

Feasibility of Laparoscopic Radical Cystectomy in Elderly Patients: A Comparative Analysis of Clinical Outcomes in a Single Institution

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Laparoscopic radical cystectomy (LRC) is a standard surgical treatment for muscle-invasive bladder cancer and high-risk non-muscle-invasive bladder cancer. LRC is a less invasive modality than conventional open surgery. Therefore, even elderly patients with invasive bladder cancer may be candidates for LRC. In this study, a comparative analysis of perioperative/oncological outcomes between elderly patients and younger patients who underwent LRC was performed to assess the feasibility of LRC in elderly patients. Sixty-eight consecutive patients who underwent LRC between October 2013 and March 2018 were enrolled and stratified into those younger than 75 years ($n=37$) and those ≥ 75 years old ($n=31$). The median follow-up period was 28.2 months. The preoperative and operative parameters and complications were similar in both groups. The 2-year overall survival (OS) was 64.4% in the younger vs. 76.4% in the elderly group ($p=0.053$), cancer-specific survival (CSS) was 79.3% vs. 81.7% ($p=0.187$), and recurrence-free survival (RFS) was 58.2% vs. 75.7% ($p=0.174$), respectively. No significant differences were observed in OS, CSS, or RFS between the groups. No significant differences were found between the groups with respect to peri-surgical/oncological outcomes. We conclude that LRC is feasible in elderly patients.

Key words: bladder cancer, laparoscopic surgery, radical cystectomy, elderly patient

The rates of bladder cancer are highest in people aged 75-84 years, with a median age of 73 at diagnosis [1]. Radical cystectomy with pelvic lymph node dissection is the gold standard treatment for muscle-invasive bladder cancer (MIBC) and for selected patients with high-risk non-muscle-invasive disease (European association of Urology (EAU) guideline 2017 <https://urowb.rorg/guideline/bladder-cancer-muscle-invasive-and-metastatic/> (accessed September 1, 2018)). However, open radical cystectomy (ORC) is a procedure with high morbidity, and it is associated with a high complication rate [2]. Among patients with mus-

cle invasion, those aged 75 years and older were less likely to undergo radical cystectomy (14%) compared with patients aged 55-64 years (48%) and those aged 65-74 years (43%). Patient age may affect treatment decisions in patients with muscle-invasive disease [3]. In recent reports, laparoscopic radical cystectomy (LRC) has been shown to be a minimally invasive approach that limits blood loss and has the benefits of less postoperative pain and faster bowel function recovery compared with ORC [4]. However, the feasibility of LRC in very elderly patients remains unclear. We performed a comparative analysis of perioperative/clinical outcomes between elderly patients (≥ 75 years) and

younger patients (<75 years) who underwent LRC.

Patients and Methods

A total of 68 consecutive patients who underwent LRC between October 2013 and March 2018 were reviewed and divided into 2 groups, those who were 75 years old or older ($n=31$), and those below 75 ($n=37$), for comparison. Both groups were assessed for perioperative outcomes, including operating time, blood loss, complications, pathological findings, recovery, and oncological outcomes. The oncological indication of radical cystectomy in our institute was high-risk non-muscle-invasive bladder cancer with BCG failure or MIBC. The final surgical indication basically depended on the patient's condition (American Society of Anesthesiologists (ASA) class <2), not on age. The study design was approved by the Ethics Committee of Ehime University Hospital (No. 1806017), and it adhered to the Declaration of Helsinki.

Statistical analysis. Comparisons between groups were performed using the Mann-Whitney U -test and chi-squared test. The log-rank test was used to compare the Kaplan-Meier curves between the groups. Associations between variables and cancer-specific survival (CSS) were analyzed using Cox proportional hazards regression for CSS analysis, with data summarized by hazard ratios with 95% confidence intervals (CIs). All analyses were performed using the IBM Statistical Package for the Social Sciences (SPSS) version 21.0

(IBM Corp., Armonk, NY, USA), and values of $p < 0.05$ were considered to indicate statistical significance.

Results

The cohort included 37 patients younger than 75 years old and 31 patients (46%) 75 years old or older (Table 1). The preoperative parameters (sex, body mass index, ASA class, Charlson comorbidity index, performance status) were similar in both groups. However, significant differences were observed in hemoglobin ($p=0.034$), albumin ($p=0.038$), and the neoadjuvant chemotherapy rate ($p=0.016$) (Table 2). As for intraoperative data, the operative time (median 444 vs. 442 min), estimated blood loss (median 500 vs. 380 mL), and rate/range of pelvic lymphadenectomy were similar in both groups. We performed construction of an ileal neobladder (27.0%) in the younger patients and ureterostomy (22.6%) in the elderly patients. But no significant difference was observed in the distribution of urinary diversion ($p=0.562$) (Table 2). The rates of peri-/postoperative complications of all grades (Clavien–Dindo classification) were 32.4% vs. 29.0% ($p=0.577$) and those of complications over grade 3 were 16.2% vs. 9.7% in the younger and elderly groups, respectively. One patient from the elderly group needed intraoperative open conversion due to hypercapnia. No other patients needed open conversion (Table 3). The pathological findings showed that the positive surgical margin rates (10.8% vs. 6.6% in the

Table 1 Demographic and clinical characteristics

	Elderly group (≥ 75) $n = 31$	Younger group ($75 <$) $n = 37$	p -value
age median (range)	79 (75–90)	69 (37–74)	
Sex (male : female)	22 : 9	30 : 7	0.327
BMI median (range)	24.2 (16.6–31.1)	22.3 (17–37.3)	0.104
ASA class (1/2/3)	11/19/1	20/16/1	0.304
CCI median (range)	1 (0–5)	0 (0–9)	0.421
PS (0/1/2/3)	17/11/1/1	29/8/0/0	0.102
Hb, g/dl median (range)	11.6 (8.8–15.6)	12.6 (8.8–18.4)	0.034
Alb, g/dl median (range)	3.8 (3.0–4.6)	4 (3.3–4.9)	0.038
cT (cT2 over) n, (%)	25 (80.6)	34 (91.9)	0.158
cT (Tis/1/2/3/4)	(2/4/14/9/2)	(1/2/22/10/2)	0.677
cN(+) n, (%)	3 (9.7)	2 (5.4)	0.415
cM1 n, (%)	0	2 (5.4)	0.292
UC dominant n, (%)	29 (93.5)	34 (91.9)	0.585
Neoadjuvant chemo n, (%)	11 (35.5)	24 (64.9)	0.016
Follow-up, m median (range)	35.4 (8.6–60.3)	23.5 (7.4–54.3)	0.044

Table 2 Operative data and pathological data

	Elderly group (≥ 75) n = 31	Younger group ($75 <$) n = 37	<i>p</i> -value
Operating time, min median (range)	444 (312–640)	442 (279–595)	0.768
EBL, ml (range)	500 (30–5,610)	380 (40–2,550)	0.392
Transfusion, n (%)	14 (45.2)	13 (35.1)	0.4
LND, n (%)	24 (77.4)	33 (89.2)	0.189
extended LND	12 (38.7)	22 (59.5)	0.088
Number of LN, n median (range)	16.5 (0–30)	20 (4–37)	0.308
Urinary diversion, n (%)			0.562
ileal conduit	18 (58.1)	21 (56.8)	
ileal neobladder	6 (19.3)	10 (27.0)	
uretrostomy	7 (22.6)	5 (13.5)	
none	0	1 (2.7)	
pT (0/Tis/1/2/3/4)	(7/3/5/4/9/3)	(9/6/5/3/10/4)	0.956
pN+, n (%)	3 (9.7)	5 (13.5)	0.46
RM1, n (%)	2 (6.5)	4 (10.8)	0.425

Table 3 Complications (peri/post operation)

	Elderly group (≥ 75) n = 31	Younger group ($75 <$) n = 37	<i>p</i> -value
Perioperative complication	2 (6.5)	3 (8.1)	0.583
conversion (hypercapnia), n	1	0	
Rectal injury, n	0	2	
Obturator nerve injury, n	1	0	
Peroneal nerve palsy, n	0	1	
Post complication, n (%)	9 (29.0)	12 (32.4)	0.315
Major (\geq class III), n (%)	3 (9.7)	6 (16.2)	0.133
	Ileus 2, abscess 1	Ileus 3, abscess 1	
		Anastomotic leak 1	
		Heart failure 1	
Minor (\leq class II), n (%)	6 (19.4)	6 (16.2)	
	Pyelonephritis, SSI	Pyelonephritis, SSI, ileus	

younger vs. elderly group, respectively) and the distributions of pathological stage were also similar between the groups. The median follow-up period was 28.2 months (Fig. 1). The 2-year overall survival (OS) rate was 64.4% in the younger vs. 76.4% in the older group ($p=0.053$), the CSS rates were 79.3% and 81.7% ($p=0.187$), and the recurrence-free survival (RFS) rates were 58.2% and 75.7% ($p=0.174$), respectively. No significant differences in OS, CSS, or RFS between the younger and elderly groups were observed. Table 4 shows the Cox proportional hazards regression analysis for CSS. In CSS, the age, sex, LND, cN(+), NAC, \geq pT3, and pN(+), RM(+) were examined via univariable analysis. Significant differences were found in \geq pT3 (hazard ratio (HR) 7.207, 95% CI 2.221–23.390,

$p=0.001$) and RM(+) (HR 5.791, 95% CI 1.803–18.597, $p=0.003$). In the multivariable analysis, a significant difference was observed in \geq pT3 (HR 4.496, 95% CI 1.139–17.741, $p=0.032$), but no significant differences were observed in age or RM(+).

Discussion

Radical cystectomy is the gold standard treatment for MIBC and for selected patients with high-risk non-muscle-invasive disease. ORC is an invasive treatment with higher rates of peri- and postoperative complications (blood loss, infection, and ileus) in elderly patients compared with LRC [5]. In urological surgery, the standard urological surgery method has switched

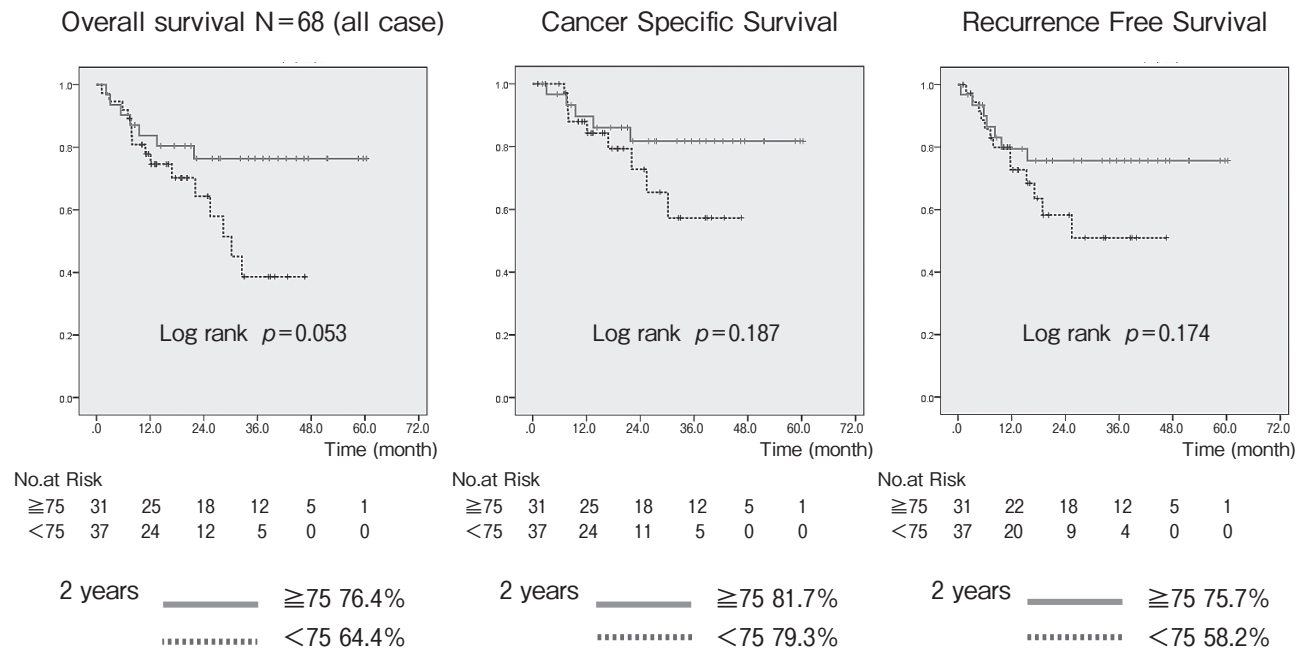


Fig. 1 Overall Survival, Cancer Specific survival, Recurrence Free Survival in LRC treatment.

Table 4 Cox proportional hazards regression analysis of cancer specific survival

	Univariable analysis			Multivariable analysis		
	HR	95% CI	p-value	HR	95% CI	p-value
Age ≥ 75 (vs < 75)	2.073	0.686–6.259	0.196			
Sex male (vs female)	2.171	0.485–9.706	0.311			
NAC	0.925	0.324–2.639	0.884			
LND	0.704	0.196–2.530	0.591			
cN (+)	2.419	0.539–10.859	0.249			
$\geq pT3$ (vs $< pT2$)	7.207	2.221–23.390	0.001	4.496	1.139–17.741	0.032
pN (+)	3.568	0.982–12.967	0.053	2.619	0.614–11.170	0.193
RM (+)	5.791	1.803–18.579	0.003	2.725	0.678–10.963	0.158

from open operation to laparoscopic/robotic surgery. Some systematic reviews have reported that LRC is a feasible and safe alternative to ORC with less blood loss and a lower transfusion requirement, a shorter length of hospital stay, and fewer complications. LRC does, however, have longer operative times [6,7]. Our data showed that the operative times were longer, but the complication rate was lower in the LRC in comparison with ORC, as reported previously [7]. The results obtained at our institute were not inferior to those of European multicenter studies in terms of the incidence of complications compared [8]. Treatment decisions should not be based on chronology alone, and

advanced age should not be a factor that precludes aggressive or curative therapy [9]. Preoperative nutritional status, serum albumin level, ASA class, and physical status are essential factors and should be considered [10-12]. In elderly patients (75 years and older), it has been reported that LRC has low rates of complications (ileus, infection). However, LRC has a longer operative time than ORC [5, 13, 14].

In a previous report, robot-assisted radical cystectomy (RARC) was shown to be associated with a lower rate of bleeding compared with ORC. However, its operative time was longer, and the rate of occurrence of complications was the same [15]. In addition, a ran-

domized trial comparing ORC, LRC, and RARC demonstrated that LRC had fewer complications than ORC and a shorter operative time than RARC [16]. At present, LRC remains the standard treatment for MIBC and selected patients with high-risk non-muscle-invasive disease.

We have typically constructed an ileal neobladder and ileal conduit for urinary diversion, and the selection of the diversion did not depend on the age of the patient. In cases with a single kidney or with a low performance status, cutaneous ureterostomy was selected with the intention of decreasing the rate of complications and shortening the operative time [17,18]. As shown in a prior report [19], an ileal conduit should be one of the standard urinary diversions for elderly patients undergoing radical cystectomy. On the other hand, cutaneous ureterostomy is also the procedure of choice for patients with limited dexterity, poor motivation, anatomical restrictions, and poor renal function.

In our results, prognostic parameters such as OS, CSS, and RFS tended to be more predictive in elderly patients than in younger patients, although the differences were not statistically significant. This trend in prognosis was caused by a tendency for more younger patients to exhibit highly malignant disease (cT2 over, cM1, pN+, and RM1).

Several studies have evaluated various factors to determine the prognosis of MIBC. Extravesical tumor (T3-T4), advanced age, non-urothelial variant histology, and a reduced number of lymph nodes removed have been established as poor prognostic factors for patients treated with radical cystectomy [8,20]. Although the current study has some limitations including its small sample size and its retrospective design, it found that advanced age was not a poor prognostic factor. Based on the results of our comparative analysis, we conclude that LRC is a feasible treatment in elderly patients. In conclusions, no significant differences were observed between the 2 groups with respect to peri-surgical/oncological outcomes. LRC in elderly patients was safe and had good results. Thus, LRC is feasible even in elderly patients.

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