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Original Article

Short- and long-term outcomes of laparoscopic radical cystectomy for bladder cancer in the elderly

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Abstract: This study aimed to evaluate the safety and efficacy of laparoscopic radical cystectomy in elderly patients. We compared the short- and long-term outcomes of laparoscopic radical cystectomy for bladder cancer between patients aged ≥ 70 years (elderly patients, *n* = 42) and those < 70 years (nonelderly patients, *n* = 89). Compared with the nonelderly group, the elderly group had a significantly high number of patients, with American Society of Anesthesiologists score II (*P* = 0.001) and comorbidity (*P* = 0.000), particularly hypertension (*P* = 0.021) and type 2 diabetes mellitus (*P* = 0.037). There was no significant difference in the pathological data between the two groups. There were no significant differences between the two groups in short-term outcomes, including blood loss, postoperative hospital stay, or incidence of 90-day postoperative complications. With respect to long-term outcomes, there were no significant differences in overall survival and disease-free survival between the two groups. In summary, laparoscopic radical cystectomy for bladder cancer was equally safe and effective in elderly and nonelderly patients.

Keywords: Laparoscopy, elderly, bladder cancer, radical cystectomy, minimally invasive surgery

Introduction

Elderly populations have been increasing worldwide, including in China. The incidence of bladder cancer has gradually increased. In China, bladder cancer was ranked as the most common urological malignancy [1-3]. Therefore, the number of elderly patients with bladder cancer is expected to increase [4-10]. Among the available surgical procedures for muscle-invasive and high-risk, recurrent, noninvasive bladder cancer, laparoscopic radical cystectomy has rapidly developed [11-20]. Previous reports have described the advantages of laparoscopic radical cystectomy for bladder cancer, such as early postoperative recovery, decreased pain, and decreased hospital stay [21-35]. However, only few studies have reprted the efficacy and safety of laparoscopic radical cystectomy for elderly patients with bladder cancer [5-8]. Here we aimed to evaluate the safety and efficacy of laparoscopic radical cystectomy for bladder cancer by retrospectively comparing short- and long-term outcomes in patients aged ≥ 70 years with relatively younger patients.

Materials and methods

This study complied with the Declaration of Helsinki. This retrospective research was approved by the Ethics Committee of Shandong Provincial Hospital. The need for informed consent from all patients was waived because of retrospective study, not prospective study.

Between January 2010 and January 2015, 131 patients with bladder cancer underwent laparoscopic radical cystectomy at our institution. All patients underwent thorough preoperative examination, including routine laboratory test, echocardiography, lung function test, chest radiography, abdominopelvic computed tomography (CT), abdominal ultrasonography, and intravenous pyelogram. Diagnostic transurethral resection and pathological examination were performed in patients with muscle-invasive bladder cancer. The oncological indications for laparoscopic radical cystectomy were as follows: (1) muscle-invasive bladder cancer T2-4a, N0-Nx, M0; (2) high-risk and recurrent nonmuscle-invasive tumors; (3) T1G3; and (4) extensive

Table 1. Baseline and preoperative characteristics of patients with bladder cancer

	Elderly (*n* = 42)	Nonelderly (*n* = 89)	Statistic value	*P* value
Age (years)	73 (70-76)	58 (37-69)	-0.874	0.000
Gender			0.052	0.820
Male	31 (73.8%)	64 (71.9%)		
Female	11 (26.2%)	25 (28.1%)		
Comorbidity	31 (73.8%)	19 (21.3%)	33.276	0.000
Chronic obstructive pulmonary disease	2 (4.8%)	0 (0.0%)		-
Hypertension	10 (23.8%)	8 (9.0%)	5.288	0.021
Type 2 diabetes mellitus	8 (19.0%)	5 (5.6%)	4.353	0.037
Stable angina	4 (9.5%)	3 (3.4%)	1.093	0.296
Chronic atrial fibrillation	3 (7.1%)	0 (0.0%)		-
Liver cirrhosis	4 (9.5%)	3 (3.4%)	1.093	0.296
ASA score				
I	19 (45.2%)	70 (78.7%)	14.626	0.000
II	21 (50.0%)	18 (20.2%)	12.100	0.001
III	2 (4.8%)	1 (1.1%)	0.454	0.515
Clinical stage			-0.033	0.974
cT1	8 (19.0%)	17 (19.1%)		
cT2	23 (54.8%)	49 (55.1%)		
cT3	11 (26.2%)	23 (25.8%)		
Indication			0.384	0.535
Primary tumor	26 (61.9%)	60 (67.4%)		
Recurrent after TURBT and/or partial cystectomy	16 (38.1%)	29 (32.6%)		

TURBT: transurethral resection of bladder tumor.

nonmuscle-invasive disease that could not be controlled by transurethral resection and intravesical therapy. According to their age during radical cystectomy, these patients were divided into two groups. The elderly group included 42 patients aged ≥ 70 years. The nonelderly group included 89 patients aged < 70 years. Surgical procedures for cystectomy, bilateral pelvic lymphadenectomy, and extracorporeal diversion have been described in the literature [36].

Baseline, preoperative, operative, postoperative, and pathological data were obtained from our hospital medical records database. The parameters analyzed were age, gender, body mass index (BMI), American Society of Anesthesiology (ASA) score, previous abdominal surgery, comorbidity, tumor factors (tumor stage, tumor histologic type, and tumor grade), and operative factors (conversion to open radical cystectomy, operating time, intraoperative blood loss, blood transfusions, time to resumption of oral intake, 90-day postoperative complications, 90-day postoperative death, and postoperative stay). The tumor TNM stage was based on the seventh edition of the TNM classification of bladder cancer that was proposed by the International Union against Cancer and American Joint Committee on Cancer [37-39]. Tumor grade was analyzed by the 1973 World Health Organization classification. Severity of 90-day postoperative complications was classified using Clavien-Dindo classification. Minor complications were classified as grades 1 and 2, whereas major complications were classified as grades 3, 4, and 5 [40-54].

Patients with high-risk disease (pT3, pT4, or lymph node positive) were evaluated using a multidisciplinary meeting for considering adjuvant chemotherapy. The initiation time of adjuvant chemotherapy was primarily determined by the patient's performance status, and the decision was based on the discretion of the patient and medical oncologist [55-59].

Postoperative follow-up was conducted at 3-month intervals during the first year, at 6-month intervals during the second year, and annually thereafter. Follow-up visits consisted of history, physical examination, and routine

Table 2. Pathological outcomes after laparoscopic radical cystectomy for bladder cancer

	Elderly (*n* = 42)	Nonelderly (*n* = 89)	Statistic value	*P* value
Pathological T stage			-0.474	0.636
pT1	4 (9.5%)	11 (12.4%)		
pT2	17 (40.5%)	38 (42.7%)		
pT3	19 (45.2%)	34 (38.2%)		
pT4	2 (4.8%)	6 (6.7%)		
Pathological N stage			-0.027	0.979
Negative	32 (76.2%)	68 (76.4%)		
Positive	10 (23.8%)	21 (23.6%)		
Lymph node harvested	14 (8-21)	16 (10-24)	-0.325	0.158
Grade (1973 WHO classification)			-0.271	0.786
Grade 1	9 (21.4%)	16 (18.0%)		
Grade 2	15 (35.7%)	34 (38.2%)		
Grade 3	18 (42.9%)	39 (43.8%)		
Residual tumor (R0/R1/R2)	42/0/0	89/0/0	0.000	1.000
Histologic type			-0.082	0.935
TCC	40 (95.2%)	85 (95.5%)		
TCC with squamous differentiation	1 (2.4%)	3 (3.4%)		
TCC with glandular differentiation	1 (2.4%)	1 (1.1%)		

TCC: transitional cell carcinoma.

Table 3. Perioperative and postoperative outcomes of laparoscopic radical cystectomy for bladder cancer

	Elderly (*n* = 42)	Nonelderly (*n* = 89)	Statistic value	*P* value
Conversion to open surgery	3 (7.1%)	8 (9.0%)	0.000	0.986
Operative time (min)	280 (230-350)	270 (240-330)	-0.548	0.540
Blood loss (ml)	240 (180-530)	260 (150-590)	-0.754	0.420
Blood transfusion	4 (9.5%)	9 (10.1%)	0.000	1.000
Resumption of oral intake (days)	5 (4-8)	4 (3-9)	-0.601	0.389
Postoperative stay (days)	13 (8-25)	11 (7-28)	-0.628	0.089
Postoperative 90-day complications	15 (3.6%)	25 (28.1%)	0.782	0.377
Major complications	4 (9.5%)	7 (7.9%)	0.000	1.000
Minor complications	11 (26.2%)	18 (20.2%)	0.586	0.443
Postoperative 90-day death	0	0		-
Adjuvant chemotherapy	21 (50.0%)	60 (67.4%)	3.667	0.055

biochemical profile. Ultrasonography of the abdomen, urography, and chest X-rays were performed at 3, 6, and 12 months postoperatively and annually thereafter, unless otherwise clinically indicated. Abdominopelvic CT scans were performed 6 months postoperatively and once per year thereafter [11-24, 60-65]. Overall survival (OS) was assessed from the date of cystectomy until the last follow-up or death by any cause. Disease-free survival (DFS) was calculated from the date of cystectomy until the date of cancer recurrence or death from any cause [66-76]. The last follow-up for the entire cohort was March 2016.

Statistical analysis

Data were calculated as mean and standard deviation for variables following normal distribution and were analyzed using *t*-tests. For non-normally distributed data, results were expressed as median and range and were compared using nonparametric tests. Differences in semi-quantitative results were analyzed using the Mann-Whitney *U*-test. Differences in qualitative results were analyzed using the chi-square test or Fisher's exact test, as appropriate. Univariate analyses were performed to identify the prognostic variables related to OS and DFS. Univariate variables with *P* values < 0.10 were selected for inclusion in the multivariate Cox proportional hazard regression model. Adjusted hazard ratios (HR), with the corresponding 95% confidence intervals (CIs), were calculated. $P < 0.05$ was considered to indicate statistical significance. The Statistical Package for the Social Sciences (SPSS) 13.0 (SPSS Inc., Chicago, IL, USA) was used for analyses.

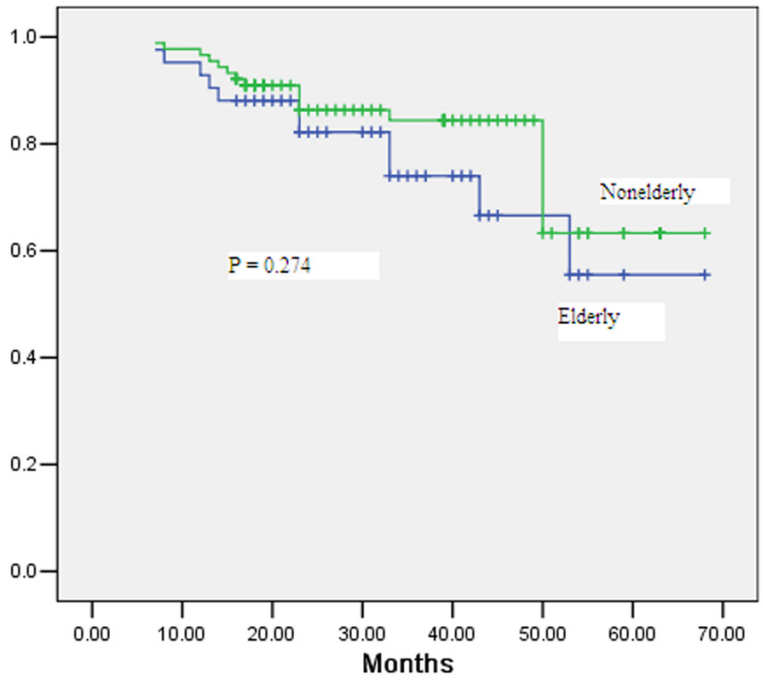

Figure 1. Overall survival of both groups.

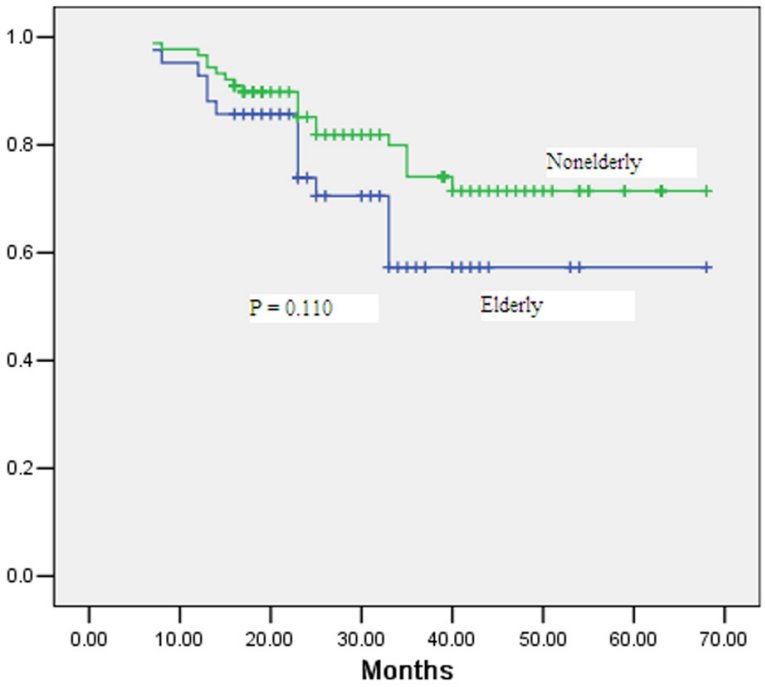

Figure 2. Disease-free survival of both groups.

Results

Short-term outcomes

Patient baseline and preoperative characteristics are summarized in **Table 1**. Patients in the elderly group had a mean age of 73 years (range 70-76 years) and those in the nonelderly group had a mean age of 58 years (range 37-69 years; P = 0.000). Elderly patients had significantly higher ASA score II (50% versus 20.2%, P = 0.001) and comorbidity rate (73.8% versus 21.3%, P = 0.000), particularly for hypertension (23.8% versus 9.0%, P = 0.021) and type 2 diabetes mellitus (19.0% versus 5.6%, P = 0.037), than nonelderly patients. There were significantly fewer elderly patients than nonelderly patients with an ASA score of I (45.2% versus 78.7%, P = 0.000).

The pathological data of the two groups are summarized in **Table 2**. There was no significant difference in the variation of pathological data between the two groups.

The intraoperative data, postoperative course, and 90-day postoperative complications are summarized in **Table 3**. There were no significant differences between both groups regarding operative time, operative blood loss, rate of blood transfusion, time to resumption of oral intake, length of postoperative stay, and 90-day postoperative complications. There were no incidences of 90-day postoperative death in any patients. There were lesser patients who underwent adjuvant chemotherapy in the elderly group than in the nonelderly group, although this difference was not significant (P = 0.055).

Long-term outcomes

The median follow-up period was similar between the two groups. Assessment of long-term outcomes is shown in **Figures 1** and **2**.

Table 4. Recurrence of bladder cancer after laparoscopic radical cystectomy

	Elderly (*n* = 42)	Nonelderly (*n* = 89)	Statistic value	*P* value
Recurrence	14 (33.3%)	19 (21.3%)	2.175	0.140
Locoregional	8 (19.0%)	10 (11.2%)	0.137	0.934
Distant	5 (11.9%)	7 (7.9%)		
Mixed	1 (2.4%)	2 (2.2%)		
Time to first recurrence (median, months)	15 (7-33)	19 (7-40)	-0.107	0.215

Table 5. Multivariate Cox regression analyses of overall survival after laparoscopic radical cystectomy for bladder cancer

Regression variables	Adjusted hazard ratio	95% CI	Beta value	*P* value
Age				0.128
< 70 years	1.00			
≥ 70 years	1.56	0.58-1.78	0.39	
ASA score			0.69	0.368
I-II	1.00			
III	1.28	0.87-1.69		
Comorbidity				0.205
No	1.00			
Yes	1.36	0.58-1.49	0.58	
Grade (1973 WHO classification)				0.106
Grade 1-2	1.00			
Grade 3	1.18	0.74-1.89	0.49	
Postoperative 90-day complications				0.236
No	1.00			
Yes	1.21	0.69-1.35	0.50	
Adjuvant chemotherapy				0.158
Yes	1.00			
No	1.36	0.48-1.98	0.60	
Pathological T stage	1.00	1.55-2.88	2.69	0.020
T_1/T_2	2.38			
T_3/T_4				
Pathological N stage			2.90	
Negative	1.00			
Positive	1.98	1.48 -2.20		0.011

There were no significant differences between the elderly and nonelderly groups in terms of 5-year OS rate ($P = 0.274$) and 5-year DFS rate ($P = 0.110$). Recurrent tumors developed in 33.3% of patients in the elderly group and in 21.3% of patients in the nonelderly group. There were no significant differences in the sites of recurrence and time to first recurrence between the two groups (**Table 4**).

Multivariate analysis revealed that depth of tumor invasion and lymph node metastasis were associated with OS (**Table 5**). Multivariate analysis revealed that depth of tumor invasion, tumor grade, and lymph node metastasis were associated with DFS (**Table 6**).

Discussion

In general, elderly patients have higher comorbidity rates than nonelderly patients. Therefore, the risk of radical cystectomy for bladder cancer was considered to be higher in the nonelderly group than in the elderly group [4-10]. Previous studies reported that postoperative mortality and morbidity increased significantly among patients aged between 65 and 80 years [4, 10]. Advanced age was an independent risk factor for mortality and morbidity after radical cystectomy [4-10]. In the present study, the comorbidity rate, particularly for cardiovascular disease and type 2 diabetes mellitus, and ASA score, among elderly patients were higher than those for nonelderly patients. However, there were no significant differences between the two groups regarding postoperative outcomes. Furthermore, the 90-day postoperative complication rate in the elderly group did not increase compared with that in the nonelderly group. These outcomes were considered to be because of a uniform perioperative treatment following clinical pathways that were conventionally applied for postoperative care of bladder cancer patients at our institution. However, the present study sug-

Table 6. Multivariate Cox regression analyses of disease-free survival after laparoscopic radical cystectomy for bladder cancer

Regression variables	Adjusted hazard ratio	95% CI	Beta value	*P* value
Age				0.301
< 70 years	1.00			
≥ 70 years	2.01	0.87-2.36	0.60	
ASA score				0.310
I-II	1.00			
III	1.20	0.69-1.69	0.80	
Comorbidity				0.108
No	1.00			
Yes	2.12	0.87-2.61	0.72	
Postoperative 90-day complications				0.209
No	1.00			
Yes	1.25	0.59-1.69	0.63	
Adjuvant chemotherapy				0.160
Yes	1.00			
No	1.65	0.87-1.79	0.90	
Pathological T stage				0.036
T_1/T_2	1.00			
T_3/T_4	2.20	2.01-2.85	1.98	
Pathological N stage				
Negative	1.00			
Positive	3.01	2.05-3.58	1.68	0.014
Grade				
Grade 1/Grade 2	1.00			0.029
Grade 3	2.36	1.87-2.96	2.01	

gested that minimally invasive laparoscopic surgery for the elderly group was not inferior to that for the nonelderly group in terms of safety [77-84].

In our study, there were no significant differences in long-term survival outcomes between the elderly and nonelderly groups. Only few previous studies have analyzed survival data of laparoscopic surgery in elderly patients [5-8]. In our study, the 5-year OS and DFS rates for elderly patients were 58% and 59% and those for the nonelderly patients were 63% and 72%, respectively. Previous studies have not shown any significant differences in long-term outcomes between nonelderly and elderly groups [5-8]. Furthermore, the long-term survival outcomes reported in previous studies were similar to ours [4-10]. However, in our study, the elderly group tended to have a higher rate of cancer recurrence. One potential explanation for this is that fewer patients in the elderly group may have undergone adjuvant chemotherapy than 11-+those in the nonelderly group [85-92].

In the past, two patterns were used to analyze the safety and validity of laparoscopic radical cystectomy in elderly patients. One analyzed the outcomes between open and laparoscopic radical cystectomy in the elderly [5, 6], whereas the other analyzed the outcomes after laparoscopic radical cystectomy between the elderly and nonelderly [7, 8]. Recently, laparoscopic radical cystectomy is a common operative procedure to treat bladder cancer because it is less invasive [11-24]. Therefore, it was necessary to integrate the analysis of the outcome data of laparoscopic radical cystectomy between nonelderly and elderly patients. In previous studies, including our own, there were no significant differences between the nonelderly and elderly with regard to short-term outcomes after laparoscopic radical cystectomy, including incidence of postoperative complications [7, 8]. Based on the abovementioned findings, laparoscopic radical cystectomy appears to be more feasible and safe in the elderly and could be selected more frequently for this population with muscle-invasive and high-risk, recurrent, noninvasive bladder cancer.

However, this study has several limitations. First, it was based on a single-center, retrospective analysis, not prospective randomized analysis. Second, the size of sample was small and the follow-up period was not very long. These limitations should be considered when interpreting our study results. In the future, a multicenter, prospective, randomized controlled study with longer follow-up period is necessary to validate the safety of laparoscopic

radical cystectomy for elderly patients with bladder cancer.

In summary, laparoscopic radical cystectomy for bladder cancer was a safe and effective treatment for elderly patients, with comparable postoperative results and long-term outcomes, although elderly patients had a greater comorbidity rate than nonelderly patients.

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Disclosure of conflict of interest

None.

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