Kaohsiung Journal of Medical Sciences (2016) 32, 191–195

Available online at www.sciencedirect.com

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journal homepage: http://www.kjms-online.com

ORIGINAL ARTICLE

Outcomes and prognostic factors of simple partial cystectomy for localized bladder urothelial cell carcinoma

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Received 30 September 2015; accepted 7 December 2015
Available online 27 March 2016

KEYWORDS
Bladder tumor;
Partial cystectomy;
Urothelial carcinoma

Abstract Radical cystectomy has remained the gold standard for recurrent superficial or muscle invasive bladder tumor. However, partial cystectomy still has a role in those who reject or have contraindications for radical cystectomy. In this study, we sought to identify predictors of bladder recurrence and overall survival after simple partial cystectomy. We included 27 patients with bladder tumor who received simple partial cystectomy without pelvic lymph node dissection between March 2000 and September 2013. Adjuvant chemotherapy or radiation therapy was prescribed according to the pathological results. Parameters were compared on the basis of bladder recurrence and overall survival. During a mean follow-up time of 39 months, five patients (18.5%) experienced bladder recurrence. An older age, a higher pathological stage, positive surgical margins, and distant metastases were significant predictors of overall survival ($p = 0.031$, $p = 0.001$, $p = 0.001$, and $p = 0.011$, respectively). Meanwhile, previous bladder instillation and positive surgical margins were significant predictors of bladder recurrence ($p = 0.026$ and $p = 0.027$, respectively). The rate of consecutive distant metastases (33.3%) was almost twice the rate of bladder recurrence (18.5%), and six patients developed consecutive distant metastases without first experiencing bladder recurrence. In patients who received a simple partial cystectomy as an alternative treatment, previous bladder instillation and positive surgical margins were significant predictors of bladder recurrence. Patients with an older age, positive surgical margins, and consecutive distant metastases had worse overall survival. Partial cystectomy with routine lymph node dissection may be a better option for achieving favorable long-term outcomes.

Conflicts of interest: All authors declare no conflicts of interest.

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http://dx.doi.org/10.1016/j.kjms.2016.02.008

Introduction

Urothelial carcinoma of the urinary bladder is strongly associated with environmental factors and age. The incidence and prevalence rates increase with age, peaking in the 8th decade of life [1,2]. In the United States in 2007, bladder urothelial carcinoma accounted for 7% of all cancers [1]. In addition to its high prevalence, bladder cancer is fatal, accounting for 3% of all cancer deaths in the United States in 2007. However, due to advancements in treatment strategies and modalities, bladder cancer mortality decreased by 5% between 1990 and 2004, despite a continuous rise in the incidence of the disease [1].

Radical cystectomy is one of the main treatment options for localized muscle invasive bladder urothelial carcinoma and select nonmuscle invasive disease. However, along with cancer control, radical cystectomy also results in some degree of reduction in the quality of life; it impacts continence, body image, and potency. These consequences make bladder preservation during treatment an important goal, for both patients and surgeons, in advanced bladder cancer cases.

A partial cystectomy with pelvic lymph node dissection can be reserved for select patients with a solitary lesion for whom radical cystectomy is otherwise contraindicated and a sufficient margin can be obtained. Some previous studies noted the comparable prognosis of radical cystectomy and partial cystectomy with adequate patient selection [3,4].

In this study, we analyzed patients who underwent simple partial cystectomy without pelvic lymph node dissection with the aim of identifying predictors of bladder cancer recurrence and overall survival in this population.

Materials and methods

Twenty-seven patients who underwent a simple partial cystectomy without pelvic lymph node dissection at our hospital between March 2000 and September 2013 were included in this study. These patients were diagnosed with bladder urothelial carcinoma, and the diagnosis was confirmed by transurethral resection of bladder tumors (TUR-BT). All patients met the criteria for radical cystectomy, but underwent simple partial cystectomy due to medical considerations or on the basis of their own decision. Computed tomography scans and bone scans were performed for staging before the operation. The absence of lymph node and distant metastases was determined by imaging studies. All bladder lesions were solitary with adequate resection margins of at least 1 cm. No neoadjuvant chemotherapy or radiation therapy was administered. Adjuvant chemotherapy or radiation therapy was prescribed according to the pathological results, i.e., if at least one of the following criteria was met: pathological Stage T3 or Stage T4 disease, or positive surgical margins.

The prognosis analysis was based on overall survival and recurrence-free survival. Parameters included general patient characteristics (sex, age, body mass index), tumor factors (pathological T stage, tumor histology, tumor size, and pathological grade), surgical factors (American Society of Anesthesiologists score and surgical margins), and previous bladder tumor conditions (previous intravesical instillation including chemotherapy or bacillus Calmette-Guerin (BCG) instillation and previous TUR-BT history and number). Here, the TUR-BT history did not refer to TUR-BT for the same bladder tumor, but to any previous superficial bladder tumor history for which bladder preservation therapy with TUR-BT was performed.

Statistical analyses were performed using SPSS version 17 software (Linkou, Taoyuan, Taiwan). Statistical methods included frequency descriptions and a Kaplan-Meier survival analysis. The study was approved by the Institutional Review Board.

Results

Patient characteristics are listed in Table 1. The mean age of patients who underwent partial cystectomy was 70.6 years (range 49—90 years). The mean follow-up time after partial cystectomy was 39.0 months. The patients were predominantly male, with a male to female ratio of 5.8.

Overall, 63% (17) of patients had pathological Stage T1 or Stage T2 disease, while Stage T3 and Stage T4 disease accounted for 33.3% (9) and 3.7% (1) of cases, respectively. The most common tumor histology was infiltrating carcinoma (74%); other histologies included papillary (14.8%), sarcomatoid (7.4%), and poorly differentiated types (3.7%). In terms of pathological grade, high-grade tumors accounted for 88.9% of all cases.

Fourteen (51.9%) patients had superficial bladder tumors for which they had previously received TUR-BT. Among these 14 patients, 11 (40.7%) had undergone TUR-BT once and three had received TUR-BT at least twice. Previous intravesical therapies including epirubicin, mitomycin, and BCG instillation were prescribed according to individual status in keeping with the National Comprehensive Cancer Network guidelines [5]. Pathological specimen examination showed that four (14.8%) patients had residual cancer at the surgical margin and 23 (85.2%) patients had clear surgical margins.

During a mean follow up of 39.0 $\pm$ 39.0 months, five (18.5%) patients experienced tumor recurrence in the bladder, nine (33.3%) patients developed distant metastasis postsurgically, and 10 (37%) patients died. Results of the univariate analysis performed using Kaplan—Meier survival curves for overall survival are shown in Table 2. Significant predictors of overall survival in patients who received partial cystectomy were: age $>$ 70 years, a higher

Table 1 Patient characteristics.

Mean patient age (y)	70.6 ± 10.7	(49–90)
Mean follow-up time (mo)	39.0 ± 39	(3.13–148.4)
Body mass index (kg/m^2)	24.4 ± 2.88	(20.7–34.4)
Sex		
Male	23 (85.2)	
Female	4 (14.8)	
Pathological T stage		
1	10 (37.0)	
2	7 (25.9)	
3	9 (33.3)	
4	1 (3.7)	
Mean tumor size (cm)	2.97 ± 1.7	
Pathological pattern		
Infiltrating	20 (74)	
Papillary	4 (14.8)	
Sarcomatoid	2 (7.4)	
Poorly differentiated	1 (3.7)	
Pathological grade		
High	24 (88.9)	
Low	3 (11.1)	
ASA score		
1	1 (3.7)	
2	13 (48.1)	
3	13 (48.1)	
Previous TUR-BT		
No	13 (48.1)	
Yes	14 (51.9)	
Previous number of TUR-BTs		
0	13 (48.1)	
1	11 (40.7)	
2	1 (3.7)	
3	1 (3.7)	
4	1 (3.7)	
Previous intravesical instillation		
Epirubicin	2 (7.4)	
Mitomycin	1 (3.7)	
BCG	1 (3.7)	
Surgical margin		
Negative	23 (85.2)	
Positive	4 (14.8)	
Bladder recurrence		
No	22 (81.5)	
Yes	5 (18.5)	
Distant metastasis		
No	18 (66.7)	
Yes	9 (33.3)	

Data are presented as mean ± SD (range) or *n* (%).
ASA score = American Society of Anesthesiologists score; BCG = bacillus Calmette–Guerin; SD = standard deviation; TUR-BT = transurethral resection of bladder tumors.

pathological T stage, positive surgical margins, and consecutive distant metastases ($p = 0.031$, $p = 0.001$, $p = 0.001$, and $p = 0.011$, respectively).

Results of the univariate analysis of recurrent-free survival are shown in Table 3. Previous bladder intravesical instillation and positive surgical margins were significant predictors of bladder tumor recurrence ($p = 0.026$ and

Table 2 Univariate analysis of predictors of overall survival.

	No. of cases	Mean survival time (mo)	No. of deaths	*p*
Sex				
Female	4	27.8 ± 10	2	0.121
Male	23	88.0 ± 16	8	
Age (y)*				
< 70	13	118.7 ± 18	2	0.031*
≥ 70	14	47.2 ± 13	8	
Body mass index (kg/m^2)				
≤ 24	12	94.7 ± 19.9	4	0.670
> 24	13	57.1 ± 12.3	4	
Pathological T stage*				
1	10	94.8 ± 11	2	0.001*
2	7	26.0 ± 7	4	
3	9	91.1 ± 25	3	
4	1	4.6	1	
Tumor size (cm)				
< 2	6	57.8 ± 10	1	0.870
≥ 2 and < 4	12	65.6 ± 15	5	
≥ 4	9	81.9 ± 23	4	
Histology				
Papillary	4	63.8 ± 12	3	0.539
Infiltrating	20	93.5 ± 18	6	
Others (sarcomatoid and poorly differentiated)	3	82.0 ± 15	1	
Pathological grade				
Low	3	88.3 ± 20	1	0.312
High	24	75.3 ± 16	9	
ASA score				
1	1		0	0.202
2	13	103.2 ± 18	4	
3	13	33.2 ± 5.4	6	
Previous TUR-BT				
No	13	67.2 ± 15	5	0.875
Yes	14	82.4 ± 20	5	
Number of previous TUR-BTs				
0	13	67.2 ± 15	5	0.440
1	11	89.4 ± 20	4	
≥ 2	3	16.1 ± 15	1	
Previous intravesical instillation				
No	24		10	0.582
Yes	3		0	
Surgical margin*				
Negative	23	93.0 ± 16	7	0.001*
Positive	4	16.5 ± 8	3	
Bladder recurrence				
No	22	92.4 ± 16	7	0.154
Yes	5	44.9 ± 23	3	
Distant metastasis*				
No	18	102.2 ± 18	4	0.011*
Yes	9	37.9 ± 14	6	

*$p < 0.05$.
ASA score = American Society of Anesthesiologists score; TUR-BT = transurethral resection of bladder tumors.

Table 3 Univariate analysis of predictors of bladder recurrence-free survival.

	No. of cases	Mean recurrence-free time (mo)	No. of deaths	*p*
Sex				
Female	4		0	0.346
Male	23		5	
Age (y)				
< 70	13	126.2	2	0.606
≥ 70	14	87.7	3	
Body mass index (kg/m^2)				
≤ 24	12	124.4	2	0.637
> 24	13	69.4	3	
Pathological T stage				
1	10	90.6	2	0.956
2	7	34.96	1	
3	9	114.1	2	
4	1		0	
Tumor size (cm)				
< 2	6	57.8	1	0.956
≥ 2 and < 4	12	93.6	2	
≥ 4 cm	9	116.3	2	
Histology				
Papillary	4	68.3	1	0.539
Infiltrating	20	118.7	4	
Others (sarcomatoid and poorly differentiated)	3		0	
Pathological grade				
Low	3		0	0.393
High	24		5	
ASA score				
1	1		0	0.774
2	13		3	
3	13		2	
Previous TUR-BT				
No	13	95.1	2	0.700
Yes	14	116.5	3	
No. of previous TUR-BTs				
0	13	95.1	2	0.078
1	11	135.2	1	
≥ 2	3	8.4	2	
Previous intravesical instillation*				
No	24	129.7	10	0.026*
Yes	3	8.1	0	
Surgical margin*				
Negative	23	129.5	3	0.027*
Positive	4	5.3	2	

*$p < 0.05$.
ASA score = American Society of Anesthesiologists score; TUR-BT = transurethral resection of bladder tumors.

$p = 0.027$, respectively). Patients with a history of more than two previous TUR-BTs appeared more likely to have tumor recurrence, although this was not statistically significant ($p = 0.078$).

Discussion

Ninety percent of urinary bladder cancers are urothelial cell carcinomas [6], with muscle invasive disease accounting for 80% of urothelial tumors at initial presentation.

Radical cystectomy remains the most frequently utilized surgical intervention for clinical Stage T2 and Stage T3 bladder urothelial carcinoma without lymph node or distant metastases. Cystectomy may also be indicated for select superficial bladder tumors, for example, recurrent pT1 high-grade tumors.

For patients in whom radical cystectomy is indicated, but who wish to preserve the urinary bladder, alternative treatments include radical TUR-BT, partial cystectomy, and neoadjuvant concomitant chemoradiotherapy. Partial cystectomy plays a role in select patients with appropriately located solitary tumors and resectable margins. A standard partial cystectomy should include bilateral pelvic lymph node dissection to confirm lymph node stage.

Previous studies have reported on prognosis with standard partial cystectomy, along with predictors of survival or recurrence. Holzbeierlein and colleagues [3] reviewed the cases of 58 select patients who underwent partial cystectomy with pelvic lymph node dissection for bladder urothelial carcinoma and were followed up for 33 months. They reported that partial cystectomy with pelvic lymph node dissection can result in comparable outcomes in specifically selected patients. In addition, concomitant carcinoma *in situ* and lymph node metastasis were found to be predictors of advanced recurrence. Smaldone and colleagues [4] reviewed the cases of 25 patients with primary solitary T2 or high-grade T1 tumors who received preoperative radiation for 5 days and a single dose of intraoperative intravesical chemotherapy followed by partial cystectomy with pelvic lymph node dissection. Over a follow-up period of 11 years, the cancer-specific 5-year survival was 84%. To the best of our knowledge, the role and prognosis of simple partial cystectomy have not been discussed in previous studies.

In this study, we aimed to identify prognostic predictors for patients who underwent a simple partial cystectomy. During a mean follow-up time of 39 months, the bladder tumor recurrence rate was 18.5%, with an overall survival rate of 63%. The significant predictors of poor overall survival were: age > 70 years, a higher T stage, positive surgical margins, and consecutive distant metastases. These predictors were similar to the prognostic factors of patients who underwent a radical cystectomy [7–9]. In addition, previous intravesical bladder instillation and positive surgical margins were significant predictors of bladder tumor recurrence. This can be explained by the fact that patients for whom intravesical instillation was indicated had a T1 high-grade tumor, coexisting carcinoma *in situ*, or a recurrent bladder tumor. These patients are at high risk for bladder tumor recurrence after partial cystectomy. Patients with positive surgical margins after a partial cystectomy also had a high probability of bladder tumor recurrence despite adjuvant chemotherapy or radiation therapy. Thus, a more aggressive follow up is important in these patients. Although not significant, patients with a history of multiple previous TUR-BTs (>2) were more likely to have bladder tumor recurrence ($p = 0.078$).

In our study, we determined that the incidence rate of consecutive distant metastases (33.3%) was almost twice that of recurrence in the bladder (18.5%). This rate was also higher than that reported for another case series of partial cystectomy with pelvic lymph node dissection [3]. Among patients with distant metastases, six developed consecutive distant metastases without first having a recurrence in the bladder. This may be due to the high potential for lymph node metastasis, even though preoperative computed tomography scans were negative for lymph node metastasis. In patients with potential lymph node metastases, the bilateral pelvic lymph nodes played an important role, not only in the staging diagnosis, but also in terms of the survival benefit, because consecutive distant metastases had a significant effect on overall survival.

Conclusion

For patients who underwent simple partial cystectomy as an alternative treatment, previous bladder instillation (due to previous high-grade or carcinoma *in situ* tumors) and positive surgical margins were significant predictors of bladder tumor recurrence. Patients aged $>$ 70 years, and those with positive surgical margins and consecutive distant metastases, had worse overall survival.

With adequate patient selection and proper postoperative follow up, simple partial cystectomy without pelvic lymph node dissection could provide a favorable prognosis for local bladder tumor recurrence. However, the lymph node or distant metastasis rate appeared relatively higher in our patients than in patients who received partial cystectomy with pelvic lymph node dissection in other reported case series. A possible reason for the variation in results may be that potential lymph node metastases were missed on preoperative images. For patients who are eligible for partial cystectomy, simultaneous lymph node dissection may result in more favorable long-term outcomes in terms of overall survival or distant metastases, even in those without suspected lymph node metastasis.

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