to PSA < 10 ng/ml and concluded that the confirmation for malignancy / screening in high – risk people should be considered when PSA value is more than 4 since sensitivity was 100%, rather than PSA more than 10 ng/ml.

Another study was conducted by Gilbertson in 1971, in which the author would have missed 12/37 cases of prostate cancer if only DRE was used to guide the biopsy and showed that DRE in combination with PSA provide better method for detection of prostate cancer than abnormal digital rectal examination alone.[24] In our study, it was found that, combination of DRE and PSA levels together would provide a better result.

All 30 patients were evaluated by MRI, obtaining T1 W, T2 W, PIRADS and dynamic curve characteristics. These sequences were evaluated for detection and localization of prostate cancer. In our study, there was extra capsular extension and urinary bladder / rectal invasion in 3.3% patients, seminal vesicle invasion in 6.7% and neurovascular invasion and lymph node metastasis in 13.3% of the patients. The results are similar to a study conducted by Guanay et al[25] wherein it was found that 32.4% of the patients showed extra capsular extension, 12.2% showed seminal vesicle invasion and 2.7% patients showed lymphovascular invasion (Fig. 1, 2).

The results of our study were in concensus with the study conducted by Junker et al[26], who prospectively evaluated the PIRADS scoring system for classifying multi-parametric MRI findings of the prostate and analysed the correlation between the PIRADS scoring system and tumour aggressiveness. The study concluded that the PIRADS scoring system showed good diagnostic accuracy and only PIRADS four and five showed high-grade prostate cancer.

A similar retrospective study by Schimmoller et al[27] found a sensitivity of 86%, a specificity of 68%, as well as PPV and

NPV of 58% and 90% respectively for detection of prostate cancer using PIRADS. Various other studies reported variable reports depending upon the field strength and sample size.

The difference in our study and previous studies may be because of the fact that our sample size was small. The possibility of selection bias as in some studies, the patients included were scheduled for radical prostatectomy because of a biopsy proven prostate. Most of our data are based on results of biopsy, which allows sampling errors that may reduce the measured specificity (Fig. 3).

The diagnosis of prostate cancer in our study was also based on the findings of dynamic curve characteristics. The study of the dynamic curves revealed that among the 30 patients suspected to have prostate cancer, majority of them i.e. 46.7% patients showed type III characteristics. In comparison with the 14 histopathologically proven cases, 12 cases were detected positive using dynamic curve, exhibiting a good sensitivity of the test. However, dynamic curve test also led to the detection of 5 false positive cases. Thus, the sensitivity of dynamic curve in detecting prostate cancer was 85.7%, specificity was 68.7%, PPV was 70.5% and NPV was 84.6%. A study by Hansford et al[28] showed that DCE MR imaging time-curve-type analysis performs poorly for differentiation of prostate cancer from healthy prostatic tissue, which differs from our study results.

In the present study, we also evaluated the role of combined PIRADS and dynamic curve analysis in the detection of prostate cancer in comparison with histopathological findings. The combination of PIRADS and dynamic curve test in the detection of prostate cancer yielded a sensitivity value of 100% showing that the two diagnostic tests when used collectively can detect the true cases appropriately. However, the specificity value obtained was 87.5%, depicting the chances of obtaining false positive results. The PPV and NPV were 100% and 93.3% respectively.

Several other studies have also proved the effectiveness of DCE-MRI in detection of prostate cancer and also as a useful aid along with histopathological tests. A study by Chen Z et al[29] has confirmed that DCE-MRI tool with PIRADS and Dynamic Curve serves as a good indicator for detection of prostate cancer.

Thus, the combination of PIRADS and Dynamic curve characteristics in DCE-MRI testing can prove as a valuable and effective tool in diagnosis of prostate cancer. In addition, it can also aid as a guide for histopathological examination for better results.

CONCLUSION

PIRADS is found to be more effective in efficiently determining the cases of prostate cancer. However, combination of PIRADS and dynamic curve type analysis in diagnosing prostate cancer proved to have a sensitivity of 100% and specificity of 87.5%. The study also proved that a combination of PIRADS and dynamic curve characteristics in DCE-MRI testing is a valuable and efficient tool in diagnosis of prostate cancer.

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