

# The Impact of Smoking in Bladder Cancer Risk-Retrospective Analysis

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**ABSTRACT** **Background:** Cigarette smoking is the most important modifiable risk factor for bladder cancer and is associated with increased incidence, recurrence, and disease progression.

**Objective:** To evaluate the association between smoking exposure and clinicopathological characteristics of bladder cancer in a single-center cohort.

**Methods:** This retrospective observational study included 54 patients diagnosed with bladder cancer and treated at the Clinic of Urology, Prishtina, between January 2000 and March 2026. Demographic data, smoking history, diagnostic procedures, treatment modalities, and histopathological findings were analyzed.

**Results:** All patients were chronic smokers, most of whom initiated smoking during early adolescence. The cohort was predominantly male (92.6%), with a mean age of 63 years. High-grade and muscle-invasive tumors were frequently observed. All patients underwent transurethral resection of bladder tumor (TUR-B), while patients with aggressive disease underwent radical cystectomy.

**Conclusion:** Smoking is strongly associated with both the development and aggressive biological behavior of bladder cancer. Early initiation and prolonged exposure significantly increase risk, emphasizing the importance of smoking cessation strategies.

**Keywords:** Bladder cancer; Smoking; Urothelial carcinoma; TUR-B; Radical cystectomy

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## INTRODUCTION

Cigarette smoking is the strongest and most consistently identified risk factor for bladder cancer, accounting for nearly half of all cases in developed countries. In addition to increasing disease incidence, smoking has been associated with more aggressive tumor biology, higher recurrence rates and increased risk of disease progression. Tobacco-derived carcinogens, including aromatic amines and polycyclic aromatic hydrocarbons, are excreted in urine, resulting in prolonged urothelial exposure and promoting genetic instability and malignant transformation [1–3]. Epidemiological evidence indicates a three- to fourfold increased risk of bladder cancer among smokers, with a long latency period [2]. Both smoking intensity and duration demonstrate a dose–response relationship [4]. Molecular mechanisms include DNA adduct formation and mutations in tumor suppressor genes [2]. Smoking also influences prognosis. In non–muscle-invasive bladder cancer [NMIBC], smoking is associated with increased recurrence and progression risks [5–7]. Smoking cessation has been shown to improve outcomes, although residual risk persists [7,8].

## MATERIALS AND METHODS

**Study design:** this is a retrospective observational cohort study.

**Study population:** A total of 54 patients diagnosed with bladder cancer and treated at the Clinic of Urology, Prishtina, between January 2000 and March 2026 were included. All patients were managed by the same surgical team, ensuring consistency in clinical approach.

## DATA COLLECTION

The following variables were analyzed:

- Smoking history (initiation age, chronic exposure),
- Sociodemographic characteristics,
- Diagnostic imaging,
- Treatment modalities,
- Histopathological findings.

## Diagnostic evaluation

### Patients underwent:

- Abdominal ultrasound examination
- Cystoscopy procedure
- Contrast CT program.

### Pathophysiology:

### Tumors were classified according to:

- WHO classification
- TNM staging system

**Treatment protocol:** all patients initially underwent transurethral resection of bladder tumor (TUR-BT). Radical cystectomy was performed in 19 patients based in pathohistological findings and after written informed consent.

## RESULTS

### Patient's data:

**Male:** 50 (92.6%) / **Female:** 4 (7.4%)

**Mean age:** 63 years (range 39–85 y.o.)

All patients reported long-term tobacco use, with initiation commonly at 14–15 years of age.

### Socialdemographic characteristics:

- **Lower education:** 34 patients / Higher education: 20 patients
- **Urban:** 23 patients / Rural: 31 patients

### Diagnostic findings:

- **Complete imaging (US + cystoscopy + CTU):** 31 patients
- **US + cystoscopy only:** 23 patients

### Treatment findings:

All patients underwent TUR-BT.

### Histopathological findings:

- Predominantly urothelial carcinoma in 23 pttts: high-grade tumors (pT1 G3, pT2 G3).
- 1 ptt: Urothelial carcinoma associated with sarcomatoid differentiation (pT2 G3).
- Urothelial carcinoma in 30 pttts (Ta,T1 Low grade)

A total of 19 pttts with aggressive disease (high-grade and muscle-invasive tumors) underwent radical cystectomy after providing written informed consent [Figure 1-5].

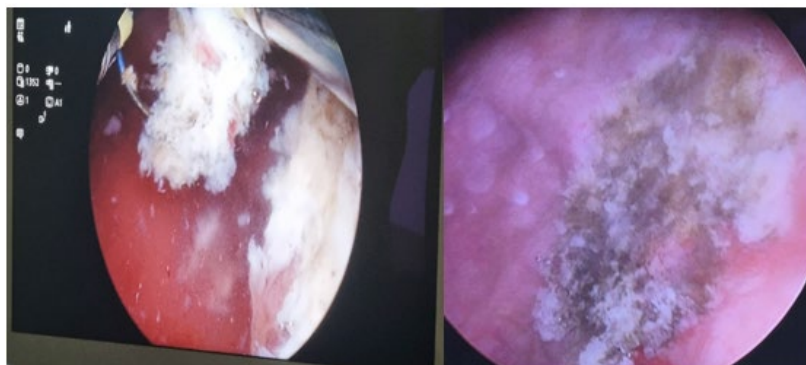


Figure: 1

Figure: 2

Figures 1 and 2: Intraoperative endoscopic view during a transurethral resection of a bladder tumor (TUR-B).

Diagnoza dhe të dhënat klinike Clinical diagnosis and data		Tu vesicæ urinariæ. Tamponata vesicæ urinariæ. Haematuria Opp: TUR-Tu vesicæ urinariæ. Detamponada et evacuatio coagulati vesicæ urinariæ - HP.	
Biopsia (citologjia) e parë apo e përsëritur First biopsy (citology) or repeated		Mjeku: Doctor Prof. Asoc. Dr. Xhevdet Çuni spec. Dr. Dardan Hoxha spz.	
Data e marrjes së materialit Date when was taken the specimen	05.09.25	Data e dërgimit Date of sent	Substanca fiksuese Fixation
Nr. i biopsisë Biopsy number	S / 9 - 25	Pranuar Received	10%FNP Perfunduar Finished
Metoda e ngjyimit Stain	HP	Numri e preparateve Number of slides	seri
<p>1. Mase e resekuar nga tumori i fshikzes urinare                      Janë pranuar materiale indore të fshikzes urinare ne shumë pjesë, me dukje te çrregullta e me madhësi se bashku deri 2x2x1.5 cm, me ngjyrë gri ne kafe te erte, me siperfaqe granulare, konsistencë mesatare. Materiali është procesuar ne tersi per ekzaminim histopatologjik.</p> <p>Histologjikisht ne prerjet serike vrehet nekroze e ekaçgjeruar iskemike hemorragjike tumorale indore me proliferim i epitelit kalimtar, me më shumë se 12 radhë, me qeliza polimorfe, hiperkrome, me aranzhim papillar, solid, tabekular dhe sarkomatoz e shoqeruar me nekroze siperfaqesore dhe detritus qelizor. Ne stromen fibromuskulare vrehen ishuj te qelizave atipike epiteliiale, me aranzhim solid , trabekular dhe sarkomatoz me qeliza atipike epiteliiale, me dukje ovale, boshtore , bizare me berthama hiperkrome. Ne strome vrehet nekroze, kongjestion vaskular, ekstravazate eritrocitare, detritus qelizor, mase e granulociteve, limfociteve dhe monociteve.</p> <p>Dg. Carcinoma urotheliale invasivum - tipi sarkomatoz et necrosis tumoralis ischemica haemorrhaica pT2_Nx_Mx</p>			
Dr. Sci. Ragip Shabani tel: 044 309 030 e-mail: s_ragip@hotmail.com		Prof. Dr. Ragip Shabani spec.	

Figure 3: Pathohistological report: High-grade urothelial carcinoma (G3) with sarcomatoid differentiation associated with extensive necrosis and haemorrhage.

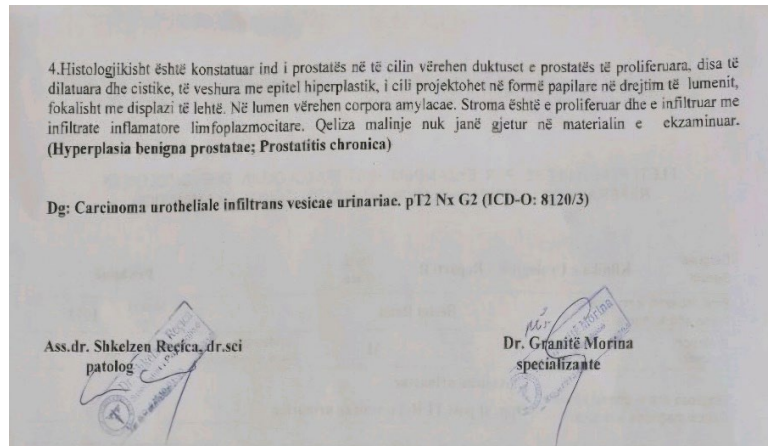


Figure 4: Invasive urothelial carcinoma of the urinary bladder, pathological stage: pT2, Nx, G2 (ICD-O: 8120/3).

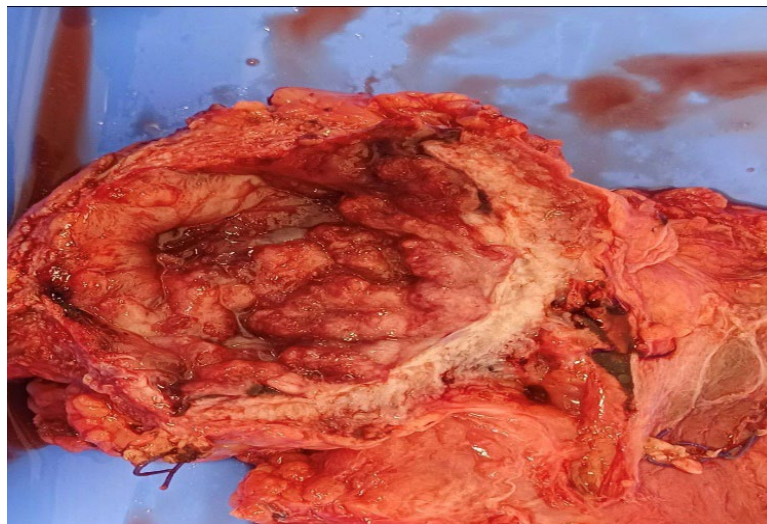


Figure 5: The specimen consists of an opened urinary bladder with attached perivesical soft tissue. On sectioning, there is a large, irregular exophytic tumor mass occupying a substantial portion of the bladder lumen.

## DISCUSSION

Our study confirms a strong association between smoking and bladder cancer, consistent with epidemiological data demonstrating a three- to fourfold increased risk (1–3). A key finding is the early initiation of smoking, supporting previous studies showing increased susceptibility to carcinogens during adolescence (4,5). Smoking was also associated with aggressive tumor characteristics, including high-grade and invasive disease. This aligns with previous findings that smoking contributes to tumor progression and worse outcomes (2,3,6). Rink et al. demonstrated that smoking predicts recurrence and progression in NMIBC (6), while meta-analyses confirm these associations (7). Smoking cessation remains crucial. Evidence shows that quitting reduces recurrence risk (6,8), although risk does not fully normalize.

## STRENGTHS

- Single-center consistency

- Uniform surgical management
- Long observation period

## LIMITATIONS

- Retrospective design
- Small sample size
- Self-reported smoking data
- Lack of environmental exposure analysis

## CONCLUSION

Smoking is a major risk factor for the development and progression of bladder cancer. Our findings highlight the impact of early initiation and prolonged exposure on tumor aggressiveness. Despite study limitations, the results emphasize the importance of smoking cessation as a key component of bladder cancer management and prevention strategies.

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