

ORIGINAL ARTICLE

Urothelial Carcinoma of the Urinary Bladder in Young Adults — Clinical Experience at Taipei Veterans General Hospital

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Background: The clinical behavior and prognosis of bladder cancer in young patients is not well defined. The aim of this study was, therefore, to evaluate the clinical behavior, pathologic characteristics and prognosis of urothelial carcinoma of the urinary bladder in young adults.

Methods: We retrospectively reviewed records from 30 young patients (23 males, 7 females; age \leq 40 years) with urothelial carcinoma of the urinary bladder who had been treated in our hospital between May 1990 and October 2003. Data were analyzed by the Kaplan-Meier method to assess disease recurrence and survival.

Results: The mean age at diagnosis was 34.3 ± 5 years (range, 22–40 years). Fifteen patients presented with pTa, 9 with pT1, 4 with pT2, 1 with pT3, and 1 with pT4. Twenty-six patients (87.2%) had low-grade bladder cancer, and the other 4 had high-grade disease. The most frequent initial presenting symptom was gross hematuria. The mean postoperative follow-up period was 72.8 months (range, 4–149 months). Fifty percent of superficial bladder cancers recurred a mean of 10.7 months (range, 3–68 months) after operation. One patient died from invasive bladder cancer after radical cystectomy, and 1 died from superficial bladder cancer due to tumor progression. The 5-year cancer-specific survival rate was 95.2% for superficial cancer and 83.3% for invasive cancer. The overall survival rate was 93.3%.

Conclusion: Urothelial carcinoma of the urinary bladder in young adults is usually associated with low grade and low stage. Invasive bladder cancer had no worse a survival rate than superficial bladder cancer. [*J Chin Med Assoc* 2005;68(6):272–275]

Key Words: gross hematuria, urinary bladder, urothelial carcinoma

Introduction

Urothelial carcinoma of the bladder in young patients is rare, and less than 1% of such tumors present in the first 4 decades of life.^{1,2} Although the biologic behavior and treatment of bladder cancer has been well studied, conflicting reports exist about clinical behavior and prognosis for patients under 40 years of age. Whether younger patients have a better prognosis than their

older counterparts has long been a subject of debate; indeed, some groups observed similar patterns of clinical behavior and prognosis for bladder cancer in young and older patients,^{1–4} whereas other investigators reported lower rates of disease recurrence and progression, and better survival, in younger patients.^{5–8} In our study, we evaluated presenting symptoms, disease recurrence and survival in patients 40 years old or younger with urothelial carcinoma of the urinary bladder.

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E-mail: ycwen2@vghtpe.gov.tw • Received: June 28, 2004 • Accepted: February 3, 2005

Methods

Study population and protocol

We retrospectively reviewed the charts of 30 consecutive patients, aged 40 years or younger, with bladder cancer treated at our institution between May 1990 and October 2003. Demographic data, initial transurethral resection pathology, recurrence and progression events, intravesical instillation therapy, radical cystectomy data, local and distant recurrence, adjuvant therapies, and disease status, were recorded. The pathologic stage of bladder cancer was assessed according to the tumor-node-metastasis (TNM) classification.⁹ Tumor grade was assessed according to the grading system established by the World Health Organization:¹⁰ grades I and II were categorized as low grade; and grade III as high grade. Patients with non-transitional cell histology, and those with a history of upper urinary tract involvement, were excluded from the study. Disease progression was defined as the conversion, by pathologic stage, of superficial to invasive bladder cancer. Death from bladder cancer, or evidence of local or distant disease recurrence, was classified as treatment failure, and patients who survived without evidence of disease, or who were lost to follow-up, were censored. Survival was defined as the time from initial presentation to the study end point, including death or censoring.

Statistical analyses

Patients were stratified into 2 subgroups according to tumor stage (superficial and invasive). Superficial bladder cancer includes pTa and pT1 tumors. Invasive bladder cancer includes pT2, pT3 and pT4 tumors. For survival analysis, we used 3 end points: disease-specific survival; disease-free recurrence in superficial and invasive bladder cancer; and disease-free progression. The Chi-squared test was used to analyze correlations in the 2 subgroups. Survival curves were plotted using the Kaplan-Meier method, with statistical significance calculated according to the log-rank test. Data were analyzed using SPSS version 11.0 (SPSS Inc, Chicago, IL, USA). A *p* value of less than 0.05 was considered statistically significant.

Results

The mean age of the patients at initial diagnosis was 34.3 ± 5 years (range, 22–40 years), and the male:female ratio was 3.3:1 (23 males, 7 females). The mean follow-up period was 72.8 months (range, 4–149 months). The most common presenting symptoms

were hematuria in 28 patients (93.3%), dysuria in 3 (10%), and flank pain in 2 (6.7%).

Of the 30 patients, 24 (80%) initially had superficial bladder cancer and 6 had invasive bladder cancer. Initial cancer staging was as follows: pTa (*n* = 15), pT1 (9), pT2 (4), pT3 (1), and pT4 (1). There were 26 low-grade and 4 high-grade cases (Table 1). All 24 patients with superficial bladder cancer underwent transurethral resection of bladder tumor. Twenty-two patients (73%) had postoperative intravesical instillation therapy, with mitomycin (*n* = 10), adriamycin (6), epirubicin (3), or thiotepa (1). Six patients with invasive bladder cancer underwent radical cystectomy. Four patients had urinary diversion with a neobladder, 1 with an ileal conduit, and 1 with a Kock pouch. Five patients (83%) with invasive bladder cancer had adjuvant cisplatin-based chemotherapy.

Young adults with urothelial carcinoma of the urinary bladder were divided into 2 age groups. As shown in Table 1, 6 of the 30 patients (20%) were diagnosed at or before age 30 years, and 24 (80%) at age 31–40 years. Among patients aged ≤ 30 years, 5 had stage Ta–T1 disease, and 1 had stage T2b disease. Among patients aged 31–40 years, 19 had stage Ta–T1 disease, and 5 had stage T2–T4 disease. The recurrence rates for superficial bladder cancer in the 2 age groups were 40% (≤ 30 years) and 52.7% (31–40 years) (Table 1). Thus, although no statistically significant differences were identified between the 2 age groups, disease recurrence, especially of superficial bladder cancer, tended to be more common in older than younger patients.

During follow-up, 12 patients (50%) with superficial bladder cancer had a postoperative recurrence within 10.7 months (range, 3–68 months). One patient (16.7%) with invasive bladder cancer had a recurrence within 6 months of operation. The proportion of patients without a recurrence of invasive bladder cancer was 84.4% (Figure 1). One patient died from invasive bladder cancer after cystectomy, and another died from superficial bladder cancer due to tumor progression. The 5-year cancer-specific survival rate was 95.2% for superficial bladder cancer and 83% for invasive bladder cancer. The overall 5-year cancer-specific survival rate was 93.3% (Figure 2).

Discussion

Urothelial carcinoma of the urinary bladder is the most common neoplasm of the urinary tract. The peak incidence occurs in the sixth decade, but the condition is rarely noted in individuals younger than 40 years old, thus giving a reported incidence of about 0.8%.^{1–4}

Table 1. Characteristics of patients treated for bladder cancer

	Age (yr)		Total	p*
	≤ 30	31–40		
Patients, n (%)	6 (20)	24 (80)	30 (100)	
Mean age (range), yr	25.2	36.6	34.3 (22–40)	
Males/females	3/3	20/4	23/7	0.65
Mean follow-up (range), mo	86.7	69.3	72.8 (4–149)	
Stage at presentation, n (%)				1.00
Ta	3	12	15 (50)	
T1	2	7	9 (30)	
T2	1	3	4 (13.4)	
T3		1	1 (3.3)	
T4		1	1 (3.3)	
Type at presentation, n (%)				
Superficial bladder cancer (Ta, T1)	5	19	24 (80)	
Invasive bladder cancer (T2–T4)	1	5	6 (20)	
Grade at presentation, n (%)				0.61
Low	5	21	26 (86.7)	
High	1	3	4 (13.3)	
Intravesical therapy of superficial cancer, n (%)	5/5	17/19	22/24 (91.7)	1.00
Cystectomy, n (%)	1	5	6 (100)	
Adjuvant chemotherapy for invasive cancer, n (%)	0	5	5/6 (83.3)	
Tumor recurrence, n (%)				
Total	2/6 (33.3)	11/24 (45.8)	13/30 (43.3)	
Superficial bladder cancer	2/5 (40)	10/19 (52.7)	12/24 (50.0)	> 0.05
Invasive bladder cancer	0/1 (0)	1/5 (20)	1/6 (16.7)	> 0.05
Tumor progression to invasive cancer, n (%)	0	2	2/24 (8.3)	
Mortality, n (%)				> 0.05
Superficial bladder cancer	0/5 (0)	1/19 (5.3)	1/24 (4.2)	
Invasive bladder cancer	0/1 (0)	1/5 (20)	1/6 (16.7)	

*For 1 age group versus the other.

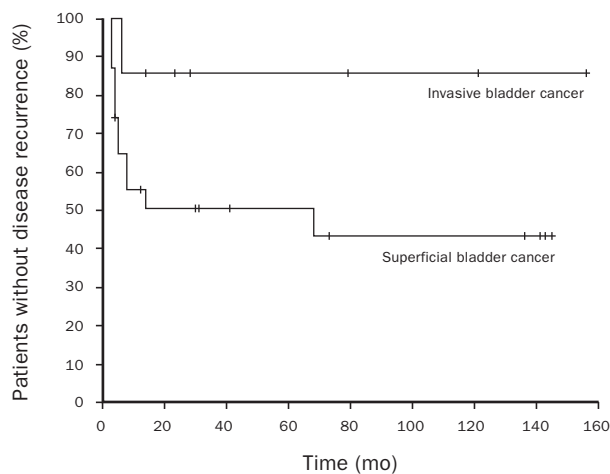


Figure 1. Proportion of patients without a recurrence of superficial (95% confidence interval, CI, 42–99 months) or invasive bladder cancer (95% CI, 96–173 months).

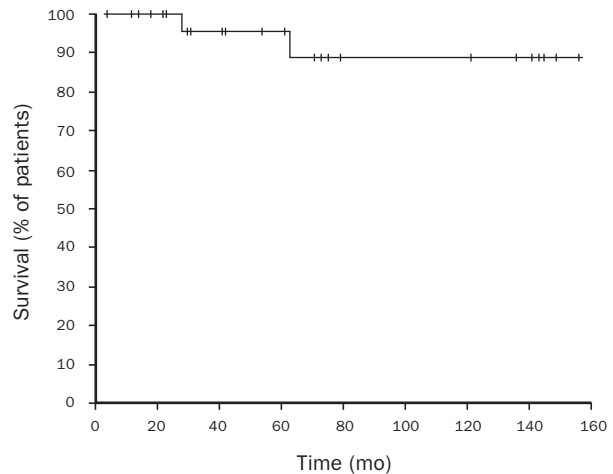


Figure 2. Overall survival rate of young adults with urothelial carcinoma of the urinary bladder (95% confidence interval, 128–160 months).

Our study, with a male:female ratio of 3.3:1, demonstrates the usual male predominance of urothelial bladder carcinoma; this ratio is similar to those in the reports of Ozbey et al¹¹ and Kurz et al.⁴ The most common presenting symptom in the young adults in our study was gross hematuria, the causes of which included infection, urolithiasis, and malignancy. The findings of gross hematuria, the main symptom of bladder cancer, and irritative bladder symptoms should be thoroughly investigated to permit the accurate, differential diagnosis of bladder cancer, especially in the young group. In our study, there was no significant difference between patients with superficial or invasive bladder cancer regarding the occurrence of gross hematuria.

In our series, 24 young patients (80%) were initially diagnosed with superficial bladder cancer, and the remaining 6 (20%) with invasive bladder cancer. Twelve patients with superficial bladder cancer had a tumor recurrence within a mean of 10.7 months. Only 2 of the 24 patients with superficial bladder cancer (8.3%) progressed to invasive bladder cancer. Our results are supported by the report of Yossepowitch and Dalbagni,¹² who documented a progression rate of 16%.

Benson et al⁵ and Madgar et al⁶ reported that tumor recurrences were age-related and tended to occur more frequently in older than younger patients. Among 6 patients aged ≤ 30 years in our study, 5 presented with stage Ta–T1 disease, and 1 with stage T2b disease; 24 patients aged 31–40 years had stage Ta–T1 disease ($n = 19$), or stage T2–T4 disease (5). Disease recurrence rates in the 2 age groups were 33.3% (≤ 30 years) and 45.8% (31–40 years). Although this difference was not statistically significant, tumor recurrence does seem to be age-related.

The prognosis for patients with invasive bladder cancer is very poor. According to Yossepowitch and Dalbagni,¹² the 5-year rate of disease-free survival after cystectomy was only 59% in 17 patients. In our series, the corresponding rate after cystectomy in 6 patients with invasive bladder cancer was 83%. This discrepancy

may be because more patients with advanced disease were evaluated in the first report: 8 patients had stage T3–4 disease,¹² whereas only 2 patients did in our study. Further investigations are now required to confirm long-term outcomes in young adults with urothelial bladder cancer.

In conclusion, patients younger than 40 years old with bladder cancer usually have low-grade and low-stage tumors. Among this age group, the survival rate in patients with invasive bladder cancer appears to be no worse than that in patients with superficial bladder cancer.

References

1. Johnson DE, Hillis S. Carcinoma of the bladder in patients less than 40 years old. *J Urol* 1978;120:172–3.
2. Wan J, Grossman HB. Bladder carcinoma in patients aged 40 years or younger. *Cancer* 1989;64:178–81.
3. Kutarski PW, Padwell A. Transitional cell carcinoma of the bladder in young adults. *Br J Urol* 1993;72:749–55.
4. Kurz KR, Pitts WR, Vaughan ED Jr. The natural history of patients less than 40 years old with bladder tumors. *J Urol* 1987;137:395–7.
5. Benson RC, Tomera KM, Kelalis PP. Transitional cell carcinoma of the bladder in children and adolescents. *J Urol* 1983;130:54–5.
6. Madgar I, Goldwasser B, Nativ O, Hanai Y, Jonas P. Long-term followup of patients less than 30 years old with transitional cell carcinoma of the bladder. *J Urol* 1988;139:933–4.
7. Fitzpatrick JM, Reda M. Bladder carcinoma in patients 40 years old or less. *J Urol* 1986;135:53–4.
8. Witjes JA, Debruyne FM. Bladder carcinoma in patients less than 40 years of age. *Urol Int* 1989;44:81–3.
9. Wittkind C, Sobin LH. *Union Internationale Contre Le Cancer TNM Classification of Malignant Tumors*, 5th edition. New York: Wiley-Liss, 1997.
10. Mostofi FM, Sobin LH, Torloni H, eds. *WHO: Histological Typing of Urinary Bladder Tumors. International Histological Classification of Tumors, No 10*. Geneva: World Health Organization, 1973.
11. Ozbey I, Aksoy Y, Bicgi O, Okyar G. Transitional cell carcinoma of the bladder in patients under 40 years of age. *Int Urol Nephrol* 1999;31:655–9.
12. Yossepowitch O, Dalbagni G. Transitional cell carcinoma of the bladder in young adults: presentation, natural history and outcome. *J Urol* 2002;168:61–6.