RESEARCH ARTICLE

Laparoscopic Versus Open Radical Cystectomy for Patients Older than 75 Years: a Single-Center Comparative Analysis

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Abstract

Background: To explore the safety, efficacy, and oncological outcome of 3-port laparoscopic radical cystectomy (LRC) compared to open radical cystectomy (ORC) in patients older than 75 years. Materials and Methods: From June 2010 to July 2014, we analyzed 16 radical cystectomies in patients older than 75 years (LRC group=8; ORC group=8). Demographic parameters, operative variables, and perioperative outcome in the 2 groups were retrospectively collected, analyzed, and compared. Results: Patients in both groups had comparable preoperative characteristics. A significantly longer operating time (476 vs. 303 min, P=0.0002) and less estimated blood loss (627 *vs.* 2,106 mL, P=0.021) were observed in the LRC group compared to the ORC group. Infection and ileus were the most common early complications after surgery. Patients who underwent ORC suffered from more postoperative infection (22.2% *vs.* 0.0%, P=0.054) and ileus (25.0% *vs.* 12.5%, P=0.521) than the LRC group, but the difference was not significant. Conclusions: Judging from this initial trial, 3-port LRC can be safely carried out in elderly patients. We suggest 3-port LRC as the primary intervention to treat muscle-invasive or high-risk nonmuscle-invasive bladder cancer in elderly patients with an otherwise relatively long life expectancy.

Keywords: Laparoscopy - radical - cystectomy - older patients - bladder cancer

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Introduction

Radical cystectomy is the standard treatment for nonmetastatic, invasive bladder cancer. Unfortunately, this treatment is associated with clinically significant perioperative complications and prolonged recovery time, further compounded by the fact that patients with this disease are typically older and often have a history of comorbidities (Chavan et al., 2014). With marked improvements in medical technology and health care, the average life span of the general population in most countries has progressively increased. It is reported that the percentage of the Japanese population more than 75-years-old will reach 26.9% by 2060 (Cabinet et al., 2014). The strong association between age and bladder cancer incidence has made treating elderly patients with muscle-invasive or high-risk nonmuscle-invasive bladder cancer a crucial, but delicate, balancing act for urologists (Froehner et al., 2009; Gakis et al., 2013).

Traditionally, radical cystectomy is performed using an open surgical technique. Although open radical cystectomy (ORC) with different types of urine diversion has proved safe for elderly patients and remains the standard of care for the treatment of muscle-invasive bladder cancer, it is associated with significant short and long-term morbidity (Mendiola et al., 2007; Froehner et al., 2009; Gakis et al., 2013). Elderly patients, especially those older than 75 years, almost always present with several comorbidities, thus putting these patients at an even greater risk of complications or mortality (Bostrom et al., 2009; Richards et al., 2012). As a result, older patients may be guided toward more conservative, less effective therapies such as radiation therapy with or without chemotherapy, or palliative transurethral resection (Mendiola et al., 2007). It is imperative for us to find ways of minimizing the perioperative morbidity and mortality in elderly patients.

Since the first report by Parra et al. (1992), laparoscopic radical cystectomy (LRC) has become a viable alternative to ORC with the advancement of laparoscopic equipment and the increased skills of urologists performing minimally invasive surgery (Sighinolfi et al., 2007; Tang et al., 2014). The elderly patient still poses several challenges to LRC, such as whether patients can tolerate the longer operation time, risk of pneumoperitoneum, and peculiar surgical position. Few studies, however, have focused on the feasibility of LRC compared to ORC in patients older than 75. We previously reported the effects of multichannel trocar use in 2-port laparoscopic

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prostatectomy for prostate cancer with the aim of achieving safer and less invasive surgeries (Nakane et al, 2013). Here, we applied the same method to 3-port LRC with the intention of exploring the surgery's safety, efficacy, morbidity, mortality, and oncological outcome in patients older than 75 by conducting an ORC-controlled, retrospective single-center study.

Materials and Methods

Between June 2010 and July 2014, 49 patients underwent LRC or ORC and urinary diversion in our institution. The median age was 69 years old (range 39 to 81). We changed the total cystectomy operation type from LRC to ORC in May 2013. Of the 49 patients, 16 were older than 75 (LRC group=8; ORC group=8). All participants were informed upon hospital admission that their clinical information might be used in a later clinical study, and their written informed consent was obtained. All procedures were performed in accordance with the ethical principles expressed in the 1995 Declaration of Helsinki. Patient information was anonymized prior to analysis. The indication for radical cystectomy was histologically diagnosed muscle-invasive bladder cancer by transurethral resection, biopsy-confirmed recurrent multifocal high-grade superficial bladder cancer, or bladder cancer in situ refractory to repeated transurethral resection. The clinical and follow-up data were retrospectively collected and analyzed from our bladder cancer database.

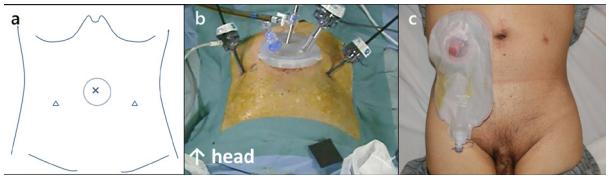

Figure 1. (a) Sham of 3-port laparoscopic radical cystectomy. (b) Multichannel trocar placed on umbilical incision and two 5-mm ports were inserted into the bilateral fossa. (c) Abdominal photograph of ileal conduit division patient, immediately postoperatively.

All patients underwent a thorough preoperative examination including routine laboratory tests, chest radiograph, intravenous pyelogram, echocardiograph, lung function test, computerized tomography or magnetic resonance imaging, and abdominal ultrasonography. Patients were graded according to the American Society of Anesthesiologists (ASA) system. Common comorbidities such as hypertension, coronary artery disease, chronic obstructive pulmonary disease, diabetes mellitus, and other chronic diseases were recorded.

All patients began a semiliquid diet 2 days prior to surgery. The day before surgery, patients began a liquid diet and underwent bowel preparation with 34 g magnesium citrate 18 hours before surgery. All patients wore compression stockings before entering the operating room. A broad-spectrum systemic antibiotic was given intravenously during induction of anesthesia. Either LRC or ORC, both with bilateral pelvic and iliac lymphadenectomy for men and women, was performed according to the procedures described by Campbell-Walsh Urology (Wein A., 2012). The LRC urinary diversion was reconstructed extracorporeally through a 5 cm supraumbilical multichannel trocar, which included the camera port.

Laparoscopic access was performed as follows. After umbilical incision, we incised the anterior rectus fascia and vertically separated the rectus muscle fibers. Next, the peritoneum was incised to the abdominal cavity. A multichannel trocar (EZ ACCESS, EZ trocar 5 mm, Lap-Protector; Hakko, Nagano, Japan) was placed just beneath the incision, allowing simultaneous use of up to 3 instruments: a 5 mm 0° lens laparoscope with a flexible tip (Olympus Surgical, Tokyo, Japan) plus 2 operative instruments. In addition, 2 5 mm ports were inserted

Table 1. Baseline Patient Characteristics

	LRC	ORC	P value
Age, median (IQR)	78 (76, 81)	79 (77, 83)	0.194*
Gender, men/women	5/3	6/2	0.590**
BMI, mean ± SD	23.9 ± 4.4	22.0 ± 4.0	0.393*
Hb, mean ± SD (g/L)	121.3 ± 17.9	125.8 ± 10.7	0.554*
Serum creatinine, mean ± SD (μmol/L)	109.3 ± 60.1	91.7 ± 34.1	0.487*
Serum albumin, mean ± SD (g/L)	36.8 ± 3.4	37.6 ± 6.9	0.756*
MC needed before surgery (n%)	3 (37.5%)	2 (25.0%)	0.590**
ASA class (n%)			0.590**
2	6 (75.0%)	5 (62.5%)	
3	2 (25.0%)	3 (37.5%)	
Surgery history (n%)			
Abdominal surgery	4 (50.0%)	1 (12.5%)	0.106**
Nephrectomy	1 (12.5%)	2 (25.0%)	0.521**
Comorbid conditions (n%)			
Coronary heart disease	1 (12.5%)	1 (12.5%)	1.000**
Hypertension	3 (37.5%)	5 (50.0%)	0.317**
Diabetes mellitus	0 (0.0%)	1 (12.5%)	0.302**
COPD	1 (12.5%)	1 (12.5%)	1.000**
Other chronic diseases	1 (12.5%)	1 (12.5%)	1.000**

*LRC = laparoscopic radical cystectomy; ORC = open radical cystectomy; IQR = Interquartile range; BMI = body mass index; Hb = hemoglobin; MC = multidisciplinary consultation; ASA = American society of anesthesiologists; COPD = chronic obstructive pulmonary disease; *Student t-test was used for statistical analysis; **Chi-square tests were used for statistical analysis.

into the bilateral fossa to facilitate the use of standard laparoscopic instruments (Figure 1).

The demographic parameters included age, gender, body mass index (BMI), comorbidities, surgical history, laboratory test results, and whether multidisciplinary consultations were needed. Operative variables were operating time (defined as anesthesia duration), estimated blood loss (EBL), and transfusion. Perioperative outcomes were time to liquid intake, time to exsufflation, time to canalization, and postoperative hospital stay. Early complication was defined as events within 90 days and late events as more 90 days after the operation (Froehner et al., 2009). Oncological outcomes, including survival and recurrence, were evaluated. The pathological tumor stage and grade were determined according to the TNM classification and the World Health Organization system of 2004, respectively (Eble et al., 2004; Sobin et al., 2009).

The chi-square test, Mann-Whitney U test, and Student t test were used to compare categorical, nonparametric, and parametric data, respectively, between the 2 groups. Differences were considered significant when P<0.05. Statistical analysis was performed with SPSS Statistics, version 19.0 (IBM Inc., Armonk, NY, USA).

Table 2. Pathological Results

	LRC	ORC	P value
Pathological stage (n%)			0.198**
Tis, T1	1 (12.5%)	5 (62.5%)	
T2	2 (25.0%)	1 (12.5%)	
T3	4 (50.0%)	2 (25.0%)	
T4	1 (12.5%)	0 (0.0%)	
Grade (n%)			0.302**
Low grade	1 (12.5%)	0 (0.0%)	
High grade	7 (78.5%)	8 (100%)	
Lymph node status (n%)			0.131*
Negative	6 (75.0%)	8 (100%)	
Positive	2 (25.0%)	0 (0.0%)	
Lymph node number	9.3 ± 1.8	5.4 ± 2.6	0.004*
Positive surgical margins	0 (0.0%)	0 (0.0%)	1.000**

*LRC = laparoscopic radical cystectomy; ORC = open radical cystectomy; *Student t-test was used for statistical analysis; **Chi-square tests were used for statistical analysis.

Results

Patients in the LRC and ORC group had comparable preoperative demographic and clinical preoperative characteristics (Table 1). Pathological results were also comparable between the 2 groups (Table 2).

There was no conversion to open surgery in the LRC group. The operative and postoperative characteristics are shown in Table 3. Significant differences were observed between the 2 groups regarding operating time, EBL, and postoperative hospital stay. The LRC group required a significantly longer mean operating time than the ORC group (476 min *vs*. 303 min, p=0.002). The median EBL was 630 mL for LRC and 1,286 mL for ORC (P=0.021). The rate of required transfusion of ORC (75.0%) was nearly twice that of LRC (37.5%) (P=0.131). The median postoperative hospital stay was 23 days for LRC and 3 days for ORC (P=0.020). Compared with preoperative data, serum albumin significantly decreased to 11.8±2.3 g/L and 12.1±6.1 g/L (both P<0.001) for LRC and ORC, respectively. Hemoglobin also significantly decreased to 11.8±7.1 g/L and 20.5±18.2 g/L (both P<0.001) for LRC and ORC, respectively. There was no significant change in serum creatinine in either group. Two patients in the LRC group and 4 in the ORC group required postoperative multidisciplinary consultation (P=0.302), a result of more complications overall in the ORC group, but the difference was not significant.

Postoperative complications are noted in Table 4. Infection and ileus were the most common early postoperative complications. Patients who underwent ORC suffered from more postoperative infections (37.5% *vs*. 0%, P=0.054) and ileus (25.0% *vs*. 12.5%, P=0.521) than those in the LRC group within 90 days after surgery, but the difference was not significant. Postoperative complications necessitated reoperation in 2 ORC group patients (Table 4), but no LRC group patients required reoperation. No patient in either group died from operation-related complications.

The median follow-up was 8 months (range 2-16 months) and 22 months (range 16-50 months) for the

Table 3. Operative and Postoperative Characteristics.

	LRC	ORC	P value
Operative time, mean ± SD (min)	476 ± 83	303 ± 99	0.002*
Estimated blood loss (mL), median (IQR)	630 (136, 1567)	1,286 (650, 5706)	0.021#
Transfusion needed (n%)	3 (37.5%)	6 (75.0%)	0.131**
Division (n%)			1.000**
Ileal conduit	4 (50.0%)	4 (50.0%)	
Ureterocutaneostomy	4 (50.0%)	4 (50.0%)	
Hb, mean ± SD (g/L)	109.5 ± 14.9	105.3 ± 12.9	0.552**
Serum creatinine, mean ± SD (μmol/L)	102.7 ± 52.6	92.2 ± 28.4	0.802**
Serum albumin, mean ± SD (g/L)	25.0 ± 3.4	25.5 ± 4.3	0.791**
MC needed after operation (n%)	2 (25.0%)	4 (50.0%)	0.302*
Time to liquid intake, mean ± SD (day)	1.8 ± 0.5	2.6 ± 1.2	0.132*
Time to nasogastric tube removal, mean ± SD (day)	0.9 ± 0.4	1.3 ± 0.7	0.209*
Time to canalization, mean ± SD (day)	11.4 ± 3.2	12.8 ± 2.2	0.451*
Time to exsufflation, mean ± SD (day)	3.8 ± 0.9	4.1 ± 0.6	0.353*
Hospital stay after surgery (day), median (IQR)	23 (18, 30)	31 (23, 50)	0.020#

*LRC = laparoscopic radical cystectomy; ORC = open radical cystectomy; Hb = hemoglobin; MC = multidisciplinary consultation; *Student t-test was used for statistical analysis; **Chi-square tests were used for statistical analysis; #Mann-Whitney U was used for statistical analysis

Table 4. Postoperative Complications

	LRC	ORC	P value
Early complications <90 days (n%)			
Infectiona	0 (0.0%)	3 (37.5%)	0.054**
Ileusb	1 (12.5%)	2 (25.0%)	0.521**
Delirium	1 (12.5%)	2 (25.0%)	0.521**
Wound dehiscence	0 (0.0%)	2 (25.0%)	0.131**
Diarrhea	1 (12.5%)	1 (12.5%)	1.000
Late complications >90 days (n%)			
Pyelonephritis	0 (0.0%)	2 (25.0%)	0.131**
Illeus	0 (0.0%)	2 (25.0%)	0.131**
Ureteral stricture	0 (0.0%)	2 (25.0%)	0.131**
Reoperation required	0 (0.0%)	2 (25.0%)	0.131**
Mortalityc (n%)			
<90 days	0 (0.0%)	0 (0.0%)	1.000
>90 days	0 (0.0%)	0 (0.0%)	1.000

[a] Patients diagnosed with infection when they presented continuous fever and antibiotics were considered the most effective treatment for resolution; [b] Ileus was diagnosed when gas-fluid levels were seen in abdominal X-rays; [c] Mortality was calculated as death attributed by operation; **Chi-square tests were used for statistical analysis

LRC and ORC group, respectively. At the last follow-up, 7 (87.5%) and 5 (62.5%) patients were alive in the LRC and ORC group, respectively. The majority of patients (85.7%, 6/7) in the LRC group and all patients in the ORC group remained disease-free. Cancer-specific death occurred in 1/1 (100%) and 0/3 (0%) patients the LRC and ORC group, respectively.

Discussion

In most countries, the general population's life expectancy is increasing, but it has been estimated that nearly 1 in 3 people older than 70 may suffer from a wide variety of malignant tumors, the main factor negatively affecting the health of elderly people, including bladder cancer. The trend is distinctly noticeable with increasing age, especially in those older than 70 (Froehner et al., 2009).

Elderly patients with muscle-invasive or high-risk nonmuscle-invasive bladder cancer who require major surgery, such as cystectomy, pose difficult challenges for the operative surgeon. This dilemma is due to the combined complexity of comorbidities and greater risk of complications and mortality in this subset of patients (Froehner et al., 2009; Morgan et al., 2011). These considerations have collectively led to delaying cystectomy for elderly patients. It is reported that only 25% of patients 70-79 years old with muscle-invasive bladder cancer were treated with radical cystectomy compared to 55% of those aged 55-59 years old (Prout et al., 2005). Recently, however, several studies have proved that age should not be a limiting factor for selecting radical cystectomy as a treatment for muscle-invasive bladder cancer (Prout et al., 2005; Froehner et al., 2009; Guillotreau et al., 2009; Zeng et al., 2014).

Although studies have proved that elderly patients can safely undergo cystectomy, this surgical procedure is always associated with a high incidence of postoperative complications and morbidity. Patients older than 75 who underwent ORC suffered an early complication rate from 38.6% to 64%, a late complication rate of 16.4% to 42%, and a 30-day postcystectomy mortality rate from 2% to 6% (Game et al., 2001; Soulie et al., 2002; Zebic et al., 2005; Sogni et al., 2008). Use of minimally invasive treatments, such as laparoscopic surgery, has been expanding rapidly, encouraged by excellent perioperative and oncological results in renal cell and prostate cancer treatments and field-wide technical developments (Richards et al., 2012). Studies have suggested that LRC could reduce blood loss, analgesic consumption, and postoperative complications and promote earlier recovery of bowel function and return to normal activity (Guillotreau et al., 2012; Richards et al., 2012). Despite these advantages, ORC is still considered the gold-standard for muscle-invasive or high-risk nonmuscle-invasive bladder cancer, especially for elderly patients (Gakis et al., 2013).Concerns regarding the unusual Trendelenburg position and tolerability of pneumoperitoneum-caused metabolic acidosis in elderly patients with limited renal reserve are contributing factors, but to our knowledge, comparative data of morbidity rate and long-term survival benefit validating these concerns for patients older than 75 are lacking (Richards et al., 2012). Compounding the lack of data, many surgeons performing LRC tend to select relatively younger patients with a healthy BMI and good comorbidity profile and typically offer the procedure only to patients with organ-confined, nonbulky bladder cancer (Murphy et al., 2008). These favorable selection criteria would also naturally encourage quicker LRC recovery with a lower probability of transfusion and other complications. Beginning after May 2013, in this study, we attempted LRC for all patients in whom a total cystectomy was indicated, effectively removing selection bias for LRC. If LRC was unable to be performed, we planned to convert to ORC, but no conversion was necessary.

Zeng et al. (2014) and Richards et al. (2012) conducted observational studies to justify the feasibility of LRC and robot-assisted radical cystectomy (RRC), respectively, compared to ORC in elderly bladder cancer patients. In spite of longer operating times (413 *vs*. 337 min), LRC achieved similar perioperative outcomes without compromising pathologic outcomes, and with less EBL (400 *vs*. 500 mL) and fewer complications (infection and ileus) compared with ORC (Zeng et al., 2014). Similar results were achieved with RRC (Richards et al., 2012), although a randomized trial by experienced surgeons at a high-volume center reported similar rates of perioperative complications among patients undergoing RRC and ORC (Bochner et al., 2014).

We performed LRC with a multichannel trocar and two 5-mm ports, although single-site, minimally invasive surgery is also appropriate in some cases (Horstmann et al., 2012). Our operation with 3-port LRC was similar to that with 5-port LRC.

In the present study, the LRC group experienced less EBL and significantly reduced infection incidence within 90 days postoperatively compared to the ORC group. Furthermore, patients in the LRC group required fewer postoperative multidisciplinary consultations (25.0% *vs*. 50.0%, P=0.302), indicating a smoother recovery. Serum albumin was significantly reduced in both groups.

The value is thought to reflect nutritional status and is strongly associated with mortality, accounting for a 2.5-fold increase in the risk of 90-day mortality per each 7 g/L decrease in serum albumin (Zeng et al., 2014). Postoperative nutritional consideration in both procedures is required to reduce the possibility of delayed recovery. Postoperative hospital stay in the LRC group was shorter than in the ORC group, but overall hospital stay in our institution was longer than in previous reports (Guillotreau et al., 2012; Richards et al., 2012). As the Japanese medical insurance system is mostly responsible for cost, duration of hospitalization is of secondary consideration for patients who are generally discharged only after sufficient wound healing. In elderly patients, this is a lengthy process, but shortened after LRC due to fewer complications and an improved rehabilitation system.

The limitations of this study should be noted. First, the nature of a retrospective study made it impossible to completely avoid selection and attrition biases, especially as LRC began after ORC and the study periods differed. A randomized, prospective study stratified and matched for age, medical comorbidity, and urinary diversion as well as long-term follow-up would be ideal for assessing the effect of LRC on elderly patients. Second, the sample size of this study was small and potentially suffered from volunteer bias. In most cases, patients older than 75 years, especially those with poor physical conditions, were reluctant to undergo such a major surgery. The results may only reflect the outcome of those elderly patients with acceptable physical conditions and more optimistic attitudes.

The results of this study demonstrate that LRC has similar efficacy compared to ORC, with fewer postoperative complications and less EBL. We suggest considering LRC as the primary intervention for treating muscle-invasive or high-risk nonmuscle-invasive bladder cancer in elderly patients with an otherwise relatively long life expectancy. However, more and larger, prospective randomized studies are needed to confirm these results.

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