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Pure Laparoscopic Radical Cystectomy with Ileal Conduit: A Single Surgeon's Mid-Term Outcomes

Bumsoo Park,[1,2,3] Byong Chang Jeong,[1,2] Seong Soo Jeon,[1,2]
Hyun Moo Lee,[1,2] Han Yong Choi,[1] and Seong Il Seo[1,2]

[1]Department of Urology, [2]Institute for Refractory Cancer Research, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul; [3]Department of Urology, Kangnam General Hospital, Yongin, Korea.

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Corresponding author: Dr. Seong Il Seo, Department of Urology, Samsung Medical Center, Sungkyunkwan University School of Medicine, 81 Irwon-ro, Gangnam-gu, Seoul 135-710, Korea.
Tel: 82-2-3410-3559, Fax: 82-2-3410-6992
E-mail: siseo@skku.edu

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Purpose: The use of laparoscopic radical cystectomy (LRC) for muscle-invasive bladder cancer is not yet widespread because of the technical difficulties of the procedure and the lengthy operating time. In this study, we report a single surgeon's experience with LRC. **Materials and Methods:** Thirty patients (25 men and 5 women) with bladder cancer underwent LRC and ileal conduit by a single surgeon between November 2007 and May 2011. An extracorporeal urinary diversion was performed through 5-6 cm midline incision for specimen extraction. **Results:** The median operating time and estimated blood loss were 527.5 minutes and 275 mL, respectively. There was no conversion to open surgery. The median time to oral intake and postoperative hospital stay were 5 days and 12 days, respectively. The rates of immediate, early postoperative and late postoperative complication were 3.3%, 20% and 20%, respectively. With 16 months of median follow-up, the overall and recurrence-free survival rates were 70% and 56.7%, respectively. **Conclusion:** LRC is feasible for the management of invasive bladder cancer and, with appropriate patient selection, can be a good alternative to open or robot-assisted radical cystectomy in the era of robot-assisted surgery.

Key Words: Urinary bladder neoplasms, cystectomy, laparoscopic surgery

INTRODUCTION

Open radical cystectomy (ORC) is the universally accepted gold standard for treating muscle-invasive, organ-confined bladder cancer (BCa). However, ORC is considered one of the most invasive surgeries in the urology field with significant morbidity and mortality rates. The perioperative complication rate before 1970 was about 35%, with a mortality rate of nearly 20%.[1] With improvements in medical, surgical, anesthetic, and intensive care techniques, the mortality rate has decreased significantly, with current estimates of about 2.5%.[2] The morbidity of this surgery still remains high, with an overall complication rate of nearly 30%.[2,3] Therefore, urologists have attempted various techniques to reduce the morbidity. At present, there is increasing interest in both laparoscopic radical cystectomy (LRC) and robot-assisted laparoscopic radical cystectomy (RALRC), indicating that min-

imally invasive radical cystectomy for muscle-invasive BCa is one of the final frontiers of urologic oncology. The main objective of using these minimally invasive technologies is to reduce procedure-related morbidity. Published reports on LRC have shown this advantage over ORC in a nonrandomized setting.[4] Also, these new techniques are believed to lead to faster recovery, shorter hospital stay, and more rapid return to daily activities compared with ORC, while yielding the same oncologic and functional outcomes.

However, the use of LRC is not yet widespread because of the technical difficulties of the procedure and the lengthy operating time (OT). Furthermore, with the recent development of the da Vinci® Surgical System (Intuitive Surgical, Sunnyvale, CA, USA), there is a trend for increasing popularity of RALRC because it provides better surgical control, better vision, decreased tiredness of the surgeon, and has a faster learning curve compared to LRC. However, RALRC has its own disadvantages, such as a higher cost. Therefore, the usefulness of LRC in the treatment of muscle-invasive BCa in the field of minimally invasive surgery should not be overlooked, even in the current era of robotic surgery.

We present a single surgeon's experience and mid-term oncologic outcomes of LRC with ileal conduit in 30 patients.

MATERIALS AND METHODS

Patient selection

Between November 2007 and May 2011, 30 consecutive patients in our department who underwent LRC by a single surgeon (S.I.S.) were enrolled in this study. Indications included 1) muscle-invasive BCa, 2) T1G3 or high-risk and recurrent superficial BCas, and 3) extensive non-muscle-invasive BCas that could not be controlled by transurethral resection and intravesical therapy. All patients underwent transurethral resection of the bladder tumor before LRC. A single surgeon performed LRC for radical cystectomy and did not perform ORC in the same period. By comparison, other surgeons in our center performed 104 ORCs in the same period.

Patient preparation

The patient bowel was prepared with oral administration of polyethylene glycol and rectal bisacodyl enema. A nasogastric tube was inserted into the stomach, and a rectal tube was positioned in the rectum up to 10 cm from the anus. An 18 F Foley catheter with 5 mL ballooning was inserted to drain the bladder before the operation. General anesthesia with endotracheal intubation was performed for all patients.

Operative technique

The patient was placed in the supine position with both arms positioned closed to the trunk and in a frog-leg position. The table was slightly flexed and set in the Trendelenburg position at 25 to 30 degrees. A 5-port transperitoneal approach was used. An approximately 12 mm vertical incision was made 2 to 3 cm above the umbilicus for the camera port. Pneumoperitoneum was established after inserting the Veress needle, after which a 12-mm dilating trocar was inserted in this area for the camera port. The remaining four ports were formed under direct laparoscopic vision to avoid any bowel injuries. The second and third ports were placed 2 cm below the umbilicus on both sides of the midclavicular line. The fourth and fifth ports were positioned 2 to 3 cm superior and medial to both sides of the anterior superior iliac spines (Fig. 1).

Bilateral pelvic lymph node dissection (PLND) was performed first or after cystectomy. The boundaries of a PLND were the aortic bifurcation proximally, the genitofemoral nerve laterally, the circumflex iliac vein and lymph node of Cloquet distally, and the hypogastric vessels posteriorly, including the obturator fossa. The lymph nodes were immediately entrapped in a Lapbag (Angiomed-Bard, Karlsruhe, Germany) and extracted through the trocar site.

After an adhesiolysis between the abdominal wall and intestines, both ureters were dissected distally and ligated using a Hem-o-lok (Teleflex Medical, Research Triangle Park, NC, USA) near the bladder and transected. The distal margins of the ureters were sent for frozen section biopsy. The lateral

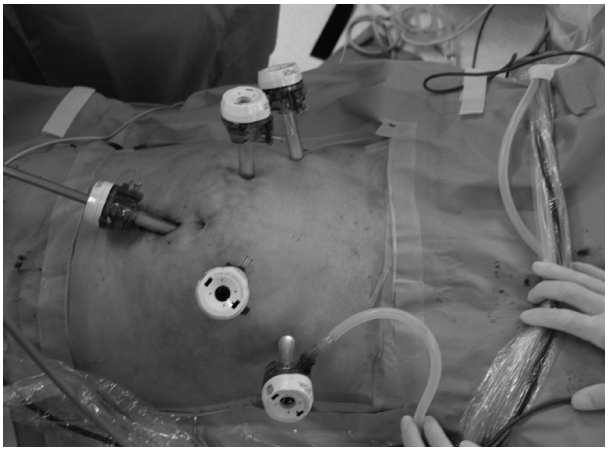

Fig. 1. Fan-shaped transperitoneal placement of 5 ports for laparoscopic radical cystectomy.

and posterior pedicles of the bladder and the prostate were divided with a Hem-o-lok or LigaSure (Covidien, Boulder, CO, USA). An inverted U-shaped anterior parietal peritoneotomy was made to expose Retzius' space, and the endopelvic fascia was incised bilaterally. The puboprostatic ligament was divided, and the dorsal vein complex was suture ligated. The apex of the prostate and the urethra were divided by scissors, and the urethral margins were sent for frozen biopsy. The specimen was placed in a Lapbag and extracted through an extended incision about 6 cm from the camera port. Then the left ureter was transposed to the right side passing under the sigmoid mesocolon.

An ileal conduit was created extracorporeally using a 6 cm-sized midline incision. This procedure was exactly the same as that of ORC, and there was no difficulty in forming an ileal conduit using the small midline incision (Fig. 2). For the five female patients, hysterectomy and bilateral salpingo-oophorectomy were performed by the gynecologic surgical team. After hysterectomy, a 100 mL Jackson-Pratt drain bag was packed in the vagina to maintain the pneumoperitoneum.

Follow-up methods

Postoperative follow-up was conducted at 6-month intervals. Follow-up visits consisted of a history, physical examination, complete blood count with differential count, routine biochemical profile, urinalysis, urine cytology, chest radiograph, and abdominal/pelvic computed tomography (CT) scans. Positron emission tomography scans were performed at 12-month intervals instead of the abdominal/pelvic CT scans at those follow-up visits. Bone scans were performed when clinically indicated. We updated the survival status of all patients through telephone contact in June 2011.

Statistical analysis

Kaplan-Meier plots were used to estimate overall survival (OS) and recurrence-free survival (RFS) for all patients. One-way analysis of variance (ANOVA) was used to estimate the learning curve. The Mann-Whitney U test was used to compare the OTs and estimated blood losses between male and female groups. All analyses were conducted using SPSS v.19.0 (SPSS Inc., Chicago, IL, USA), and a p value <0.05 was considered to be statistically significant.

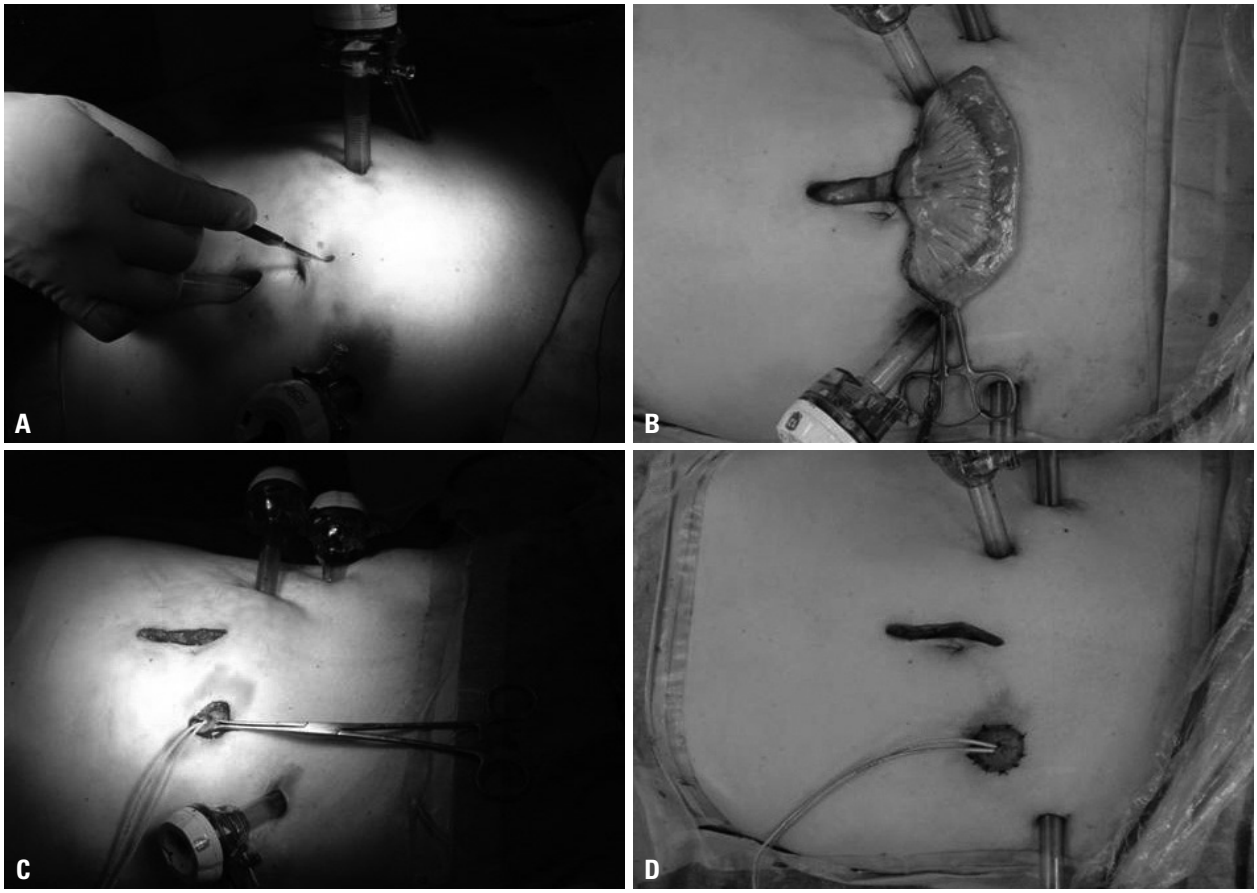

Fig. 2. Procedures for extracorporeal ileal conduit urinary diversion. (A) Mini-laparotomy incision about 6 cm at midline with extending the camera port. (B) Extracorporeal formation of the ileal conduit segment. (C) Formation of stoma. (D) Completion of extracorporeal ileal conduit urinary diversion.

RESULTS

Patient characteristics

The median age and body mass index were 63 years (range 45 to 81) and 22.65 kg/m^2 (range 18.14 to 30.08), respectively. Patients were stratified according to the American Society of Anesthesiologists classification: class 1, 6 patients (20%); class 2, 17 patients (56.7%); class 3, 7 patients (23.3%). Seven patients (23.3%) had a history of previous abdominal surgery, 2 of whom underwent open or laparoscopic nephroureterectomy with bladder cuff resection for previous upper tract urothelial carcinomas (Table 1).

Operative data

Radical cystectomy was completed laparoscopically without conversion to the open technique in all patients, and there was no perioperative mortality. The median OT was 527.5 min (range 330 to 1039). The median estimated blood loss (EBL) was 275 mL (range 100 to 2000), with a transfusion rate of 13.3% (4 of 30). Fig. 3 demonstrates sequential changes in OT and EBL, which also reflect the single surgeon's learning curve. To statistically evaluate the surgeon's learning curve, we divided the 30 patients into 3 groups (first, middle, and last 10 cases) and compared the OTs and EBLs using one-way ANOVA. However, there were no significant differences in OT (p=0.257) and EBL (p=0.667) between those groups.

The mean number of lymph nodes removed was 19.3 (range 6 to 36), 17 (range 6 to 30) in the standard PLND of 14 patients (46.7%) and 21.4 (range 9 to 36) in the extended PLND of 16 patients (53.3%). The median pain numerical rating scale measured on the day immediately after surgery was 5 of 10. The median time to oral intake was 5 days (range 4 to 7), and the median postoperative hospital stay was 12 days (range 9 to 30) (Table 2).

Complications

Complications were classified as immediate, early postoperative, and late postoperative and were graded according to the modified Clavien classification system.[5] In this series, we observed 3.3% (1 of 30), 20% (6 of 30), and 20% (6 of 30) immediate, early postoperative, and late postoperative complications, respectively (Table 3). Intraoperative obturator nerve injury occurred in one patient, but it was immediately repaired using a sural nerve graft by the plastic surgical team, and the patient underwent postoperative rehabilitation. Three patients had a bowel ileus in the early postoperative period but were easily managed by nil per os and active ambulation without any further bowel complications. All other perioperative complications listed were managed medically or surgically without any further sequelae.

Histopathologic and oncologic outcomes

Most tumors were urothelial carcinoma (28 of 30, 93.3%). There were two non-urothelial carcinomas, including one adenocarcinoma and one large cell neuroendocrine carcinoma. Of the total population, 6.7% (2 of 30) had carcinoma *in situ* (pTis), 40% had organ-confined disease (stage pT2

Table 1. Preoperative Patient Characteristics

Characteristics	Values
Gender	
Women, n (%)	5 (16.7)
Men, n (%)	25 (83.3)
Median age, yrs (range)	63 (45-81)
Median body mass index, kg/m^2 (range)	22.65 (18.14-30.08)
Median ASA score	2
ASA class, n (%)	
1	6 (20)
2	17 (56.7)
3	7 (23.3)
Smoking history, n (%)	13 (43.3)
Mean pack-yr (range)	16.85 (0-140)
Previous abdominal or pelvic surgery, n	
Repair of bowel perforation	2
Open NUx with bladder cuff resection	1
Laparoscopic NUx with bladder cuff resection	1
Herniorrhaphy	1
Laparoscopic cholecystectomy	1
Resection of ovarian cyst	1
Preoperative clinical T stage, n (%)*	
cTa	2 (6.7)
cT1	5 (16.7)
cT2	22 (73.3)
cT3	1 (3.3)
Tis associated	0 (0)
Preoperative histological grade, n (%)*	
Grade I	1 (3.3)
Grade II	6 (20)
Grade III	21 (70)
Unclassified*	2 (6.7)

ASA, the American Society of Anesthesiologists; NUx, nephroureterectomy.
*For non-urothelial carcinomas.

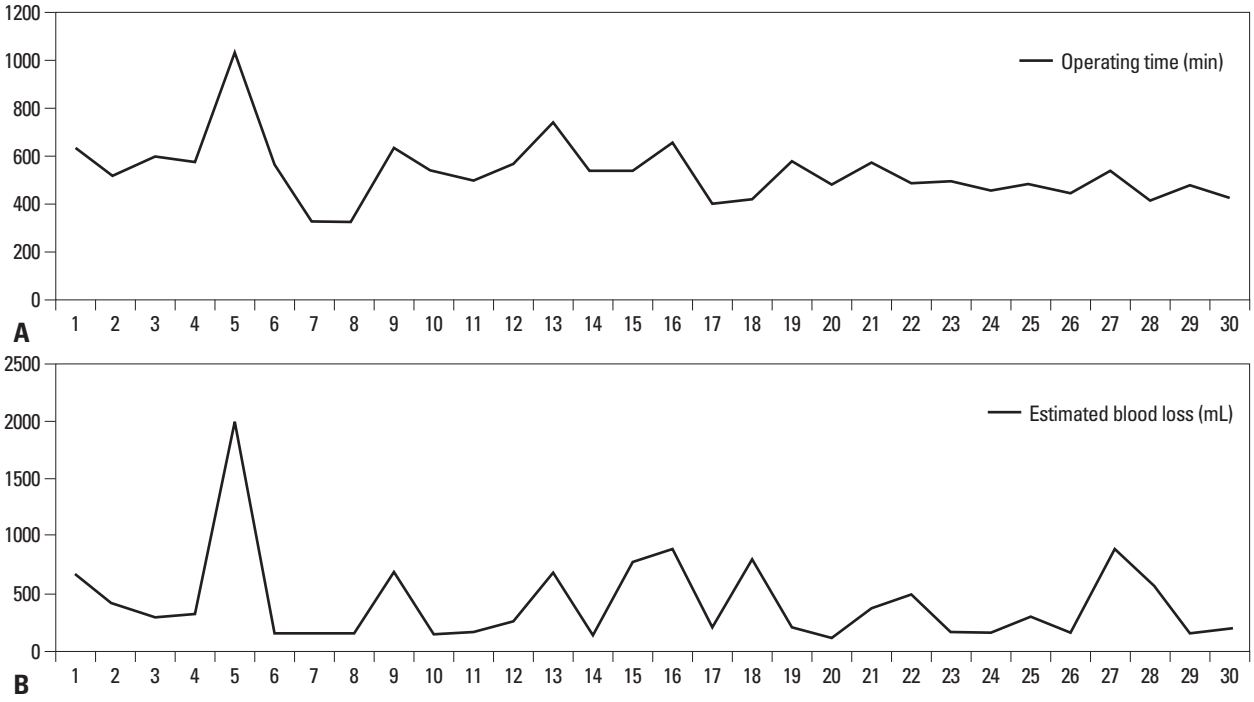

Fig. 3. Sequental changes in operating time (A) and estimated blood loss (B) reflecting the surgeon's learning curve.

Table 2. Operative Data

Parameters	Values
Median (range) operating time, min	527.5 (330-1039)
Median (range) estimated blood loss, mL	275.0 (100-2000)
Transfusion rate, n (%)	4 (13.3)
Conversion rate, n (%)	0 (0)
Mean (range) no. of lymph nodes removed, n	19.3 (6-36)
Urethrectomy, n (%)	5 (16.7)
Perioperative complication rate, n (%)	13 (43.3)
Perioperative mortality rate, n (%)	0 (0)
Median (range) pain NRS	5 (2-10)
Median (range) time to oral intake, days	5 (4-7)
Median (range) postoperative hospital stay, days	12 (9-30)

NRS, numerical rating scale.

or less), 30% had locally advanced extravesical disease (stage pT3), and 23.3% had prostatic invasions (stage pT4). Node-positive disease was found in 26.7% of patients. No patient had positive surgical margins (Table 4). Patients who had non-organ-confined disease or positive lymph nodes were given adjuvant chemotherapy after recovery.

The median clinical follow-up in this series was 16 months (range 0.8 to 42.6 months). Twelve patients (40%) had evidence of recurrent disease (local recurrence in 2 and distant metastasis in 10 patients). At the final telephone interview, the status of 3 patients (10%) was unavailable, 21 patients (70%) were alive with 3 (14.3%) having distant metastasis, producing an OS of 70% and an RFS of 56.7% (Fig. 4).

DISCUSSION

LRC was developed in an attempt to decrease the perioperative morbidity of the treatment without compromising the oncologic results. Since Gill, et al.[6] reported two cases of LRC for the first time in 2000, many others have reported on the safety and feasibility of LRC.[4,7-12] Although the mean OT is generally longer in LRC compared to ORC, it is evident that mean EBL, transfusion rate, and analgesic requirement are less in LRC.[13,14] Nevertheless, LRC is still not a very commonly performed procedure in many institutions possibly because of two major controversies.

The first controversy regarding LRC is its oncologic outcome. There have been very few reports on the oncologic outcomes of LRC compared to those of ORC. This lack of information is possibly because only short-term follow-up of LRC series is currently available, which makes it difficult to compare the LRC data set with data from ORC series. In a matched-pair comparative study by Ha, et al.,[15] there were no significant differences between the ORC and LRC groups in terms of overall, cancer-specific, and recurrence-free survival. Recently, Huang, et al.[16] reported that the estimated 5-year OS, cancer-specific survival, and RFS were 73.7%, 81.3%, and 72.6%, respectively. Their report

Table 3. Surgical Complications Stratified by the Clavien Classification System

Clavien grading system	Complications	No. (%)	Management
Immediate (during surgery)		1 (3.3)	
IIIb	Obturator nerve injury	1 (3.3)	Sural nerve graft
Early postoperative (within 30 days)		6 (20)	
I	Bowel ileus	3 (10)	NPO with active ambulation
II	Deep vein thrombosis	1 (3.3)	Enoxaparin with warfarin
IIIa	Wound dehiscence	1 (3.3)	Wound irrigation and repair
IIIb	Wound dehiscence	1 (3.3)	Wound irrigation and repair
Late postoperative (after 30 days)		6 (20)	
II	Urinary tract infection	2 (6.7)	Parenteral antibiotics
II	Deep vein thrombosis	1 (3.3)	Warfarin administration
II	Lymphedema	1 (3.3)	Diosmin/hesperidin with rehabilitation
IIIb	Pouch stone	1 (3.3)	Flexible cystoscopic stone removal
IIIb	Parastomal hernia	1 (3.3)	Repair of the hernia

NPO, nil per os (nothing by mouth).

is encouraging when compared to the oncologic outcomes of the largest ORC series by Stein, et al.[2] which showed that the estimated 5-year OS and RFS were 60% and 68%, respectively. In terms of recurrence rates, the results of the LRC series by Huang, et al.[16] are encouraging because they showed a local recurrence rate of 6.4% and a distant metastasis rate of 14.6%, while the ORC series by Stein, et al.[2] showed a 7.3% local recurrence rate and a 22.2% distant metastasis rate. However, the data for the long-term oncologic outcomes of LRC are still lacking, and thus, the true oncologic effectiveness of LRC has not yet been established. Therefore, oncologic equivalency or noninferiority of LRC over ORC will only be determined in the context of adequately powered randomized clinical trials with primary outcome measures of composite complications rate and oncologic outcome.

The second controversy about LRC is its loss of prominence in the current era of robotic surgery. The da Vinci® robot system has advantages over the pure laparoscopic surgical system, while conserving the conventional advantages of laparoscopic surgery. Guru, et al.[17] conducted a total of 297 surveys regarding surgeons' attitudes toward robot-assisted surgery and showed that 78% of respondents felt that it was required or beneficial to have training in robot-assisted surgery. Until now, only one study has compared LRC with RALRC.[18] This study reported that there was no significant difference in mean OT, but showed significantly less EBL, lower transfusion rate, and less time to oral intake in the RALRC group.[18] At least one postoperative complication was experienced by 21% of patients in the RALRC group and 50% of patients in the LRC group.[18] Although it may seem that RALRC is superior to LRC, more studies need to be performed to compare the functional and oncologic outcomes of LRC and RALRC.

Table 4. Histopathologic and Oncologic Outcomes

Outcome	Values
Urothelial carcinoma, n (%)	28 (93.3)
Adenocarcinoma, n (%)	1 (3.3)
Large cell neuroendocrine carcinoma, n (%)	1 (3.3)
Pathologic T stage, n (%)	
pTa	1 (3.3)
pT1	4 (13.4)
pT2	7 (23.3)
pT3	9 (30)
pT4	7 (23.3)
pTis	2 (6.7)
Pathologic N stage, n (%)	
pN-	22 (73.3)
pN+	8 (26.7)
Histological grade, n (%)	
Grade I	0 (0)
Grade II	4 (13.3)
Grade III	24 (80)
Unclassified*	2 (6.7)
Positive surgical margin, n (%)	0 (0)
Oncologic follow-up	
Median follow-up, months (range)	16 (0.8-42.6)
Overall survival, n (%)	21 (70)
Recurrence-free survival, n (%)	17 (56.7)
Recurrence, n (%)	12 (40)
Local recurrence	2 (6.7)
Distant metastasis	10 (33.3)
Port-site recurrence	0 (0)

*For non-urothelial carcinomas.

Cost is the major disadvantage of robot-assisted surgery including RALRC. In a cost-analysis study of RALRC ver-

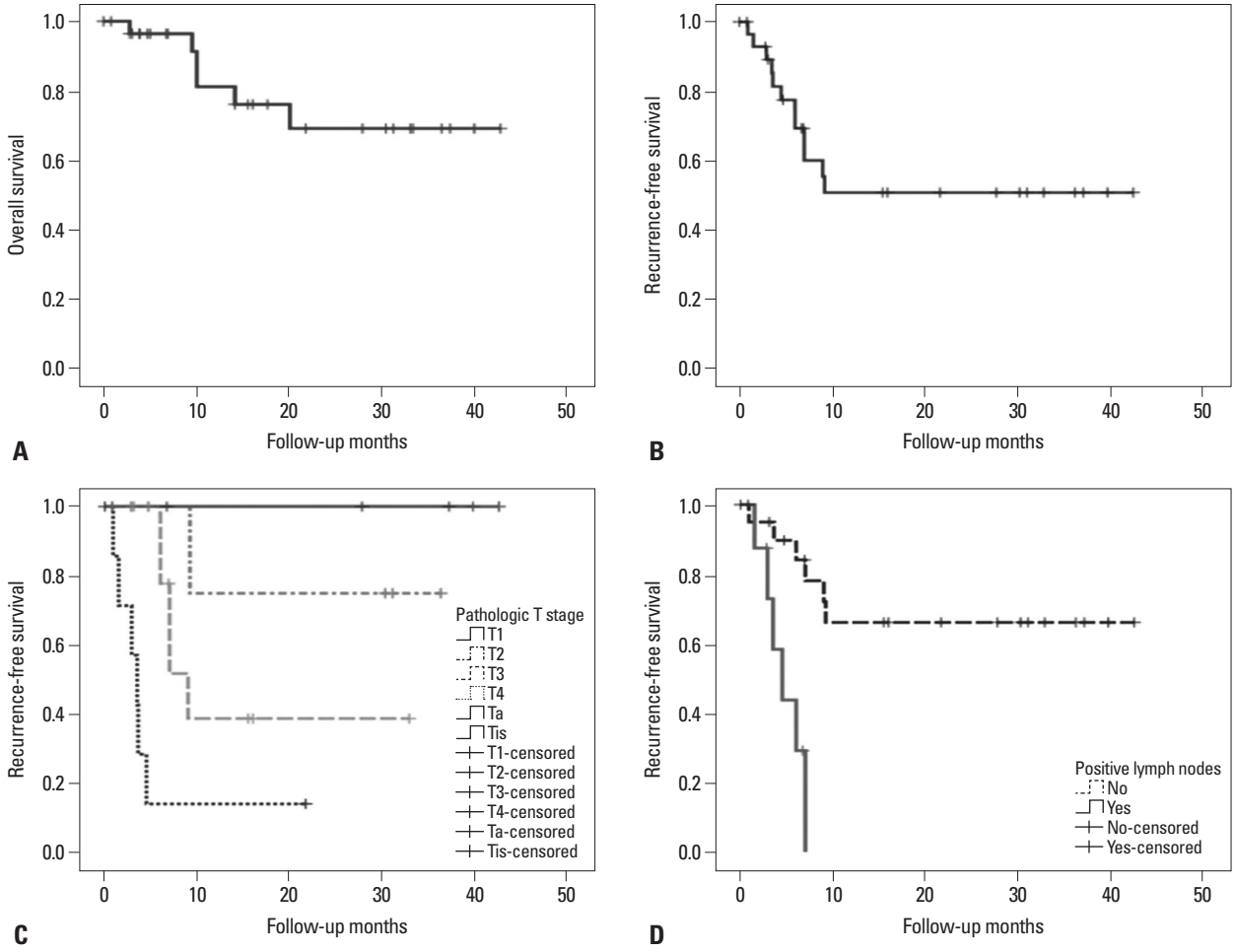

Fig. 4. Kaplan-Meier plots (A) for overall survival, (B) for recurrence-free survival, (C) for recurrence-free survival stratified by pathologic T stages, and (D) by lymph node involvement status.

sus ORC, Smith, et al.[19] reported that RALRC is associated with an overall higher financial cost. Gregori, et al.[20] compared the costs of LRC and ORC and reported that LRC is associated with a reduction in costs compared to the open approach. Therefore, although direct cost comparison analysis between LRC and RALRC is lacking in the literature, it can be indirectly inferred that RALRC is associated with an overall higher financial cost than LRC. Thus, LRC can be a reasonable alternative in minimally invasive radical cystectomy even in the current era of robot-assisted surgery.

In our series, the median OT, EBL and transfusion rate were 527.5 min, 275 mL and 13.3%, respectively, results are similar with those of other series, except for OT, which is relatively longer than those recorded in other series. A number of intraoperative factors may have affected this result. In general, we spent about two hours and 30 min for PLND, one hour and 30 min for cystectomy, and two hours for conduit creation and stoma formation. We think that relatively longer time spent for PLND was attributable to trying to do a more meticulous dissection. We mainly use Hem-o-lok clipping for bladder pedicle dissection without using Endo-GIA stapler (United States Surgical Corp., Norwalk, CT, USA) for insurance issues, and this could be another factor for the longer OT. The OT was longer especially in female patients because the surgery was performed in combination with a gynecologic surgical team, which could result in an additional hour of surgical time. When comparing the OT and EBL between males and females using the Mann-Whitney U test, there was a significant difference in the OT (p=0.004) but no difference in EBL (p=0.122) (data not shown). Wound complication rate in our series was 6.7% (2/30) which is less than those of current ORC series (9 to 15%),[21-23] suggesting an advantage of LRC in terms of wound outcome.

We recently published an article that compared complications between ORC and RALRC in the same institution.[24] The study included other surgeons' ORC series. Based on this study, EBL (1063.4 mL vs. 275 mL) and the transfu-

Table 5. Perioperative Data of Our Series and the Open Radical Cystectomy Series in the Same Institution in the Similar Period

	Our LRC series	Our ORC series[24]
Period	Nov 2007-May 2011	Sep 2008-Mar 2011
Surgeon	Single surgeon (S.I.S.)	Four surgeons (except S.I.S.)
No. of patients	30	104
Follow-up, months	16*	Not reported
Operating time, min	527.5*	494.3†,‡
Estimated blood loss, mL	275*	1063.4†
Transfusion rate, %	13.3	56.7
Complication rate, %	43.3	74.0
Perioeprative mortality rate, %	0	2.9
Time to oral intake, days	5*	Not reported
Hospital stay, days	12*	27.1†

LRC, laparoscopic radical cystectomy; ORC, open radical cystectomy.
*Median.
†Mean.
‡In cases of ileal conduit.

sion rate (56.7% vs. 13.3%) were higher in our ORC series than our LRC series. Moreover, overall complication rate (74.0% vs. 43.3%), perioperative mortality rate (2.9% vs. 0%), and the hospital stay (27.1 days vs. 12 days) were also higher in our ORC series than our LRC series. Although this was not a statistical comparative analysis, overall perioperative parameters were favorable in the LRC series compared to our ORC series, except that OT was longer in the LRC series (Table 5).

During a follow-up period of 0.8 to 42.6 months, our OS and RFS were 70% and 56.7%, respectively. Although the RFS was lower than that of the larger LRC series,[16] OS was similar. In the literature, RFS after ORC varies between 62% and 68% at 5 years and 50% and 60% at 10 years, with OS ranging between of 59% and 66% and 37% and 43%, respectively.[25] In contrast an RALRC series report with 1-2 years of follow-up found RFS and OS to be 86-91% and 90-96%, respectively.[25] Thus, especially for RFS, the oncologic outcome of our LRC series was relatively unfavorable compared to the current ORC and RALRC series. One of the possible reasons for this is that more than 50% of patients had over pT3 on final pathology (30% pT3 and 23.3% pT4). Therefore, although the sample size was small, we conducted a brief subgroup analysis with patients who had pT2 or less, and the result showed a RFS of 92.8% (13/14) and OS of 100% (14/14) (data not shown).

Our study has several limitations that should be discussed. This is the retrospective design with relatively small number of patients in a single institution. Thus, it is difficult to sufficiently determine the learning curve and oncologic outcomes. Moreover, because of the relatively shorter follow-up period in our series, this result needs to be further examined with a longer period of follow-up time.

In conclusion, LRC is a feasible procedure for the management of muscle-invasive BCa and, if the patient selection is appropriate and possibly limited to pT2 or lower, it can be a good alternative to ORC or RALRC in the era of robot-assisted surgery. Extracorporeal urinary diversion with a small incision decreases the total OT and, at the same time, maintains the benefits of laparoscopic surgery. However, the long-term oncologic outcomes after LRC and comparisons with ORC and RALRC should be investigated further.

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