Bladder Cancer

Prospective Assessment of Vesical Imaging Reporting and Data System (VI-RADS) and Its Clinical Impact on the Management of High-risk Non–muscle-invasive Bladder Cancer Patients Candidate for Repeated Transurethral Resection

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Abstract

Background: Vesical Imaging Reporting and Data System (VI-RADS) score is adopted to provide preoperative bladder cancer (BCa) staging. Repeated transurethral resection of bladder tumor (Re-TURBT) is recommended in most of high-risk non–muscle-invasive bladder cancers (HR-NMIBCs) due to possibility of persistent/understaged disease after initial TURBT. No diagnostic tools able to improve patient’s stratification for such recommendation exist.

Objective: To (1) prospectively validate VI-RADS for discriminating between NMIBC and muscle-invasive bladder cancer (MIBC) at TURBT, and (2) evaluate the accuracy of VI-RADS for identifying HR-NMIBC patients who could avoid Re-TURBT and detecting those at higher risk for understaging after TURBT.

Design, setting, and participants: Patients with BCa suspicion were offered multiparametric magnetic resonance imaging (mpMRI) before TURBT. According to VI-RADS, a cutoff of ≥3 to define MIBC was assumed. TURBT reports were compared with preoperatively recorded VI-RADS scores to assess mpMRI accuracy in predicting Re-TURBT outcomes. Performance of mpMRI was assessed by receiver operating characteristic curve analysis. 

Intervention: Multiparametric MRI of the bladder before TURBT.

Outcome measurements and statistical analysis: Sensitivity, specificity, positive (PPV) and negative (NPV) predictive values were calculated for mpMRI performance in patients undergoing TURBT and for HR-NMIBC patients candidate for Re-TURBT. Performance of mpMRI was assessed by receiver operating characteristic curve analysis. 

Results and limitations: A total of 231 patients were enrolled. Multiparametric MRI showed sensitivity, specificity, PPV, and NPV for discriminating NMIBC from MIBC at
1. Introduction

When first diagnosed via transurethral resection of bladder tumor (TURBT), most of bladder cancers (BCa) are Ta-T1 non–muscle-invasive bladder cancers (NMIBCs) according to the tumor, node, and metastasis (TNM) classification system [1,2]. NMIBCs represent a heterogeneous category of tumors associated with, depending on the risk profile, high recurrence (30–80%) and progression (25–50%) rates, and leading to cancer death after bladder-sparing treatment within 5 yr in about 16–23% of cases [3]. In contrast, patients with high-grade (HG) muscle-invasive bladder cancers (MIBCs) are at a significant risk of developing metastatic disease, with a 5-yr overall survival (OS) rate of 68% after radical cystectomy (RC) for patients with pathologically organ-confined BCa (pT2), compared with 25–30% for those with extravesical extension [4,5].

Surgical management of NMIBC and MIBC tumors are therefore completely different, with initial TURBT being the first diagnostic and therapeutic procedure for NMIBC and only a diagnostic procedure for MIBC patients suitable for RC [6,7]. Notably, TURBT is operator dependent; therefore, presence of residual disease (reflecting incomplete BCa resection) varies widely with operators’ experience, increasing recurrence rates, progression, and finally cancer-related death [8,9]. About 7–30% of NMIBCs are understaged after TURBT, increasing up to 45% when resection does not include detrusor muscle [10,11]. Based on these issues, European Association of Urology guidelines recommend a second look and resection (repeated TURBT [Re-TURBT]) 2–6 wk following primary TURBT for all T1 tumors as well as for those in which no detrusor muscle in the specimen was included [12].

Multiparametric magnetic resonance imaging (mpMRI) for BCa is expanding and becoming increasingly accurate in providing high tissue contrast resolution, being able to finely differentiate bladder wall layers [13,14]. In particular, recent retrospective experience reported promising outcomes implementing Vesical Imaging Reporting and Data System (VI-RADS) score previously described [15], which was demonstrated to be a reliable image-guided approach to assess the presence of muscle invasiveness in the pre-TURBT setting [16].

The aim of this study was to validate the diagnostic accuracy of VI-RADS scoring system in discriminating NMIBC from MIBC in a large prospective single-center cohort of patients who underwent mpMRI of the bladder as an initial diagnostic tool before TURBT.

As the secondary endpoint, we aimed to verify, specifically for HR-NMIBC category, potential clinical application of VI-RADS score as a predictor of adverse pathology at Re-TURBT in order to investigate the performance of mpMRI for the selection of patients who could potentially avoid unnecessary Re-TURBT, and on the contrary, to detect those at higher risk for understaged disease after primary resection who should not miss Re-TURBT.

2. Patients and methods

2.1. Patient population and study design

This prospective study received formal Institutional Review Board and Ethical Committee approval. The study was conducted in line with the European Urology and Good Clinical Practice guidelines accordingly to ethical principles laid down by the latest version of the Declaration of Helsinki. Written informed consent was obtained for all patients enrolled in the study.

Between December 2017 and May 2019, all patients referred to our institutions for BCa suspicion were offered mpMRI before TURBT as per institution protocol. Patients with contraindication to perform mpMRI were excluded (ie, patients with impaired renal function; patients with claustrophobic disorder, with MR “unsafe” or “conditional” devices; and those who could not attain adequate bladder distension).

Each patient underwent mpMRI of the bladder to evaluate diagnostic accuracy of VI-RADS score in discrimination between NMIBC and MIBC at initial TURBT. According to secondary endpoint, following TURBT, patients diagnosed with low-risk NMIBC (LR-NMIBC), primary...
and/or concomitant carcinoma in situ (CIS), MIBC, and non-urothelial bladder carcinoma were excluded from this secondary-aim analysis. All patients selected for undergoing Re-TURBT due to high-risk Ta-T1 NMIBC were further evaluated to assess the level of concordance between Re-TURBT outcomes and preoperatively determined VI-RADS scores. The study design is summarized in Fig. 1.

2.2. Imaging acquisition protocol

All patients underwent the same mpMRI protocol at 3 Tesla scan (Discovery 750; GE, Italy). According to VI-RADS [15], T2-weighted sequences were acquired in axial, coronal, and sagittal planes; diffusion-weighted images were acquired in axial plane with high $b$ values ($b = 0–800–1000$, up to $2000\text{s/mm}^2$), and dynamic contrast-enhanced images were acquired in axial plane with a temporal resolution of 5 s. Imaging parameters and VI-RADS scoring flowchart are summarized in Supplementary Table 1 and Supplementary Fig. 1. Patients were administered an intramuscular antispasmodic agent and instructed to drink 500–1000 ml of water 30 min before the examination to obtain adequate bladder distension. All examinations were reviewed by two urogenital radiologists, blinded to clinical
Both readers assigned a VI-RADS score (1–5) to each lesion (up to 3 per patient), and for each patient, only the one with the highest VI-RADS score was considered. A VI-RADS cutoff score of ≥3 to define MIBC was assumed. Differences in opinion were resolved by consensus, assuming the most experienced reader’s opinion as the definitive one. A schematic representation of each VI-RADS category is shown in Supplementary Fig. 2.

2.3. TURBT, Re-TURBT, and histopathologic reports

All patients underwent conventional bipolar white-light TURBT within 6 wk after mpMRI at our institution. Re-TURBT was performed within 2–6 wk after initial surgery, by the same two experienced surgeons, at the scar site/sites of first resection for all T1 patients as well as for those with HG-Ta missing muscularis propria in the resection specimen. All tumor samples were analyzed by two experienced uropathologists. Outcomes from Re-TURBT reports (absence of cancer and/or persistent NMIBC vs upstaging to MIBC) were compared with the preoperative VI-RADS scores in order to assess diagnostic accuracy of mpMRI with pathologic reports (standard reference).

2.4. Statistical analysis

To assess the performance of mpMRI in differentiating between NMIBC and MIBC (aim 1), sensitivity, specificity, positive (PPV) and negative (NPV) predictive values were calculated for the whole cohort of patients who underwent mpMRI before TURBT, using TURBT for LR-NMIBC, Re-TURBT for HR-NMIBC, and RC for MIBC results as standard of reference. The performance of mpMRI was assessed by means of receiver operating characteristic (ROC) curve analysis. Inter-reader agreement analysis was performed with K statistics in order to investigate variability.

Table 1 – Patient characteristics and VI-RADS evaluation for bladder cancer lesions for the whole cohort (n = 231*).

<table>
<thead>
<tr>
<th>Variables</th>
<th>VI-RADS 1 (n = 37 (16))</th>
<th>VI-RADS 2 (n = 122 (52.8))</th>
<th>VI-RADS 3 (n = 31 (13.4))</th>
<th>VI-RADS 4 (n = 29 (12.6))</th>
<th>VI-RADS 5 (n = 12 (5.2))</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>Median 66 IQR 63–69</td>
<td>64 IQR 62–66</td>
<td>68 IQR 64–71</td>
<td>67 IQR 64–70</td>
<td>69 IQR 65–71</td>
</tr>
<tr>
<td>No. of lesions</td>
<td>Unifocal 15 (40.5)</td>
<td>68 (55.7)</td>
<td>6 (19.4)</td>
<td>8 (27.6)</td>
<td>4 (33.3)</td>
</tr>
<tr>
<td>Multifocal</td>
<td>22 (59.5)</td>
<td>54 (44.3)</td>
<td>25 (80.6)</td>
<td>21 (72.4)</td>
<td>8 (66.6)</td>
</tr>
<tr>
<td>Lesion diameter (cm)</td>
<td>≤3</td>
<td>31 (83.8)</td>
<td>109 (89.3)</td>
<td>9 (29)</td>
<td>3 (10.3)</td>
</tr>
<tr>
<td>&gt;3</td>
<td>6 (16.2)</td>
<td>13 (10.7)</td>
<td>22 (71)</td>
<td>26 (89.7)</td>
<td>9 (75)</td>
</tr>
<tr>
<td>T stage</td>
<td>Ta</td>
<td>10 (27)</td>
<td>51 (41.8)</td>
<td>5 (16.1)</td>
<td>0</td>
</tr>
<tr>
<td>T1</td>
<td>27 (73)</td>
<td>66 (54.1)</td>
<td>7 (22.6)</td>
<td>3 (10.3)</td>
<td>0</td>
</tr>
<tr>
<td>≥T2</td>
<td>0</td>
<td>5 (4.1)</td>
<td>19 (61.3)</td>
<td>26 (89.7)</td>
<td>12 (100)</td>
</tr>
<tr>
<td>Concomitant CIS</td>
<td>1 (2.7)</td>
<td>10 (8.2)</td>
<td>6 (19.3)</td>
<td>7 (24.1)</td>
<td>2 (16.7)</td>
</tr>
<tr>
<td>Pathologic grade</td>
<td>Low grade</td>
<td>11 (29.7)</td>
<td>62 (50.8)</td>
<td>5 (16.1)</td>
<td>0</td>
</tr>
<tr>
<td>High grade</td>
<td>26 (70.3)</td>
<td>60 (49.2)</td>
<td>26 (83.9)</td>
<td>29 (100)</td>
<td>12 (100)</td>
</tr>
</tbody>
</table>

CIS = carcinoma in situ; IQR = interquartile range; n = number; VI-RADS = Vesical Imaging Reporting and Data System.

*Patients with non-urothelial carcinoma of the bladder (n = 5, 2.1%) were excluded from definitive analysis.

Fig. 2 – ROC curve representing VI-RADS score performance in discriminating NMIBC from MIBC at initial TURBT (whole cohort; n = 231). Criterion ≥3 to define MIBC was assumed. AUC = area under the curve; CI = confidence interval; MIBC = muscle-invasive bladder cancer; n = number; NMIBC = non-muscle-invasive bladder cancer; ROC = receiver operating characteristics; TURBT = transurethral resection of bladder tumor; VI-RADS = Vesical Imaging Reporting and Data System.
performance in mpMRI reading. To evaluate intrareader agreement, each reader randomly reviewed a subset of images (one-fourth of patients in each pathologic T-stage category) within 3 mo from the end of enrollment.

As for secondary outcome, sensitivity, specificity, PPV, and NPV were calculated for the use of mpMRI for HR-NMIBC patients undergoing Re-TURBT. Final diagnosis after TURBT, Re-TURBT, and/or RC was considered the gold standard for detecting MIBC. ROC analysis was also performed.

All statistical analysis was performed by using software MedCalc (version 15.6.1; MedCalc Software bvba, Ostend, Belgium). All tests were two sided, and statistical significance was set at $p < 0.05$.

### 3. Results

Overall 288 patients with a primary suspicion of BCa were prospectively enrolled. Out of these, 52 (18%) cases did not meet the inclusion criteria and were consequently excluded from further evaluation (Fig. 1). A total of 236 patients underwent mpMRI before TURBT. Clinical features and tumor characteristics of the whole population are summarized in Table 1.

#### 3.1. Primary aim: prospective validation of VI-RADS score in NMIBC and MIBC differentiation before TURBT

Out of 236 cases, five (2.1%) with non-urothelial carcinoma of the bladder were excluded. Accordingly, a total of 231 patients were evaluated. The performance of mpMRI to discriminate NMIBC from MIBC tumors provided sensitivity and specificity of 91.9% (95% confidence interval [CI]: 82.2–97.3) and 91.1% (95% CI: 85.8–94.9), respectively. The PPV and NPV were 77.5% (95% CI: 65.8–86.7) and 97.1% (95% CI: 93.3–99.1), respectively. The area under the curve (AUC) was 0.94 (95% CI: 0.91–0.97). ROC curve analysis for this primary endpoint is summarized in Fig. 2. Inter-reader agreement was overall good ($\kappa = 0.81$, 95% CI: 0.65–0.93), with only 17 cases reporting disagreement between readers. In 14 of these cases, discrepancies were of 1 VI-RADS point (eg, VI-RADS category 3 vs 2 or category 3 vs 4). In three cases, the discrepancy was between categories 2 and 4. We did not find any tendency to over- or underestimate one reader compared with the other. Intrareader agreement was near perfect for both readers ($\kappa > 0.92$).

#### 3.2. Secondary aim: assessment of VI-RADS score as a predictor of Re-TURBT pathology outcomes for HR-NMIBCs

Forty-two (18.2%) patients with MIBC at initial TURBT, 58 (25.1%) with LR-NMIBC, and 17 (7.3%) with CIS were excluded. A total of 114 patients were considered for final analysis. Among this subpopulation, 28 (24.5%) had no detrusor muscle in the primary TURBT specimen. Of these patients, eight (28.6%) were HG-Ta, 11 (39.3%) were HG-T1, and nine (32.1%) were LG-T1. Clinical and tumor features of HR-NMIBCs are summarized in Table 2. After Re-TURBT, absence of cancer was found in 58 (50.9%) patients, 36 (31.6%) were diagnosed with persistent HR-NMIBCs, and 20 (17.5%) were upstaged to MIBC. Multiparametric MRI before

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**Table 2 – Patient characteristics and VI-RADS assessment only for HR-NMIBCs (n = 114).**

<table>
<thead>
<tr>
<th>Variables, n (%)</th>
<th>VI-RADS 1 n = 30 (26.3)</th>
<th>VI-RADS 2 n = 61 (53.5)</th>
<th>VI-RADS 3 n = 10 (8.8)</th>
<th>VI-RADS 4 n = 8 (7)</th>
<th>VI-RADS 5 n = 5 (4.4)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients</td>
<td>n = 30 (26.3)</td>
<td>n = 61 (53.5)</td>
<td>n = 10 (8.8)</td>
<td>n = 8 (7)</td>
<td>n = 5 (4.4)</td>
</tr>
<tr>
<td>Age (yr)</td>
<td>Median 65</td>
<td>66</td>
<td>66</td>
<td>63</td>
<td>72</td>
</tr>
<tr>
<td></td>
<td>IQR 61–68</td>
<td>63–68</td>
<td>63–71</td>
<td>63–65</td>
<td>64–74</td>
</tr>
<tr>
<td>No. of lesions</td>
<td>Unifocal 9 (30)</td>
<td>17 (27.9)</td>
<td>2 (20)</td>
<td>4 (50)</td>
<td>2 (40)</td>
</tr>
<tr>
<td></td>
<td>Multifocal 21 (70)</td>
<td>44 (72.1)</td>
<td>8 (80)</td>
<td>4 (50)</td>
<td>3 (60)</td>
</tr>
<tr>
<td>Lesion diameter (cm)</td>
<td>≤3 25 (83.3)</td>
<td>53 (86.9)</td>
<td>3 (30)</td>
<td>2 (25)</td>
<td>2 (40)</td>
</tr>
<tr>
<td></td>
<td>&gt;3 5 (16.6)</td>
<td>8 (13.1)</td>
<td>7 (70)</td>
<td>6 (75)</td>
<td>3 (60)</td>
</tr>
<tr>
<td>TURBT T stage</td>
<td>Ta 4 (13.3)</td>
<td>3 (4.9)</td>
<td>1 (10)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>T1 26 (86.7)</td>
<td>58 (95.1)</td>
<td>9 (90)</td>
<td>8 (100)</td>
<td>5 (100)</td>
</tr>
<tr>
<td>TURBT pathologic grade</td>
<td>Low grade 4 (13.3)</td>
<td>12 (19.7)</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>High grade 26 (86.6)</td>
<td>49 (80.3)</td>
<td>10 (100)</td>
<td>8 (100)</td>
<td>5 (100)</td>
</tr>
<tr>
<td>Detrusor muscle in TURBT report</td>
<td>Present 19 (63.3)</td>
<td>51 (86.6)</td>
<td>8 (80)</td>
<td>8 (100)</td>
<td>5 (100)</td>
</tr>
<tr>
<td></td>
<td>Absent 11 (36.7)</td>
<td>10 (16.4)</td>
<td>2 (20)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Re-TURBT outcomes</td>
<td>Absence of BCa 27 (90)</td>
<td>52 (85.2)</td>
<td>4 (40)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Persistent NMIBC 3 (10)</td>
<td>6 (9.8)</td>
<td>1 (10)</td>
<td>1 (12.5)</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Upstaged MIBC (≥T2) 0</td>
<td>3 (5)</td>
<td>5 (50)</td>
<td>7 (87.5)</td>
<td>5 (100)</td>
</tr>
</tbody>
</table>

BCa = bladder cancer; HR-NMIBC = high-risk non–muscle-invasive bladder cancer; IQR = interquartile range; MIBC = muscle-invasive bladder cancer; n = number; NMIBC = non–muscle-invasive bladder cancer; Re-TURBT = transurethral resection of bladder tumor; TURBT = transurethral resection of bladder tumor; VI-RADS = Vesical Imaging Reporting and Data System.
TURBT showed sensitivity and specificity of 85% (95% CI: 62.1–96.8) and 93.6% (95% CI: 86.6–97.6), respectively, to identify patients diagnosed with MIBC at Re-TURBT. PPV and NPV were 74.5% (95% CI: 52.4–90.1) and 96.6% (95% CI: 90.5–99.3), respectively. The AUC was 0.93 (95% CI: 0.87–0.97). ROC curve analysis was summarized in Fig. 3. Case examples of VI-RADS scoring within HR-NMIBCs are shown in Figs. 4 and 5.

4. Discussion

BCa prognosis and management mostly reflect tumor stage at primary diagnosis. The VI-RADS scoring system has been developed with the intent of standardizing staging, diagnosis, and eventually in future therapeutic response, through a consensus-driven approach to reproducible imaging and reporting.

Fig. 3 – ROC curve representing VI-RADS score performance as a predictor of adverse pathology (MIBC) at Re-TURBT report among HR-NMIBC patients (n = 114). Criterion >3 to define MIBC was assumed. AUC = area under the curve; CI = confidence interval; HR: high risk; n = number; MIBC = muscle-invasive bladder cancer; NMIBC = non-muscle-invasive bladder cancer; Re-TURBT = repeated transurethral resection of bladder tumor; ROC = receiver operating characteristics; VI-RADS = Vesical Imaging Reporting and Data System.

Fig. 4 – A 68-yr-old man presenting with hematuria and bladder mass reported after flexible cystoscopy underwent mpMRI before primary TURBT. (A) T2W imaging showing an exophytic lesion on the left-lateral wall, >1 cm in the greatest dimension, with a low SI stalk and an equivocal SI of the muscularis propria. VI-RADS score for T2W imaging was 3. (B) DWI (b = 2000). (C) ADC map, showing an exophytic lesion with restricted diffusion, low SI slack on DWI, and muscularis propria with a continuous intermediate signal on DWI. VI-RADS score for DWI was 2. (D) DCE imaging. (E) Perfusion map showing early enhancement of the lesion and inner layer without early enhancement of the muscularis propria. DCE was assigned a VI-RADS category of 2. Overall VI-RADS score was 2. T stage after TURBT identified HG-T1, while Re-TURBT resulted in absence of cancer at primary tumor site. ADC = apparent diffusion coefficient; DCE = dynamic contrast enhanced; DWI = diffusion weighted imaging; HG = high grade; mpMRI = multiparametric magnetic resonance imaging; SI = signal intensity; Re-TURBT = repeated transurethral resection of the bladder tumor site; T2W = T2 weighted; TURBT = transurethral resection of the bladder tumor; VI-RADS = Vesical Imaging Reporting and Data System.
Clinical application of preoperative VI-RADS score for NMIBC versus MIBC discrimination at primary resection has been validated recently, with good diagnostic accuracy by different groups. First, Barchetti et al [17] in a retrospective series reported significant diagnostic outcomes in MIBC discrimination confirmed at TURBT with a good inter-reader agreement between two experienced genitourinary radiologists (AUC 0.92 and 0.87 for readers 1 and 2, respectively; \( \kappa = 0.73 \)). In addition, Ueno et al [18] definitively confirmed the excellent performance with fine reproducibility of VI-RADS score in muscle-invasive tissue detection with an intraclass correlation coefficient of 0.85 (95% CI: 0.8–0.89) among five different readers, achieving high diagnostic performance represented by a pooled AUC of 0.90 (95% CI: 0.87–0.93). To date, the most recent and large retrospective validation of VI-RADS criterion \( \geq 2 \) for MIBC detection was published by Wang et al [19]. The authors demonstrated high diagnostic performance (AUC of 0.94) and the highest inter-reader agreement ever reported (\( \kappa = 0.92 \)). These studies, therefore, have to be considered the initial evidence testifying clinical reliability of VI-RADS as a pre-TURBT tool to identify patients suffering from MIBC. However, their retrospective nature and single-center design should be advocated as the primary limitation. To our knowledge, our study represents the first large prospective analysis demonstrating high diagnostic reliability of VI-RADS score, specifically cutoff 1–2 versus 3–5, in differentiating superficial from invasive disease at TURBT (sensitivity 91.9%, 95% CI: 82.2–97.3; specificity 91.1%, 95% CI: 83.8–94.9; PPV 77.5%, 95% CI: 65.8–86.7; NPV 97.1%, 95% CI: 93.3–99.1; inter-reader \( \kappa = 0.81 \), 95% CI: 0.65–0.93).

Our assessed secondary aim has to be considered a future ambitious perspective analyzing the applicability of VI-RADS score in the management of patients diagnosed with HR-NMIBC at TURBT, who, in the majority of cases, are currently candidate for Re-TURBT.

A number of quality issues, some potentially linked to the experience of the surgeon, indeed suggest that the initial TURBT may be inadequate in a high percent of these patients, with residual tumor rates varying between 33% and 76% for all the cases, achieving 27–72% and 33–78% for Ta and T1 tumors, respectively. Even more strikingly, underestimation of tumor depth invasion at first TURBT has been evidenced in up to 7–30% of cases, increasing up to 45–51% in those with HG-T1 tumors undergoing RC or in those where no muscle was detected in the specimen after initial resection [20,21].

As nicely advocated by Babjuk [22], Re-TURBT should therefore be considered an “emergency rescue” performed because of the uncertain quality of the first TURBT. However, this early repeated resection is not devoid of relevant and severe intra- and/or postoperative

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Fig. 5 – A 59-yr-old woman with ultrasound suspicious for BCa underwent mpMRI before primary TURBT. (A) T2W imaging showing a lesion of \( \geq 1 \) cm at the posterior wall of the bladder with intermediate SI that extends to the muscularis propria. T2W imaging was assigned a VI-RADS category of 4. (B) DWI \( b = 2000 \) and (C) ADC maps showing a lesion with significant restricted diffusion, extending through the muscularis propria. VI-RADS score of DWI was 4. (D) DCE imaging and (E) perfusion map showing early and heterogeneous enhancement of the lesion, which extended through the muscularis propria. DCE was assigned a VI-RADS category of 5. Overall VI-RADS score was 4. T stage after TURBT was HG-T1 NMIBC. After 4 wk, Re-TURBT was performed, resulting in T2 stage. The patient underwent RC and the stage was confirmed to be pT2b, N0, M0. ADC = apparent diffusion coefficient; BCa = bladder cancer; DCE = dynamic contrast enhanced; DWI = diffusion weighted imaging; HG = high grade; mpMRI = multiparametric magnetic resonance imaging; NMIBC = non–muscle-invasive bladder cancer; RC = radical cystectomy; Re-TURBT = repeated transurethral resection of the bladder tumor site; SI = signal intensity; T2W = T2 weighted; TURBT = transurethral resection of the bladder tumor; VI-RADS = Vesical Imaging Reporting and Data System.
complications together with significant socioeconomic implications and health-care–related costs [23,24].

Among available studies present in literature, none have based their findings on any preoperative/intraoperative tool for the identification of the ideal Re-TURBT HR-NMIBC candidate. In a large retrospective series, Angulo et al [25] basically demonstrated that performing Re-TUR did not impact long-term progression-free and disease-specific survival (hazard ratio [HR] = 0.77, 95% CI: 0.6–1.7; \( p = 0.9 \) and HR = 1.46, 95% CI: 0.8–2.6; \( p = 0.21 \), respectively). Another large prospective randomized study from the Nordic Association of Urology [26] revealed that tumor status at repeat TUR had a marginal role in influencing long-term cancer-specific survival (CSS; HR = 2.32, 95% CI: 0.7–7.74, \( p = 0.16 \) and HR = 3.03, 95% CI: 0.89–10.34, \( p = 0.07 \) for high-risk Ta and T1, respectively). Interestingly, Gontero et al [27] demonstrated, when stratifying patients according to presence/absence of detrusor muscle at TURBT, how the impact of Re-TURBT had only borderline effect on CSS (HR = 0.31, 95% CI: 0.09–1.08, \( p = 0.07 \)) for those with absence of muscularis propria in the resection specimen. Even more surprisingly, in those cases with muscle included in the TURBT specimen, Re-TURBT either did not improve or only slightly improved CSS and OS (CSS, HR = 1.6, 95% CI: 1.1–2.31, \( p = 0.01 \); OS, HR = 1.23, 95% CI: 0.97–1.56, \( p = 0.09 \)).

In our cohort of HR-NMIBC patients, we demonstrated a good concordance in discriminating the absence of cancer/persistent NMIBC versus upstaging to MIBC at Re-TURBT (sensitivity and specificity: 85%, 95% CI: 62.1–96.8 and 93.6%, 95% CI: 86.6–97.6, respectively; PPV and NPV: 74.5%, 95% CI: 52.4–90.1 and 96.6%, 95% CI: 90.5–99.3, respectively), confirming our hypothesis of VI-RADS score as an interesting potential predictor of adverse pathology at Re-TURBT. Even if cases on adequate concordance between VI-RADS 1–2 and absence of MIBC at Re-TURBT (\( n = 94, 82.4\% \)) were quantitatively more significant than those on concordance between VI-RADS 3–5 and detection of understaged disease at Re-TURBT (\( n = 20, 17.5\% \)), we still should be cautious advocating mpMRI as a predictive criterion for the selection of patients who could eventually avoid Re-TURBT. This is also due to the significant rate of persistence of NMIBC detected at Re-TURBT in our series (\( n = 36, 31.5\% \)). These findings are in line with the available literature confirming the pitfalls of initial TURB in providing complete eradication of BCa in HR-NMIBC patients. Different experience analyzing new intraoperative imaging methods such as photodynamic diagnosis (PDD) has shown a reduction in the rate of persistent disease down to 15% of cases [28,29]. A future combined approach of mpMRI imaging and PDD-TURBT may improve preoperative detection and intraoperative resection of bladder neoplasms, potentially reducing the need for early restaging procedures.

Despite promising outcomes, our series is not devoid of limitations. First and more importantly, diagnosis of CIS cannot be made with imaging methods; therefore, mpMRI cannot be adopted yet for this large portion of per-definition high-risk cases. Second, although our results are prospective, these were obtained with a small-sized, single-center sample, leading to all our MRI acquisitions being achieved by the same highly performing 3 T magnet and making applicability of our results to clinical routine slightly difficult. At this point, large multicenter randomized experience has been acknowledged as the remaining step before assuming VI-RADS as a standardized, reliable, reproducible, and highly performing preoperative tool for BCa staging.

Finally, even though we are not hiding our enthusiasm for future clinical applications of mpMRI and VI-RADS score for BCa management, their role as a diagnostic tool for patients candidate for Re-TURBT still need to be confirmed. In addition, we admit that we are still far from avoiding unnecessary secondary resections. However, mpMRI of the bladder might be considered for future predictive models in order to assess the risk of understaged MIBC after first resection, thus improving adequate diagnosis and prognosis of this large proportion of bladder tumors.

5. Conclusions

VI-RADS score is a novel imaging tool leading urologist to properly differentiate patients with superficial or muscle-invasive disease before TURBT. In this study, we tested the ability of VI-RADS score ≤2 as a clinical predictor of noninvasive disease at Re-TURBT. Improvement of the diagnostic performance of mpMRI and of the quality issues of primary TURBT will be mandatory prior to consider VI-RADS as a reliable stratification tool for patients candidate for avoiding early repeated resection. At the same time, we tested the VI-RADS cutoff of ≥3 as a predictor of understaged MIBC at TURBT with the intent for future identification of false-negative cases that should definitely not miss repeated resection of the primary tumor site.

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Appendix A. Supplementary data

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