Clinical Features and Treatment Outcomes of Large Bladder Tumors Nearly Filling the Bladder

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Purpose: The prognosis and clinical management of bladder tumors nearly occupying the entire bladder cavity remain poorly defined due to limited available data. This study aimed to evaluate the clinical features and treatment outcomes of patients presenting with bladder tumors nearly filling the bladder at initial diagnosis.

Materials and Methods: After obtaining ethical approval, a retrospective analysis was conducted on 51 patients diagnosed between 2017 and 2024 with primary bladder tumors nearly filling the bladder. All underwent transurethral resection of bladder tumor (TURBT). The clinical and pathological data were analyzed using descriptive statistics and multivariable logistic regression.

Results: The mean age was 76.24 ± 11.7 years, with a median follow-up of 9.73 months (range: 3–84 months). Hematuria was the most frequent symptom (74.5%). Muscle-invasive disease was identified in 43.1% of cases at initial diagnosis, exceeding the 25% generally reported in newly diagnosed bladder cancer cohorts ($p < .001$). Complete resection was achieved in 68.6%, while 31.4% required repeat TURBT (re-TURBT). Among patients initially diagnosed with non-muscle-invasive tumors, 31.1% were found to have muscle invasion upon second resection. Treatments comprised intravesical immunotherapy (48.6%), radical cystectomy (25.7%), chemoradiation (14.3%), and systemic chemotherapy (11.4%).

Conclusion: Bladder tumors nearly filling the bladder cavity are associated with high rates of muscle invasion and pose significant challenges in treatment and management. Larger, prospective multicenter studies are warranted to validate these findings and optimize management in this high-risk population.

Keywords: bladder neoplasms; urinary bladder neoplasms; transurethral resection of bladder tumor; carcinoma in situ; cystectomy; chemoradiotherapy

INTRODUCTION

Bladder cancer is the tenth most commonly diagnosed cancer worldwide, with approximately 549,000 new cases and 200,000 deaths annually.(1) Over the past several decades, its incidence has been rising, particularly in developing countries. However, a deceleration in this increase has been observed in recent years.(2) According to the 2013 data from the Ministry of Health, bladder cancer ranks as the third most common cancer among men in Turkey, following lung and prostate cancers. Additionally, mortality rates due to bladder cancer in Turkey stand at 6.6 per 100,000 individuals, placing the country among the highest globally in bladder cancer-related deaths.(3)

The primary therapeutic and diagnostic procedure for bladder tumors is transurethral resection of bladder tumor (TURBT), which allows for histopathological evaluation and initial treatment.(4) Approximately 75% of bladder tumors are non-muscle-invasive at diagnosis, classified as Ta or T1 stage. Despite TURBT, recurrence rates reach up to 60% within the first year, with progression rates up to 15%.(5) Several factors influencing recurrence and progression have been identified, including whether the tumor is primary or recurrent, the number of tumors, the presence of carcinoma in situ (CIS), tumor grade, and tumor size.(6)

Tumor size has been increasingly recognized as a critical prognostic factor in bladder cancer. Both the European Association of Urology (EAU) and the National Comprehensive Cancer Network (NCCN) guidelines acknowledge tumor size as a key variable in risk stratification, setting a threshold at 3 cm.(7) However, beyond this threshold, a clear predictive value for tumor size has not been established, particularly for tumors exceeding this limit.

Despite the well-documented significance of tumor size in risk assessment, limited data are available on the clinical course of bladder tumors that nearly fill the bladder. The scarcity of literature on this subject highlights a gap in understanding the prognosis of such large tumors. This study aims to evaluate the clinical outcomes of patients who, at initial diagnosis, presented with a bladder almost entirely occupied by a tumoral lesion.

MATERIALS AND METHODS

Study Population

After obtaining approval from the Mugla Sitki Kocman University Ethics Committee, this retrospective study analyzed patients diagnosed with bladder tumors between 2017 and 2024. A total of 51 consecutive patients

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Table 1. Demographic and Clinical Characteristics.

Characteristic	Patients, n (%)
Gender	Male: 47 (92.2)
	Female: 4 (7.8)
Presenting Symptoms	Hematuria: 38 (74.5)
	Pain: 4 (7.8)
	Irritative Symptoms: 9 (17.6)
Renal Function (eGFR)	>60 mL/min: 34 (66.7)
	<60 mL/min: 17 (33.3)
Complete TURBT in a Single Session	Yes: 35 (68.6)
	No (required two sessions): 16 (31.4)
Preoperative Erythrocyte Transfusion	Required: 10 (19.6)
	Not required: 41 (80.4)

Abbreviations: eGFR, estimated glomerular filtration rate; TURBT, transurethral resection of bladder tumor.

with primary bladder tumors nearly filling the bladder who underwent TURBT during this period were included.

Inclusion and Exclusion Criteria

Patients with histopathologically confirmed bladder carcinoma and complete medical records—including age, date of diagnosis, presenting symptoms, preoperative blood transfusion status, bladder function tests (BFT), treatment date, pathological findings, disease stage, number of operations, and completeness of tumor resection—were eligible. Complete TURBT was defined as macroscopic removal of all visible tumor tissue, with clear visualization of the whole bladder for any residual tumor. The completeness of resection and residual tumor were documented in the operative report. Patients were excluded if they had a history of recurrent bladder cancer, prior bladder cancer treatment, incomplete medical records, or evidence of metastatic disease at diagnosis.

Procedures

Tumors occupying nearly the entire bladder were defined by three senior urologists as cases in which normal-appearing bladder mucosa was visible in no more than one-fifth (≤20%) of the bladder surface area. The extent of visible normal mucosa was assessed intraoperatively by the operating urologist and verified by at least one of the other senior urologists. Interobserver agreement was reached through a review of operative notes and mutual intraoperative evaluations.

Statistical Analysis

Data were analyzed using SPSS version 26.0 software (IBM Corp., Armonk, NY, USA). Continuous variables were summarized as mean ± standard deviation (SD) or median with range, while categorical variables were described as numbers and percentages. The normality of the distribution of continuous variables was assessed using the Kolmogorov-Smirnov test and visual inspection of Q-Q plots. For continuous variables, comparisons between two independent groups were analyzed with the Student's *t*-test for normally distributed data and the Mann-Whitney *U* test for non-normally distributed data. The assumption of homogeneity of variances for the t-test was assessed using Levene's test. Fisher's exact test was used for comparing categorical variables when any expected cell count was less than 5; otherwise, the chi-square test was used. Differences between observed proportions and reference population values were evaluated using one-sample proportion tests.

A multivariable logistic regression analysis was performed to identify independent predictors of muscle invasion at initial TURBT. Variables included in the model were age, sex, presence of CIS, tumor grade, and renal function status. The overall model fit was assessed using the Likelihood-Ratio Test. Results were reported as odds ratios (OR) with 95% confidence intervals (CI). A p-value of $< .05$ was considered statistically significant.

RESULTS

A total of 51 patients were included in the study. The mean age was 76.24 ± 11.7 years, and the median follow-up period was 9.73 (3–84) months. Of the patients, 47 (92.2%) were male, and 4 (7.8%) were female. The most common presenting symptom was hematuria, which was observed in 38 (74.5%) patients, followed by irritative urinary symptoms in 9 (17.6%) patients and pain in 4 (7.8%) patients (**Table 1**).

Evaluation of renal function revealed that 34 (66.7%) patients had an estimated glomerular filtration rate (eGFR) above 60 mL/min/1.73 m², whereas 17 (33.3%) had an eGFR below this threshold, indicating impaired renal function. Preoperative erythrocyte transfusion was required in 10 (19.6%) patients, while 41 (80.4%) did not require transfusion. Complete transurethral resection of bladder tumor (TURBT) was achieved in 35 (68.6%) patients in a single session, whereas 16 (31.4%) required a second session for complete resection (**Table 1**).

The proportion of muscle-invasive disease was 43.1% (22 of 51; 95% CI 29.3–57.8). When compared with the approximate 25% prevalence generally reported in population-based bladder cancer cohorts,(1, 8) this rate was statistically higher ($p < .001$), reflecting a higher initial disease burden in this cohort. Similarly, low-grade tumors accounted for 31.9% (15 of 47; 95% CI 19.1%–47.1%), which was statistically lower ($p = .003$) than the approximately 60% prevalence reported in reference populations (**Table 2**).[9]

A total of 12 patients were lost to follow-up after the

Table 2. Histopathological Findings.

Pathological Features	1st TURBT, n (%)	2nd TURBT, n (%)
Tumor Type	Urothelial Carcinoma (UCC): 47 (91.5)	Urothelial Carcinoma (UCC): 29 (100)
	Non-UCC: 4 (8.5)	Non-UCC: 0
Carcinoma in Situ (CIS)	Present: 3 (5.9)	Present: 2 (6.8)
	Absent: 48 (94.1)	Absent: 27 (93.2)
Tumor Grade	Low-Grade: 15 (31.9)	Low-Grade: 9 (31.1)
	High-Grade: 32 (68.1)	High-Grade: 20 (68.9)
Tumor Stage (pT Classification)	pT1: 29 (56.9)	pT1: 20 (68.9)
	pT2: 22 (43.1)	pT2: 9 (31.1)

Abbreviations: TURBT, transurethral resection of bladder tumor; CIS, carcinoma in situ; UCC, urothelial carcinoma.

Table 3. Post-TURBT Treatment Modalities.

Treatment Modality	NMIBC Patients, n (%)	MIBC Patients, n (%)	Total Patients, n (%)
Intravesical BCG Therapy	17 (85.0)	0 (0)	17 (48.6)
Radical Cystectomy	3 (15.0)	6 (40.0)	9 (25.7)
Chemoradiation	0 (0)	5 (33.3)	5 (14.3)
Systemic Chemotherapy Alone	0 (0)	4 (26.7)	4 (11.4)
Total	20 (100)	15 (100)	35 (100)

Abbreviations: TURBT, transurethral resection of bladder tumor; NMIBC, non-muscle-invasive bladder cancer; MIBC, muscle-invasive bladder cancer; BCG, Bacillus Calmette–Guérin.

first TUR, and 4 additional patients were lost after the second TUR, leading to their exclusion from further analysis (**Figure 1**). Among the 29 patients initially diagnosed with stage T1 disease, 9 (31.1%) were upstaged to stage T2 upon re-evaluation at the second TURBT, highlighting the high risk of initial understaging in very large bladder tumors. The second resection was typically performed within 4 weeks (IQR 3–6 weeks) of the initial procedure (**Table 2**).

Perioperative complications were observed in 11 patients (21.6%), the majority classified as Clavien–Dindo grade I–II. Eight patients (15.7%) experienced postoperative hematuria; 3 of these patients (5.9%) were the cases in which the procedure was terminated due to suspected bladder perforation. None of the perforations were intraperitoneal, and all were managed conservatively. Among the remaining patients with postoperative hematuria, 3 (5.9%) were managed conservatively, while 2 (3.9%) required re-operation for bladder clot retention (Clavien–Dindo grade IIIa). In addition, 3 patients (5.9%) developed febrile urinary tract infections, all of which resolved with antibiotic therapy. The median duration of postoperative bladder drainage was 3 days (IQR 2–7), and the median length of hospital stay was 4 days (IQR 3–7).

Following TURBT, treatment allocation was determined by pathological staging for the 35 patients who remained in follow-up. Among the 20 patients with non-muscle-invasive bladder cancer (NMIBC), the primary treatment was intravesical immunotherapy, with 17 (85.0%) receiving Bacillus Calmette-Guérin (BCG) therapy. The remaining 3 (15.0%) NMIBC patients underwent radical cystectomy. For the 15 patients with muscle-invasive bladder cancer (MIBC), 6 (40.0%) were treated with radical cystectomy, 5 (33.3%) received trimodal therapy with chemoradiation, and 4 (26.7%) were treated with systemic chemotherapy alone. Despite treatment, 3 patients (5.9%) succumbed to the disease during follow-up (**Table 3**).

To identify factors associated with muscle invasion at diagnosis, a multivariable logistic regression analysis was conducted. The overall model was statistically significant (likelihood-ratio $p = .021$). The analysis revealed that high tumor grade was the only independent predictor of muscle invasion (OR 5.98, 95% CI 1.15–31.10, $p = .034$). Patients with high-grade tumors were nearly six times more likely to have muscle-invasive disease compared to those with low-grade tumors. While other factors were not statistically significant, some trends were notable. Impaired renal function was associated with a nearly four-fold increase in the odds of muscle invasion (OR 3.96), though the confidence interval was wide and included 1.0 (95% CI 0.71–21.95). The effects of age and presence of CIS were minimal, with odds ratios close to 1.0 (Table 4).

DISCUSSION

Bladder tumors that nearly fill the bladder present a unique clinical challenge due to their high rates of muscle invasion, increased recurrence risk, and more aggressive disease progression. Our study demonstrates that these tumors are frequently muscle-invasive at diagnosis (43.1%, as detailed in Table 2), a rate statistically higher than the approximately 25% prevalence reported in population-based bladder-cancer cohorts.[4,8] This difference should be interpreted contextually rather than inferentially, since reference data originate from broader and less advanced populations. These findings align with previous research indicating that tumor size is an independent risk factor for worse oncological outcomes in bladder cancer patients.[7,10] Large bladder tumors have been associated with increased tumor burden, more aggressive histological features (including higher rates of lymphovascular invasion and variant histology),[11-14] and poorer survival rates. Studies suggest that tumors larger than 3 cm have higher recurrence and progression rates.[15,16] In our cohort, the high percentage of muscle-invasive disease at initial TURBT underscores tumor size's pivotal role in disease severity. Recurrence rates in bladder cancer remain a critical concern, with studies reporting recurrence in up to 60% of cases within the first year.[17,18] Correspondingly, 31.1% of patients with initially diagnosed T1 disease progressed to T2 upon repeat TURBT, underscoring the necessity of early re-TURBT in patients with large tumors—a practice reinforced in the literature, where nearly 30% of patients initially staged as T1 are found to have muscle invasion upon re-evaluation.[19]

Table 4. Multivariate analysis of the predictor of muscle invasive disease at first operation.

Variable	Odds Ratio (OR)	95% Confidence Interval (CI)	*P*-value
Age	1.05	0.98 – 1.12	.152
Sex (Male vs. Female)	1.18	0.11 – 12.34	.891
CIS (Present vs. Absent)	8.15	0.52 – 127.21	.134
Grade (High vs. Low)	5.98	1.15 – 31.10	.034
Renal Function (Impaired vs. Normal)	2.56	0.64 – 10.16	.181

Abbreviations: CIS, carcinoma in situ; TURBT, transurethral resection of bladder tumor; OR, odds ratio; CI, confidence interval.

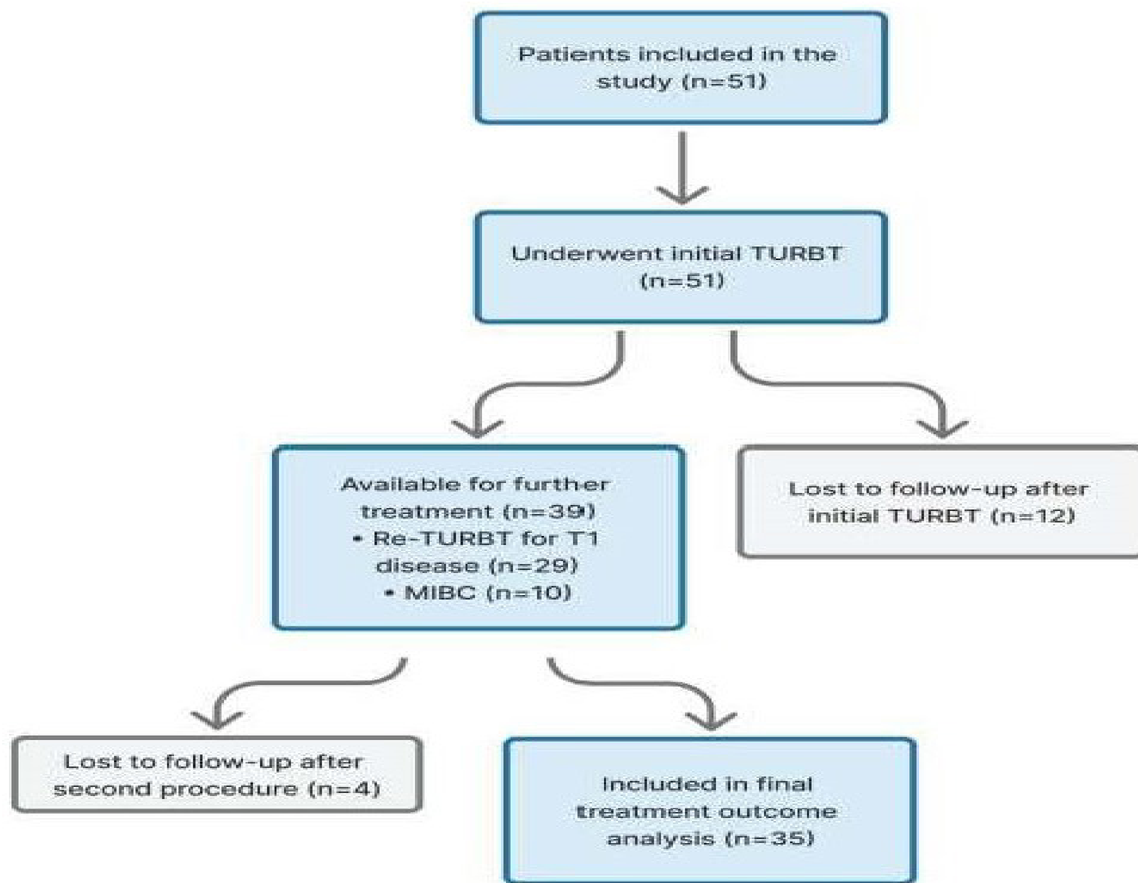

Figure 1. Flow diagram for the study.

Despite complete TURBT being achieved in 68.6% of patients in a single session, the remaining required a second session, highlighting the technical difficulty in resecting large tumors. Studies have demonstrated that incomplete resection is associated with significantly higher recurrence and progression risks.[20] The European Association of Urology (EAU) recommends complete resection whenever possible, but in cases of large tumors, radical cystectomy is often considered earlier in the disease course.[4] In our cohort, 25.7% of patients underwent radical cystectomy, a proportion comparable to large-scale studies evaluating muscle-invasive bladder cancer treatment patterns,[21] and consistent with findings that patients with large bladder tumors often require early cystectomy due to high recurrence and progression rates.[22] Additionally, recent evidence suggests that bladder-preserving approaches, such as trimodal therapy (TMT) with chemoradiation, may be effective in select patients with large tumors;[23] however, long-term survival outcomes remain uncertain.

Our study found that 48.6% of patients received intravesical BCG therapy following TURBT. The efficacy of BCG in large tumors remains a topic of debate, with some studies indicating reduced efficacy due to higher tumor burden and increased likelihood of BCG failure. A recent analysis demonstrated that the response rates to BCG in large tumors are significantly lower than those in smaller tumors, suggesting a need for alternative treatment strategies in this subgroup.[24]

For patients with muscle-invasive disease, systemic chemotherapy was administered to 14.3% in conjunction with radiotherapy and 11.4% as monotherapy. The role of neoadjuvant chemotherapy (NAC) in bladder cancer management has been widely studied, with recent meta-analyses indicating a 5–10% absolute survival benefit.[25] However, there is emerging evidence that large tumors may exhibit intrinsic resistance to systemic chemotherapy, necessitating personalized therapeutic approaches.[26]

A significant proportion of our patients (33.3%) had impaired renal function (eGFR < 60 mL/min/1.73 m²), a factor that can impact treatment choices. Previous research has shown that renal insufficiency is common in bladder cancer patients due to chronic obstruction, hydronephrosis, and advanced age. This is particularly relevant in the context of chemotherapy selection, as renal dysfunction limits the use of cisplatin-based regimens, which remain the standard for muscle-invasive disease.[27]

Renal function impairment represents the most frequent cause of cisplatin ineligibility, affecting up to 30–50% of patients with muscle-invasive or metastatic urothelial carcinoma. According to the Galsky criteria, an eGFR or creatinine clearance below 60 mL/min is sufficient to preclude cisplatin-based chemotherapy, leading to undertreatment in a substantial proportion of patients.[28] For cisplatin-ineligible individuals, alternatives such as gemcitabine–carboplatin or immune checkpoint inhibitors (e.g., pembrolizumab, nivolumab, or the enfortumab vedotin–pembrolizumab combination) have

emerged as effective and better-tolerated options in recent trials.[29]

Additionally, 19.6% of our patients required preoperative erythrocyte transfusion, suggesting a high burden of tumor-related anemia. Large bladder tumors are associated with increased bleeding risks, necessitating closer perioperative monitoring and optimization. A study reported that patients with large tumors frequently experience higher rates of perioperative complications, including prolonged hospital stays and increased transfusion requirements.[30]

This study has several limitations. Its retrospective and single-center design may limit the generalizability of the findings. The intraoperative assessment used to define tumors “nearly filling the bladder” was subjective, and standardized imaging-based size measurements were not applied. Adjusted multivariable analyses were limited by the modest sample size. The follow-up period was relatively short and variable, and loss to follow-up in 16 (31.4%) patients introduces potential attrition bias. These factors should be considered when interpreting the results, and future prospective multicenter studies with objective volumetric criteria and standardized follow-up are warranted.

CONCLUSIONS

Our findings confirm that bladder tumors occupying nearly the entire bladder cavity are associated with increased rates of muscle invasion, recurrence, and progression. These tumors pose significant challenges in surgical resection, disease monitoring, and treatment response. Therefore, our results support the consideration of multimodal treatment approaches, including early radical cystectomy and systemic therapies, for optimal patient outcomes. Future research should focus on developing personalized treatment strategies to improve survival outcomes in this high-risk patient population through larger, prospective studies.

SUMMARY

Patients with very large bladder tumors have a higher risk of aggressive forms of cancer and complications. Early detection, aggressive treatment, and careful follow-up are crucial for improving outcomes in these challenging cases.

CONFLICT OF INTEREST

The authors report no conflict of interest.

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