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Application of Vesical Imaging–Reporting and Data System in Evaluation of Urinary Bladder Cancer Using Multiparametric Magnetic Resonance Imaging: A Hospital-Based Cross-Sectional Study

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Abstract

Background Multiparametric magnetic resonance imaging (mp-MRI) of urinary bladder (UB) is a novel imaging to predict detrusor muscle invasion in Bladder cancer (BC). The Vesical Imaging–Reporting and Data System (VI-RADS) was introduced in 2018 to standardize the reporting of BC with mp-MRI and to diagnose muscle invasion. This study was performed to evaluate the role of mp-MRI using VI-RADS to predict muscle invasive BC.

Methods This prospective study was carried from June 2020 to May 2021 in a tertiary care institute. Thirty-six patients with untreated BC underwent mp-MRI followed by transuretheral resection of the tumor (TURBT). Mp-MRI findings were evaluated by two radiologists and BC was categorized according to VI-RADS scoring system. Resected tumors along with separate biopsy from the base were reported by two pathologists. Histopathological findings were compared with VI-RADS score and the performance of VI-RADS for determining detrusor muscle invasion was analyzed.

Results VI-RADS scores of 4 and 5 were assigned to 9 (25%) and 15 (41.7%) cases, respectively, while 4 (13.3%) cases had VI-RADS score 3 on mp-MRI. VI-RADS 1 and 2 lesions were observed in six (16.7%) and two (5.5%) cases, respectively. On histopathology, 23 cases (63.9%) had muscle-invasive cancer and 13 cases (36.1%) had non–

Keywords
- bladder cancer
- multiparametric
- magnetic resonance imaging
- detrusor
- staging

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muscle-invasive cancer. The sensitivity and diagnostic accuracy of mp-MRI in predicting muscle invasive BC was 95.6 and 80.6%, respectively.

Conclusion Mp-MRI has high sensitivity and diagnostic accuracy in predicting muscle invasive BC and should be advocated for evaluation of BC prior to surgery.

Introduction

Bladder cancer (BC) is a common urological malignancy among adults. In India, BC is the ninth most common cancer accounting for 3.9% of all cancer cases as per the Indian Cancer Registry data.[1] BC is three to four times more common in men as compared with women.[2] BC has a high recurrence rate and up to 80% of patients with non–muscle invasive BC relapse within 5 years,[3] and nearly 30% of patients progress to muscle invasive disease on long-term surveillance after primary treatment.[4]

Majority of BC are urothelial in origin (90%) while approximately 6 to 8% are squamous cell carcinomas and only a few are adenocarcinomas.[5] Up to 25% of urothelial cancers show a mixed histology including small-cell neuroendocrine, micropapillary, sarcomatoid, and plasmacytoid components and have worse prognoses than the pure urothelial cancers.[5] Cigarette smoking and exposure to chemical carcinogens are the commonest etiologic factors for urothelial tumors. Cigarette smoking is presumed to be the causative factor in 50 to 60% of men and one-third of women with BC.[6,7] Risk factors for squamous cell cancer of UB include long-term catheterization, nonfunctioning bladder, urinary tract calculi, and chronic infection by *Schistosoma haematobium*.[8]

Urothelial tumors can be divided in non–muscle-invasive, (~80–85%) and muscle-invasive (20–25%) types, whereas squamous-cell carcinoma and adenocarcinoma are nearly almost invasive at the time of diagnosis.[7] Majority of urothelial lesions are low-grade lesions, may be multifocal, arise from a hyperplastic epithelium and generally have a good prognosis with recurrence rates of approximately 50%.[8,9] If left treated, they have a propensity to become muscle invasive tumors. Muscle-invasive BCs are aggressive tumors and have a bad prognosis. So, the early diagnosis and management can reduce the morbidity and mortality in these patients and for that imaging can play an important role.

Though contrast-enhanced computed tomography (CECT) is commonly performed for BC, magnetic resonance imaging (MRI) is superior to CT for local staging of BC. This is attributed to the ability of MRI to clearly differentiate the layers of the urinary bladder wall which in-turn enables an accurate assessment of the depth of tumor invasion and its extra-vesical extension.[10] Distinction between muscle-invasive and non–muscle-invasive BC is of great importance in planning the treatment and prognosticating the disease. Transurethral resection of bladder tumor (TURBT) is the method of choice for treating non–muscle invasive BC with or without adjuvant intravesical chemotherapy,[11] whereas muscle-invasive disease is managed with radical cystectomy, radiotherapy, chemotherapy, or a combination of these depending on the staging.[12] Adequate preoperative assessment of BC facilitates in counseling the patients and also planning the treatment. Until now, BC is staged with combination of clinical, pathological, and radiologic findings.[13] Further muscle infiltration on TURBT is missed in up to 25 to 36% of invasive BC.[14–16]

Multiparametric MRI (mp-MRI) can provide a noninvasive opportunity to decrease the errors in local staging through better anatomical visualization. Mp-MRI includes morphologic imaging techniques like high-resolution T2-weighted (T2W) imaging and functional imaging techniques such as dynamic contrast enhanced (DCE) imaging and diffusion-weighted imaging (DWI). Few studies exist in literature signifying the role of MRI in predicting muscle invasive BC.[17–21] To standardize and propose a consensus-driven approach for mp-MRI in local BC staging, the Vesical Imaging-Reporting and Data System (VI-RADS) was introduced in 2018.[22] This system predicts the likelihood of detrusor muscle invasion in BC using a five point VI-RADS scoring system. Therefore this pilot study was performed to determine the applicability of mp-MRI using VI-RADS scoring system to predict muscle invasive urinary BC in our setup.

Materials and Methods

Patient Population

This prospective study was performed from June 2020 to May 2021 after the clearance from the institutional ethics committee and included 58 patients of BC who visited the urology outpatient department during that period. These patients were diagnosed clinically and then urinary bladder lesion was confirmed by cystoscopy and radiological investigations.

Exclusion criteria included patients with contraindications to MRI (cardiac pacemaker or metallic implants), deranged renal function, patients with urethral stricture, those who could not hold urine, patients with history of claustrophobia, and those with recurrent bladder. These accounted for 22 of 58 patients (20.7%) and so only 36 patients were included for final study.

Magnetic Resonance Imaging Parameters

The mp-MRI of the urinary bladder was performed in all the patients after at least 4 to 6 hours of fasting. Adequate bladder distension was achieved by instructing the patient not to void urine for approximately 2 hours before imaging or by asking the patient to drink 500 to 1,000 mL of water 30 minutes before MRI examination. Imaging was performed with 1.5-T MRI machine (Magnetom ESSENZA; Siemens Healthcare, Germany) from aortic bifurcation to the inferior

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margin of the pubic symphysis. Each patient was subjected to three main components of mp-MRI (high-resolution T2W, DWI, and DCE MRI). Additional sequences included T1W images and axial T2W images with fat suppression. Turbo spin-echo (TSE) T2W sequences were obtained in axial, coronal, and sagittal planes with field of view (FOV) of 12 to 20 cm and slice thickness/gap of 3 mm/0.3 mm. For DWI, echo-planar sequence in axial plane was obtained with 16- to 22-cm field of view and 3-mm slice thickness and *B*-values of 0, 400, 800, and 1,200 were used. DCE scan was obtained using volumetric interpolated breath hold sequence (VIBE) after administering intravenous gadopentetate dimeglumine at a dose of 0.1 mmol/kg at a rate of 2.5 mL/s followed by 20 mL of saline flush. Minimum of five sets of contrast-enhanced images were obtained after injection of contrast.

Image Analysis

T2W, DWI, and DCE were scored for each patient with a 5-point VI-RADS scoring system. VI-RADS scoring was performed independently by two experienced uroradiologists in all the cases to predict detrusor muscle invasion. In case of any discordance between the two readers, the final scoring was obtained with consensus. In patients with multiple tumors, tumor with the largest size was selected. Bladder tumors were scored using the VI-RADS scoring system as laid out in the literature.[22] DWI (first) and DCE (second) were the dominant sequences for risk estimation while T2W sequence was used a first pass guide, especially for categories 1 to 3[22]:

1. VI-RADS 1 (muscle invasion is highly unlikely): structural category (SC), DCE, and DWI category 1.
2. VI-RADS 2 (muscle invasion is unlikely to be present): SC, DCE, and DWI category 2; both DCE and DWI category 2 with SC category 3.
3. VI-RADS 3 (the presence of muscle invasion is equivocal): SC, DCE, and DWI category 3; SC category 3, DCE or DWI category 3, and the remaining sequence category 2.
4. VI-RADS 4 (muscle invasion is likely): at least SC and/or DWI and DCE category 4; the remaining category 3 or 4; SC category 3 plus DWI and/or DCE category 4; SC category 5 plus DWI and/or DCE category 4.
5. VI-RADS 5 (invasion of muscle and beyond the bladder is very likely): at least SC plus DWI and/or DCE category 5; the remaining category 4 or 5.

Statistical Analysis

VI-RADS score of 3 and above was used as a cut-off value to predict detrusor muscle invasion. All patients were subjected to TURBT or cystectomy. In patients who underwent TURBT, a piece of detrusor muscle tissue at the tumor base was also removed for histopathological evaluation. Histopathological examination was performed by two experienced pathologists for detrusor muscle invasion. All categorical data were expressed as number and proportion. The diagnostic performance of VI-RADS score in predicting muscle invasion was evaluated by the calculating sensitivity, specificity, and diagnostic accuracy using 2×2 tables in Microsoft Excel. The interobserver agreement and weighted kappa value were calculated using Statistical Package for Social Sciences.

Results

A total of 36 patients, including 32 (88.9%) men and 4 (11.1%) women, were included in this study with an age range of 42 to 85 years. Solitary lesions were seen in 31 (86.1%) cases while multifocal tumors were observed in 5 (13.9%) cases in our study. Majority of BC occurred on the lateral posterior wall (86.1%; 31/36) with only a few cases located in bladder dome (5.5%; 2/36) and in bladder neck (8.3%; 3/36). Involvement of ureteric orifice was observed in 8 (22.2%) cases only.

VI-RADS score was calculated in all the patients using a combination of T2W, DWI, and DCE images for predicting detrusor muscle invasion. Excellent consistency was obtained between the two readers for predicting muscle invasive disease with a weighted kappa value of 0.92. The discordant scoring was observed in the tumors involving bladder neck and ureteric orifice only (8.3%; 3/36) and the final scoring was obtained with consensus between the two readers. Two cases of BC (6.7%) were scored as VI-RADS 1 on mp-MRI. VI-RADS scores of 2 and 3 were assigned to six (16.7%) and four (11.1%) cases, respectively. VI-RADS scores of 4 and 5 were assigned to 9 (25%) and 15 (41.7%) cases, respectively. A score of 3 or greater for VI-RADS was used to predict muscle invasive BC.

On histopatholgical examination, 23 patients (63.9%) had muscle-invasive cancer, while 13 patients (36.1%) had non–muscle-invasive cancer. All the cases of VI-RADS 1 and 83.3% (five of six) cases of VI-RADS 2 on mp-MRI in our study were non–muscle invasive on histopathology. In patients with VI-RADS 3 score on mp-MRI, detrusor muscle invasion on histopathology was seen in two cases (50%) only with other two cases being non–muscle invasive. Three patients (33.3%) with VI-RADS 4 and one patient (6.7%) of VI-RADS 5 score on mp-MRI had non–muscle-invasive disease with rest of the patients having detrusor muscle invasion on histopathology (►Table 1).

VI-RADS score of 3 or greater was used as cut-off value in predicting detrusor muscle invasion and sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and diagnostic accuracy of VI-RADS score was calculated (►Table 1). Mp-MRI was 95.6% sensitive and 53.8%

Table 1 Distribution of patients according to VI-RADS score and histopathological correlation

VI-RADS score on mp-MRI	Histopathology (36)	
	Muscle invasive (23)	Non–muscle invasive (13)
1	0	2
2	1	5
3	2	2
4	6	3
5	14	1
Total	23 (63.9%)	13 (36.1%)

Abbreviations: mp-MRI, multiparametric magnetic resonance imaging; VI-RADS, vesical imaging–reporting and data system.

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Table 2 Performance of mp-MRI using VI-RADS in detecting muscle-invasive disease

VI-RADS score and number of cases	Sensitivity	Specificity	PPV	NPV	Accuracy
1 (2 cases)	0	100	–	100	–
2 (6 cases)	0	100	–	83.3	83.3
3 (4 cases)	100	–	50	–	50
4 (9 cases)	100	–	66.7	–	66.7
5 (15 cases)	100	–	93.3	–	93.3
Total (36 cases)	95.6	53.8	78.6	87.5	80.6

Abbreviations: mp-MRI, multiparametric magnetic resonance imaging; NPV, negative predictive value; PPV, positive predictive value; VI-RADS, vesical imaging–reporting and data system.
Note: Data in 95% confidence intervals.

specific in predicting muscle invasive BC with a diagnostic accuracy of 80.6% (►Table 2).

Discussion

Precise preoperative diagnosis of detrusor muscle invasion is very important in management of BC as management and prognosis for non–muscle invasive (stage T1 or lower) and muscle-invasive (stage T2 or higher) BC are different.[13] TURBT is the standard technique for confirming the presence or absence of detrusor muscle invasion, it also provides pathologic subtype and grade, and in some cases, it can be curative.[18,23] However, TURBT underestimates T-stage in up to 40% of patients and is inaccurate at determining tumor grade in up to 15% of patients, and frequently needs to be repeated.[24] Also, adherence to guidelines recommending repeat TURBT varies widely between urologists.[25]

MRI is a promising tool in the imaging and assessment of BC. Though histopathologic diagnosis remains the gold standard for BC diagnosis and staging,[26] the use of MRI speeds up the diagnostic part and therefore patient management. Introduction of mp-MRI (including high-resolution T2W, DWI, and DCE sequences) is helpful in both anatomic and functional evaluation of the local staging and grading of bladder cancer with relatively high accuracy.[17] The VI-RADS, introduced recently, suggests the predictability of detrusor muscle invasion using the 5-point scoring system on mp-MRI. So we evaluated the usefulness of VI-RADS scoring system in predicting muscle invasive BC and to validate its use in routine clinical practice.

In our study, all the cases with VI-RADS 1 (►Fig. 1) and 83.3% cases with VI-RADS 2 (►Fig. 1) score on mp-MRI had no evidence of detrusor muscle invasion on histopathology. Also majority of VI-RADS 4 (6/9; 67.7%) and VI-RADS 5 (►Fig. 2) lesions (14/15; 93.3%) were muscle invasive on histopathological evaluation. In patients with VI-RADS 3 (►Fig. 3) score on mp-MRI, detrusor muscle invasion was observed on histopathology in two cases (50%) only with other two2 being non–muscle invasive. So as per our observation, VI-RADS scoring system had 100% diagnostic

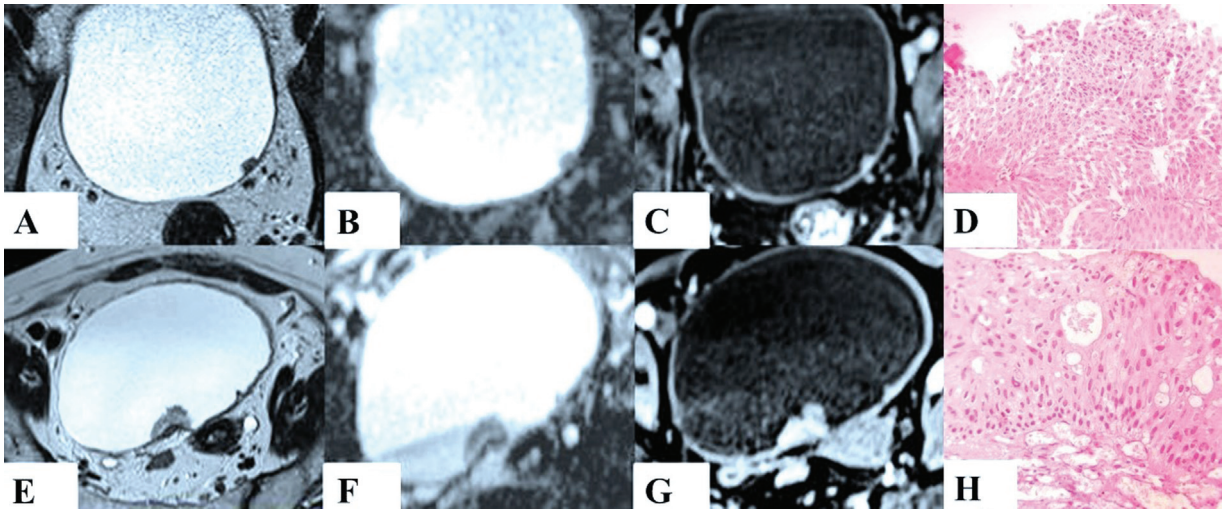

Fig. 1 VI-RADS 1 and 2 lesions. **(A)** coronal T2W, **(B)** axial DWI and **(C)** DCE images showing tiny bladder tumor (<1 cm) located along left posterior and lateral wall with preserved low-signal intensity muscular layer and no abnormal enhancement. **(E)** Axial T2W, **(F)** DWI, and **(G)** DCE images showing small bladder tumor (>1 cm) with preserved low-signal intensity muscular layer and no abnormal enhancement. Histopathology sections **(D and H)** showing low-grade urothelial carcinoma without deep smooth muscle involvement (H&E: ×20 and ×40). DCE, dynamic contrast enhanced; DWI, diffusion-weighted imaging; H&E, hematoxylin and eosin; T2W, T2-weighted; VI-RADS, vesical imaging–reporting and data system.

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accuracy for VI-RADS 1, 83.3% accuracy for VI-RADS 2, and 93.3% accuracy for VI-RADS 5 lesions in predicting muscle invasive disease. Only VI-RADS 4 (67.7%) and VI-RADS 3 lesions (50%) had relatively lower accuracy in predicting detrusor muscle invasion. Wang et al[13] in their study had 100% diagnostic accuracy for tumors scored as VI-RADS 1, 4, and 5 and 95% accuracy for VI-RADS 2 tumors. This difference could be attributable to inadequate or indeterminate yield of TURBT specimens in our study. This difference could also be attributable to use of lower strength magnet (1.5 T) in our study as compared with Wang et al[13] who used 3.0-T MRI for their study.

Sensitivity of VI-RADS scoring in predicting muscle-invasive BC was calculated using a VI-RADS score of 3 or greater as cut-off value. Mp-MRI was 95.6% sensitive in predicting muscle invasive BC with a diagnostic accuracy of 80.6%, PPV of 78.6% and NPV of 87.5%, respectively. Carando et al[27] in their meta-analysis observed that using a cut-off value of VI-RADS score of >2, sensitivity, specificity, PPV, and NPV in predicting muscle invasive disease were 78 to 91.9%, 85 to 91%.1, 69 to 78%, and 88 to 97.1%, respectively, while considering a VI-RADS score cut-off value of >3, the sensitivity, specificity, PPV, and NPV were 77 to 94.6%, 43.9 to 96.5%, 51.6 to 86%, and 63.7 to 93%, respectively. Wang et al[13] observed a sensitivity of 87.1%, specificity of 96.5%, and accuracy of 94.1%, suggesting that VI-RADS can well reflect the muscle-invasive BC when the VI-RADS score is 3 or greater. Recent meta-analysis have also demonstrated that mp-MRI can provide good diagnostic performance for predicting muscle invasive BC.[28,29]

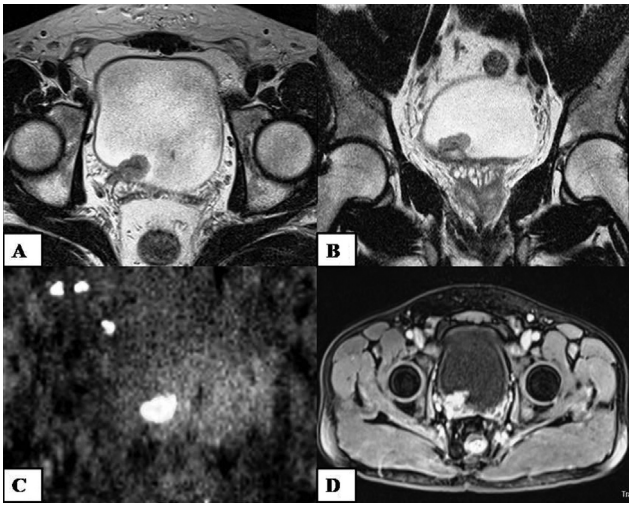

Fig. 3 VI-RADS 3 lesion on mp-MRI. **(A)** Axial and **(B)** Coronal T2W images in a patient shows a hypointense tumor stalk located at the right vesicouretric junction with no clear interruption of low-signal intensity muscular layer. **(C)** DWI image shows no clear interruption of low signal intensity muscular layer. **(D)** DCE image shows no early enhancement of muscularis propria suggesting a VI-RADS score of 3. DCE, dynamic contrast enhanced; mp-MRI, multiparametric magnetic resonance imaging; T2W, T2-weighted; VI-RADS, vesical imaging–reporting and data system.

In our study, excellent consistency was observed between the two readers for predicting muscle-invasive disease, using VI-RADS 3 as the cut-off limit. The only discrepancies observed were related to tumors in the bladder neck and

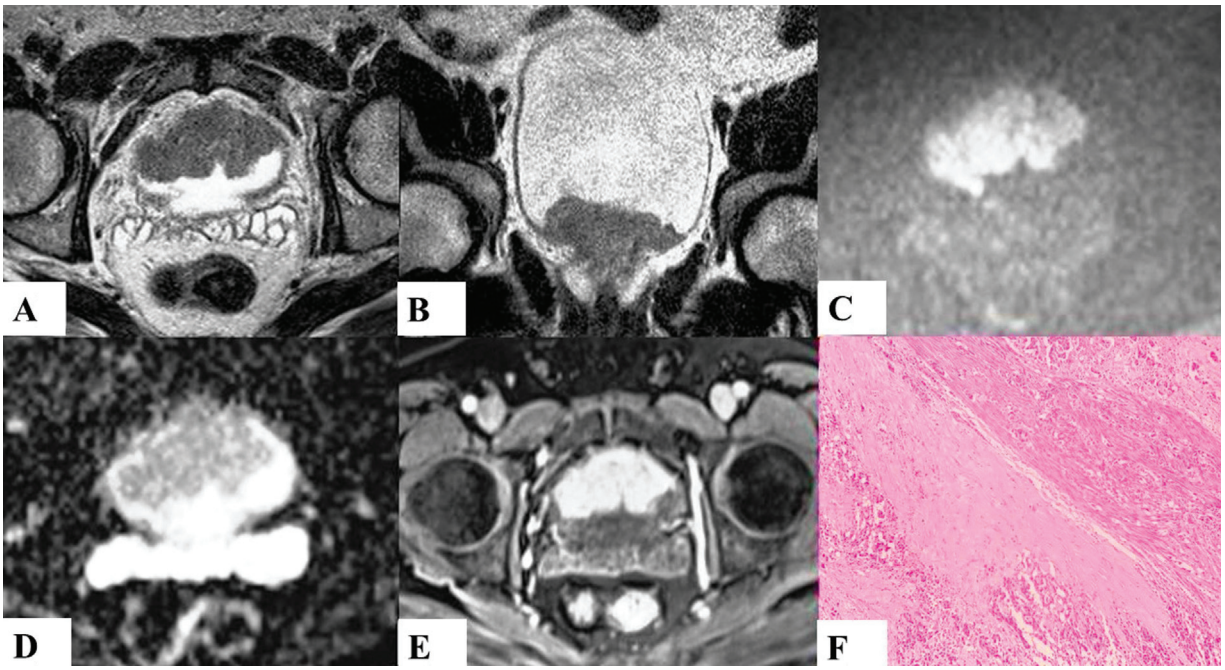

Fig. 2 VI-RADS 5 lesion. **(A)** Axial and **(B)** Coronal T2W images showing a broad based tumor in the bladder neck with clear disruption of low-signal intensity muscularis layer and extension into peri-vesical fat. **(C)** DWI and **(D)** corresponding ADC images showing clear disruption of muscularis layer. **(E)** DCE image showing early enhancement of muscularis with extension of the enhancing lesion into perivesical fat. **(F)** Histopathology section showing high grade urothelial carcinoma with deep smooth muscle invasion (H&E; ×20). DCE, dynamic contrast enhanced; H&E, hematoxylin and eosin; T2W, T2-weighted; VI-RADS, vesical imaging–reporting and data system.

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ureteral orifices (three cases), and this presumably may be associated with anatomic locations of the tumor.[13]

Limitations

There were a few limitations in our study. First the sample size was small and so more such studies should be performed in future to further validate the results obtained in our study. Second the tumor with the largest burden on MRI was selected in patients with multiple tumors, thereby leading to selection bias. Third the study was performed using 1.5-T MRI which has somewhat less contrast resolution as compared with 3-T MRI. Previously published study in literature has demonstrated improved diagnostic accuracy of 3.0-T MRI compared with 1.5-T MR in T2 staging of BC.[30] However in a resource poor country, like India, availability of 3.0-T MRI is extremely limited and has a higher cost as compared with 1.5-T MRI.

Conclusion

VI-RADS is a novel and comprehensive scoring system in predicting the detrusor muscle invasion in BC with good sensitivity, specificity, and diagnostic accuracy for detecting detrusor muscle invasion. VI-RADS scoring using mp-MRI plays a significant role in improving BC detection and staging and is strongly recommend in the prediction of detrusor muscle invasion, preoperatively. Further research must also be conducted to validate the results obtained in our study.

Note

The study was performed at the Government Medical College, Jammu.

Ethical Approval

The study was approved by Institutional Ethics Committee of the Hospital (IRB Number: IEC/GMC/Cat A/2020/157).

Funding

None.

Conflict of Interest

None declared.

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