

# Clinicopathological profile of urothelial carcinoma of the bladder: A five-year retrospective study

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## ABSTRACT

**Background and Objectives.** Urothelial carcinoma of the bladder is more common than urothelial carcinoma of the upper urinary tract. Carcinoma of the bladder is the tenth most common cancer in the world, with 570,000 new cases and 213,000 deaths annually. Men are significantly more likely than women to develop bladder cancer, with an incidence of 9.5 per 100,000 and a mortality of 3.3 per 100,000, which are rates approximately four times those seen among women globally. Clinicopathological profiling is highly significant in bladder carcinoma because the majority of specimens are received through TURBT.

**Materials and Methods.** This observational descriptive study takes a retrospective approach. The population of this study consists of paraffin blocks obtained from biopsy, transurethral resection of bladder tumor, and cystectomy that were used to diagnose urothelial carcinoma of the bladder through histopathological analysis in the Dr. Soetomo General Academic Hospital between January 2018 and December 2022. The demographic and histopathological data were taken from the patients' medical records. **Results.** The majority of patients were men (88%). The average age of the patients was 58.65 years, with a range of 21–80 years and peak incidence occurring at 51–60 years (39%). The procedure most frequently employed was TURBT (68.48%), and squamous differentiation was the most frequent histologic finding (87.5%). The most common type of urothelial carcinoma of the bladder found on urine cytopathology examination was negative for high-grade urothelial carcinoma (81%).

**Conclusions.** The clinicopathological profile is very important in determining the prognostic factor in urothelial carcinoma of the bladder. Most patients herein were men in the age group of 51–60 years. The procedure most frequently employed was TURBT. Most tumors comprised urothelial carcinoma with squamous differentiation, and the majority was negative for high-grade urothelial carcinoma on urine cytopathological examination.

**Keywords:** urothelial carcinoma, bladder, clinicopathology, profile, urine cytopathology

## INTRODUCTION

Carcinoma of the bladder is the most common type of carcinoma, ranking tenth in the world with 570,000 new cases and 213,000 deaths annually. Men are more likely than women to develop urothelial carcinoma of the bladder, with an incidence of 9.5 per 100,000 and mortality of 3.3 per 100,000. These numbers are four

times higher than those for women worldwide. It occurs most frequently in southern Europe (Greece, Spain, Italy), Western Europe (Belgium and the Netherlands), and North America [1].

The morphology of invasive urothelial carcinoma can be recognized in the morphology of other tumors. The invasion of tumor cells into the muscularis propria is a significant factor in the morphological evaluation of

invasive urothelial carcinoma. The understanding of tumor invasion patterns is crucial because this can provide insights into the prognosis [2]. Tumor invasion is characterized by the presence of non-intact basement membranes and the tumor growing into underlying stromal tissue [3]. Squamous differentiation is characterized by the presence of keratinization and/or intercellular bridging [4].

The clinicopathological profile is very important in urothelial carcinoma of the bladder because the majority of specimens received are small [5]. The aim of this study is to identify the clinicopathological profile of urothelial carcinoma of the bladder in patients at Dr. Soetomo General Academic Hospital, Surabaya, Indonesia between January 2018 and December 2022.

## MATERIALS AND METHODS

This observational descriptive study takes a retrospective approach. This study's data were derived from paraffin blocks from biopsy, transurethral resection of bladder tumor (TURBT), and cystectomy materials that were diagnosed through histopathology as urothelial carcinoma of the bladder in the Anatomical Pathology Unit of the Central Laboratory Installation of the Dr. Soetomo General Academic Hospital between January 2018 and December 2022. Urothelial carcinoma of the bladder was identified in 92 patients who met the inclusion criteria during histological examination. The histopathological data herein included the tumor type and the differentiation.

The data on the patients, including their examination number, age, sex, and specimen procedure, in addition to the histopathological diagnoses of invasive urothelial carcinoma of the bladder from biopsy, TURBT, and cystectomy were analyzed herein. Urine cytology diagnosis was analyzed according to the Paris System. The patients who had tumors in other organs and distant metastases were omitted from the analysis, as were patients who had received any type of neoadjuvant and chemotherapy-based systemic treatment. All the data were taken from the patients' medical records.

## RESULTS

The analysis of the data from 2018-2022 demonstrated that 92 patients were diagnosed with urothelial carcinoma of the bladder in the Anatomical Pathology Unit of the Central Laboratory Installation in the Dr. Soetomo General Academic Hospital in Surabaya, Indonesia. This sample comprised 81 (88.04%) men and 11 (11.96%) women, indicating a male-to-female incidence ratio of 7.4:1. The age range of the subjects was 21-80 years, with a mean age of 59.65 years. Peak incidence occurred in those aged 51-60 years (39.13%), followed by those aged 61-67 years (28.26%).

**TABLE 1.** Demographic data of patients with urothelial carcinoma of the bladder

Sex	n = 92
Male	81 (88.04)
Female	11 (11.96)
Age	
21-30 years	1 (1.09)
31-40 years	4 (4.35)
41-50 years	12 (13.04)
51-60 years	36 (39.13)
61-70 years	26 (28.26)
71-80 years	13 (14.13)

Biopsy, TURBT, and cystectomy are interventional procedures used to confirm the diagnosis of invasive urothelial carcinoma of the bladder, the frequency of which is presented in Table 2. The most widely used intervention was TURBT, having been used in 63 cases (68%).

**TABLE 2.** Frequency of surgical procedures used to diagnose urothelial carcinoma of the bladder

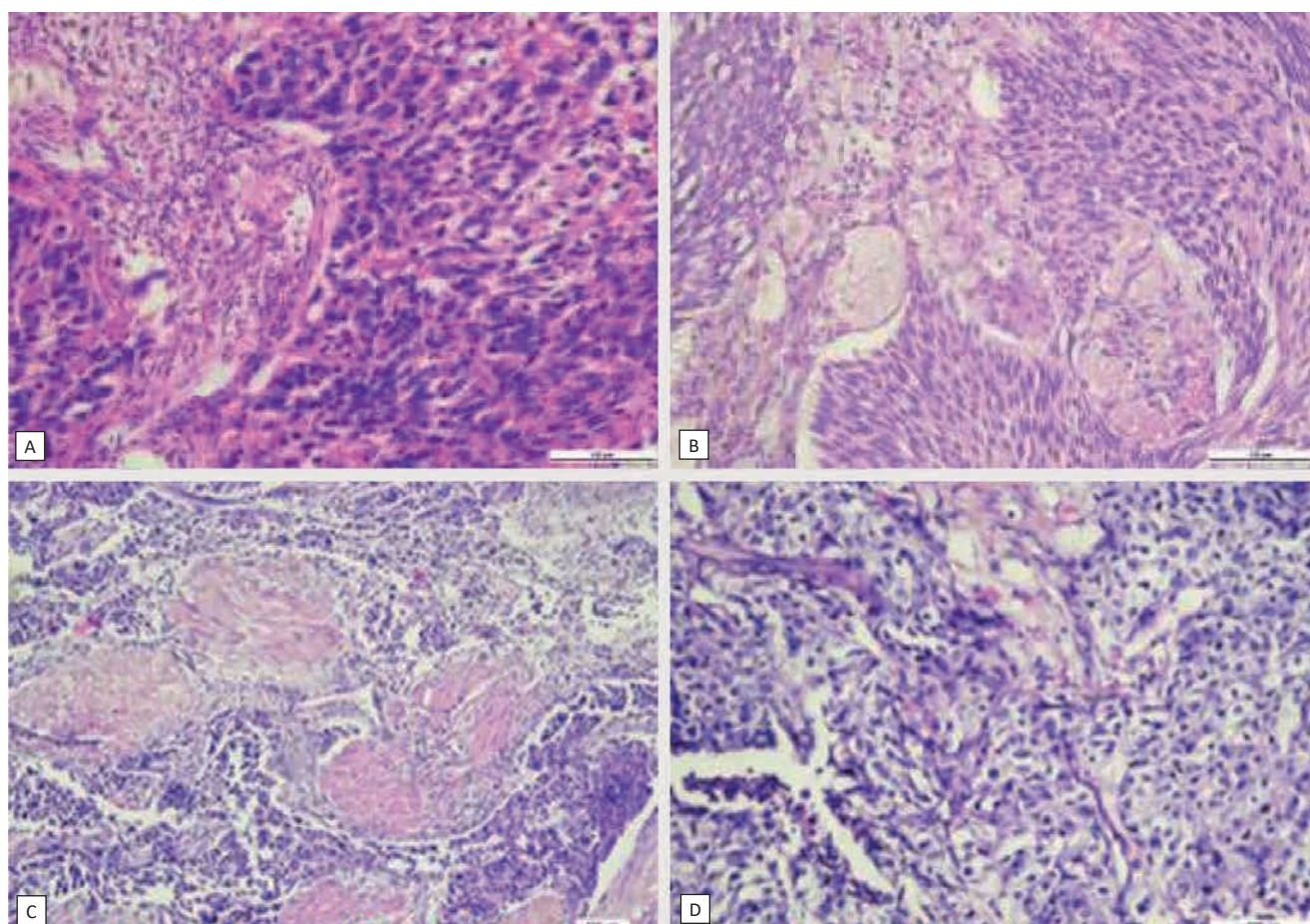
	Surgical procedure	Frequency	Percentage	Valid percentage
Valid	Biopsy	17	18.48	18.48
	TURBT	63	68.48	68.48
	Cystectomy	12	13.04	13.04
Total		92	100	100

Based on the histopathological analysis, all cases of urothelial carcinoma of the bladder in this study involved invasion into the stroma and/or muscularis propria (100%). Of the four types of differentiation seen in urothelial carcinoma of the bladder, two were observed herein: squamous differentiation (92.59%, n=25) and glandular differentiation (7.41%, n=2). No Mullerian or trophoblastic differentiation was observed. The remaining 65 cases could not be graded because the specimens were too small. Figure 1 provides an overview of the differentiation types.

**TABLE 3.** Types of differentiation in urothelial carcinoma of the bladder

Histopathological feature	n
Type of tumor (n = 92) Invasive urothelial carcinoma	92 (100%)
Type of differentiation (n = 27)	
Squamous differentiation	25 (92.59%)
Glandular differentiation	2 (7.41%)
Mullerian differentiation	0
Trophoblastic differentiation	0

Urine cytological examination was also conducted by comparing the outcomes of the histological tissue examinations between patients with invasive urothelial carcinoma of the bladder and then analyzing the patients' prior urine cytology examinations.



**FIGURE 1.** (A, B) Invasive urothelial carcinoma with stromal invasion (200x); (C) invasive urothelial carcinoma with muscularis propria invasion (100x); (D) invasive urothelial carcinoma with squamous differentiation (200x)

Urine cytopathological examination was not conducted on all patients as only 31 patients underwent urine cytopathological examination before the histopathological diagnoses were made. At 25 cases (81%), the majority of the urine cytopathological examinations were negative for high-grade urothelial carcinoma. The results of the urine cytopathological examinations are presented in Table 4.

**TABLE 4.** Urine cytopathology according to the Paris System

Invasive urothelial carcinoma (derived from histopathological examination)	n
	<b>92 (100%)</b>
Urine cytological examination (n = 31)	Frequency
Nondiagnostic	0
Negative for high-grade urothelial carcinoma	25 (80.65%)
Atypical urothelial carcinoma	5 (16.13%)
Suspicious for high-grade urothelial carcinoma	0
High-grade urothelial carcinoma	1 (3.23%)
Low-grade urothelial carcinoma	0
Other	0

## DISCUSSION

In this study, the clinicopathological profile of invasive urothelial carcinoma of the bladder was descrip-

tively assessed. The clinicopathological data comprised the distribution of the number of cases annually over the five-year period reviewed as well as the distribution based on age, sex, surgical procedure, histological differentiation, and outcome of the urine cytopathological examinations.

### Gender

In this study, men accounted for 81 cases (88%) of invasive urothelial carcinoma of the bladder, while women accounted for 11 cases (12%). Thus, the ratio of men to women was 7.4:1. Men worldwide develop invasive urothelial bladder cancer three to four times more frequently than women [4]. This difference could be explained by tobacco usage as up to 50% of both men and women who develop bladder cancer are smokers, which present a significant risk factor. In addition, men and women have different hormonal systems and differing hormonal biology [6,7].

### Age

The age range of the research subjects was 21-80 years, with a mean age of 59.65 years. Peak incidence was found in the group aged 51-60 years (39.13%). In-

vasive urothelial carcinoma of the bladder is typically found in adults over 65, but younger and older people over 70 have been diagnosed with it in the United States [4,6]. Indeed, a study of patients in New York in 2014 found that the group aged 60-70 years saw the highest incidence. Another study by Gree Dalton Grossfeld in Chicago in the same year determined that the most common age for invasive urothelial carcinoma was 70 years [8].

### Histopathological characteristics

Invasion of tumor cells into the stroma and/or muscularis propria informs the diagnosis of invasive urothelial carcinoma. In this study, invasive urothelial carcinoma of the bladder with squamous differentiation was the most common type as it accounted for 25 cases, which was followed by invasive urothelial carcinoma of the bladder with glandular differentiation, which was observed in two cases. Mullerian differentiation and trophoblastic differentiation were not observed herein.

To date, there have been no studies on the type of differentiation of urothelial carcinoma of the bladder. However, studies show that invasive urothelial carcinoma accounts for 95% of urothelial carcinoma of the bladder diagnoses, with squamous cell carcinoma accounting for 3% and adenocarcinoma comprising the remaining 2%. Conversely, Gree Dalton Grossfeld's Chicago study found that urothelial carcinoma accounted for 90%, squamous cell carcinoma comprised 5–10%, and adenocarcinoma accounted for 2% [8].

According to other findings, radical cystectomy is more effective than radiation or TURBT, making it the recommended gold standard treatment for muscle-invasive bladder urothelial carcinoma [9].

### Urine cytopathology

The data from patients with bladder urothelial carcinoma were retrospectively used to compile the urinary cytopathological examination data for this investigation. At 25 cases (81%), the majority of the urine cytology results were negative for high-grade urothelial carcinoma, and the least frequent diagnostic category was high-grade urothelial carcinoma, with one case (3%).

This is contrary to Kagawa's results, which indicate that, when urinary cytology is reported as negative for high-grade urothelial carcinoma according to the Paris System, there is a low probability of high-grade urothelial carcinoma being present. These results support the implementation of the Paris System in clinical practice [10].

Patients can use the following procedure to obtain a urine sample [11]:

1. The first morning urine sample should be collected.
2. The patient must urinate into a sterile container without solution. At least 30mL of midstream urine must be collected.
3. The patient must close the container tightly.
4. The patient must collect three samples over three consecutive days, following the same procedure each time.

There is a discrepancy in the study findings, which is due to practitioners only collecting one urine sample from each patient, resulting in suboptimal outcomes and subpar urine cytology screening results. Collaboration between the pathologist and practitioner is also necessary for obtaining the best possible urine cytopathological examination results, which will aid in determining the diagnosis.

## CONCLUSION

Clinicopathological profiling is very important for determining the prognostic factor in urothelial carcinoma of the bladder. Herein, most of the patients were men aged between 51 and 60 years, and the majority of them were at an advanced stage. The cytopathological examination of the urine determined that the majority of them were negative for high-grade urothelial carcinoma. Collaboration between pathologists and practitioners is required to get the best urine cytopathology examination results, which will aid in.

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