



Magnetic resonance radiographic features which might lead to misdiagnosis of muscle-invasive bladder cancer based on vesical imaging reporting and data system: the application experience of a single center

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Background: The Vesical Imaging Reporting and Data System (VI-RADS) has been widely used for diagnosing muscle-invasive bladder cancer (MIBC), yet instances of misdiagnosis persist. However, limited research discusses the factors affecting its accuracy. This study aimed to evaluate the diagnostic efficacy of the VI-RADS in our center and to preliminarily identify possible magnetic resonance imaging (MRI) characteristics of misdiagnosis.

Methods: From January 2018 to February 2023, a consecutive series of 211 participants pathologically diagnosed with bladder cancer (BC) who underwent an MRI exam were retrospectively enrolled. MRI was interpreted by 2 radiologists with different levels of experience, the diagnostic performance was validated using the receiver operating characteristic (ROC) curve, and VI-RADS ≥ 4 was considered to indicate MIBC-positive status. The clinical and radiographic characteristics of the true-positive (TP), true-negative (TN), false-positive (FP), and false-negative (FN) groups were analyzed using Kruskal-Wallis test or Fisher exact test.

Results: With VI-RADS ≥ 4 as the cutoff value, the area under the ROC curves (AUCs) were 0.951 (0.912–0.976) and 0.847 (0.791–0.893) for the more-experienced reader and less-experienced reader, respectively, with good interobserver agreement ($\kappa=0.74105$). The median tumor size in the TP (more experienced: 57 cases; less experienced: 44 cases) and FP (more experienced: 8 cases; less experienced: 9 cases) groups was larger than that in the TN (more experienced: 141 cases; less experienced: 139 cases) group for the more-experienced reader (TP: 28 mm; FP: 31 mm; TN: 19 mm; $P<0.001$ and $P=0.031$, respectively) and the less-experienced reader (TP: 31 mm; FP: 28 mm; TN: 19 mm; $P<0.001$ and $P=0.042$, respectively). The tumor base in the TP and FP groups was larger than that in the TN group for the more-experienced reader (TP: 37 mm; FP: 48 mm; TN: 15 mm; both $P<0.001$) and for the less-experienced reader (FP: 42 mm; FP: 36 mm; TN: 15 mm; $P<0.001$ and $P=0.022$, respectively). The median tumor base in the TP group was

larger than that in the FN group for the less-experienced reader (TP: 42 mm; FN: 17 mm; P=0.004).

Conclusions: We observed good to excellent AUCs with good interobserver agreement among radiologists with different levels of expertise using VI-RADS. Large tumor size and wide tumor base affected the accuracy of VI-RADS in MIBC diagnosis.

Keywords: Multiparametric magnetic resonance imaging (mpMRI); muscle-invasive bladder cancer (MIBC); Vesical Imaging Reporting and Data System (VI-RADS)

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Introduction

Bladder cancer (BC) is the most common malignant urothelial tumor (1). As the ninth most common tumor in the world, the prevalence of BC in males is approximately three times higher than that in females, but the mortality rate of female patients is higher than that of male patients (2,3). Muscle invasion of BC has a considerable influence on the choice of treatment modalities and on prognosis (4). Patients with non-muscle-invasive BC (NMIBC) may be able to preserve their bladder, while patients with muscle-invasive BC (MIBC) may require bladder removal. There are differences in the quality of life between patients receiving these two different treatments (5). Therefore, it is crucial to accurately differentiate MIBC from NMIBC before surgery.

The proper methods for the preoperative diagnosis of BC muscle invasion have long been examined by radiologists. In recent years, the role of magnetic resonance imaging (MRI) in differentiating BC muscle invasion has been gradually discovered. Compared with computed tomography (CT), MRI has better soft-tissue resolution and multiplanar and multiparametric imaging capability, which have made it an important staging modality for BC (6,7). On the basis of multiparametric MRI (mpMRI), the Vesical Imaging Reporting and Data System (VI-RADS) was released in May 2018 as a standard imaging and diagnostic method for BC (8). Thus far, it has substantial advantages in BC staging by means of the VI-RADS score. Some studies have shown that the VI-RADS score has a good diagnostic effect for BC (9-13), and Kufukihara *et al.* reported accuracy of the VI-RADS score to be significantly higher than that of cystoscopy (14). Meanwhile, some surgeons and radiologists have also made use of the VI-RADS score to open new perspectives in the treatment process, such as assessing

whether a patient needs repeated transurethral resection of the bladder tumor (TURBT) (15,16) or evaluating stage changes after chemotherapy (17). However, the application of the VI-RADS score has also reached a plateau.

A standard method has been established to minimize the impact of experience on accuracy. However, through reviewing the abovementioned studies and during the clinical application of the VI-RADS score in our center, we found that those “experienced” readers had significantly higher accuracy. Moreover, it is unclear which characteristics may be responsible for this discrepancy, and thus it remains to be determined whether diagnostic accuracy can be improved through greater attention to certain characteristics. Based on our experience with imaging reads and data from Sun Yat-sen University Cancer Center, we conducted a preliminary study of the characteristics that may influence the accuracy of the VI-RADS score. We present this article in accordance with the STARD reporting checklist (18) (available at <https://qims.amegroups.com/article/view/10.21037/qims-23-356/rc>).

Methods

Patient selection

The study conformed to the provisions of the Declaration of Helsinki (as revised in 2013) and was approved by the Medical Ethics Committee of Sun Yat-sen University Cancer Center, written informed consent was waived for this retrospective study. The institutional electronic medical records and Picture Archiving and Communication Systems (PACS) database were searched to identify patients with BC who underwent mpMRI examinations between January 2018 and February 2023. We retrospectively collected all the consecutive cases during this period and

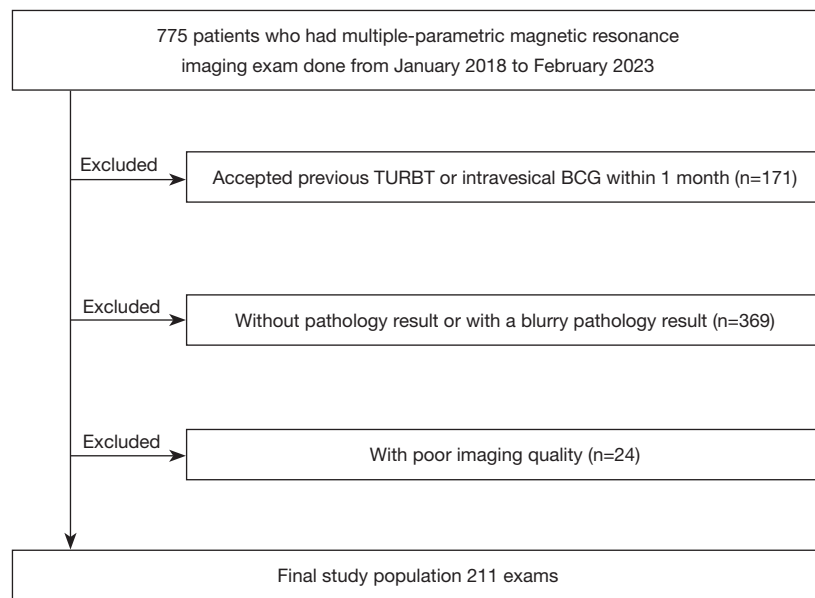


Figure 1 Flowchart showing the patient selection process. TURBT, transurethral resection of bladder tumor; BCG, Bacille Calmette-Guerin.

initially identified 775 exams. The exclusion criteria were as follows: (I) ambiguous pathology results or no pathology result within 1 month after examination; (II) poor imaging quality; and (III) administration of previous TURBT and intravesical Bacille Calmette-Guerin (BCG) treatment within 1 month. Ultimately, 211 tests were included in the study population (Figure 1).

Radiographic and clinical characteristics

Image analysis was performed by two board-certified abdominal radiologists [a reader with more experience (ME) with 16 years of experience in bladder imaging; and a reader with less experience (LE) with 3 years of experience in bladder imaging] who had no knowledge of the clinical, laboratory, or pathological information regarding the participants after reviewing a training session of 20 external cases (Table S1). The two readers proceeded only after reviewing a training session of 20 external cases. They then independently assessed the radiographic characteristics of the participants and were each unaware of the other's results and clinical information.

The readers assessed imaging quality, analyzed key characteristics (location, number, size, growth pattern, stalk, and base width), and assessed the VI-RADS (8) category for each nodule.

The following clinical information was extracted from our electronic medical record database: age, sex, first visit, special comorbidities (including a history of tumors or other urinary disorders), surgical information, and pathology results. The pathological findings of the American Joint Committee on Cancer (AJCC) T stage (19) were as follows: T_a papillary noninvasive tumor; T₁ tumor invading the subepithelial connective tissue; T₂ tumor invading the muscle; T₃ tumor invading the perivesical tissue; T_{4a} tumor invading the prostate, uterus, or vagina; and T_{4b} tumor invading the pelvic or abdominal wall.

Imaging acquisition

All patients underwent multiphase parametric bladder MRI on a 3.0 T magnet scanner (Discovery MR750, GE Healthcare, Wauwatosa, USA; Ingenia 3.0 T CX, Philips Healthcare, Best, The Netherlands). The MRI protocol consisted of the following scanning sequences: a respiratory-triggered fast spin-echo or turbo spin-echo T₁-weighted sequence; a respiratory-triggered fast spin-echo or turbo spin-echo T₂-weighted sequence; a diffusion-weighted sequence using respiratory-triggered single-shot echo-planar sequence with b values of 0 and 1,000 s/mm², respectively; and a dynamic contrast-enhanced MRI performed after administration of an intravenous injection

Table 1 Patient and tumor characteristics

Characteristics	Value
Age, years	62 [15]
Sex	
Female	23 (10.9)
Male	188 (89.1)
Previous history of urothelial cancer	
First-time tumor	148 (70.1)
Recurring tumor	63 (29.9)
TURBT	63 (29.9)
Neoadjuvant chemotherapy	40 (19.0)
BCG therapy	19 (9.0)
No. of tumors per patient	
1 tumor	150 (71.1)
2 tumors	17 (8.1)
≥3 tumors	44 (20.8)
Histological grade	
Low	58 (27.5)
High	153 (72.5)
AJCC T stage	
Ta	94 (44.5)
Tis	0 (0.0)
T1	55 (26.1)
T2	35 (16.6)
T3	24 (11.4)
T4	3 (1.4)
Surgical method	
Radical cystectomy	55 (26.1)
Bladder cuff excision	5 (2.3)
TURBT	151 (71.6)

Data are shown as n (%) or median [IQR]. TURBT, transurethral resection of the bladder tumor; BCG, Bacille Calmette-Guerin; AJCC, American Joint Committee on Cancer; IQR, interquartile range.

of gadolinium-based contrast material (0.1 mmol/kg body weight; Magnevist; Bayer Schering Pharma, Leverkusen, Germany). The initial contrast image was acquired at 25 or 24 s after the beginning of injection and was followed by the same sequences 4 to 6 times every 25 or 24 s. The MRI

techniques are summarized in detail in [Table S2](#).

Statistical analysis

Categorical variables are expressed as numbers and percentages, and continuous variables are expressed as medians and interquartile ranges because they were not normally distributed. The receiver operating characteristic (ROC) curve and area under the curve (AUC) were determined. We evaluated the sensitivity, specificity, accuracy, cutoff value, and the Cohen kappa coefficient (κ) (to measure interobserver agreement) of the VI-RADS score in identifying BC. κ values (level of agreement) were defined as follows: 0.00–0.20, poor; 0.21–0.40, fair; 0.41–0.60, moderate; 0.61–0.80, good; and 0.81–1.0, excellent. For between-group comparisons for the clinical and radiographic characteristics of the true positive (TP), true negative (TN), false positive (FP), and false negative (FN) groups in diagnosing MIBC, we used the Kruskal-Wallis test (adjusted by Bonferroni correction) or Fisher exact test where appropriate. A P value <0.05 was considered statistically significant. The ROC curve was drawn using MedCalc 18.2.1 (MedCalc Software, Mariakerke, Belgium) software, and SPSS 25.0 (IBM Corp., Armonk, NY, USA) was used for other statistical analyses.

Results

Baseline demographics

Among the total of 211 cases, 55 (26.1%) pathological specimens were collected through radical cystectomy, 5 (2.3%) through bladder cuff resection, and 151 (71.6%) through TURBT. NMIBCs accounted for 70.6% (Ta and T1) of the 211 cases, and MIBCs accounted for 29.4% (T2, T3, and T4) ([Table 1](#)).

Diagnostic performance of the VI-RADS score and interobserver agreement

The frequencies of MIBCs for each VI-RADS score for each reader are shown in [Table 2](#).

The diagnostic performance of the VI-RADS score with each different reader is shown in [Figure 2](#). The cutoff value of both ROC categories was VI-RADS ≥ 4 . The AUC for reader ME was 0.951 (0.912–0.976), which was outstanding, and for reader LE, it was 0.847 (0.791–0.893), which was also excellent. Agreement between the readers was

Table 2 Frequency of MIBC and NMIBC for each VI-RADS score for each reader

Reader	VI-RADS				
	1	2	3	4	5
Reader ME	22 (10.4)	115 (54.5)	9 (4.3)	39 (18.5)	26 (12.3)
MIBC	0 (0.0)	4 (3.5)	1 (11.1)	32 (82.1)	25 (96.2)
NMIBC	22 (100.0)	111 (96.5)	8 (88.9)	7 (17.9)	1 (3.8)
Reader LE	19 (9.0)	112 (53.1)	14 (6.6)	42 (19.9)	24 (11.4)
MIBC	1 (5.3)	10 (8.9)	5 (35.7)	26 (61.9)	20 (83.3)
NMIBC	18 (94.7)	102 (91.1)	9 (64.3)	16 (38.1)	4 (16.7)

Data are shown as n (%). MIBC, muscle-invasive bladder cancer; NMIBC, non-muscle-invasive bladder cancer; VI-RADS, Vesical Imaging-Reporting and Data System; reader ME, reader with more experience; reader LE, reader with less experience.

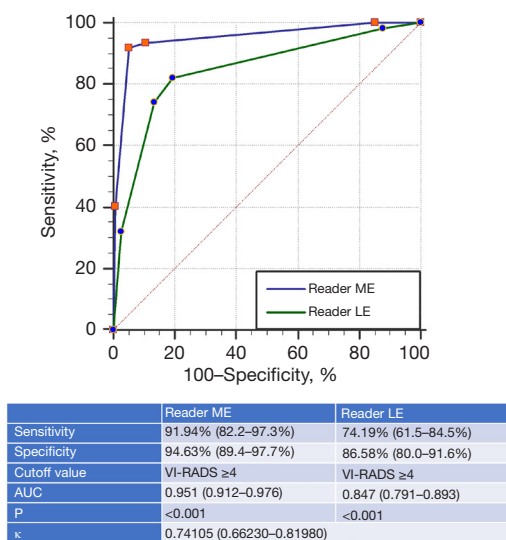


Figure 2 Comparison of ROC curve analysis for both readers. Reader ME, reader with more experience; reader LE, reader with less experience; VI-RADS, Vesical Imaging Reporting and Data System; AUC, area under the curve; ROC, receiver operating characteristic.

substantial ($\kappa=0.74105$) (details in [Table S3](#)).

Characteristics influencing the accuracy of the VI-RADS score

Table 3 lists several characteristics and their effects on the TN, TP, FN, and FP rates of the two readers. The TP and FP groups had a larger tumor size and wider tumor base compared to the other two groups. There was no statistically significant difference among the TN, TP,

FN, and FP groups in terms of sex or age in either reader. Significant differences for reader ME were observed in the tumor number ($P=0.002$), tumor size ($P<0.001$), and tumor base width ($P<0.001$) as well as in tumor size ($P<0.001$) and tumor base width for reader LE ($P<0.001$).

Table 4 shows the pairwise comparison of the TN, FN, TP, and FP groups in terms of tumor number, tumor size, and tumor base width. For reader ME, the tumor size in the FP and TP groups was significantly larger than that in the TN group ($P=0.031$ and $P<0.001$, respectively); meanwhile, the tumor base width in the TP and FP groups was significantly larger than that in the TN group ($P<0.001$ and $P<0.001$, respectively). For reader LE, the tumor size in the FP and TP groups was significantly larger than that in the TN group ($P=0.042$ and $P<0.001$, respectively); meanwhile, the tumor base width in the TN group was significantly smaller than that in the TP and FP groups ($P<0.001$ and $P=0.022$, respectively), and the tumor base width in the FN group was significantly smaller than that in the TP group ($P=0.004$) (*Figures 3–5*).

Discussion

Our study confirmed that when the cutoff value of VI-RADS was ≥ 4 (reader ME: sensitivity 91.94%, specificity 94.63%, AUC 0.951; reader LE: sensitivity 74.19%, specificity 86.58%, AUC 0.847), the VI-RADS score had high diagnostic validity and reliability in predicting MIBC. The influence of tumor size and tumor base width on MIBC prediction with the VI-RADS score was also noted.

Since its inception, the VI-RADS score has been widely recognized by radiologists and urologists as a highly valuable aid for clinical decision-making (15,16,20).

Table 3 Comparison of differences between TP, FP, TN, and FN

Characteristics	N	Male	Age, years	Tumor number	Tumor size, mm	Tumor base, mm
Total	211	188 (89.1)	62 [15]	1 [1]	23 [18]	18 [24]
Reader ME						
TP	57	55 (96.5)	62 [16]	1 [0]	28 [19]	37 [46]
FP	8	7 (87.5)	58 [11]	1 [0]	31 [22]	48 [32]
TN	141	121 (85.8)	63 [15]	1 [1]	19 [16]	15 [13]
FN	5	5 (100.0)	64 [19]	5 [5]	20 [14]	17 [20]
P value		0.115	0.567	0.002	<0.001	<0.001
Reader LE						
TP	44	42 (95.5)	63 [15]	1 [0]	31 [19]	42 [40]
FP	9	7 (77.8)	53 [8]	1 [2]	28 [19]	36 [23]
TN	139	120 (86.3)	64 [14]	1 [1]	19 [16]	15 [13]
FN	19	19 (100.0)	58 [15]	1 [2]	23 [15]	17 [22]
P value		0.822	0.098	0.071	<0.001	<0.001

Data are shown as n (%) or median [IQR]. TP, true positive; FP, false-positive; TN, true negative; FN, false negative; reader ME, reader with more experience; reader LE, reader with less experience; IQR, interquartile range.

Table 4 Pairwise comparison of accuracy

Characteristics	Adjusted P value					
	TN vs. FN	TN vs. TP	TN vs. FP	FN vs. TP	FN vs. FP	TP vs. FP
Reader ME						
Tumor number	0.732	0.031	0.226	0.086	0.063	1.000
Tumor size	1.000	<0.001	0.031	1.000	1.000	1.000
Tumor base	1.000	<0.001	<0.001	0.508	0.219	1.000
Reader LE						
Tumor size	1.000	<0.001	0.042	0.160	0.482	1.000
Tumor base	0.801	<0.001	0.022	0.004	0.702	1.000

TN, true negative; FN, false negative; TP, true positive; FP, false positive; reader ME, reader with more experience; reader LE, reader with less experience.

In this study, with VI-RADS ≥ 4 as the cutoff value for identifying MIBC, the AUCs of the VI-RADS score were greater than 0.80 for both readers, and the interobserver agreement was $\kappa=0.74105$, further supporting VI-RADS as a stable scoring system for BC. This was consistent with previous findings (21-26). However, it seems that the accuracy of VI-RADS depends in part on the experience of the radiologists (24), as the reader ME had higher accuracy and sensitivity than did reader LE (*Figure 2*).

To improve the diagnostic accuracy of the VI-RADS score for MIBC, we evaluated the influence of age, sex, tumor number, tumor size, tumor base width, and other characteristics on the accuracy of the VI-RADS score. Among these, age and sex had no effect on the results, while tumor size and tumor base width seemed to reduce the accuracy of diagnosis from both readers.

The Kruskal-Wallis test (adjusted with Bonferroni correction) showed that larger tumor size was associated

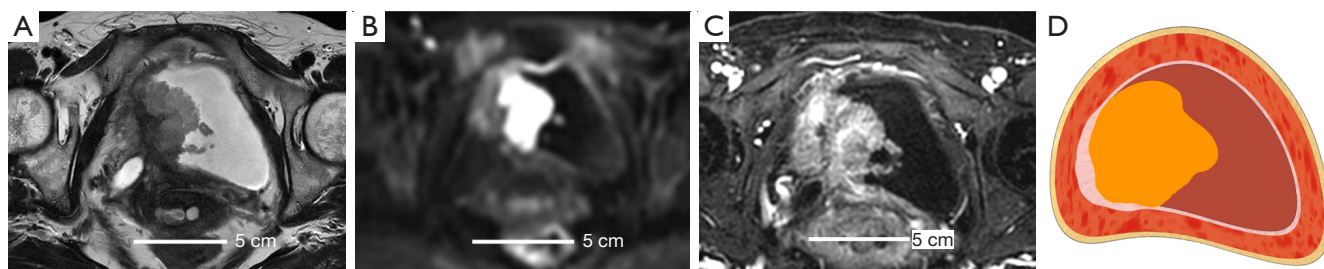


Figure 3 Misdiagnosed case 1. T2WI (A), DWI (B), DCE imaging (C), and schematic diagram (D) of a 52-year-old woman with pT1 high-grade urothelial carcinoma (pathological specimen from radical cystectomy), which was rated as VI-RADS 4 by reader LE due to a large tumor size of 44 mm × 26 mm × 42 mm. T2WI, T2-weighted image; DWI, diffusion-weighted imaging; DCE, dynamic contrast-enhanced; VI-RADS, Vesical Imaging-Reporting and Data System; reader LE, reader with less experience.

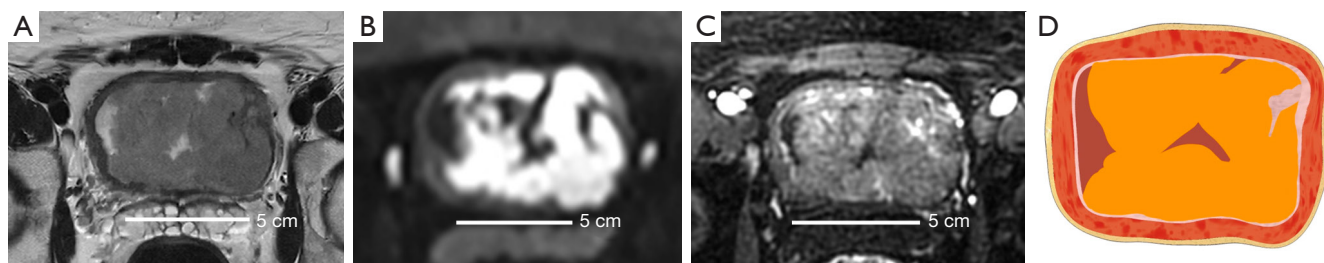


Figure 4 Misdiagnosed case 2. T2WI (A), DWI (B), DCE imaging (C), and schematic diagram (D) of a 52-year-old man with pT1 high-grade urothelial carcinoma (pathological specimen from radical cystectomy), which was rated VI-RADS 4 by reader LE due to a total tumor base of 151 mm and a large tumor size of 73 mm × 47 mm × 24 mm. T2WI, T2-weighted image; DWI, diffusion-weighted imaging; DCE, dynamic contrast-enhanced; VI-RADS, Vesical Imaging-Reporting and Data System; reader LE, reader with less experience.

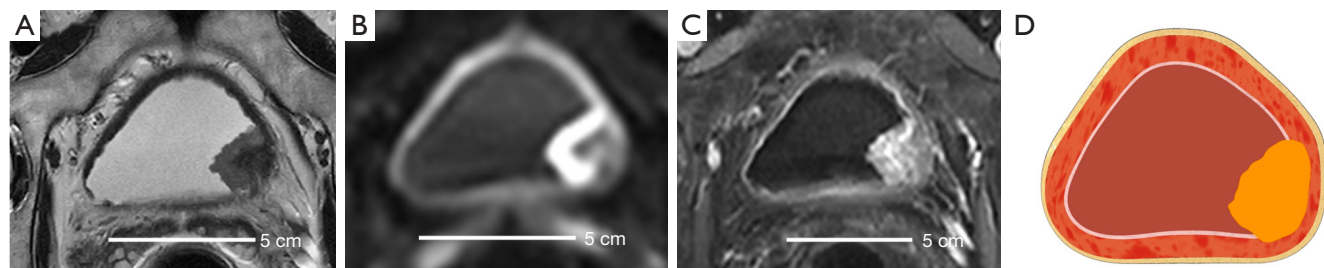


Figure 5 Misdiagnosed case 3. T2WI (A), DWI (B), DCE imaging (C) and schematic diagram (D) of a 76-year-old woman with pT2 high-grade urothelial carcinoma (pathological specimen from TURBT), which was rated as VI-RADS 2 by reader ME and reader LE due to its smaller tumor size, narrower tumor base, and its suspected stalk. T2WI, T2-weighted image; DWI, diffusion-weighted imaging; DCE, dynamic contrast-enhanced; TURBT, transurethral resection of the bladder tumor; VI-RADS, Vesical Imaging-Reporting and Data System; reader ME, reader with more experience; reader LE, reader with less experience.

with a higher incidence of FP for reader ME (TN *vs.* FP, $P=0.031$) and reader LE (TN *vs.* FP, $P=0.042$). The notion that a larger tumor size indicates greater malignancy (27) causes less attention to be paid to the other tumor traits. Our findings suggest that a tumor with a large size may

lead to misjudgment and the greater occurrence of FPs (Figures 3, 5). To avoid errors related to tumor size, certain biases need to be avoided, and the significance of a large tumor should not be overestimated.

The width of the tumor base was also positively

associated with a higher FP rate for reader ME (TN *vs.* FP, $P < 0.001$) and for reader LE (TN *vs.* FP, $P = 0.022$). We believe this can be attributed to a wider the tumor base involving a larger area of examination (Figures 3,4). Oğuz *et al.* (28) also found that the error rate of VI-RADS in flat lesions was increased. Indeed, we have observed that a flat lesion has a relatively wider base, which is consistent with our results. Therefore, more careful confirmation of the continuity of the low-signal line in the T2WI sequence may yield greater accuracy when tumors with a wider base are encountered. To improve the diagnostic accuracy of VI-RADS for MIBC with a wide base, we first need to determine the extent of the tumor base, and then carefully observe the entire base in each plane to determine whether or not it is invading the muscle.

In the scoring of reader ME, we observed a significant difference in tumor number between groups ($P = 0.002$), but there was no significant difference between groups in the pairwise comparison. This might be due to the lack of FN cases and high dispersion.

To improve the VI-RADS, many studies have been conducted in a variety of areas. Researchers continue to explore more applications of the VI-RADS scenario to meet clinical needs. In addition to applying VI-RADS to assess MIBC in newly diagnosed patients, some researchers have attempted to apply VI-RADS to assess the depth of infiltration in patients after TURBT or chemotherapy as a noninvasive and complementary approach (14,17). In a different vein, some studies have focused on how to improve the VI-RADS by using a high b value in the diffusion-weighted imaging (DWI) sequence (29) via a biplanar (axial and sagittal) reduced field of view DWI sequence (30), without use of a dynamic contrast-enhanced sequence (31) or other methods. However, macroscopic radiographic characteristics are the most immediate basis for radiologists to make judgments in their daily work. Thus far, few studies have focused on the effect of macroscopic image characteristics on the accuracy of VI-RADS. Several studies (24,32,33) have revealed the effect of tumor location on the accuracy of the VI-RADS, especially at the ureteral orifice and bladder diverticuli. Meng *et al.* (34) reported that discrepancies between T2WI and DWI affected the application of VI-RADS. Our research focused on the effects of tumor number, tumor size, and tumor base width, indicating that these negatively impacted the diagnostic accuracy of VI-RADS.

Some other limitations of our study are worth mentioning. First, we employed a retrospective design, and

all cases were reviewed by two radiologists. It is possible that the performance of mpMRI could differ when evaluated prospectively. Second, a sample size of 211 patients and two readers may not be sufficiently large to avoid data-dredging bias. Further improvement with a larger sample size is expected in the future. Third, 71.6% of the tumor specimens came from TURBT but not radical cystectomy, and it has been proven that the pathological results of radical cystectomy specimens are more accurate (35). However, this is a common and inevitable problem, and we plan to address this issue in future work. Nevertheless, this study is a reminder that greater attention should be paid to certain radiographic-based errors when the VI-RADS score is being used.

In this study, we validated the stability and superiority of the VI-RADS score in diagnosing MIBC. When using a cutoff of VI-RADS ≥ 4 , we obtained an AUC > 0.8 for both readers. Large tumor size and a wide tumor base also led to misdiagnosis. To reduce FNs and FPs and improve the accuracy of the VI-RADS, tumors with large sizes or wide bases should be more conscientiously examined. In addition, larger, prospective, and multi-institutional studies are needed to determine the exact impact of these characteristics.

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Footnote

Reporting Checklist: The authors have completed the STARD

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at <https://qims.amegroups.com/article/view/10.21037/qims-23-356/coif>). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013) and was approved by the Medical Ethics Committee of Sun Yat-sen University Cancer Center. Individual consent for this retrospective analysis was waived.

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