

Association Between Voiding Dysfunction and Intravesical Recurrence in Non-Muscle-Invasive Bladder Cancer

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Abstract

Background

Post-void residual (PVR) urine volume may reflect impaired bladder emptying and prolonged urothelial exposure to urinary carcinogens; however, its association with intravesical recurrence in patients with non-muscle-invasive bladder cancer (NMIBC) remains incompletely defined. This study evaluated the association of preoperative PVR volume, PVR ratio, and uroflowmetric parameters with intravesical recurrence in male patients with NMIBC.

Methods

This retrospective, single-center cohort study included male patients who underwent transurethral resection of bladder tumor for NMIBC between January 2018 and January 2026. Of 596 patients screened, 106 with complete preoperative uroflowmetry, PVR measurements, clinicopathological data, and follow-up information were included. Patients with a voided volume < 150 mL were excluded. The PVR ratio was calculated as $PVR / (PVR + \text{voided volume})$. Patients were categorized according to the occurrence of intravesical recurrence during follow-up. Receiver operating characteristic (ROC) curve analysis was used to assess discrimination for recurrence, and logistic regression analyses were performed to evaluate associations between voiding parameters and recurrence.

Results

Intravesical recurrence occurred in 31 of 106 patients (29.2%). Median PVR volume was significantly higher in patients with recurrence than in those without recurrence (250 vs. 50 mL, $p < 0.001$), as was the median PVR ratio (0.56 vs. 0.14, $p < 0.001$). In contrast, maximum urinary flow rate, mean flow rate, and voided volume did not differ significantly between the groups. PVR volume showed the highest discrimination for intravesical recurrence (AUC 0.962, 95% CI 0.926–0.990), whereas the PVR ratio had an AUC of 0.902 (95% CI 0.842–0.950). Each 50-mL increase in PVR was associated with higher odds of recurrence (OR 4.47, 95% CI 2.52–7.94; $p < 0.001$), and the association remained significant after multivariable adjustment (aOR 6.31, 95% CI 2.84–13.98; $p < 0.001$). Similarly, each 0.10 increase in PVR ratio was independently associated with recurrence (aOR 2.80, 95% CI 1.83–4.27; $p < 0.001$). In exploratory threshold analyses, $PVR \geq 150$ mL yielded 100% sensitivity and 88.0% specificity for recurrence.

Conclusions

Higher preoperative PVR volume and PVR ratio were independently associated with intravesical recurrence in male patients with NMIBC, whereas conventional uroflowmetric flow parameters showed

limited discriminatory ability. PVR may represent an easily obtainable clinical parameter that provides complementary information to established clinicopathological risk assessment. The exploratory 150-mL threshold requires external validation before clinical implementation.

Introduction

Bladder cancer is one of the most common malignancies of the urinary tract, and approximately 75% of patients present with non-muscle-invasive bladder cancer (NMIBC) at the time of diagnosis [1]. Despite transurethral resection of bladder tumor (TURBT) and risk-adapted adjuvant intravesical therapies, NMIBC requires long-term, risk-stratified surveillance because of its high recurrence rate and the risk of progression in selected patient subgroups [2]. Current European Association of Urology (EAU) risk stratification incorporates patient age, tumor number, tumor size, pathological stage, tumor grade, and the presence of concomitant carcinoma in situ (CIS) as major prognostic variables [3]. Similarly, the European Organisation for Research and Treatment of Cancer (EORTC) risk tables include tumor number, tumor size, prior recurrence rate, pathological stage, CIS, and tumor grade as key variables for estimating the risks of recurrence and progression [4]. Nevertheless, the predictive performance of currently available risk stratification models, including EORTC, CUETO, and EAU models, may remain limited at the individual patient level, particularly in populations treated with contemporary intravesical therapies [5].

Lower urinary tract symptoms and voiding dysfunction are common among older individuals, in whom bladder cancer is also more prevalent; however, these factors are not routinely incorporated into current NMIBC risk stratification systems. Moderate-to-severe lower urinary tract symptoms have been reported to be associated with an increased risk of intravesical recurrence in patients with NMIBC [6]. Increased post-void residual (PVR) urine volume may lead to urinary stasis, thereby prolonging urothelial exposure to urinary carcinogens and exfoliated tumor cells and potentially increasing the risk of intravesical recurrence [7]. Higher PVR volumes have also been associated with a reduced response to standard treatment in both male and female patients with NMIBC [8]. However, studies suggesting that the association between PVR and recurrence in high-risk NMIBC may differ according to whether bacillus Calmette–Guérin (BCG) therapy is administered indicate that this relationship may be influenced by intravesical treatment [9]. More recent prospective data have further supported increased residual urine volume as a potential marker associated with intravesical recurrence [10].

A substantial proportion of previous studies have been single-center and retrospective, with considerable heterogeneity in patient populations, PVR threshold values, follow-up duration, and intravesical treatment protocols. Moreover, the assessment of voiding dysfunction has generally focused on absolute PVR volume, whereas other parameters that may provide a more comprehensive assessment of voiding function, including maximum urinary flow rate, mean urinary flow rate, voided volume, and residual urine ratio, have been less extensively investigated. Because absolute PVR volume may be influenced by voided volume and total bladder volume, the PVR ratio, calculated as **PVR/(PVR + voided volume)**, may provide a more standardized measure of bladder emptying efficiency.

The present study aimed to evaluate the associations of preoperative PVR volume, PVR ratio, and uroflowmetric parameters with intravesical recurrence, recurrence-free survival, and disease progression in patients undergoing TURBT for NMIBC. We also investigated whether these voiding parameters provide prognostic information independent of established clinicopathological risk factors. We hypothesized that increased PVR volume and PVR ratio, together with reduced maximum urinary flow rate, would be associated with a higher risk of intravesical recur

Materials and Methods

Study Design and Patient Population

This retrospective, single-center, observational cohort study was conducted at the Department of Urology, Hitit University Çorum Erol Olçok Training and Research Hospital. The medical records of 596 patients who underwent transurethral resection of bladder tumor (TURBT) for non-muscle-invasive bladder cancer (NMIBC) between January 2018 and January 2026 were retrospectively reviewed.

The study was approved by the Hitit University Ethics Committee (Decision No. 2026 – 183). Owing to the retrospective nature of the study, the requirement for written informed consent was waived by the ethics committee. The study was conducted in accordance with the principles of the Declaration of Helsinki. Following ethical approval, patient data were retrieved from the hospital information management system, medical records, operative reports, pathology reports, cystoscopic follow-up records, laboratory results, imaging findings, uroflowmetry records, and post-void residual (PVR) urine volume measurements.

The study was specifically designed to investigate the potential association between voiding dysfunction and NMIBC recurrence in male patients, with particular consideration of lower urinary tract dysfunction potentially related to benign prostatic hyperplasia and prostatic bladder outlet obstruction. Therefore, female patients were excluded to reduce sex-related anatomical and functional heterogeneity in voiding characteristics.

Patients without preoperative uroflowmetry or PVR measurements, those with a voided volume < 150 mL, and those with incomplete clinical, pathological, or follow-up data were excluded. Because uroflowmetry and PVR measurements were not routinely performed in all patients during the retrospective study period, a substantial proportion of the initial cohort lacked the voiding parameters required for the present analysis. Following eligibility assessment, 106 male patients with available preoperative uroflowmetry and PVR data, together with complete clinicopathological and follow-up information, were included in the final analysis.

The primary objective of the study was to evaluate the association of preoperative PVR volume, PVR ratio, and uroflowmetric parameters with intravesical tumor recurrence during follow-up in male patients with NMIBC. Secondary objectives were to investigate the associations of these voiding parameters with disease progression and other clinicopathological prognostic factors.

Data Collection and Evaluated Variables

Patient age, body mass index, and comorbidities were recorded. Whether patients presented with primary or recurrent tumors, a history of previous TURBT, and intravesical therapies administered either before or after the index TURBT were also assessed.

To evaluate voiding function, preoperative PVR volume, maximum urinary flow rate (Q_{max}), mean urinary flow rate (Q_{ave}), and voided volume were recorded. Only uroflowmetry measurements obtained before TURBT were considered. Uroflowmetry measurements with a voided volume < 150 mL were considered insufficient for reliable assessment, and these patients were excluded from the study. In patients with more than one eligible preoperative uroflowmetry measurement, the measurement closest to the date of TURBT was used.

PVR volume was measured as part of routine clinical practice. Patients were instructed to void spontaneously and, upon returning after voiding, PVR volume was measured using transabdominal ultrasonography. The same ultrasound device was used for PVR assessment throughout the study period; however, information regarding the manufacturer and model of the device could not be retrieved from the retrospective records. In patients with multiple PVR measurements, the eligible preoperative measurement closest to the date of TURBT was included in the analysis.

To standardize residual urine burden relative to the estimated total bladder volume, the PVR ratio was calculated using the following formula:

$$\text{PVR ratio} = \text{PVR} / (\text{PVR} + \text{voided volume})$$

Bladder emptying efficiency (BEE) was calculated as follows:

$$\text{BEE} = 1 - \text{PVR ratio}$$

Tumor-related variables included tumor location, tumor number, maximum tumor diameter, primary or recurrent tumor status, pathological stage, tumor grade, presence of concomitant carcinoma in situ (CIS), lymphovascular invasion, and variant histology. Based on the available clinicopathological data, patients were categorized into low-, intermediate-, high-, and very-high-risk groups according to the European Association of Urology (EAU) risk classification. Pathological staging was recorded according to the TNM classification used during the study period, whereas tumor grading was recorded according to the World Health Organization (WHO) grading system reported in the pathology records during the corresponding period.

Treatment and Follow-up

All patients underwent TURBT for the NMIBC episode evaluated in the present study. Postoperative follow-up was assessed using cystoscopy records, pathology reports, and clinical follow-up data.

Information regarding the administration of adjuvant intravesical therapy and whether the treatment included bacillus Calmette–Guérin (BCG) was obtained from the medical records.

Intravesical recurrence was defined as the detection of a new bladder tumor during follow-up by cystoscopic evaluation and/or histopathological examination.

Disease progression was defined as progression to a higher pathological stage, development of muscle-invasive bladder cancer ($\geq T2$), regional lymph node involvement, or metastatic disease during follow-up. An increase in tumor grade alone was not considered disease progression.

Outcomes

The primary outcome was the association of preoperative PVR volume, PVR ratio, bladder emptying efficiency, and uroflowmetric parameters with the development of intravesical recurrence during follow-up.

Secondary outcomes included the associations of PVR volume and other voiding parameters with disease progression, as well as the associations of clinicopathological variables, including tumor number, tumor size, pathological stage, tumor grade, presence of CIS, EAU risk group, and intravesical therapy, with intravesical recurrence.

Statistical Analysis

Statistical analyses were performed using IBM SPSS Statistics for Windows, version 31.0 (IBM Corp., Armonk, NY, USA). Before analysis, the dataset was reviewed on a patient-by-patient basis to identify duplicate records, missing data, and clinically inconsistent values.

The distribution of continuous variables was assessed using histograms, Q–Q plots, and the Shapiro–Wilk test. Normally distributed continuous variables were expressed as mean $\pm$ standard deviation, whereas non-normally distributed variables were presented as median and interquartile range (IQR). Categorical variables were expressed as number and percentage [n (%)].

The study population was divided into two groups according to whether intravesical recurrence occurred during follow-up. Continuous variables were compared between groups using the independent-samples Student's t-test or Mann–Whitney U test, as appropriate according to their distribution. Categorical variables were compared using Pearson's chi-square test or Fisher's exact test when expected cell counts were low.

The discriminatory ability of PVR volume, PVR ratio, bladder emptying efficiency, maximum urinary flow rate (Q_{max}), mean urinary flow rate (Q_{ave}), and voided volume for intravesical recurrence was evaluated using receiver operating characteristic (ROC) curve analysis. The area under the curve (AUC) and corresponding 95% confidence intervals were calculated for each parameter.

For PVR volume, thresholds of ≥ 50 , ≥ 100 , ≥ 150 , and ≥ 200 mL were evaluated. Thresholds of ≥ 0.20 and ≥ 0.30 for the PVR ratio, < 0.80 and < 0.70 for bladder emptying efficiency, and < 10 and < 15 mL/s for Qmax were also assessed. Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were calculated at each threshold to evaluate discrimination for intravesical recurrence. These threshold analyses were considered exploratory and were not regarded as validated clinical decision cutoffs.

Logistic regression analysis was used to identify factors associated with intravesical recurrence. PVR volume was analyzed as a continuous variable per 50-mL increase, whereas the PVR ratio was analyzed per 0.10-unit increase. Univariable logistic regression analyses were initially performed. Subsequently, multivariable logistic regression models adjusted for EAU risk group and intravesical treatment status were constructed to control for potential confounding factors. Because of the close mathematical and clinical relationship between PVR volume and the PVR ratio, these variables were not entered simultaneously into the same multivariable model and were instead evaluated in separate models. Similarly, because bladder emptying efficiency is the mathematical complement of the PVR ratio, these two variables were not included together in the same regression model.

Given the limited number of recurrence events, the number of covariates included in the multivariable models was restricted to reduce the risk of overfitting. Results were reported as odds ratios (ORs), adjusted odds ratios (aORs), 95% confidence intervals (CIs), and p values.

Kaplan–Meier analysis and other time-to-event survival analyses were not performed; the primary analysis was based on whether intravesical recurrence occurred during the follow-up period.

All statistical tests were two-sided, and a p value < 0.05 was considered statistically significant.

Results

Patient Population and Baseline Clinicopathological Characteristics

A total of 106 male patients with non-muscle-invasive bladder cancer (NMIBC) were included in the study. During follow-up, intravesical recurrence occurred in 31 patients (29.2%), whereas no recurrence was observed in 75 patients (70.8%). There was no significant difference in age between patients with and without recurrence [median, 70.0 vs. 71.0 years; $p=0.997$]. Similarly, no significant between-group differences were observed with respect to smoking history, anticoagulant use, alpha-blocker use, or 5-alpha-reductase inhibitor use.

Among the clinicopathological variables, tumor size was numerically greater in patients who developed recurrence; however, this difference did not reach statistical significance [median, 4.0 vs. 3.0 cm; $p=0.208$]. No significant differences were observed between the groups in terms of the presence of multiple tumors, concomitant carcinoma in situ (CIS), or repeat transurethral resection of bladder tumor (re-TURBT). In contrast, the proportion of patients who received intravesical therapy was significantly

higher in the recurrence group than in the non-recurrence group [74.2% vs. 50.7%; $p=0.026$]. Similarly, the proportion of patients who received BCG-containing intravesical therapy was significantly higher among patients who developed recurrence [71.0% vs. 45.3%; $p=0.016$] (Table 1).

Table 1. Comparison of Clinical and Tumor Characteristics According to Intravesical Recurrence Status

Variable	Overall (n=106)	No recurrence (n=75)	Recurrence (n=31)	p value
Age, years	70.5	71.0	70.0	0.997
Smoking history, n (%)	70 (66.0)	49 (65.3)	21 (67.7)	0.812
Anticoagulant use, n (%)	32 (30.2)	19 (25.3)	13 (41.9)	0.090
Alpha-blocker use, n (%)	66 (62.3)	49 (65.3)	17 (54.8)	0.311
5-alpha-reductase inhibitor use, n (%)	3 (2.8)	2 (2.7)	1 (3.2)	1.000
Tumor size, cm	3.0	3.0	4.0	0.208
Multiple tumors, n (%)	41 (38.7)	28 (37.3)	13 (41.9)	0.658
Concomitant CIS, n (%)	16 (15.1)	13 (17.3)	3 (9.7)	0.386
Repeat TURBT, n (%)	58 (54.7)	42 (56.0)	16 (51.6)	0.680
Intravesical therapy, n (%)	61 (57.5)	38 (50.7)	23 (74.2)	0.026
BCG-containing therapy, n (%)	56 (52.8)	34 (45.3)	22 (71.0)	0.016

Note: Statistical significance was defined as $p<0.05$. Statistically significant p values are shown in bold.

Abbreviations: BCG, bacillus Calmette–Guérin; CIS, carcinoma in situ; TURBT, transurethral resection of bladder tumor.

Uroflowmetric and Bladder Emptying Parameters

When uroflowmetric parameters were compared according to recurrence status, no significant differences were observed between patients with and without recurrence in terms of Qmax, mean flow rate, or voided volume. Median Qmax was 13.0 mL/s in the non-recurrence group and 14.0 mL/s in the recurrence group ($p=0.848$). Median mean flow rate was 6.0 mL/s in both groups ($p=0.853$). Similarly, there was no significant difference in voided volume between the groups (200.0 mL vs. 195.0 mL, $p=0.986$).

In contrast, PVR volume was markedly higher in patients who developed recurrence. Median PVR volume was 50.0 mL in the non-recurrence group and 250.0 mL in the recurrence group ($p<0.001$). Likewise, the PVR ratio was significantly higher in the recurrence group (0.56 vs. 0.14, $p<0.001$), whereas bladder emptying efficiency was significantly lower in patients with recurrence (0.44 vs. 0.86, $p<0.001$) (Table 2).

Table 2. Comparison of Voiding Parameters According to Intravesical Recurrence Status

Variable	Overall (n=106)	No recurrence (n=75)	Recurrence (n=31)	p value
Qmax, mL/s	14.0	13.0	14.0	0.848
Mean flow rate, mL/s	6.0	6.0	6.0	0.853
Voided volume, mL	200.0	200.0	195.0	0.986
PVR volume, mL	90.0	50.0	250.0	<0.001
PVR ratio	0.24	0.14	0.56	<0.001
Bladder emptying efficiency	0.76	0.86	0.44	<0.001

Note: Statistical significance was defined as $p < 0.05$. Statistically significant variables are shown in bold.

Abbreviations: PVR, post-void residual urine volume; Qmax, maximum urinary flow rate.

ROC Analysis

The discriminatory performance of PVR volume, PVR ratio, bladder emptying efficiency, and uroflowmetric parameters for intravesical recurrence was evaluated using receiver operating characteristic (ROC) curve analysis. PVR volume demonstrated the highest discriminatory performance for intravesical recurrence (AUC, 0.962). The PVR ratio and reduced bladder emptying efficiency also showed strong discriminatory performance (AUC, 0.902 for both). In contrast, Qmax, mean flow rate, and voided volume showed poor discriminatory ability, with AUC values of 0.512, 0.512, and 0.501, respectively (Table 3).

Table 3. Discriminatory Performance of Voiding Parameters for Intravesical Recurrence

Parameter	AUC	95% CI
PVR	0.962	0.926–0.990
PVR ratio	0.902	0.842–0.950
Reduced bladder emptying efficiency	0.902	0.839–0.956
Qmax	0.512	0.392–0.626
Mean flow rate	0.512	0.387–0.619
Voided volume	0.501	0.381–0.614

Abbreviations: AUC, area under the curve; CI, confidence interval; PVR, post-void residual urine volume; Qmax, maximum urinary flow rate.

Cut-off Analyses

In analyses using different PVR thresholds, the recurrence rate increased markedly with increasing PVR volume. Among patients with PVR ≥ 50 mL, the recurrence rate was 44.9%, whereas no recurrence was observed in patients with PVR < 50 mL ($p < 0.001$). At a PVR threshold of ≥ 100 mL, the recurrence rate was 62.0%, whereas at a threshold of ≥ 150 mL it was 77.5% ($p < 0.001$ for both). A PVR cut-off of ≥ 150 mL demonstrated 100% sensitivity, 88.0% specificity, a positive predictive value of 77.5%, and a negative predictive value of 100% for intravesical recurrence.

Similar associations were observed for the PVR ratio and bladder emptying efficiency. Among patients with a PVR ratio ≥ 0.20 , the recurrence rate was 51.7%, whereas no recurrence was observed below this threshold ($p < 0.001$). The recurrence rate was also 51.7% among patients with bladder emptying efficiency < 0.80 , and this threshold was significantly associated with intravesical recurrence ($p < 0.001$). In contrast, Qmax thresholds of < 10 mL/s and < 15 mL/s were not significantly associated with recurrence ($p = 0.618$ and $p = 1.000$, respectively) (Table 4).

Table 4. Performance of Exploratory Thresholds for Intravesical Recurrence

Threshold	Recurrence rate, criterion met (%)	Recurrence rate, criterion not met (%)	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	p value
PVR ≥ 50 mL	44.9	0.0	100.0	49.3	44.9	100.0	< 0.001
PVR ≥ 100 mL	62.0	0.0	100.0	74.7	62.0	100.0	< 0.001
PVR ≥ 150 mL	77.5	0.0	100.0	88.0	77.5	100.0	< 0.001
PVR ≥ 200 mL	83.3	7.9	80.6	93.3	83.3	92.1	< 0.001
PVR ratio ≥ 0.20	51.7	0.0	100.0	61.3	51.7	100.0	< 0.001
PVR ratio ≥ 0.30	58.3	5.2	90.3	73.3	58.3	94.8	< 0.001
BEE < 0.80	51.7	0.0	100.0	61.3	51.7	100.0	< 0.001
BEE < 0.70	57.4	6.8	87.1	73.3	57.4	93.2	< 0.001
Qmax < 10 mL/s	33.3	28.0	25.8	78.7	33.3	72.0	0.618
Qmax < 15 mL/s	28.6	30.0	51.6	46.7	28.6	70.0	1.000

Abbreviations: BEE, bladder emptying efficiency; NPV, negative predictive value; PPV, positive predictive value; PVR, post-void residual urine volume; Qmax, maximum urinary flow rate. Threshold analyses were exploratory and should not be interpreted as externally validated clinical decision cut-offs.

Logistic Regression Analysis

In logistic regression analysis, PVR volume was strongly associated with intravesical recurrence. In univariable analysis, each 50-mL increase in PVR was associated with significantly higher odds of recurrence (OR, 4.47; 95% CI, 2.52–7.94; $p<0.001$). In the model adjusted for age, EAU risk group, and intravesical treatment status, PVR volume remained independently associated with recurrence (adjusted OR, 6.31; 95% CI, 2.84–13.98; $p<0.001$).

The PVR ratio was also significantly associated with recurrence in both univariable and multivariable analyses. Each 0.10-unit increase in the PVR ratio was associated with increased odds of recurrence in univariable analysis (OR, 2.46; 95% CI, 1.76–3.44; $p<0.001$), and this association remained significant after adjustment (adjusted OR, 2.80; 95% CI, 1.83–4.27; $p<0.001$). In contrast, Qmax was not significantly associated with intravesical recurrence in univariable analysis ($p=0.782$) (Table 5).

Table 5. Logistic Regression Analysis for Intravesical Recurrence

Variable	OR	95% CI	p value
PVR, per 50-mL increase	4.47	2.52–7.94	<0.001
PVR, per 50-mL increase – adjusted	6.31	2.84–13.98	<0.001
PVR ratio, per 0.10-unit increase	2.46	1.76–3.44	<0.001
PVR ratio, per 0.10-unit increase – adjusted	2.80	1.83–4.27	<0.001
Qmax, per 5-mL/s decrease	1.04	0.80–1.34	0.782
Age	1.00	0.95–1.05	0.925
High/very-high EAU risk	1.17	0.50–2.72	0.717
Intravesical therapy	2.80	1.11–7.05	0.029
BCG-containing therapy	2.95	1.20–7.24	0.018
CIS	0.51	0.13–1.94	0.323
Multiple tumors	1.21	0.52–2.85	0.658

Abbreviations: BCG, bacillus Calmette–Guérin; CI, confidence interval; CIS, carcinoma in situ; EAU, European Association of Urology; OR, odds ratio; PVR, post-void residual urine volume; Qmax, maximum urinary flow rate. “Adjusted” refers to the multivariable model adjusted for age, EAU risk group, and intravesical treatment status.

Discussion

The principal finding of the present study is that increased post-void residual (PVR) urine volume was strongly and independently associated with intravesical recurrence in male patients undergoing TURBT for non-muscle-invasive bladder cancer (NMIBC). Median PVR volume was 250 mL in patients who developed recurrence compared with 50 mL in those without recurrence; similarly, the PVR ratio was markedly higher and bladder emptying efficiency was lower in the recurrence group. In ROC analysis, PVR volume demonstrated an AUC of 0.962, while the PVR ratio and bladder emptying efficiency each showed an AUC of 0.902, suggesting that impaired bladder emptying may have clinical relevance in identifying NMIBC patients at increased risk of recurrence. In contrast, Qmax, mean urinary flow rate, and voided volume were not associated with recurrence, indicating that the residual urine burden after voiding may be more relevant to recurrence risk than instantaneous flow characteristics.

Current NMIBC risk stratification systems are primarily based on clinicopathological variables such as age, tumor number, tumor size, pathological stage, tumor grade, and the presence of concomitant carcinoma in situ (CIS) [11]. However, the predictive performance of these models may be limited at the individual patient level, particularly in cohorts treated with different intravesical treatment protocols. In our study, PVR volume and PVR ratio remained independently associated with recurrence after adjustment for age, EAU risk group, and intravesical treatment status, suggesting that post-void bladder emptying may provide complementary information to established clinicopathological risk models. Nevertheless, PVR should not be regarded as a replacement for existing EAU or EORTC risk classification systems, but rather as a potentially useful and easily measurable clinical variable that may complement these established tools [12].

Previous studies investigating the relationship between lower urinary tract dysfunction and bladder tumor recurrence generally support our findings. Lunney et al. reported that tumor recurrence was more frequent in NMIBC patients with moderate or severe lower urinary tract symptoms and that symptom severity may represent an independent predictor of recurrence [13]. In a study of 53 male smokers, Gül et al. found that mean PVR volume was higher in patients who developed recurrence, although the difference did not reach statistical significance, possibly because of the small sample size [14]. Sazuka et al., in a cohort of 305 patients with NMIBC, demonstrated that increased PVR volume and preoperative pyuria were independent risk factors for intravesical recurrence [15]. These findings support the possibility that PVR is not only a marker of lower urinary tract symptoms but may also be associated with the clinical course of NMIBC.

Al-Zubi et al. evaluated 119 patients with NMIBC according to PVR levels and reported shorter recurrence-free survival, particularly among patients with PVR $\geq$ 60 mL [16]. Di Gianfrancesco also demonstrated that increased PVR was associated with a poorer response to standard treatment in both male and female patients with NMIBC [17]. In a recent prospective study, Maeda et al. reported that residual urine volume was significantly higher in the recurrence group than in the non-recurrence group among male patients, and that residual urine volume remained an independent risk factor in

multivariable analysis [18]. The strong association between PVR and recurrence observed in our adjusted analyses, together with its high ROC performance, is consistent with these previous findings and further supports the relationship between impaired bladder emptying and intravesical recurrence.

Several mechanisms may underlie the association between increased PVR and intravesical recurrence. Prolonged urinary retention within the bladder may increase urothelial exposure to potentially carcinogenic substances excreted in the urine, including aromatic amines and polycyclic aromatic hydrocarbons derived from tobacco smoke. Urinary stasis may also promote chronic inflammation, pyuria, and recurrent urinary tract infections, thereby creating a microenvironment that may facilitate tumor development or implantation. In addition, tumor cells shed into the urine after TURBT may remain in contact with the urothelium for longer periods in the presence of incomplete bladder emptying, potentially increasing the likelihood of intravesical implantation [19]. Although these mechanisms are biologically plausible, the observational nature of the available evidence does not establish a causal relationship.

The lack of association between Qmax or mean urinary flow rate and recurrence in our study is noteworthy. Uroflowmetric flow parameters may be influenced by several factors, including voided volume, patient effort during voiding, detrusor contractility, bladder outlet obstruction, and measurement conditions. Therefore, a single Qmax measurement may not always accurately reflect true bladder emptying dysfunction. PVR volume, in contrast, directly reflects the absolute amount of urine remaining in the bladder after voiding. The association of both PVR ratio and bladder emptying efficiency with recurrence suggests that bladder emptying parameters adjusted for estimated total bladder volume may also provide prognostic information. However, the higher AUC observed for absolute PVR volume compared with the PVR ratio suggests that, in this patient population, absolute residual urine burden may be a stronger discriminatory parameter than proportional measurements.

In the cut-off analysis, a PVR threshold of ≥ 150 mL yielded 100% sensitivity, 88% specificity, a positive predictive value of 77.5%, and a negative predictive value of 100%, representing one of the most clinically notable findings of the study. The absence of recurrence below this threshold suggests that lower PVR values may have potential negative predictive value for recurrence. However, there is currently no universally accepted threshold defining clinically significant PVR. The International Continence Society PVR measurement module similarly notes that no universally accepted cut-off exists for defining significant residual urine volume [20]. Likewise, recent evaluations have emphasized that PVR measurements are influenced by measurement timing, technique, and intra-individual variability, and that no standardized cut-off has been established for defining “high” or “significant” PVR [21,22]. The substantial intra-individual variability observed in repeated PVR measurements further supports the need for cautious interpretation of thresholds derived from a single measurement or a single patient cohort [23]. Because the 150-mL threshold in the present study was evaluated and tested within the same cohort, the observed performance may be subject to optimism bias. Therefore, this threshold should not currently be considered a definitive clinical decision limit, but rather a candidate cut-off requiring validation in independent and larger patient cohorts.

The higher rates of intravesical therapy and BCG-containing treatment among patients who developed recurrence may initially appear unexpected. However, this finding should not be interpreted as indicating that intravesical therapy increases the risk of recurrence. Because intravesical treatments, particularly BCG, are more frequently administered to patients with intermediate- and high-risk NMIBC, this association may largely reflect the higher baseline disease risk underlying the treatment indication [24]. Although BCG is the standard treatment for high-risk NMIBC, persistent disease or recurrence may still occur in a subset of patients despite adequate therapy [25]. Moreover, not only the administration of BCG but also completion of induction therapy and appropriate maintenance treatment are important determinants of oncological outcomes; maintenance therapy has been shown to reduce recurrence risk and prolong recurrence-free survival [26,27]. In our study, PVR remained independently associated with recurrence after adjustment for intravesical treatment status, suggesting that the observed relationship was not solely attributable to treatment selection. Nevertheless, further analyses incorporating details such as the type of intravesical agent, induction and maintenance regimens, total number of instillations, treatment adherence, and criteria for adequate BCG are warranted.

An important clinical aspect of the present study is that PVR is a non-invasive, low-cost, easily repeatable parameter that is widely available in routine urological practice. In patients with high PVR before TURBT, a more detailed assessment of potential bladder outlet obstruction, detrusor underactivity, urinary tract infection, and concomitant medications may be considered. However, the current findings do not provide sufficient evidence to support medical or surgical treatment of bladder outlet obstruction solely for the purpose of reducing NMIBC recurrence risk. Whether reducing residual urine volume can actually lower the risk of recurrence can only be determined through prospective and preferably interventional studies.

This study has several limitations. First, its retrospective and single-center design introduces the potential for selection and information bias. Although the medical records of 596 patients who underwent TURBT for NMIBC were initially screened, only 106 male patients with available preoperative uroflowmetry, PVR measurements, and the required clinicopathological data were included in the final analysis. The fact that uroflowmetry and PVR measurements were not routinely obtained in all patients during clinical practice may therefore represent an important source of selection bias.

The inclusion of male patients only limits the generalizability of the findings to female patients. In addition, although patients with a voided volume <150 mL were excluded to improve the reliability of uroflowmetric measurements, this criterion may limit the applicability of the findings to patients with lower voided volumes.

PVR and uroflowmetry measurements were based on assessments performed at a single preoperative time point. Although PVR was measured using the same ultrasonography device following spontaneous voiding as part of routine clinical practice, the interval between voiding and ultrasonographic measurement was not consistently documented in the retrospective records, and information regarding the manufacturer and model of the ultrasound device could not be retrieved. Furthermore, PVR may be

affected by bladder filling and intra-individual variability, which may have contributed to measurement variability.

Not all potential confounding variables could be included in the models, including prostate volume, International Prostate Symptom Score (IPSS), objectively assessed bladder outlet obstruction, detrusor contractility, pyuria, urinary tract infection, previous recurrence burden, and details of intravesical treatment. In particular, the type of intravesical agent, BCG induction and maintenance regimens, total number of instillations, and criteria for adequate BCG treatment could not be modeled in detail. Therefore, the possibility of residual confounding cannot be excluded.

The presence of only 31 intravesical recurrence events limited the number of covariates that could be included in multivariable regression models and increased the potential risk of overfitting. Accordingly, the models were constructed parsimoniously. Because the PVR ratio and bladder emptying efficiency are mathematically complementary measures, they should not be interpreted as independent prognostic factors.

Finally, recurrence was evaluated as a binary outcome according to whether intravesical recurrence occurred during follow-up rather than as a time-to-event outcome. Differences in follow-up duration among patients could not therefore be fully accounted for and may have influenced the findings. In addition, the evaluated PVR thresholds were assessed in the same cohort and were not externally validated, which may have resulted in overestimation of sensitivity, specificity, and predictive values. In particular, the 150-mL threshold should therefore be regarded as an exploratory candidate cut-off for future studies rather than as a validated clinical decision threshold.

Conclusion

In this retrospective cohort, increased preoperative post-void residual (PVR) urine volume and PVR ratio were significantly associated with intravesical recurrence in male patients with non-muscle-invasive bladder cancer (NMIBC), and these associations remained significant after adjustment for clinical risk factors in multivariable analyses. In the present cohort, PVR volume demonstrated greater discriminatory ability for intravesical recurrence than Qmax, mean urinary flow rate, and voided volume.

Although a PVR threshold of ≥ 150 mL showed high sensitivity and specificity in exploratory analyses, this value should not be regarded as a validated clinical decision threshold because it was evaluated within the same cohort. Rather than replacing established NMIBC risk stratification systems, PVR should be considered a readily obtainable candidate clinical parameter that may provide complementary information to conventional clinicopathological assessment.

Larger, multicenter prospective studies using standardized PVR measurement protocols are warranted to validate these findings in independent patient populations and to more accurately define the relationship between residual urine burden and intravesical recurrence.

Abbreviations

AUC: Area under the curve

BCG: Bacillus Calmette–Guérin

BEE: Bladder emptying efficiency

CI: Confidence interval

CIS: Carcinoma in situ

EAU: European Association of Urology

EORTC: European Organisation for Research and Treatment of Cancer

IQR: Interquartile range

NMIBC: Non-muscle-invasive bladder cancer

NPV: Negative predictive value

OR: Odds ratio

aOR: Adjusted odds ratio

PPV: Positive predictive value

PVR: Post-void residual urine volume

Qave: Mean urinary flow rate

Qmax: Maximum urinary flow rate

ROC: Receiver operating characteristic

TURBT: Transurethral resection of bladder tumor

WHO: World Health Organization

Declarations

Ethics approval and consent to participate

The study was approved by the Hitit University Ethics Committee (Decision No. 2026-183). Owing to the retrospective nature of the study, the requirement for obtaining written informed consent from individual

participants was waived by the ethics committee. All procedures were conducted in accordance with the principles of the Declaration of Helsinki. Patient data were anonymized prior to analysis.

Consent for publication

Not applicable.

Availability of data and materials

The datasets generated and/or analyzed during the current study are not publicly available because they contain potentially identifiable clinical information and are subject to institutional data protection requirements. De-identified data may be available from the corresponding author upon reasonable request and subject to applicable ethical and institutional approvals.

Clinical trial number: not applicable.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

Mustafa Serdar Çağlayan, Ahmet Taşcı, Alpkon Torun, Burak Çağlar Öztürk, Cemil Aydın, and Musa Ekici contributed to the conception and design of the study. Data collection and clinical data acquisition were performed by the study investigators. Ahmet Taşcı contributed to data analysis, interpretation of the results, and preparation of the initial manuscript draft. All authors contributed to the critical revision of the manuscript for important intellectual content, read and approved the final manuscript, and agreed to be accountable for all aspects of the work.

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