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ViradsAnd Bladder Cancer Staging Using Multiparametric Magnetic Resonance Imaging

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ABSTRACT

Background: The Vesical Imaging–Reporting and Data System (VI-RADS) could be a recently created framework of the bladder cancer staging usingmultiparametric MRI (mpMRI), which can be utilized to anticipate the nearness of invasion of the bladder wall muscle in cases of cancer of the bladder.

Aim: The aim of the study isto defineVI-RADS as a standard approach of imaging and reporting systemusing mpMRI with T2-weighted imaging (T2WI), diffusion-weighted imaging (DWI), and dynamic contrast-enhanced imaging (DCE MRI) for accurate Bladder Cancer staging.

Method: The study was done in ZagazigUniversity Hospital. Eighty patients with lower urinary tract symptoms and urinary bladder mass detected by ultrasound were scheduled for elective multiparametric magnetic resonance imaging in the period from February 2020 to January 2021.

Results: In our study,low-grade bladder cancer regarding histopathological grading represented a higher percentage than tumors of high-grade type with 56.6%, and according to mp MRI, we had 46 patients with NMIBC representing 60.5 % while VIRADS distribution among 76 patients with bladder cancer was as follow V1=12, V2=26, V3=10, V4= 14, V5=14 cases respectively and we founda highly statistically significant association between tumor histopathological grading and mp MRI where P value < 0.001

Conclusion: This study has shown thatthe score related to VIRADSshows up to be a good and impressiveradiological methodthat can be used before the operation for the definition and prediction of invasion of the detrusor muscle (NMIBC vs. MIBC) in bladder cancer usingmpMRI.

Keywords:
Neoplasms; urinary bladder; Anatomicaland functional magnetic resonance imaging; Diffusion-weighted imaging; Imaging with administration; Validity of results.

1. Introduction

The cancer of the bladder is a disease of life-threatening effect and regarding the human malignancies is one of the highest rate and more dangerous one to deal with. Most Bladder

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cancers are carcinomas of the urothelial cell , and stratified by histology into cancers of low and high grade [1]. The tumors of high grade are subdivided into tumors withmuscle invasion and tumorsswithout. Non–muscle-invasive bladder cancers are always of low grade and have an inactive common history[2].

The grade of bladder cancer is detected by analysis of tumor samplespathologically according to World Health Organization (WHO) 2004 bladder cancer grading criteria [3].Treatmentis pointed at lessening nearby repeat and arrange movement and keeping up quality of life. Muscle-invasive bladder cancers (MIBCs) are forceful tumors with an inauspicious forecast. The victory of management is subordinate on the stage of the essential mass and condition of the nearby lymph nodes [4].

Bladder cancer management depends mainly on clinical features, pathological and radiological findings.MRI isstrongly accurate in the diagnosis and local staging of bladder cancer, with using cystoscopy and results of pathologic staging remaining finally a strong standard regarding references[5].

Staging mpMRI has a great outcome in plans of management. It has high efficacy in determining the extent of tumor, organ metastasis, and lymph node metastasisand is considered an accurate procedure that gives a perfect tissue differentiate determination, being able to distinguish the stratifications of the bladder wall with no need for organization of radiation[6].

Anatomic MR techniques (T2WI) providesdata on the masssite, bladder wall invasion, and depth within the wall but may result in over staging becausefibrosis or inflammation associated with the tumor can be similar to the hypointensity of the muscularis propria. Functional techniques of MRI, especially the DWI and associated ADC , have demonstratedtheirability in the assessment of biological behaviors such as cellularity and have demonstrated their effectiveness in the management of the cancer of the bladder, especially in the evaluation of the tumor grade[7].

Respecting thestory of the success ofmpMRI and the Reporting and Data (RAD) scoring system in different cancertypes (Different previous RADS, such as PI-RADS for the Prostate and BI-RADS for the Breast Cancer), VI-RADS have assessed this in bladder cancer[8].

VI-RADS suggests a scoring system of fivepointsfor the definitionof the nearness or the nonappearance of bladder cancer invasion using T2W imaging, DWI, and DCE signal, and appearance to form an overall risk of score invasion. VI-RADS is a review on the diagnosis, monitoring of treatment, and detection of cancer bladder return back and aims to provide guidelines on detecting and local staging of Bladder Cancer on the base ofmpMRI[9].

2. Patients and Method

2.1. Patients

This study was carried out at the Radio-diagnosis department (MRI unit), ZagazigUniversity Hospital. A total number of 80 patients with diagnosed bladder mass were referred from the urology department for elective multiparametric MRI in the period from February 2020 to January 2021.They were 60 males (79%) and 16 females (21%), their age ranged from 45to 85 years (mean age= 65 years ±12.02).Four patients out of Eighty with metastatic deposits to the urinary bladder from nearby organs were excluded from the study, so we had seventy-six patients full fill the inclusion criteria of the study.

The patients were referred by a urologist for suspicion of having bladder mass suspected clinically and confirmed by pelvic, abdominal US; all patients were subjected to mpMRI final diagnosis of thepatients was reached by comparing to postoperative histopathological results.

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2.1.1. Patient Inclusion Criteria:

1-Patients of any age and any sex.
2-Patients with urinary bladder mass in pelvic, abdominal ultrasound.
3- Untreated patients with bladder cancer and cases having received the first TURBT asa diagnostic toolonly, but not those who are performing TURBT for the second time.

2.1.2. Patient Exclusion Criteria:

1-Patients with urinary bladder mass and unfit for operation.
2-Patients with metastatic deposits to the urinary bladder from nearby organs.
3-Patients have contraindications for MRI, including:
Patients with: Heart pacemakers Implanted electronic devices,Intracranial metal clips, Insulin pumps,Implanted hearing device aids.
4-Patients with renal impairment (GFR less than 30).
Full history was taken. A patient clinical assessment was performed. Revision of previous laboratory and other radiological investigations(pelvic, abdominal US), pathological results in case of TURBT was done prior to mpMRI examination.Informed consent was written and taken from all patients who participated; the study took the approval by the ethical research committee of the Faculty of Medicine, ZagazigUniversity; the study was done according to the code of ethics of the world medical association (Declaration of Helsinki) for studies including humans.

2.1.3. Patient preparation

- All patients were informed about the steps and the importance of MRI examination to be cooperative with the machine operator.
- Before the examination, patients had a food fasting 6-h and tookantispasmodic injected intramuscularly.
- They were asked to drink water (500 to 1000 ml) in a period of 30 minutes to expandthe urinary bladder adequately andnot to void 1-2h before imaging.

2.2. Image acquisition

Examination of the urinary bladder through mp-MRI was actualized using 1.5-T Magnetic resonance imagingsystems (Achieva-class IIa, Philips Medical Systems, and Optima 450 GEM, GE Healthcare) with anexternal surface coil of multichannel phased-array was put on the patient's abdomen and pelvis.
The MRI protocol was focused on the pelvis with determining of T staging and VI-RADS-score.
Two-dimensional fast spin echo axial, sagittal, and coronal T2WI (Echo Time (TE) = 90–100 ms, Repetition Time (TR) = 2250–3500 ms, Matrix = 256 × 256,BW = 20–83 KHz,Sectionthickness/Gap = 4–6 mm/1–2 mm, Field of view (FOV) = 20 cm);Axial DWI was done during free breathing using fast spin echo-planar imaging sequence (monodirectional gradient multi-section) with 0 and 800–1000 s/mm2 b values of (TE = 90–100 ms, TR = 3500–4500 ms, matrix = 256 × 256,BW = 142 KHz , Section thickness/Gap = 4–6 mm/ 1–2 mm, FOV = 36 cm).The calculation of ADC map was doneautomatically.

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High-resolution Isotropic Volume Excitation (THRIVE) axial, sagittal, and coronal 3D T1WI or T1-WI liver Acquisition with Volume Acquisition (LAVA) Dynamic Contrast-Enhanced (TE = 4.7 ms, TR = 16.4 ms, flip angle = 15, Section thickness = 3 mm, Matrix = 352 × 352) with a temporal resolution of five seconds after injection of 0.1 mmol/kg of Gd through intravenous routeat a rate of two ml/second, followed by saline flush injecting.A first post-contrast acquisition was done after injection of the contrast by 30 seconds, followed by four consecutive sequences taken every 30s.
In casesbladder showed air within (from cystoscopy or indwelling catheter), MRI was delayed two to three days after to avoid the Susceptibility artifact of DWI's.

2.3. Image reconstruction and interpretation

As regards the analysis of the image, all radiological examinations were transferred andwent under review on a Picture Archiving and Communication Systems (PACS) (Magic view, GE, Milwaukee, WI, USA). T2WI followed by diffusion weighted-MR images and then dynamic contrast-enhanced -MR images were interpreted respecting the T1 and T2WI image sets, and the tumor wasrelegatedto a T stage in every sequence when more than one tumor wasdetected: the highest T stage represented the final T stage of the patient.
A VI-RADS of the five-points score is developed using the separate MRI sequences T2W, DWI, and DCE MRI and predicts the probability of muscle invasion.
The probability of muscle invasion by bladder cancer can be established by the VI-RADS using a 5-point scoring system to:
Highly unlikely of invasion of the muscle ; (VI-RADS 1).
Unlikely of invasion of the muscle ; (VI-RADS 2).
Equivocal finding of invasion of the muscle; (VI-RADS 3).
Likely of invasion of the muscle; (VI-RADS 4).
Very likely of invasion of the muscle ; (VI-RADS 5).

2.4. Statistical analysis

Data were collected, coded, entered, and analyzed using Microsoft Excel software. Data were then imported into Statistical Package for the Social Sciences (SPSS version 23.0) software for analysis. Qualitative data were represented as numbers and percentages, and quantitative data were represented by mean ± SD. Differences between quantitative paired groups were tested by Student t-test and paired-test for significance. P-value was set at <0.05 for significant results and <0.001 for a highly significant result.

3. Results

3.1. VIRADS distribution among 76 patients

The most common VIRADS group was V2 including 26 pateints with 43.3 percentage **(Table 1).**

Table 1.VIRADS distribution among 76 patients

Value	Number (N)	Percentage %
V1	12	15.7 %
V2	26	34.3%
V3	10	13.2%
V4	14	18.4%

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V5	14	18.4%
Total	76	100

3.2. The Percentage of NMIBC versus MIBC

Among 76 pateints, 46 patients with NMIBC (60.5%) and 30 patients with MIBC with (39.5%) **(Table 2)**.

Table 2.The Percentage of NMIBC versus MIBC.

Value	Number (N)	Percentage %
NMIBC	46	60.5
MIBC	30	39.5
Total	76	100

3.3. Histopathological grading

Among 76 cases, there were 43 cases with low-grade tumors and 33 cases with high-grade tumors(Table 3).

Table 3. Histopathological grading

Value	Number (N)	Percentage %
Low grade	43	56.5
High grade	33	43.5
Total	76	100

3.4. Consistency of detrusor muscle invasion by histopathology versus mp MRI on the base of VIRADS score.

In our study, there were 46/76 NMIBC by mp MRI while 42/76 by histopathology, and In our study, there were 30 /76 NMIBC by mp MRI while 34/76 by histopathology (Table 4& chart).

Table 4. Consistency of detrusor muscle invasion by histopathology versus mp MRI on the base of VIRADS score

Variable	**NMIBC**		**MIBC**		
	N	**%**	**N**	**%**	**Total**
mp MRI	**46**	60.5%	30	39.5%	76
Histopathology	**42**	55.3%	34	44.7%	76

This table shows that there was highly statistical significant association between tumor histopathological grading and mp MRI where P value < 0.001.

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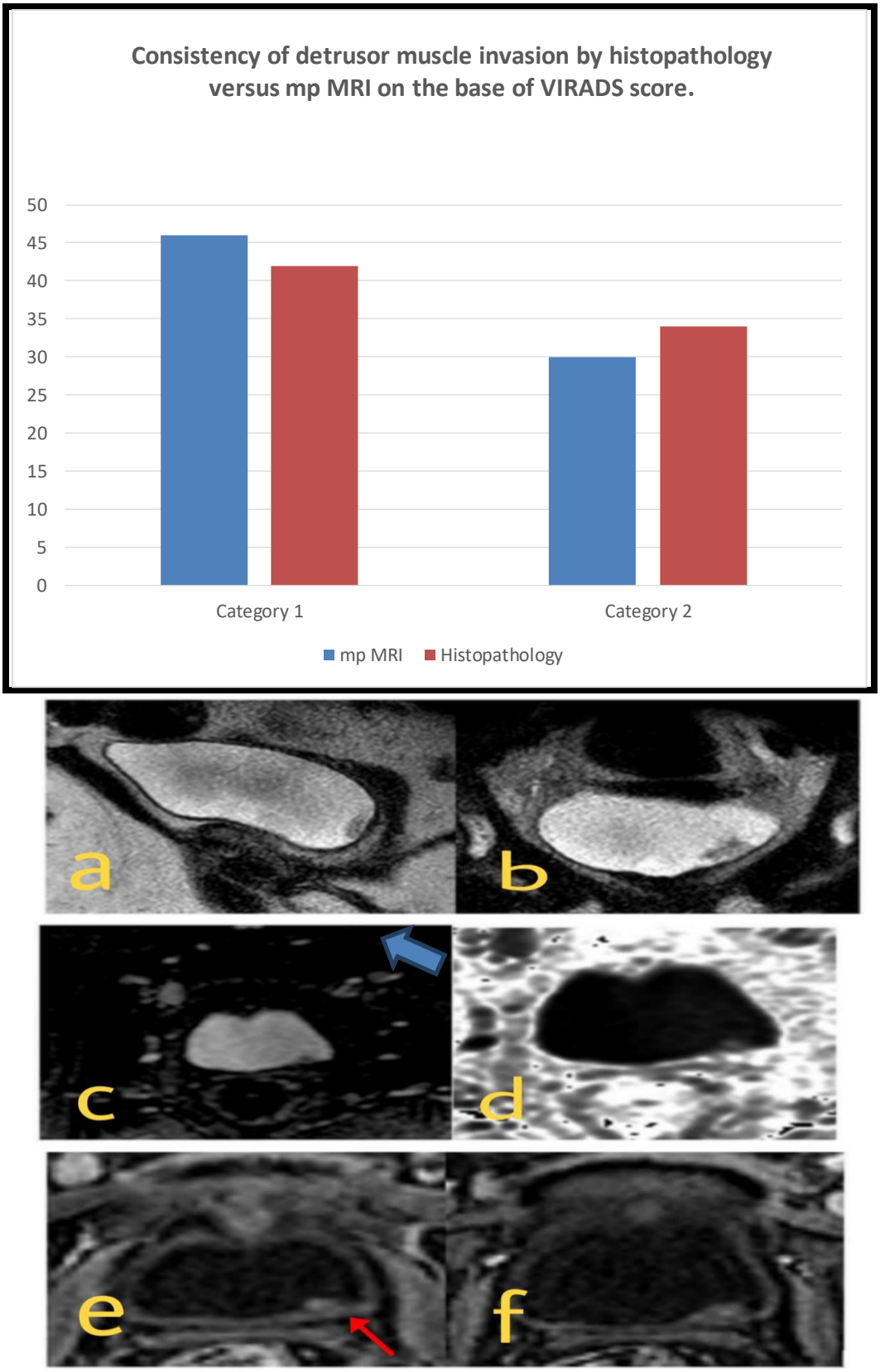

Figure (1).A 50-year-old female patient complaining of dysuria. Sagittal (a) and coronal (b) T2WI images show a mass with no sort of muscle invasion seen at left posterolateral UB wall within bladder trigone peripherally, seen polypoidal in shape seen not interrupting the underlying detrusor muscle of low signal intensity, without perivesical fat extension. DWI (c)

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and ADC map image (d) show low diffusion restricted of the mass with diffusion facilitation of muscle layer excludes muscle invasion and high ADC value of 1.3 × 10–3 s/mm2, DCE-MRI (e,f) displaying the mass enhanced intensely without disrupting enhancement of muscle layer denoting nonmuscle invasion (arrow). Multi-Parametric MRI agrees with NMIBC (Stage T1) and VI-RADS I, which are histopathologically confirmed.

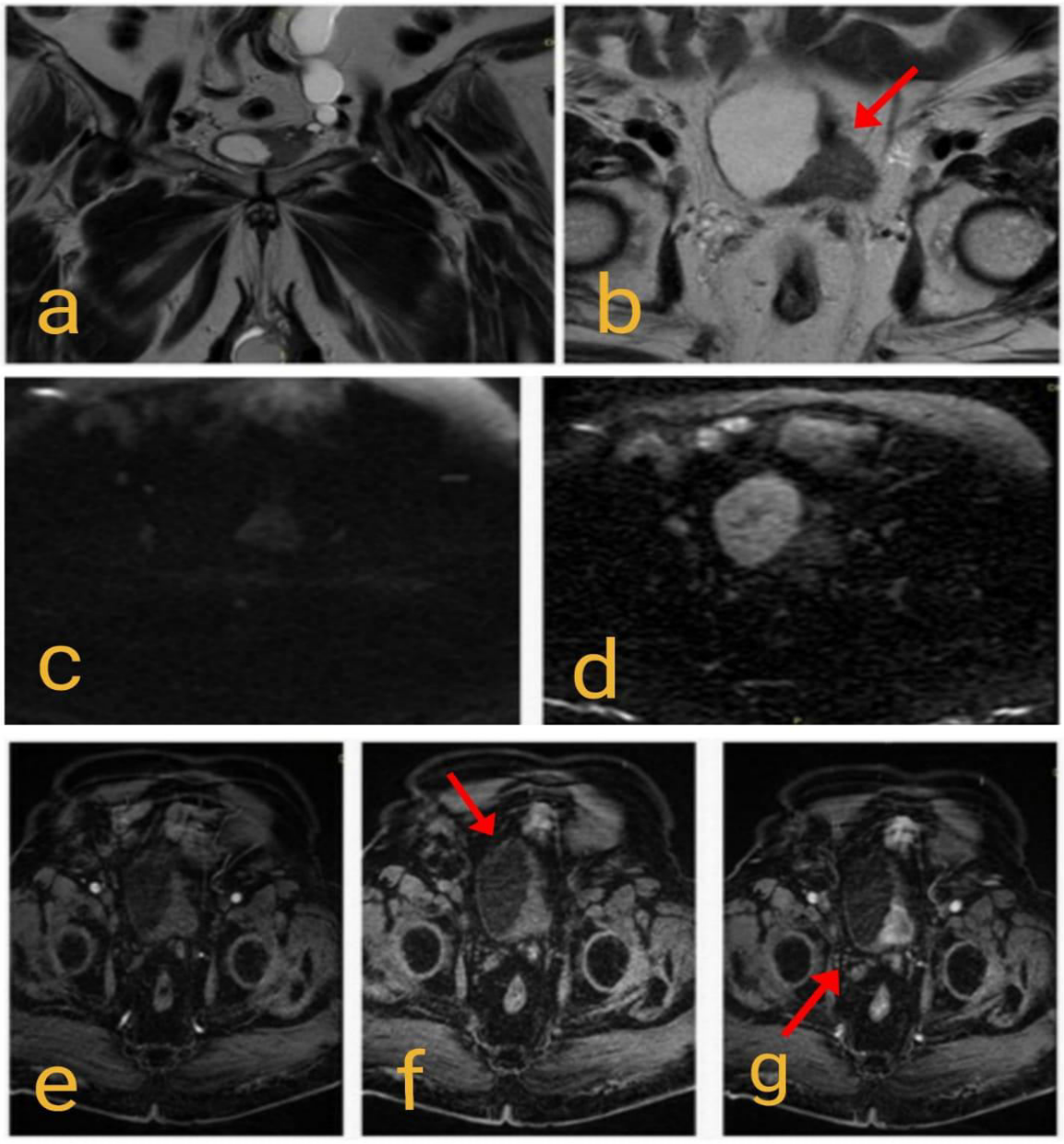

Figure (2).A 65-year-old male patient with a history of recurrent hematuria. Coronal (a) and axial (b) T2WI images shows muscle-invasive left posterolateral UB endophytic mass lesion involving the left vesicoureteric junction with subsequent left-sided moderate hydronephrosis, the mass seen interrupted the underlying detrusor muscle of low signal intensity, without perivesical fat extension (arrows). DWI (c) and ADC map image (d) show highly diffusion restricted of mass with diffusion facilitation of muscle layer exclude muscle invasion and low ADC value about 0.7 × 10–3 s/mm2 pointing to malignant nature, DCE-MRI (e) non-contrast subtracted image and (f and g) early arterial phase image are showing

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early intense enhancement of the mass with the disrupted enhancement of muscle layer denoting muscle invasion (arrow). Multi-Parametric MRI are consistent with MIBC (Stage T2) and VI-RADS IV, which are histopathologically confirmed.

4. Discussion

Bladder carcinoma is the 10thmost common danger around the world,the 6th commonest malignancy in males, and the seventeenth commonest femalescancer[10]. The larger part isTransitional cell carcinomas, either low-grade or high-grade entities. Clinical administration of bladder cancers is decided primarily based on segregating non-muscle-invasive bladder cancers from muscle-invasive bladder cancers. Non-muscle-invasive bladder cancers can be treated conservatively with resection of bladder tumor through transurethral route and intravesical ingrained. On the other hand, muscle-invasive bladder cancers require more serious medications, counting radical cystectomy[11].

VI-RADS was outlined and actualized to make an organized reporting system for interpreting mp-MRI in BCastaged locally. The admixing of T2-weighted imaging, diffusion-weighted imaging, and dynamic contrast-enhanced imaging is the base for making astandard reporting system through the VI-RADS. VI-RADS provides scores of 5-points that detect the possibility of the invasion of the detrusor muscle by BCa . VIRADS has taken great interest and applicability, as described by many publications, and has been received by numerous radiologists and hospitals in clinical schedule [8,14].

In this study, the majority of the patients (79 %) were males, and the minority of the patients (21%) were females;similar findings have been reachedbyAfifi et al., [15],who reported that the male: female ratio was 10:1. Regarding the mean age group in our study, the was 65 years; this was in agreement withMakboul et al., [16],who reported that the mean age group among 32 patients is 57.16 ± 7.32 years.

Histopathological grades of the tumor play acrucial role in the prediction of the outcome of the treatment plans. Gupta et al.[17]studied 60 patients with bladder tumors; there were 45 patients (75%) with low-grade tumors, while 15 patients (25 %) had high-grade tumors. This matches our study results which include 43 patients (60.5 %) with low-grade tumors and 33 patients (39.5 %) with high-grade tumors.

By Applying the VIRADS scoring system to bladder mass assessment regarding the point of detrusor muscle invasion and therefore giving accurate staging, Among 76 patients, we found 12 cases with V1 representing 17.7 %, 26 cases with V2 representing 34.3 %, 10 cases with V3 of 13.2 % , 14 cases having V4 of percentage 18.4 % and the same result for V5 of 14 cases and 18.4% percent, Near similar findings reached by the study ofGhanshyam et al., [18]who reported that V4 and V5 representing the highest number of patients included for 15 patients in each category.

In our study,mpMRI detects 46 patients with NMIBC, about 60.5 % of all patients and 30 patients with MICB, representing 39.4%; this is in concordance with previous studies of Hong et al. [19], who found that 20 patients out of 32 had NMIBC and eight patients with MIBC.

In our study, there was significance between VIRADS score and histopathology regarding the differentiation between NMIBC and MIBC (P <0.001). These results were inconsistent with Juri et al.[20],who reported that the diagnostic ability of the VI-RADS for the bladder cancer staging according to the T-staging has been comparatively good, but there are some false - positive or false-negative cases still detected

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5. Limitations

1. It was a single experience of the institute with a sample of small size,so it's difficult to make the resulting general.
2. mpMRI is very expensive, not easily available, and VIRADS needs experience and a learning curve of high level.
3. UsingmpMRIto detect the VIRADS score is useless in cases of carcinoma in situ.

6. Conclusion and Recommendations

We concluded that the score of VIRADS is a radiological tool that is perfect, easy to interpret, and applicable for the detection ofthe invasion of the bladder wall by BC in conditions before operations which can help in improvingthe management plan and explaining prognosis to the patients and is recommended highly to be applicable in practice every day.

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