RESEARCH ARTICLE

Histopathological Evaluation of Urothelial Carcinomas in Transurethral Resection Urinary Bladder Tumor Specimens: Eight Years of Single Center Experience

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Abstract

Background: Urothelial carcinoma (UC) is a malignant neoplasm that most commonly occurs in the urinary bladder. The primary aim of this study was to evaluate the clinicopathologic features, recurrence and progression in patients with bladder urothelial cancer. Materials and Methods: The medical records of patients diagnosed with UC in the state pathology laboratory between January 2006 and July 2014 were retrospectively included. Carcinomas were categorized according to age, gender, histologic grade, tumor configuration, pathologic staging, recurrence status, and progression. Results: A total of 125 (113 men, 12 women) patients were examined. The mean age was 65.9 years and the male-to-female urothelial cancer incidence ratio was 9.4:1. Low-grade UCs were observed in 85 (68%) and high-grade in 40 (32%). A papillary tumor pattern was observed in 67.2% of the UCs. Cases were classified with the following pathological grades: 34 (27.2%) cases of pTa, 70 (56%) of pT1, and 21 (16.8%) of pT2. Recurrence occurred in 27 (21.6%) patients. Ten progressed to a higher stage (pT1 to pT2), and three cases to higher grade (low to high). We also analyzed the results separately for 70 (56%) patients 65 years of age and older. Conclusions: With early detection and diagnosis of precursor lesions in older patients, by methods such as standard urologic evaluation, urinary cytology, ultrasound scanning and contrast urography, and cystoscopy, in addition to coordinated efforts between pathologists and urologists, early diagnosis may reduce the morbidity and mortality of patients with urothelial carcinoma.

Keywords: Age - bladder cancer - histologic grade - gender - pathologic stage - progression - recurrence

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Introduction

Worldwide, urinary bladder cancer is the seventh most common malignancy of the urinary tract (Lopez-Beltran et al., 2004)and accounts for approximately 3.2% of all cancers (Parkin et al., 1999). An estimated 74,690 new cases and 15,580 deaths will occur in 2014 in the United States (Siegel et al., 2014). These tumors usually occur in the geriatric population with a male predominance (male to female, ratio; 3.5:1). The median age at the time of diagnosis is 69 years old for men and 71 years old for women (Parkin et al., 1999; Taylor et al., 2009). Epidemiologic studies have reported important risk factors for urinary bladder carcinomas are cigarette-smoking and occupational exposure to aromatic amines. Other risk factors include biomarker/genetic susceptibility, fluid consumption and water pollutants, environmental pollution (arsenic), gender (male), socioeconomic status, coffee consumption, urinary tract disease (stone, inflammation), schistosoma haematobium infection, exposure to ionizing radiation, cyclophosphamide, and other pharmaceutical agents (phenacetin) (Negri et al., 2007; Burger et al., 2013). The most common symptoms and signs are haematuria, pain, dysuria, less often appetite, weight loss, respiratory findings, renal insufficiency either from clinical manifestations locally, advanced or metastatic disease (DeSouza et al., 2014; Shephard et al., 2012). The two man categories of urothelial carcinoma include noninvasive papillary UC, and invasive UC. Urothelial carcinoma (UC) patients have at presentation a limited mucosa-submucosa invasion (superficial, also known nonmuscle invasive) in 80% of patients, as dictated by staging of the primary tumor, pTa and pT1 (Cheng et al., 2012) while 10-20% of newly diagnosed patients present with invasive carcinoma (Eble et al., 2013). Urothelial carcinoma (so-called transitional cell) is the most common type of urinary bladder carcinoma (Lopez-Beltran et al., 2004). The major prognostic factor for urothelial tumors is the histologic grade. A histologic system for classifying urothelial tumors has been proposed; papilloma, papillary neoplasm of low malignant potential, low-grade papillary carcinoma, and high-grade papillary carcinoma (Rosai, 2011). The five year survival rate for patients with noninvasive UC treated with cystectomy is about 78.6%, while UC with invasion of the detrusor muscle is approximately 6-40% (Skinner,

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Table 1. Distribution of Histologic Grade, Pathologic Stage, Mean Age and Gender in Patients with Urothelial Carcinomas (n = 125) of the Urinary Bladder

Histologic grade			Gender		Mean Age (Years)
			Male	Female	Male/Female
Low-grade	Pathologic Staging	pTa	27 (31.80%)	5 (5.90%)	63.9/64.0
		pT1	47 (55.30%)	4 (4.70%)	66.3/74.0
		pT2	2 (2.40%)	0 (0.00%)	75.0/0
		Total	76 (89.40%)	9 (10.60%)	68.4/69.0
High-grade	Pathologic Staging	pTa	1 (2.50%)	1 (2.50%)	80.0/75.0
		pT1	19 (47.50%)	0 (0.00%)	63.4/0
		pT2	17 (42.50%)	2 (5.00%)	66.9/72.0
		Total	37 (92.50%)	3 (7.50%)	70.1/73.5

1977). The recurrence rate after transurethral resection is 30-60%, and 10-15% of patients develop progression with advanced disease (invasion of the muscle) (Vedder et al., 2014). The aim of the present study was to clarify the histopathologic features and patient characteristics of UC diagnosed in urinary bladder specimens.

Materials and Methods

Study design

In this retrospective study, four micrometer thick formalin-fixed and paraffin-embedded sections created from transurethral resection of bladder tumor (TURBT) specimens of patients with urothelial carcinoma were-examined. The specimens were stained with hematoxylin–eosin. We excluded non-invasive papillary urothelial neoplasm of low malignant potential, squamous cell carcinoma, adenocarcinoma, small cell carcinoma and other neoplasms. All samples were obtained from State Hospital's pathology laboratory between January 2006 and July 2014. All cases were categorized according to age, gender, histologic grade, tumor configuration, microscopic tumor extension or pathologic staging (primary tumor, pT), recurrent tumors and patient age; ≤40 years, 41 to 50 years, 51 to 60 years, 61 to 70 years, 71 to 80 years, and >81 years. Histologic grade was categorized as low-grade or high-grade; pathologic staging was categorized as pTa, noninvasive papillary carcinoma; pT1, tumor invades subepithelial connective tissue (lamina propria); pT2, tumor invades muscularis propria (detrusor muscle) according to the classification of the College of American Pathologists (CAP), World Health Organization (WHO) 2004/ International Society of Urologic Pathology (ISUP) Consensus Classification and the tumor node metastasis (TNM) Classification of Malignant Tumours (UICC 2009) (Lopez-Beltran et al., 2004; Sobin et al., 2009; College of American Pathologists, (CAP) 2014).

Statistical analyses

Data were analyzed using Statistical Package for Social Sciences (SPSS) software (version 21.0 for Windows, IBM Corp. Released 2012. IBM SPSS Statistics for Windows, Armonk, NY: IBM Corp.). A student t-test was used to compare averages, a chi-square test was used to determine the dispersion of the two groups (low vs high-grade), and a Kruskal-Wallis-H test was used to determine the dispersion of pathologic staging group. All differences associated with a chance probability of 0.05 or less were considered statistically significant. Continuous variables are presented as mean ± standard deviation (SD).

Table 2. Correlations between Pathologic Stage and Histologic Grade

	PathologicStage			Total
Histologic Grade	pTa	pT1	pT2	
Low-grade	32 (25.6%)	51 (40.8%)	2 (1.6%)	85 (68%)
High-Grade	2 (1.6%)	19 (15.2%)	19 (15.2%)	40 (32%)
Total	34 (27.2%)	70 (56.0%)	21 (16.8%)	125(100%)

Results

Patient characteristics

A total of 125 carcinomas of the urinary bladder with histologic urothelial carcinoma (UC, transitional cell) in cases examined between January 2006 and July 2014 were reported.

Age

The mean age of the patients was 65.96 ± 12.1 years (range 37 to 88 years). The median age detected in men for UC was 65.58 years, and in women was 69.58 years. Distribution of cases among age groups was: ≤40 years, 1.6%; 41 to 50 years, 9.6%; 51 to 60 years, 23.2%; 61 to 70 years, 25.6%; 71 to 80 years, 25.6%; and >81 years, 14.4%. Cases ≤60 years of age comprised 34.4% of patients, while ≥61 years of age comprised 65.6% of patients. No statistically significant difference was found between age or age groups and histologic grade or pathologic staging (P=0.968, 0.318, 0.986, 0.394, respectively).

Gender

There were 113 male (90.4%) and 12 female (9.6%) cases in this study. No differences could be shown between the histologic grade and pathologic staging with respect to gender (P=0.588, 0.205, respectively).

Histologic grade

Low-grade UCs (LGUCs) were detected in 85 (68%) cases while high-grade UCs were identified in 40 (32%) of the cases (see Table 1, 2, 3). LGUCs were encountered in 85 of 125 patients, including 32 (37.6%) with pTa; HGUCs were encountered in all patients, including 19 (47.5%), and 19 (47.5%) with pT1 or pT2, respectively. A statistically significant correlation between histologic grade and pathological staging was observed (P=0.000).

Table 3. Distribution of Histologic Grade, Pathologic Stage, and Age group in Patients with Urothelial Carcinomas (n=125) of the Urinary Bladder

Histologic Grade			Age Group <64 year n (%)	Age Group ≥65 year n (%)	Total n (%)
Low-grade	Pathologic Stage	pTa	15 (17.6%)	17 (20%)	32 (37.6%)
		pT1	23 (27.1%)	28 (32.9%)	51 (60%)
		pT2	0 (0%)	2 (2.4%)	2 (2.4%)
	Total		38 (44,7%)	47 (55.3%)	85 (100%)
High-grade	Pathologic Stage	pTa	0 (0%)	2 (5%)	2 (5%)
		pT1	8 (20%)	11 (27.5%)	19 (47.5%)
		pT2	9 (22.5%)	10 (25%)	19 (47.5%)
	Total		17 (42.5%)	23 (57.5%)	40 (100%)
Total	Pathologic Stage	pTa	15 (12%)	19 (15.2%)	34 (27.2%)
		pT1	31 (24.8%)	39 (31.2%)	70 (56%)
		pT2	9 (7.2%)	12 (9.6%)	21 (16.8%)
	Total		55 (44%)	70 (56%)	125 (100%)

Tumor configuration

The vast majority of tumors exhibited a papillary configuration (67.2%), and less often a solid/nodule, or mixed (papillary and solid) configuration. Tumors with a predominantly papillary configuration were found in 88.2% of all patients in pTa, in 67.1% of all patients pT1, in 33.3% of all patients with pT2, in 78.8% of all patients with low-grade malignancy, and in 42.5% of all patients high-grade malignancy (Figures 1a, 1b). There was also a significant correlation between tumor configuration and histologic grade or pathologic staging (P=0.004, 0.000, respectively).

Pathologic staging (primary Tumor, pT)

pTa (noninvasive papillary carcinoma) was observed in 34 (27.2%) cases, pT1 (tumor invades subepithelial connective tissue (lamina propria)) and pT2 (tumor invades muscularis propria (detrusor muscle)) in 70 (56%) cases and, 21 (16.8%) patientscases, respectively. Thirty-four patients (27.2%) found to havewith UC wereas classified diagnosed with noninvasive carcinoma, 91 (72.8%) patients were diagnosed with (72.8%) invasive carcinoma (lamina propria invasion, muscularis propria-detrusor muscle invasion) and 104 (83.2%) patients (83.2%) with nonmuscle invasive bladder cancer (Figure 1c). Of those, noninvasive carcinoma occurred in 34 of 125 patients (27.7%), including 32 (25.6%) LGUC, and two2 (1.6%) with HGUC. Invasive carcinoma was encountered in 91 of 125 patients (72.8%), including 53 (42.4%) with LGUC, and 38 (30.4%) with HGUC. A correlation was detected between invasive status and histologic grade of tumor (P=0.000). Muscle invasive urothelial carcinoma was more common in males than in females (15.2% and 1.6%, P=0.052).

Patient characteristics of recurrent tumors

Recurrence was observed in 27 of the 125 (21.6%) patients in all tumors; however, 98 (78.4%) patients did not have a recurrence (Table 4). The mean age of patients was 67.4 ± 12.6 (range 37 to 86) years old. Recurrent UC was observed in 21 (77.8%) of the males and in six (22.2%) of the female cases in this study. There was a correlation or significant statistical association between recurrent tumors and gender (P=0.012). Low-grade UC had a recurrence

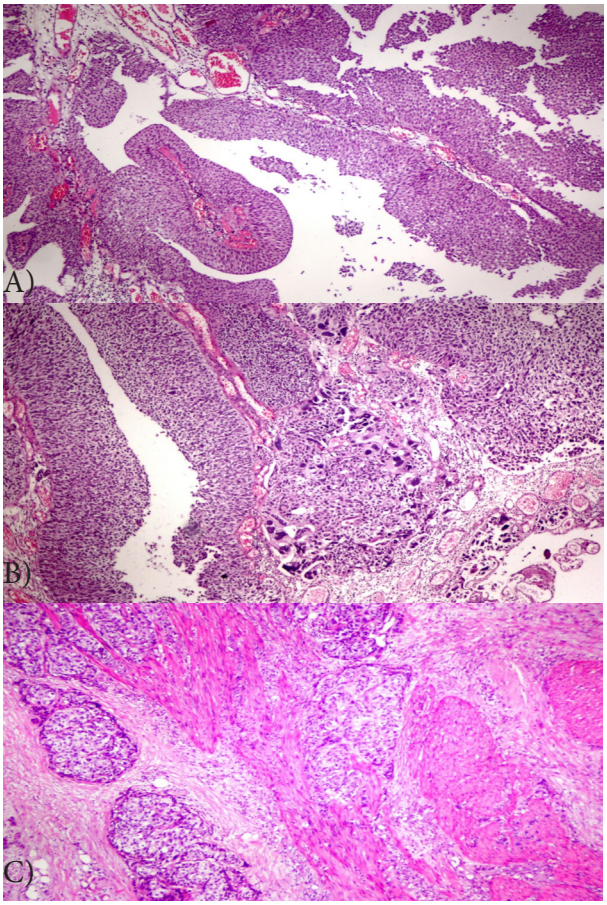

Figure 1. Urothelial Carcinomas. A) Low-grade papillary, Pathologic Staging, pTa;noninvasive (Hematoxylin-Eosin, original magnification ×40 objective). B) High-grade urothelial carcinoma, papillary, Pathologic Staging, pT1; tumor invades subepithelial connective tissue-lamina propria (Hematoxylin-Eosin, original magnification ×40 objective). **C)** Pathologic Staging, pT2: Tumor invades muscularis propria (detrusor muscle) (Hematoxylin-Eosin, original magnification ×100 objective)

in 19 cases (70.4%) and high-grade UC had a recurrence in 8 (29.6%). Tumor recurrences were observed in pTa, pT1 and pT2 in 10 (37%), 16 (59.3%), 1 (3.7%) case, respectively. There was a significant correlation between recurrent bladder cancer and pathologic staging (P=0.040). No statistically different relationship was found between

recurrent disease and histologic grade of tumor (P= 0.768). Twenty-three (85.2%) patients had one recurrence, three (11.1%) patients had two recurrences, and one (3.7%) patient had three recurrences. The mean count of episodes was 1.18.

Recurrence of year

Cases of UC were recorded during an eight-year period. Recurrence of UC within ≤1 year following the first transurethral resection was seen in 15 (55.6%) patients and >1 year in 12 (44.4%) patients. The mean process time to first recurrence at follow-up was 11.9 months (minimum 1, maximum 36 months). Cases with UC recurrence had a rate of 81.5% at the 24 month follow-up period. All patients had no evidence of extravesical extension, no metastasis and no evidence of death. The association recurrence for the years and also pathologic staging were statistically significant (P=0.028). There was no correlation between recurrence for years and histologic grade (P=0.510).

Stage or grade progression

Ten patients (37%, all total recurrent cases) were diagnosed as having tumour progression from pT1 carcinomas to pT2 carcinomas in later transurethral resections. Three patients showed progression from a low to high grade tumor. In two patients with tumour recurrence, the tumor progressed to muscle invasion.

Older patients (≥65 years)

We analyzed the results in 70 patients (56%) 65 years of age and older. Low-grade and high-grade UC was found approximately in 67.1% and 32.9% of older patients, respectively. Nineteen patients (27.1%) were pTa and 39 patients (55.7%) were pT1 and 12 patients (17.1%) were pT2. There were 69.6% (18/27 cases) with recurrent bladder carcinoma who were 65 years of age and older. No statistically significant relationship was found between older patients and histologic grade of tumor, pathologic staging and recurrence (P=0.819, 0.939, 0.210, respectively). Analysis according to tumor histology showed a trend; the elderly (>81 years) patients had outcomes were noted with low-grade histology 13 patients (10.4%) and high-grade histology 5 patients (4%). Four patients (3.2%) were pTa and 9 patients (7.2%) were pT1 and 5 patients (4%) were pT2.

Table 4. Clinicopathologic Features and Tumor Recurrences

		Age Group	
		<64 yrs	≥65 yrs
		n	n
Gender	Male	8	13
	Female	1	5
Pathologic Staging	pTa	4	6
	pT1	5	11
	pT2	0	1
Histologic Grade	Low-grade	5	14
	High-grade	4	4
Interval to recurrencemonths	<12 months	6	9
	12-24 months	2	5
	>24 months	1	4
Progression pT	No	4	13
	Progression	5	5
Progression HG	No	9	15
	Progression	0	3
Muscularispropria (detrusor muscle)	Not identified	2	5
	Present	7	13

Adequacy of material to identify muscularis propria (detrusor muscle)

Muscularis propria (detrusor muscle) was identified in 97 (77.6%) transurethral resection specimens in total and the muscularis propria was not identified in 28 (22.4%) cases. The muscularis propria was absent in 1/28 (3.5%) high-grade Ta and 18/28 (64%) T1 specimens.

Discussion

Urothelial carcinoma is the most common carcinoma of the urinary bladder, accounting for more than 90% of all primary carcinomas (Lopez-Beltran et al., 2004). Urinary bladder cancer has the fourth highest new cases of cancer diagnosed in men in 2014 in the United States (Siegel et al., 2014) and the seventeenth most frequently diagnosed cancer in women worldwide (Kakehi et al., 2010). In European Union countries, the mortality rate in men is 7.2 to 6.1/100,000 and in women approximately 1.3/100,000 (La Vecchia et al., 2010). The major risk factor for developing bladder cancer is cigarette smoking in a dose-dependent for both sexes (Burch et al., 1989), with an four-fold increased incidence compared to nonsmokers. Occupational polycyclic aromatic hydrocarbons are also responsible for approximately twenty percent of bladder cancer (Chu et al., 2013). Occupational hazards are one of several risks in the development of bladder cancer. An increased risk of urinary bladder carcinoma as an occupational risk for workers (eg, dye, rubber, leather, aluminum) have been reported (Silverman et al., 1992). The incidence of bladder cancer is predominantly seen more in men than women (Lippka et al., 2013). Investigations on this subject are numerous and clear data is available. Horstmann et al reported the incidence of urinary bladder cancer male-to-female ratio to be 2:1 (Horstmann et al., 2008), Hoke et al observed this ratio to be 1.33 to 1 (Hoke et al., 1999)while Quirk et al and Koyuncuer demonstrated the ratio of male-to-female patients to be 3.2:1, 3.76:1 respectively (Quirk et al., 2004). Thus, the ratio of male to women often differs between studies. Gupta et al reported a male to female ratio of 8.6:1 (Gupta et al., 2009). In our study, gender differences were seen in men more than women, with their onset being closer to those mentioned in the Gupta et al. In our study, we found, an overwhelming incidence in men, with a male:female ratio of 9.4:1. As far as we know, bladder cancer occurs almost exclusively in the geriatric population. Urinary bladder cancer tends to occur in the elderly (Hoke et al., 1999), but it does occur in young adults (Nomikos et al., 2011), and pediatric cases have also been reported (Stanton et al., 2013; Wang ZH et al., 2012). In a previous study, Horstmann et al. reported the mean age in males to be 62, and females to be 67; Hoke

et al observed the mean age in males to be 74.2, and in women to be 67.3, Gupta et al,Quirk et al and Koyuncuer described that men age 60.2, 65.3, 62.9 respectively (Hoke et al., 1999; Quirk et al., 2004; Horstmann et al., 2008; Gupta et al., 2009; Koyuncuer, 2013). In our study, urothelial carcinoma presentation had a mean age 65.9 (men, women mean age: 65.9 years vs 69 years, respectively) similar to that reported in the literature. In a recent study, researchers found 44.7% of UC cases to be a low-grade malignancy and 55.3% to be a high-grade malignancy (Gupta et al., 2009)and, Cheng and colleagues examined 105 transurethral resections of bladder tumor (TURBT) specimen and found 12.3% patients to have low-grade carcinoma 87.7% to have high-grade carcinoma (Cheng et al., 2000).

In our study, low-grade UC was seen in more than half of the cases, and thus our rates were different from the literature findings. The results were contrary to the neoplastic conditions of the urinary bladder of several previous published studies. Pan et al found low to high grade urothelial carcinoma that accounted for 46.6% and 39.4% in transurethral resection specimens, respectively (Pan et al., 2010). In another series, 77.8% of low grade papillary UC and 22.2% of high grade papillary urothelial carcinoma was observed (Koyuncuer, 2013). Oosterhuis et al reported a 75.8% of low grade papillary urothelial carcinoma, 24.2% high grade papillary urothelial carcinoma findings among 186 patients with urothelial carcinoma (Oosterhuis et al., 2002). In our study the rate observed is in accordance with the literature. Low-grade UC was seen in 85 (68%) cases while 40 (32%) cases were high-grade UCs. Low grade tumours, on the other hand, are associated with increased survival or longer cancer free intervals (Schapers et al., 1994). However, Jimenez et al demonstrated that the pathologic T stage was associated with the progression of invasive muscle carcinoma. The authors commented that the histologic grade is not a prognostic indicator for urothelial carcinoma to invade the muscle (Jimenez et al., 2000). The published results concerning a papillary tumor configuration in a given histologic grade have also been reported. Schned et al reported low-grade papillary lesions with a papillary configuration in 60% of tumors and high-grade papillary carcinomas account for 22.6% while non-papillary urothelial carcinoma accounts for 10.1%. The authors also reported that a papillary configuration was seen in LGPUC which accounted for 93.7% in pTa, 6.3% in pT1 or pT2, in HGPUC which accounted for 35.1% in pTa, 64.9% in pT1 or pT2 (Schned et al., 2008). In our study, the papillary tumor configuration was seen at a rate similar to the literature. In our study, we found that the papillary growth pattern of the tumour was detected in 32.9% of pTa, in 45.9% of pT1 of all LGPUC and in 5% of pTa, in 20% of pT1, in 17.5% of pT2 of all HGPUC. Mostofi et al argued that the growth pattern of the tumour serves as a prognostic factor. Papillary carcinoma throughout have a particularly favorable prognosis as compared to an infiltrating and mixed growth pattern (Mostofi et al., 1973). Tumor configuration with an infiltrative pattern also has a poor prognosis (Lopez-Beltran et al., 2004). Andius and colleagues showed that a stage T1 bladder cancer with a solid tumor configuration relationship has a higher risk of progression and poor prognosis (Andius et al., 2007). As previously noted, microscopic tumor extension (or pathologic staging) in TURBT specimens with bladder cancer has been reported, in 14.3% (15 cases) with pTa carcinoma, in 52.4% (55 cases) with pT1 carcinoma and 33.3% (35 cases) with pT2 carcinoma (Cheng et al., 2000). In our study, pT1 was seen in more than half of the cases, and thus our rates were similar to the literature findings. In our study, over seventy-seven percent of patients with invasive carcinoma are pT1 in contrast to twenty three percent of the patients with pT2. However, Choi et al observed pathologic staging in TURBT and cystectomy pathology results, in 41.5% with pTa carcinoma, in 21.5% with pT1 carcinoma and 14% with pT2 carcinoma (Choi et al., 2007). The recurrence and progression rate with respect to urinary bladder carcinoma is also variable in the published series. In a recent study by Chamie and colleagues, they observed bladder cancer recurrence rates of 39.1% and a rate of progression of 33%. In the same study, the ten-year recurrence, progression and mortality was 74.3%, 33.3%, and 12.3%, respectively (Chamie et al., 2013). Superficial bladder cancer (pTa,pT1) has a documented recurrence rate of 50.8% (Akagashi et al., 2006). Herr et al reported that low grade papillary bladder tumors show a mean number of recurrence episodes of 6.6 and observed a 67% recurrence rate. The authors observed a 17% progression rate grade or stage obtained in 215 cases treated (Herr et al., 2007).

In a literature review of several reports of low-grade papillary urothelial carcinoma, recurrence rates range from 34-72% and progression rates range from 4-10.5%; for high-grade urothelial carcinoma, recurrence rates range from 43-74%. Miyamoto et al recently reported that low-grade urothelial carcinoma had a higher rate (53.8%) of recurrence. In the same study, the mean period at diagnosis of recurrence and progression was 13.9 months (2 months to 72 months) and 25.1 months, respectively (Miyamoto H et al., 2010). In another study, the recurrence and progression rate was 37%, 0% and 54%, 15% for low grade and high grade superficial bladder cancer, respectively (Millán-Rodríguez et al., 2000). Alsheikh and colleagues detected 48.2% of the low-grade papillary carcinoma in series recurred (four months to seven years) and two of the patients had a grade progression and two of the patients had invasion of the muscle (Alsheikh et al., 2001). On the other hand, in the literature it was shown that nonmuscle invasive bladder cancer is associated with a higher risk of one year and five year recurrence rate of 15-61% and 31-78%, respectively (van der Heijden et al., 2009). In our series, 21.6% of the urothelial carcinomas exhibited a recurrence; recurrence tumors had a progression rate of 37%. In our study, the recurrence, progression and mean course of time to first recurrence was seen at a rate in accordance with the literature. Several factors are thought to contribute to the development of this recurrence, including incomplete TUR, implantation of tumour cells, de novo or new tumor and other factors (van der Heijden et al., 2009; Bryan et al., 2010). We believe this is a reason for the early recurrence of urothelial carcinoma both for predominantly

incomplete TUR (residual tumour) and de novo or new tumours. More than half of the patients in our series had a recurrence occur at less than one year after transection. In a study of 30% cases, patients' age ranged from 70-80 years, and 6% of patients were more than 80 years old having undergone a radical cystectomy for bladder cancer (Nielsen et al., 2007). In another study of 404 patients with radical cystectomy for bladder carcinoma, the median age was 74 years, with 87% of patients being between 70-79 years and 13% being more than 80 years old (Figueroa AJ et al., 1998). Therefore, we found patients to be 65 years and older. On the other hand, patients aged 70 and older have an association with an increased risk of mortality in bladder cancer and in another study, cases aged 70 years and older had a death rate of 2.8% (Chamie et al., 2013; Figueroa et al., 1998). In our study, 22.4% of the cases did not demonstrate a muscularis propria in their TUR specimen and their rate was different compared to published studies. If muscle was present in the sample, 2 pT1 specimens were upstaged in all cases of progression. Maruniak et al reported the detrusor muscle was not identified in 51% of cases (Maruniak et al., 2002).

In conclusion, the mortality rate is low today, owing to the fact that scientists are conducting extensive research and exhaustive investigations in this field. In our study, the overwhelming majority of urothelial carcinoma is composed of males with a peak incidence in the seventh decade. We believe that this difference likely is due to cigarette smoking and occupational, environmental risks or lifestyle factors. We observed that low-grade UCs and pathologic staging pT1 in all patients was detected in more than half of cases. These results in stage and grade of cancers probably are due to geographic, ethnic differences, tumour heterogeneity or other factors. Low grade carcinoma and stage pT1 bladder cancer were predominant in women. In this study, females were older at the age of detection and but had a low rate of muscle invasion and a lower rate of high grade carcinomas than males. Muscle invasive urothelial carcinoma was more common in males than in females.

This study included two patients in the third decade of life and three patients with low grade carcinomas that progressed to high carcinomas and two patients that progressed to muscle invasion in bladder cancer. However, the study demonstrated that two patients under the age of 40 years presented with pathologic stage Ta, noninvasive and low grade tumors. Recurrent tumors were found more commonly in male than female patients. The grade of recurrent disease was most frequently low grade. The patient's pathology stage or grade such as prognostic factors depends on incomplete or complete TUR. This made five-year survival, especially in the first year, easy to plan for recurrence or progression.

With early detection and diagnosis of precursor lesions in older patients, by methods such as standard urologic evaluation, urinary cytology, ultrasound scanning and contrast urography, and cystoscopy, in addition to coordinated efforts between pathologists and urologists, early diagnosis may reduce the morbidity and mortality of patients with urothelial carcinoma.

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