Original Article

Radical cystectomy for bladder cancer: oncologic outcome in 271 Chinese patients

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Abstract

Few large scale studies have reported the oncologic outcome of radical cystectomy for treating bladder cancer in China; hence, we lack long-term prognostic information. The aim of the current study was to determine the survival rate and prognostic factors of patients who underwent radical cystectomy for bladder cancer in a Chinese medical center. We retrospectively analyzed clinicopathologic data from 271 bladder cancer patients who underwent radical cystectomy between 2000 and 2011. Univariate and multivariate analyses were conducted to identify independent prognostic predictors for this cohort. Median follow-up was 31.7 months (range, 0.2–139.1 months). Thirty-day mortality was (1.4%). The 5-year recurrence-free survival, cancer-specific survival (CSS), and overall survival rates were 61.6%, 72.9%, and 68.0%, respectively. The 5-year CSS rates of patients with T1–T4 disease were 90.7%, 85.0%, 51.0%, and 18.0%, respectively. Patients with organ-confined disease had a higher 5-year CSS rate than those with extravesical disease (81.4% vs. 34.9%, $P < 0.001$). For the 38 patients (14%) with lymph node involvement, the 5-year CSS rate was 27.7%—significantly lower than that of patients without lymph node metastasis ($P < 0.001$). The 5-year CSS rate was much higher in patients with low grade tumor than in those with high grade tumor (98.1% vs. 68.1%, $P < 0.001$). Multivariate Cox regression showed that patient age (hazard ratio, 2.045; $P = 0.013$) and T category (hazard ratio, 2.213; $P < 0.001$) were independent predictors for CSS. These results suggest that radical cystectomy is a safe and effective method for treating bladder cancer in Chinese patients. Old age and high T category were associated with poor prognosis in bladder cancer patients who underwent radical cystectomy.

Key words Bladder cancer, radical cystectomy, prognosis

Muscle-invasive bladder cancer is lethal. Unfortunately, approximately 30% of bladder cancers have invaded muscle by the time of diagnosis[1]. According to statistical data from the American Cancer Society[2], there would be 73,510 new bladder cancer cases and 14,880 deaths due to bladder cancer in 2012 in the United States. In China, bladder cancer is one of the most common urinary malignancies and the eighth most common malignancy among males[3]. The most effective treatment for muscle-invasive bladder cancer is radical cystectomy combined with pelvic lymph node dissection. Studies in Western countries have reported 5-year survival rates of 54.5%–68%[4,5] in bladder cancer patients who underwent radical cystectomy. However, few large scale studies have reported the oncologic outcome of radical cystectomy for treating bladder cancer in China; hence, we lack long-term prognostic information. This makes it difficult to assess prognosis and deliver preoperative patient education. Here, we report the survival details of a group of 271 Chinese bladder cancer patients who underwent radical cystectomy combined with pelvic lymph node dissection.

Patients and Methods

Patients

A total of 271 patients (239 males and 32 females) with a median

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age of 60 years (range, 35–89 years) were enrolled in this study. All were preoperatively diagnosed with muscle-invasive bladder cancer. Radical cystectomy with pelvic lymph node dissection was performed as described previously[6]. Eleven patients received neoadjuvant chemotherapy and 47 patients received adjuvant chemotherapy. Five patients underwent radiation therapy. TNM staging was performed according to the system outlined by the American Joint Committee on Cancer (2002)[7]. Tumor grade was classified according to the 2004 World Health Organization classification[8].

Follow-up

All patients were followed at 3-month intervals during the first 2 years after surgery and at 6-month intervals thereafter. Follow-ups comprised physical examination, blood chemistry analysis, and functional evaluation. Chest radiography and abdominal ultrasonography were performed every half a year. The first follow-up abdominal computed tomography (CT) examination was performed 3 months after surgery and once per year thereafter. A complete check-up was performed in patients with any evidence of recurrence or metastasis. Tumor recurrence, including local relapse and distant metastasis, was confirmed by CT or magnetic resonance imaging.

Statistical analysis

The primary end point of the study was cancer-specific survival (CSS), which was calculated from the date of surgery to the date of death or last follow-up. Recurrence-free survival (RFS) was calculated from the date of surgery to the date of tumor recurrence. Overall survival (OS) was calculated from the date of surgery to the date of death. Survival curves were determined using the Kaplan-Meier method and compared using the log-rank test. Thirty-day mortality means any death happened within 30 days after radical cystectomy. All P values were two-tailed and $P < 0.05$ was considered significant. Data were analyzed using SPSS version 13.0 (SPSS Inc., Chicago, IL, USA).

Results

Clinicopathologic data

Detailed clinicopathologic data are listed in **Table 1**. In this patient cohort, 107 (39.5%) had recurrent tumor before radical cystectomy. Regarding the type of urinary diversion used, conduit and neobladder accounted for 43.2% and 55.7% of procedures, respectively. Only 3 patients received other types of urinary diversion (continent cutaneous pouch or cutaneous ureterostomy). The median operation time was 325 min, and the median estimated blood loss was 500 mL, with a transfusion rate of 56.5%. Seven (2.6%) patients needed re-operation for severe complications, and there were 4 (1.4%) deaths in the first 30 days after surgery. Pathology showed that most patients had high grade urothelial cancer. Of the 271 patients, 212 (78.2%) had tumor confined to the bladder, whereas 59 (21.8%) had extravesical disease; 233 (86.0%) had negative lymph nodes,

Table 1. Clinicalpathologic features, intraoperative data, and hospitalization duration of 271 patients with bladder cancer

Characteristic	No. of cases (%)
Median age[a] (years)	60 (53, 69)
Male patients	239 (88.2)
Recurrent tumor	107 (39.5)
Tumor multiplicity	162 (59.8)
Gross hematuria	204 (75.3)
Urinary irritation symptoms	75 (27.7)
Smoking history	150 (55.4)
Histologic subtype	
Urothelial carcinoma	237 (87.5)
Nonurothelial carcinoma	34 (12.5)
Grade	
High	180 (75.9)
Low	57 (24.1)
T category	
pTa–T1	78 (28.8)
pT2a	67 (24.7)
pT2b	30 (11.1)
pT3a	36 (13.3)
pT3b	27 (10.0)
pT4	31 (12.1)
N category	
N−	233 (86.0)
N+	38 (14.0)
Organ-confined disease	212 (78.2)
Form of urinary diversion	
Conduit	117 (43.2)
Neobladder	151 (55.7)
Others	3 (1.1)
Median operation time[a] (min)	325 (275, 380)
Median length of postoperative hospital stay[a] (days)	17 (13, 23)
Reoperation	7 (2.6)
Deaths within 30 days after surgery	4 (1.4)
Median estimated blood loss[a] (mL)	500 (400, 800)
Transfusion required	153 (56.5)
Cancer recurrence	82 (30.3)
Cancer death	55 (20.3)
Death for any reason	68 (25.1)

[a]These data are presented as median with interquartile range in parentheses.

whereas 38 (14.0%) had local lymph node metastasis.

Prognosis

Median follow-up time was 31.7 months (range, 0.2–139.1

months). During follow-up, 82 patients developed recurrence and 55 died from bladder cancer. Detailed 5-year CSS data are listed in **Table 2**. The 5-year RFS, CSS, and OS rates were 61.6%, 72.9%, and 68.0%, respectively (**Figure 1**). The 5-year CSS rate in patients with T1–T4 disease was 90.7%, 85.0%, 51.0%, and 18.0%, respectively (**Figure 2A**). Patients with organ-confined disease had higher 5-year CSS rate than those with extravesical disease (**Figure 2B**, 81.4% vs. 34.9%, *P* < 0.001). Thirty-eight patients (14%) had lymph node tumor involvement; the 5-year CSS rate in these patients was 27.7%, which was significantly lower than that in patients without lymph node

metastasis (**Figure 2C**, *P* < 0.001). Regarding histologic subtype, patients with urothelial carcinoma (UC) had a better prognosis than those with non-UC (**Figure 2D**, 5-year CSS rate, 75.4% vs. 56.3%; *P* = 0.042). The 5-year CSS rate was much higher in patients with low grade UC than in those with high grade UC (**Figure 2E**, 98.1% vs. 68.1%, *P* < 0.001).

Univariate and multivariate analysis

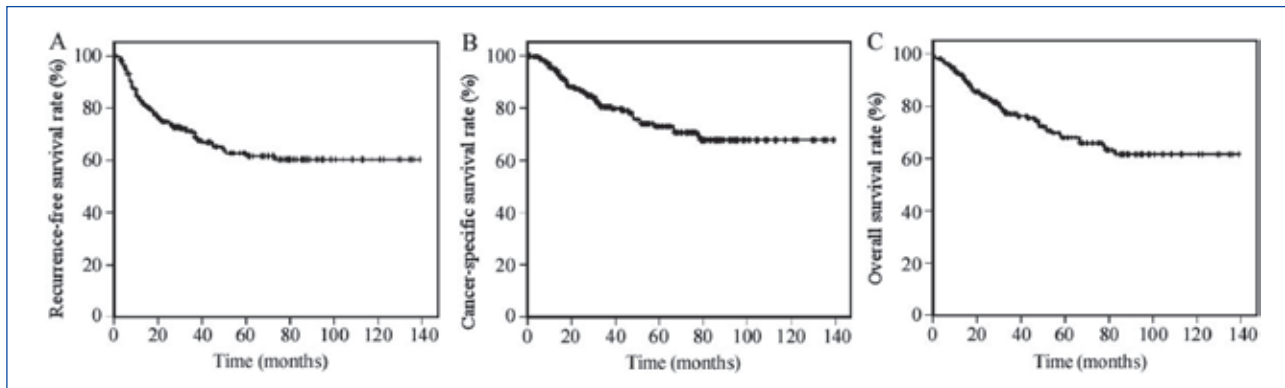To find independent predictors for CSS, we performed Cox

Figure 1. Recurrence-free, cancer-specific, and overall survival curves for the patient cohort. A, 5-year recurrence-free survival rate is 61.6%. B, 5-year cancer-specific survival rate is 72.9%. C, 5-year overall survival rate is 68.0%.

Table 2. Recurrence-free, cancer-specific, and overall survival after radical cystectomy

Characteristic	No. of cases	5-year survival rate					
		Recurrence-free	*P*	Cancer-specific	*P*	Overall	*P*
T category			<0.001		<0.001		<0.001
Ta–T1	78	79.5%		90.7%		84.5%	
T2	97	73.7%		85.0%		81.0%	
T3	63	33.4%		51.0%		49.1%	
T4	33	34.2%		18.0%		10.9%	
Depth of invasion			<0.001		<0.001		<0.001
Organ-confined	212	70.4%		81.4%		77.3%	
Extravesical	59	26.7%		34.9%		27.7%	
N category			<0.001		<0.001		<0.001
N⁻	233	66.7%		77.2%		72.4%	
N⁺	38	18.2%[a]		27.7%		24.9%	
Histologic subtype			0.001		0.042		0.043
UC	237	65.3%		75.4%		70.4%	
Non-UC	34	37.7%		56.3%		52.3%	
Total group	271	61.6%		72.9%		68.0%	
Tumor grade			0.003		<0.001		0.002
Low grade	57	83.1%		98.1%		90.0%	
High grade	180	59.5%		68.1%		64.1%	

UC, urothelial carcinoma; Non-UC, non-urothelial carcinoma. [a] This is 4-year recurrence-free survival rate.
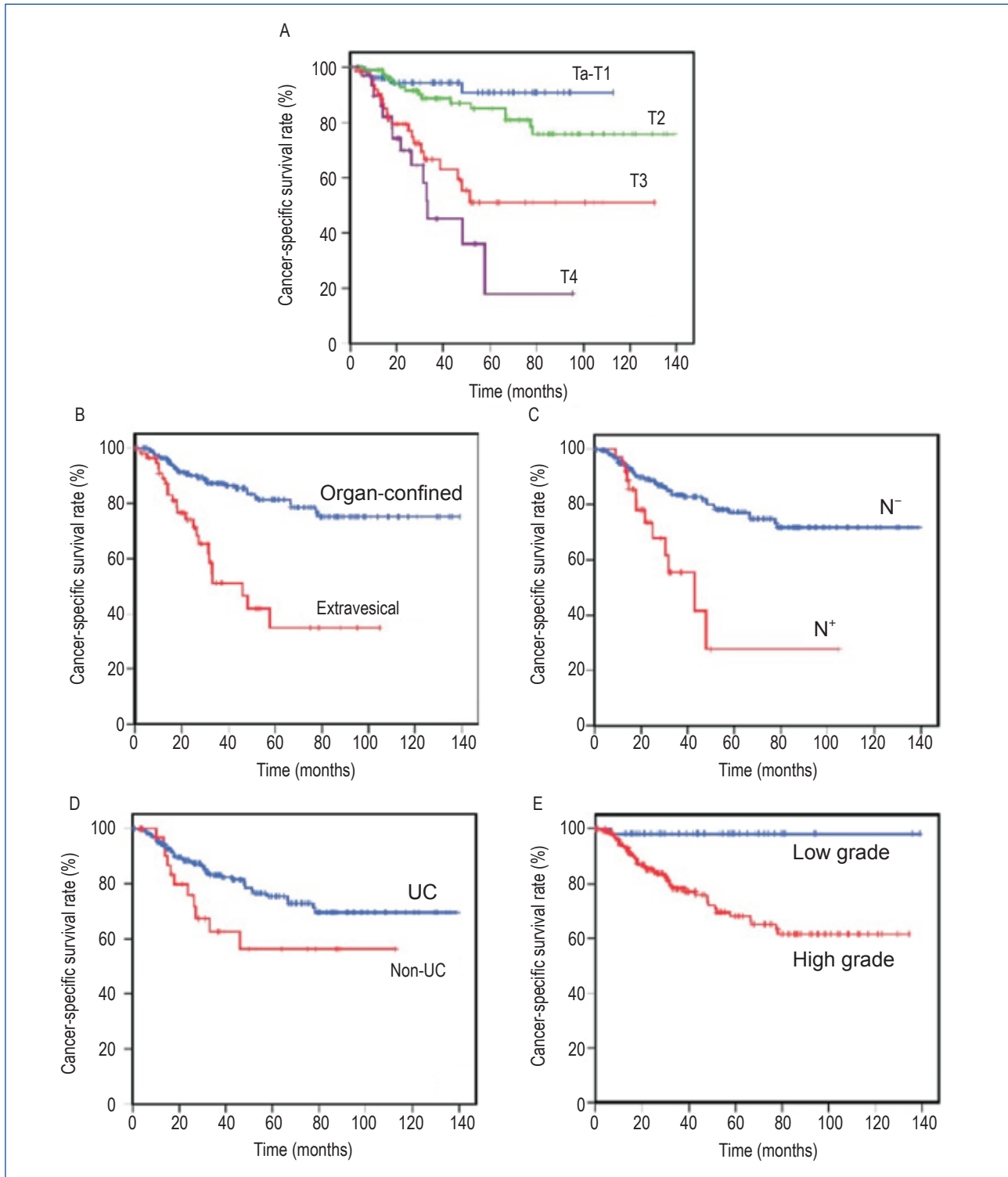
Figure 2. Cancer-specific survival (CSS) curves for subgroups. A, the 5-year CSS rates in patients with T1–T4 disease are 90.7%, 85.0%, 51.0%, and 18.0%, respectively (*P* < 0.001). B, patients with disease confined to the bladder had a cumulative 5-year CSS rate of 81.4%, compared with 34.9% for those with extravesical disease (*P* < 0.001). C, CSS curves according to lymph nodes status. N⁺, patients with lymph node metastasis; N⁻, patients without lymph node metastasis. D, CSS curves according to histological subtype. UC, patients with urothelial carcinoma; Non-UC, patients with non-urothelial carcinoma. E, among urothelial carcinoma patients, low grade cases had higher CSS rate than high grade cases (98.1% vs. 68.1%, *P* < 0.001).

regression analysis. Univariate analysis showed that patient age, T category, N category, and histologic subtype were significant predictors for survival (**Table 3**). In multivariate analysis, patient age (hazard ratio, 2.045; *P* = 0.013) and T category (hazard ratio, 2.213; *P* < 0.001) were independent predictors for CSS in the whole group (**Table 3**). However, in the cohort of patients with urothelial carcinoma, T category (hazard ratio, 1.889; *P* = 0.001) and tumor grade (hazard ratio, 8.563; *P* = 0.038) were independent predictors for CSS.

Discussion

In the present study, we reported a group of 271 patients who underwent radical cystectomies, with 5-year RFS, CSS, and OS rates of 61.6%, 72.9%, and 68.0%, respectively. On subgroup analysis, the 5-year CSS rates of patients with T1–T4 disease were 90.7%, 85.0%, 51.0%, and 18.0%, respectively. This study provides long-term prognostic information of a group of Chinese patients, who underwent radical cystectomy for bladder cancer. This makes it possible to assess prognosis and deliver preoperative patient education.

Radical cystectomy plus pelvic lymph node dissection is the gold standard treatment for muscle-invasive bladder cancer. However, the procedure is time consuming and physically demanding for surgeons; hence, few surgeons specialize in this operation. Furthermore, patients may refuse to undergo the procedure due to the high risk of intraoperative and postoperative complications. For these reasons, there have been few large scale studies focusing on the long-term oncologic outcome of bladder cancer patients who underwent radical cystectomy. In China, there are even fewer of these studies. In 2002, Sun *et al*.[9] reported 196 radical cystectomies. With a median follow-up of 6.6 years in 135 patients, the reported 5-year survival rate was 66.2%. However, the statistical method used in this study was not standardized. In 2008, Niu *et al*.[10] reported the outcome of 356 radical cystectomies at Chinese institutes. The 5-year disease-free survival rate was 48%, 73%, 44%, 22%, and 0% for the whole

group and patients with T2a, T2b, T3 and T4 disease, respectively. However, these data were collected from three centers, and the procedure and extent of surgery may have differed between them. Hence, the 5-year disease-free survival rate was not high (48%) in this cohort. Recently, Xu *et al*.[11] reported their experience with laparoscopic radical cystectomy. The oncologic outcome was satisfactory, with a 5-year CSS rate of 83.3%. However, most of the patients in this study (81%) had early stage (T2 or T1) disease, which may have contributed to the high survival rate. Huang *et al*.[12] provided the most detailed information on oncologic outcome, reporting estimated 5-year OS, CSS, and RFS rates of 73.7%, 81.3%, and 72.6%, respectively, in a group of 171 patients who underwent laparoscopic radical cystectomies. However, the sample size was relatively small in this study. In the present study, the data came from a single center and included detailed follow-up. Thus, any differences in surgical procedure or extent were minimized, and the prognostic information can be considered accurate. Moreover, our results are comparable with those in the Western literature (**Table 4**)[13-16]. In addition to the oncologic outcome, we investigated the intraoperative parameters and mortality of radical cystectomy. Mean operation time and estimated blood loss were 325 min and 500 mL, respectively. The re-operation rate and mortality were also acceptable at 2.6% and 1.4%, respectively. In summary, our study provides evidence that radical cystectomy is a safe and effective method for treating bladder cancer in Chinese patients.

Predictors of the survival of radical cystectomy patients differ between studies. For example, in a very large scale Egyptian study[17], the authors reported 2,720 cases of bladder cancer, 49.4% of which were squamous tumors and treated with radical cystectomy. They considered tumor stage, histologic grade, and lymph node status as independent variables affecting the probability of survival. In a Canadian study, the authors declared that pathologic T category greater than 2, positive lymph nodes, unknown lymph node status, lymphovascular invasion, and positive surgical margins were

Table 3. Univariate and multivariate analysis of prognostic parameters

Variable	Univariate analysis			Multivariate analysis		
	HR	95% CI	*P*	HR	95% CI	*P*
The whole group						
Age	1.941	1.131–3.332	0.016	2.045	1.163–3.593	0.013
T category	2.274	1.715–3.015	<0.001	2.213	1.612–3.037	<0.001
N category	3.137	1.646–5.981	0.001	1.809	0.901–3.632	0.095
Histologic subtype	1.961	1.012–3.800	0.046	1.483	0.718–3.063	0.287
Urothelial carcinoma						
Age	1.641	0.903–2.982	0.104	1.512	0.820–2.786	0.185
T category	2.301	1.688–3.137	<0.001	1.889	1.314–2.714	0.001
N category	3.880	1.900–7.925	<0.001	2.021	0.940–4.347	0.072
Grade	15.326	2.110–111.339	0.007	8.563	1.124–65.242	0.038

HR, hazard ratio; CI, confidence interval.

Table 4. The 5-year cancer-specific survival rate after radical cystectomy: a comparison of the present study and published Western reports

Report/study	No. of cases	5-year cancer-specific survival rate (%)				
		Ta–T1	T2	T3	T4	N⁺
Shariat *et al.*[13]	888	81	72	44	28	35
Hautmann *et al.*[14]	788	90	72	43	28	21
Madersbacher *et al.*[15]	507	76	74	52	36	33
Manoharan *et al.*[16]	432	81	70	44	16	29
Present study	271	91	85	51	18	28

associated with decreased CSS, whereas a surgeon procedure volume of 5 to 9 per year was independently associated with improved CSS[18]. In the present study, patient age and T category were independent predictors for CSS, which is consistent with the results of previous reports[17-19]. Hence, in patients with poor prognostic factors, continued follow-up may be helpful in detecting tumor recurrence. Recently, scholars have developed nomograms combining prognostic information from clinicopathologic data and biomarkers to predict the prognosis of bladder cancer patients. These nomograms have been considered reasonable and accurate for such predictions[20,21].

There are limitations to this study. First, it was retrospective; hence, bias is present. Second, the sample size was not very large. A further cooperative study using nomograms to predict prognosis in multiple Chinese medical centers is ongoing.

Conclusions

Radical cystectomy is a safe and effective method for the treatment of bladder cancer in Chinese centers. The prognosis of this group of Chinese bladder cancer patients was satisfactory and comparable with that reported in Western countries. Old age and high T category were associated with a poor prognosis in bladder cancer patients who underwent radical cystectomy.

Acknowledgment

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