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Influence of tumor characteristics (Lesion type, stage, grade) on postoperative outcomes following holmium laser resection – A cross-sectional observational study.

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Abstract

Background
Transurethral resection of the bladder tumor (TURBT) is the usual treatment for these tumors, which is followed by further intravesical chemotherapy or immunotherapy. But problems, including bleeding, obturator nerve reflex (ONR), and bladder perforation, are linked to TURBT.
Objectives- The study primarily evaluated the impact of tumor attributes, including lesion kind, stage, and grade, on the results of surgery after Holmium laser resection.

Materials and methods
It was a cross-sectional, observational study. The study was carried out in the Department of Urology, Mahatma Gandhi Medical College and Research Institute, Puducherry, India. The study was conducted for one and a half years, that is, from December 2021 to Jun 2023. In all, 24 patients were enrolled.

Results
Seven patients (29.2%) had numerous lesions, compared to the majority of 17 patients (70.8%) who had single lesions. Ten (41.7%) patients had high-grade cancers, whereas 14 (58.3%) patients had low-grade tumors. With a p-value of 0.017, patients with many lesions needed many more analgesic vials after surgery. Catheterization time, hospital stay, analgesic use, and operation time did not significantly change between the T1 and Ta stages.

Conclusion
This study demonstrates that among the various tumor characteristics evaluated, only the presence of multiple lesions significantly influenced postoperative outcomes, specifically resulting in increased analgesic requirements.

Recommendations
Larger, multicenter studies are recommended to validate these findings and assess long-term outcomes.

Keywords: *Tumor, Bladder, Holmium Laser, Outcomes, Transurethral resection of the bladder tumor*
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Introduction

The most common type of cancer found in the urinary system is bladder cancer. Ninety percent of bladder cancers are urothelial carcinomas, the most common histologic type in the US and Europe. Non-urothelial carcinomas, however,

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are more prevalent in other parts of the world. Furthermore, though they are less common, urothelial malignancies can also arise in the ureter, urethra, or renal pelvis [1].

Transurethral resection of the bladder tumor (TURBT) is the usual treatment for these tumors, which is followed by further intravesical chemotherapy or immunotherapy. But problems, including bleeding, obturator nerve reflex (ONR), and bladder perforation, are linked to TURBT. To improve the safety and efficacy of TURBT, substitute techniques such as laser surgery and bipolar plasma kinetics have been created. Because laser treatments don't pierce deeply, they cause less pain and bleeding. Additionally, depending on the tumor's size, the laser strength can be changed [2, 3].

There are some hazards associated with conventional transurethral resection of bladder tumors (CM-TURBT), especially when lateral bladder wall tumors are included. One of these dangers is that ONR may occur during surgery, which could result in a bladder perforation. When lateral tumors are removed by TURBT, the current flow through the obturator nerve may cause ONR, which can cause the bladder to perforate and cause abrupt muscular contractions. Thermal injuries can also result from CM-TURBT's high temperature range of 100°C to 300°C at the treatment site [4].

However, when the tumor tissue is removed using laser procedures, no current flows during the treatment; therefore, the obturator nerve is not stimulated. For individuals with tumors in the lateral bladder wall and non-muscle-invasive bladder cancer (NMIBC), this is particularly beneficial. Thus, the use of laser methods helps prevent ONR-induced bladder perforation [5,6].

The study primarily evaluated the impact of tumor attributes, including lesion kind, stage, and grade, on the results of surgery after Holmium laser resection.

Methodology

Study design

This was a cross-sectional, observational study conducted to assess the outcomes of en bloc laser resection for superficial bladder tumors.

Study setting

The study was carried out in the Department of Urology at Mahatma Gandhi Medical College and Research Institute, Puducherry, India. This is a tertiary care teaching hospital providing specialized urological services, including diagnostic imaging, surgical interventions, and follow-up care for bladder cancer patients. The study was conducted throughout one and a half years, from December 2021 to June 2023.

Sample size and procedure

A total of 24 patients were enrolled in the study. All patients were over the age of 18 and had a diagnosis of superficial bladder tumor (Tis, Ta, T1 N0 M0) confirmed by imaging and cystoscopic examination. The sample size was determined based on the number of eligible cases presenting to the department during the study period, given the strict inclusion and exclusion criteria and the relatively low prevalence of cases requiring this specific surgical technique at the center.

Inclusion and exclusion criteria

Inclusion criteria

- Patients aged >18 years.
- Diagnosed with superficial bladder tumor (Tis, Ta, T1 N0 M0) without evidence of extravesical extension, lymphatic metastasis, or invasion of nearby organs.

Exclusion criteria

- History of tumors or prior anti-tumor therapy.
- Severe systemic diseases (e.g., severe infections, renal or liver disease).
- Other urological conditions such as urethral calculi, prostatic hyperplasia, or urethral stricture.
- Non-papillary, widespread, or muscle-invasive bladder tumors >3 cm.

Data collection

Clinical and pathological staging was done according to the TNM 2017 classification. Diagnosis and staging involved cystoscopy, computed tomography (CT) of the kidney, ureter, and bladder (KUB), ultrasound (USG), and other standard preoperative investigations. Written informed

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consent was obtained in the patient's preferred language before inclusion.

Study procedure

After preoperative clearance, surgeries were performed under spinal or general anesthesia based on the anesthetist's assessment or the patient's preference. A 1 cm safety margin was maintained from the tumor base for en bloc resection. The laser was programmed to deliver a 40–50 Hz frequency with 1–2 Joules of energy. Saline irrigation was used throughout the procedure. After tumor excision, biopsy samples were collected from at least two locations at the mucosal margin and tumor base for histopathological assessment. Postoperatively, a 20F Foley catheter was inserted, and saline irrigation was continued in cases of hematuria until bleeding subsided.

Bias - Potential sources of bias, such as selection bias and reporting bias, were minimized by applying strict inclusion and exclusion criteria and using standardized surgical and diagnostic protocols throughout the study. All patients were operated on by experienced urologists using the same technique and laser parameters to ensure procedural consistency.

Statistical analysis

Descriptive statistics such as means and proportions were calculated for continuous and categorical variables, respectively. The Mann-Whitney U test was used to compare non-parametric variables. A p-value of <0.05 was considered statistically significant. Data were entered in Microsoft Excel 2016 and analyzed using SPSS version 26.0 (IBM Corp., Armonk, NY, USA).

Ethical considerations

The study was approved by the Institutional Ethics Committee of Mahatma Gandhi Medical College and Research Institute, Puducherry, India. Ethical approval was obtained before the commencement of the study.

Results

During the study period, 31 patients were assessed for eligibility. Of these, 4 patients did not meet the inclusion criteria (either due to tumor size >3 cm or muscle-invasive disease), and 3 patients declined to participate. Thus, 24 patients were confirmed eligible and were enrolled in the study. All 24 participants completed the study and were included in the final analysis.

The study included 24 patients with a median age of 62 years (range: 45 to 78 years). Among them, 54.2% (n=13) had diabetes mellitus, 33.3% (n=8) had hypertension, and 20.8% (n=5) had coronary artery disease (CAD), making diabetes mellitus the most common comorbidity. Four patients (16.7%) had no significant comorbidities.

Thirteen (54.2%) patients had diabetes mellitus, eight (33.3%) had hypertension, and five (20.8%) had CAD, making it the most common comorbidity overall. Of the patients, four (16.7%) did not have any serious comorbidities. The study participants' clinical profiles are displayed in Table 1.

Table 1. Clinical profile of study participants

Characteristics	Frequency (n)	Percentage (%)
Symptoms		
Hematuria	14	58.3%
Lower Abdominal Pain	04	16.7%
Frequent Urination	03	12.5%
Incidental Finding	03	12.5%
Smoking Habit		
Smokers	06	25.0%
Non-smokers	18	75.0%
Comorbidities		

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Diabetes Mellitus	13	54.2%
Hypertension	08	33.3%
Coronary Artery Disease (CAD)	05	20.8%
No Comorbidities	04	16.7%

Seven patients (29.2%) had numerous lesions, compared to the majority of 17 patients (70.8%) who had single lesions. Ten (41.7%) patients had high-grade cancers, whereas 14 (58.3%) patients had low-grade tumors. Tumor characteristics among study participants are shown in Table 2.

Table 2. Characteristics of the tumor among study participants

Characteristics	Frequency (n)	Percentage (%)
Type of Lesion		
Single	17	70.8%
Multiple	07	29.2%
Staging of Tumor		
T1	15	62.5%
Ta	09	37.5%
Grading of Tumor		
Low Grade	14	58.3%
High Grade	10	41.7%

With a p-value of 0.017, patients with many lesions needed many more analgesic vials after surgery. Catheterization time, hospital stay, analgesic use, and operation time did not significantly change between the T1 and Ta stages. The effect of tumor features on postoperative outcomes is shown in Table 3.

Table 3. Impact of tumor characteristics on postoperative outcomes

Tumor Characteristic	Postoperative Outcomes	Group	Median (IQR)	P-value
Lesion Type	Catheterization Time (days)	Single	2.00 (1.00–2.50)	0.144
		Multiple	1.00 (1.00–2.00)	
	Hospital Stay (days)	Single	2.00 (1.00–3.00)	0.080
		Multiple	1.00 (1.00–1.00)	
	Analgesic Vials Used	Single	1.00 (1.00–2.00)	0.017
		Multiple	2.00 (2.00–3.00)	
	Operative Time (minutes)	Single	35.00 (27.50–37.50)	0.626
		Multiple	30.00 (25.00–40.00)	
Tumor Stage	Catheterization Time (days)	T1	2.00 (1.00–2.00)	0.655
		Ta	1.00 (1.00–2.00)	

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	Hospital Stay (days)	T1	2.00 (1.00–3.00)	0.350
		Ta	1.00 (1.00–2.00)	
	Analgesic Vials Used	T1	1.00 (1.00–2.00)	0.298
		Ta	2.00 (1.00–3.00)	
	Operative Time (minutes)	T1	30.00 (25.00–35.00)	0.562
		Ta	35.00 (30.00–40.00)	
Tumor Grade	Catheterization Time (days)	Low Grade	2.00 (1.00–2.00)	0.900
		High Grade	1.50 (1.00–2.00)	
	Hospital Stay (days)	Low Grade	2.00 (1.00–3.00)	0.680
		High Grade	1.00 (1.00–2.00)	
	Analgesic Vials Used	Low Grade	1.00 (1.00–2.00)	0.090
		High Grade	2.00 (1.00–3.00)	
	Operative Time (minutes)	Low Grade	30.00 (25.00–35.00)	0.420
		High Grade	35.00 (30.00–40.00)	

Discussion

This study assessed the clinical outcomes of en bloc holmium laser resection in patients with superficial bladder tumors. Hematuria was the most common presenting symptom, and diabetes mellitus was the most frequent comorbidity, followed by hypertension and coronary artery disease. Tumor analysis revealed that most cases involved single lesions, with T1 tumors more common than Ta tumors. Additionally, low-grade tumors were observed slightly more frequently than high-grade tumors.

A significant finding was the higher postoperative analgesic requirement among patients with multiple lesions compared to those with single lesions ($p = 0.017$). However, catheterization time, hospital stay, and operative time did not differ significantly based on lesion type, tumor stage, or tumor grade.

In terms of tumor staging, 37.5% of cases were classified as stage Ta, while 62.5% were classified as stage T1. These findings are comparable to those reported by earlier studies [7], where 44% of cases were at stage T1 and 56% at stage Ta. In contrast, another study [8] reported 50% of cases at stage Ta and 38% at stage T1. Other studies have found a predominance of stage Ta (66.7%) over stage T1 (33.3%), while some have reported a higher proportion of stage Ta (56.9%) and a lower proportion of stage T1 (15.7%) [9,10]. Such variations in staging distribution across studies may be attributed to differences in patient selection criteria, tumor characteristics, and diagnostic approaches.

Regarding tumor grading, 41.7% of tumors in the present study were classified as high grade, while 58.3% were classified as low grade. One study [7] reported a slightly lower proportion of high-grade tumors (33%), whereas another study [8] observed a notably smaller proportion of high-grade tumors (8.5%). These differences could reflect variations in referral patterns, population characteristics, and pathological assessments across different study settings.

The findings of this study are consistent with existing evidence supporting the efficacy of holmium laser resection in the treatment of bladder malignancies [5, 6]. This technique allows for precise tumor excision with excellent hemostatic control, resulting in reduced postoperative bladder irrigation requirements, minimal clot formation, and shorter catheterization durations. The superior coagulative

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properties of the holmium laser contribute to the creation of a nearly bloodless surgical field during tumor resection.
The findings indicate that en bloc holmium laser resection is a safe and effective surgical technique for the management of superficial bladder tumors, with favorable short-term clinical outcomes and minimal postoperative complications. However, variations in tumor characteristics across studies underscore the importance of larger, multicentric studies to further validate these observations.

Generalizability

The findings are specific to a single-center study with a small sample size. Results may not be generalizable to broader populations or different healthcare settings.

Conclusion

This study demonstrates that among the various tumor characteristics evaluated, only the presence of multiple lesions significantly influenced postoperative outcomes, specifically resulting in increased analgesic requirements. Holmium laser en bloc resection appears to be a safe and consistent technique for superficial bladder tumors.

Limitations

There are a couple of significant drawbacks to this study, though. One of the limitations was the small number of patients, which might affect the efficiency and the duration of time.

Recommendations

Further research, including larger-scale studies, is necessary to validate these observations and enhance our understanding of TURBT procedures' efficacy and safety.

List of abbreviations

CT- Computed Tomography
USG- Ultrasonography
NMIBC- Non-muscle-invasive bladder cancer
CAD- Coronary Artery Disease
ONR- Obturator nerve reflex
TURBT- Transurethral resection of the bladder tumor
CM-TURBT- Conventional transurethral resection of bladder tumors

Conflict of interest

The authors declare no competing interests related to this study.

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Author contributions

All authors contributed to the study design, data collection, analysis, and manuscript preparation.
All authors approved the final manuscript.

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