



Original Article

Comparison of open and laparoscopic radical cystectomy as regards long-term oncological outcomes for bladder cancer

Thanachai Sirikul, Supon Sriplakich, Akara Amantakul

Division of Urology, Department of Surgery, Faculty of Medicine, Chiang Mai University, Chiang Mai, Thailand

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Abstract

Objective: Recently, the laparoscopic technique has become widely accepted as a minimally invasive modality which reduces morbidity and provides similar oncological outcomes to open surgery. However, the number of clinical trials comparing laparoscopic and open radical cystectomy are limited. The objectives of this study are to compare the long-term oncological outcomes between open radical cystectomy (ORC) and laparoscopic radical cystectomy (LRC) for bladder cancer.

Materials and Methods: Out of 144 radical cystectomy patients admitted to our institute from January 2006 to December 2016, 87 patients were categorized as being in the LRC group, and 57 patients in the ORC group. Baseline characteristics, perioperative variables, and pathology results were collected retrospectively. Oncological outcomes including overall survival (OS), recurrence-free survival (RFS) and cancer-specific survival (CSS) were analyzed and compared between the two groups.

Results: The mean age of the patients was 64.19 ± 9.89 years in the ORC group and 61.90 ± 10.47 years in the LRC group. The most frequent urinary diversion procedure in both groups was ileal conduit. All pathology results between the LRC group and the ORC group showed no statistical significance. The median follow-up duration was 57.18 ± 44.68 months in the ORC group and 53.96 ± 34.97 months in the LRC group. There was no statistically significant difference in overall survival (OS), recurrence-free survival (RFS) and cancer-specific survival (CSS) between the groups ($p = 0.322, 0.946, \text{ and } 0.528$, respectively).

Conclusion: Our study demonstrated that the long-term oncological outcome of LRC is comparable to ORC in the management of bladder cancer. LRC is an alternative option to open radical cystectomy and is safe, effective, and feasible. However, further large comparative studies with adequate long-term follow-up are recommended to support our results.

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Corresponding author: Akara Amantakul

Address: Division of Urology, Department of Surgery, Faculty of Medicine, Chiang Mai University, Chiang Mai 50200, Thailand

E-mail: Pop_akara@hotmail.com

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Introduction

Bladder cancer is one of the top ten most common adult malignancies worldwide.¹ The incidence and prevalence rates show a correlation with age, male gender, and smoking behavior, but varies across geographic regions or countries.^{2,3} In Thailand, bladder cancer is the ninth most common malignancy in men. In Chiang Mai, Northern Thailand, this is particularly the case with bladder cancer being the sixth most common malignancy in men, the estimated incidence being 5.7 per 100,000 population.⁴

Invasive bladder cancer is represented in almost 20-40% of bladder cancer patients worldwide. Furthermore, more than 85% die within 2 years if not treated.⁵ There are around 80 patients treated for bladder cancer at Maharaj Nakorn Chiang Mai Hospital every year and each year about 16 cases (20%) have an invasive form of the disease which requires radical surgery.⁴

There are many surgical approaches, including open radical cystectomy (ORC), laparoscopic radical cystectomy (LRC), or other minimally invasive radical cystectomy. Open radical cystectomy with pelvic lymphadenectomy has long been the treatment of choice for management of bladder cancer.⁶⁻⁸ However, de Badajoz et al. performed the first LRC in 1993,⁸ and more recently, laparoscopic surgery has been accepted as a minimally invasive treatment reducing morbidity in comparison to open surgery. Several studies have shown that LRC is technically achievable and oncologically safe.⁷⁻⁹

The advantages of laparoscopic surgery include lower estimated blood loss, lower need for transfusion, less pain killer requirements, fewer post-operative complications, a shorter postoperative convalescence period, and less surgical scarring.^{5,7,10,11} Importantly, the oncologic outcomes of laparoscopic surgery are comparable to conventional surgery.¹²⁻¹⁴

However, comparative studies that compare LRC with ORC as regards long-term oncologic outcomes are limited. In addition, robot-assisted laparoscopic radical cystectomy (RALRC) may not be a viable option for most Thai people because of financial concerns. Thus, LRC is an additional choice for the management of bladder cancer.^{8,12-18}

The objective of our study was to compare open and laparoscopic radical cystectomy as

regards long-term oncological outcomes of bladder cancer at Maharaj Nakorn Chiang Mai Hospital.

Materials and Methods

This study was retrospective in nature, medical records from January 2006 to December 2016 were reviewed and included patients aged more than 18 years old, who underwent open or laparoscopic radical cystectomy for bladder cancer at Maharaj Nakorn Chiang Mai Hospital. Exclusion criteria were palliative cystectomy, intra-operative unresectable tumor, simultaneous nephrectomy, and non-urothelial histologic subtype. The study protocol was approved by the Ethical Committee of Chiang Mai University (Research ID: 6454/ Study Code: SUR-2562-06454). Data pertaining to 144 patients fulfilled the inclusion criteria and were analyzed. Of the 144 patients, 57 patients had undergone ORC, and 87 patients LRC. The follow-up data were collected by either chart review or telephone contact. Survival status of all patients was last updated in December 2020.

The operative procedures were similar in both groups with the exception of approach. The technique for LRC, the same as was reported by Lin et al.⁷ and Haber et al.¹⁹, has been previously described. Standard pelvic lymphadenectomies were performed in our center, and the most common extracorporeal urinary diversion was ileal conduit.

Postoperatively, patients were admitted for at least 7-14 days. Clear liquid diets were started at postoperative day 5 progressing to a full diet within 7 to 10 days, depending on clinical response.

Patient baseline characteristics, intra-operative data, pathological findings and postoperative complications were assessed. Mean and standard deviation (SD) were used to express quantitative data and comparisons between the two groups were made using a Mann Whitney U test. Count and percentage were used for qualitative data and comparisons between the two groups were made using Fisher's exact test. Primary outcomes, including overall survival (OS), recurrence-free survival (RFS), and cancer-specific survival (CSS) were analyzed by Kaplan-Meier survival analysis and the two groups were compared using the log-rank test. A p value less than 0.05 was considered statistically significant. SPSS version 21 was used to analyze statistical data.



Results

Patient demographics

The baseline characteristics of all 144 patients, divided into the ORC group and the LRC group, are shown in Table 1. The mean age was 64.19 ± 9.89 years in the ORC group and 61.90 ± 10.47 years in the LRC group. The ratio of male to female in the ORC group was lower than the LRC group; the difference between the two genders was statistically significant ($p = 0.006$).

The majority of ASA scores in both groups were class 2. An ASA score of 3 was given to 8 (14.04%) patients in the ORC group and 3 (3.45%) patients in the LRC group. The comparisons between the ASA scores of the LRC group and the ORC group were statistically different ($p = 0.041$). The other preoperative data, including body mass index (BMI), clinical T stage, clinical N stage and clinical M stage showed no difference between the LRC group and the ORC group ($p = 0.993$, 0.041, 0.089, and 0.665, respectively).

Perioperative data and complications

Perioperative data are shown in Table 2.

Type of urinary diversion was similar between the ORC group and the LRC group ($p = 0.236$). Ileal conduit was the most frequent urinary diversion. A colonic conduit was the outcome in two patients in the ORC group (3.51%) because they had previously received radiation.

The mean values of anesthetic pain control (total morphine) were 17.65 ± 17.55 mg in the ORC group and 23.13 ± 16.83 mg in the LRC group ($p = 0.062$). Patients in the LRC group received fewer epidural blocks than patients in the ORC group ($p < 0.001$).

The mean length of hospital stay was 14.47 ± 6.38 days in the ORC group and 15.13 ± 7.88 days in the LRC group ($p = 0.602$).

Operative time was significantly shorter in the ORC group compared with the LRC group ($p < 0.001$). However, estimated blood loss and blood transfusion rates were significantly higher in the ORC than in the LRC group ($p < 0.001$ and < 0.001 , respectively).

There was a statistically significant difference in the incidence of perioperative complications (Clavian-Dindo classification) between the two

Table 1. Baseline characteristics of patients who underwent open radical cystectomy (ORC) and laparoscopic radical cystectomy (LRC) at Maharaj Nakorn Chiang Mai Hospital between January 2006 and December 2016.

Characteristics	ORC n = 57	LRC n = 87	P-value
Age, Mean (SD)	64.19 (9.89)	61.90 (10.47)	0.191
Gender, n (%)			0.006
Male	43 (75.44)	81 (93.10)	
Female	14 (24.56)	6 (6.90)	
Body mass index (kg/m ²), Mean (SD)	22.16 (3.53)	22.15 (3.50)	0.993
ASA score, n (%)			0.041
1	8 (14.04)	20 (22.99)	
2	41 (71.93)	64 (73.56)	
3	8 (14.04)	3 (3.45)	
Clinical T stage, n (%)			0.089
< T2	1 (1.75)	0	
T2	26 (45.61)	53 (60.92)	
T3	22 (38.60)	29 (33.33)	
T4a	8 (14.04)	5 (5.75)	
Clinical N stage, n (%)			0.665
N0	53 (92.98)	76 (87.36)	
N1	2 (3.51)	4 (4.60)	
N2	2 (3.51)	4 (4.60)	
N3	0	3 (3.45)	
Clinical M stage, n (%)			0.396
M0	56 (98.25)	87 (100)	
M1	1 (1.75)	0	

Table 3. Pathological outcomes for open radical cystectomy (ORC) and laparoscopic radical cystectomy (LRC) at Maharaj Nakorn Chiang Mai Hospital.

Pathologic Outcomes	ORC	LRC	P-value
Grade, n (%)			1.000
LG	7 (12.28)	10 (11.49)	
HG	50 (87.72)	77 (88.51)	
Concomitant CA prostate, n (%)			0.648
Yes	1 (1.75)	4 (4.60)	
No	56 (98.25)	83 (95.40)	
Concomitant CIS, n (%)			0.246
Yes	3 (5.26)	10 (11.49)	
No	54 (94.74)	77 (88.51)	
Pathologic T stage, n (%)			0.945
< T2	18 (31.58)	28 (32.18)	
T2	21 (36.84)	31 (35.63)	
T3	10 (17.54)	13 (14.94)	
T4	8 (14.04)	15 (17.24)	
Pathologic N stage, n (%)			0.075
LN positive	18 (31.58)	16 (18.39)	
LN negative	39 (68.42)	71 (81.61)	
LN count, Mean (SD)	15.07 (9.45)	12.78 (7.60)	0.112
Number of LN Positive, Mean (SD)	2.5 (1.95)	2.56 (2.06)	0.194
Surgical margin, n (%)			1.000
Positive	7 (12.28)	12 (13.79)	
Negative	50 (87.72)	75 (86.21)	
LVI, n (%)			0.865
Positive	26 (45.61)	38 (43.68)	
Negative	31 (54.39)	49 (56.32)	

LG = low grade, HG = high grade, CIS = carcinoma in situ, LN = lymph node, LVI = lymphovascular invasion.

groups ($p = 0.028$). Severe complications (Clavien-Dindo class 4 to 5) were 9 in the ORC group and 3 in the LRC group.

Pathology results

Pathology results for each group are shown in Table 3.

There was not statistical difference between the ORC group and the LRC group in pathologic grade, concomitant prostate cancer, concomitant CIS, pathological T stage, pathological N stage, lymph node count, positive lymph node number, surgical margin, or LVI ($p = 1.000, 0.648, 0.246, 0.945, 0.068, 0.112, 0.194, 1.000$, and 0.865 , respectively).

Oncological outcomes

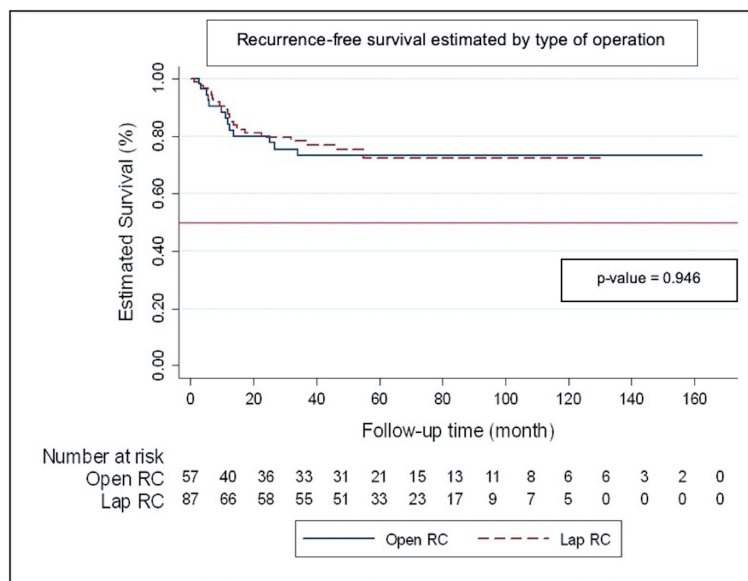
The median follow-up time was 57.18 ± 44.68 months in the ORC group and 53.96 ± 34.97 months in the LRC group; 31 patients (21.53%)

were followed for more than 10 years. Overall, patient deaths at the time of analysis were 35 (61.40%) in the ORC group and 57 (65.52%) in the LRC group.

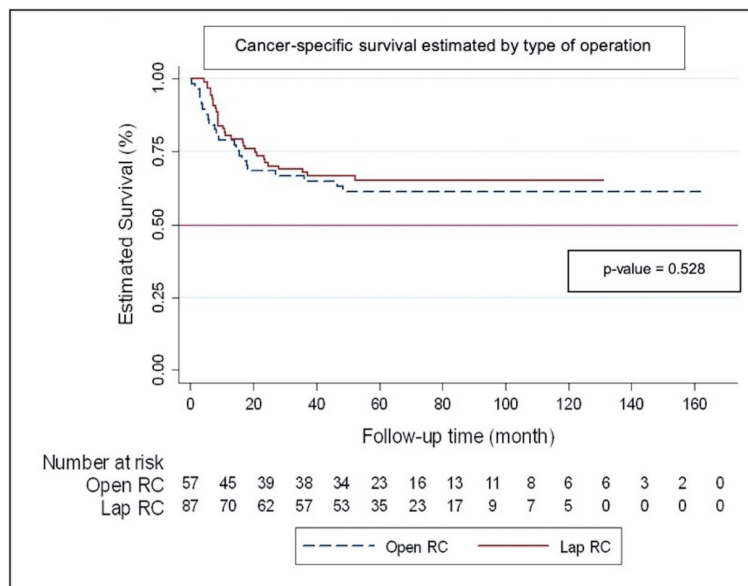
Recurrent bladder cancer was found in 13 patients in the ORC group and in 21 patients in the LRC group. Patients who died from bladder cancer numbered 23 (40.35%) and 29 (33.33%) in the ORC group and the LRC group, respectively.

There was no statistical difference in overall survival (OS), recurrence-free survival (RFS), and cancer-specific survival (CSS) between the ORC group and the LRC group ($p = 0.322, 0.946$, and 0.528 , respectively, Figure 1).

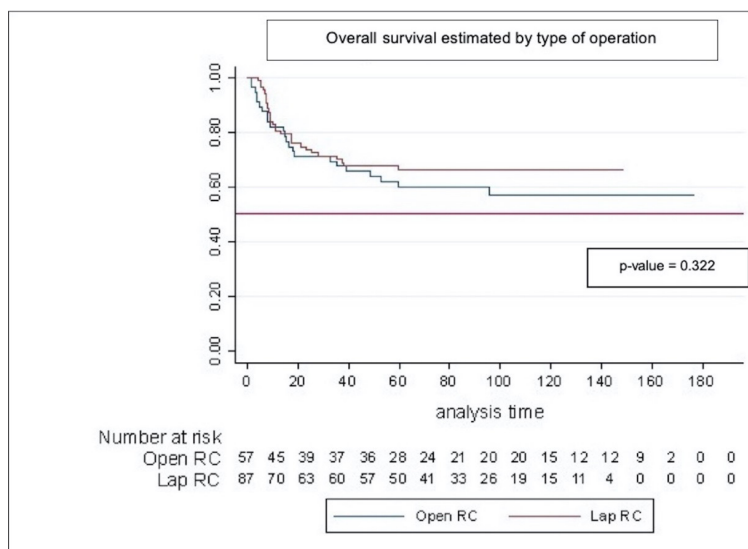
A subgroup analysis of our study demonstrated that there was no statistically significant difference between cancer-specific survival in the ORC group and the LRC group, in terms of organ confined cancer ($\leq T2$), extravesical involvement by cancer ($\geq T3$), no LN metastasis (N0), and



(A) Recurrence-free survival (RFS)



(B) Cancer-specific survival (CSS)



(C) Overall survival (OS)

Figure 1. Comparison of: (A) recurrence-free survival (RFS) between the LRC group and the ORC group, (B) cancer-specific survival (CSS) between the LRC group and the ORC group, (C) overall survival (OS) between the LRC group and the ORC group by Kaplan-Meier survival analysis and log-rank test

LN metastasis (N+) ($p = 0.075, 0.235, 0.602$, and 0.345 , respectively).

Discussion

The world today has an ageing society. Because of the developments in health care and medical technology, the proportion of the elderly has become progressively larger in the majority of countries. In correlation with the increase in age the incidence and prevalence rates of bladder cancer increase.¹⁸

Advanced age is associate with multiple medical conditions, increasing the need and therefore the risk involved in surgical procedures. Minimally invasive modalities such as laparoscopic techniques, are of increasing interest for the management of bladder cancer because LRC has lower associated morbidity than ORC.^{7,8,10,18} However, the gold standard treatment remains ORC.⁶

The perioperative variables of our study demonstrated that estimated blood loss and transfusion rates were significantly higher in the ORC group, but the operative time was significantly shorter in comparison to the LRC group. The analgesic requirement was comparable between the two groups because the ORC group received more epidural analgesic blocks than the LRC group but the LRC group had a higher morphine intake. Omar et al.⁵ showed that during LRC intraoperative blood loss, transfusion rate, and postoperative opioid consumption was significantly lower, recovery time was significantly more rapid, and hospital stay was significantly shorter than in ORC, but operative time was significantly longer. Lin et al.,⁷ Tae et al.,⁹ and Guillotreau et al.¹⁰ report findings similar to Omar et al.⁵ Our study showed that the duration of hospital stay of the two groups was similar. Due to policies of our institution, the most frequent urinary diversion procedure was ileal conduit; duration of admission was about 14 days.

The severe complications identified in our study were lower in the LRC group than in the ORC group. Omar et al.⁵ observed 155 patients in a single center who underwent radical cystectomy and followed up for a mean of 53 months. Results showed that the LRC group had significantly more intraoperative complications than the ORC group. However, severe complications were significantly more frequent in the ORC

group but no statistical differences were shown as regards individual complications between the ORC and LRC groups. Zeng et al.¹⁸ found that the ORC group experienced more complications than the LRC group. Lin et al.⁷ and Omar et al.⁸ found the same results. However, no differences were found in mild and severe complications in a study by Hemal et al.¹³

Comparison between the oncological outcomes from LRC with ORC for bladder cancer remains limited, in terms of the number of patients and long-term follow-up duration. Several comparative studies from many centers have demonstrated similar oncological results in 3 to 5 year follow-up. Ha et al.¹² reported comparable oncological outcomes between LRC and ORC in a 3-year follow up. They included 70 patients (34 patients who underwent ORC and 36 patients LRC) in 1996 to 2003, and the median follow-up was 21 months (3-56 months). The other studies by Tae et al.,⁹ Hemal et al.,¹³ Gillion et al.,¹⁴ and Zeng et al.¹⁸ reported similar oncological results in mid-term duration. Interestingly, Tae et al.⁹ concluded that the oncological outcomes were not dependent on the surgical approach. In Thailand, Nisaworn et al.¹⁶ reported comparable results from the different types of surgical approach as regards 5-year survival outcomes. In a longer term study, Snow-Lisy et al.¹⁵ compared minimally invasive surgery with ORC. The median follow-up was 5.5 years. The data showed comparable outcomes in both groups. In addition, their study had 9 patients (7%) who were followed for more than 10 years.

T Lin et al.⁷ conducted a RCT that compared oncological outcomes of LRC with ORC. However, the study pool was too small to be conclusive.

Our study demonstrated that the oncological outcomes in the long term were comparable between the ORC group and the LRC group with a median follow-up time of more than 50 months, 31 patients (21.53%) having a longer than 10 year follow-up.

Several factors impacted the oncological outcomes, specifically, lymph node count and surgical margin⁹. The high quality of radical cystectomy, an adequate lymph node yield of more than 10 lymph nodes, and the positive surgical margin (PSM) rate varied from 0% to 13%.^{9,12} Furthermore, a greater number of lymph nodes dissected proved to be beneficial and improved



the survival outcome¹². Recently, extended pelvic lymphadenectomies have been recommended.¹⁴ In this study, median lymph node counts were comparable in both groups ($p = 0.112$), and both gave adequate yields, although we performed standard lymphadenectomies. Rates of positive surgical margins were no different between the groups and ranged from 0% to 13.79%. This was comparable to the standard for radical cystectomy.

Limitations

There were several limitations to this study, the main ones being the retrospective nature which always gives variability in determination of data and also there were selection biases. The surgical approach was mainly chosen by the surgeon in conjunction with patient preference. The economic status of the patient also had an impact. This study was heterogeneous as different surgeons performed radical cystectomies, there was a difference in the ratio of male to female in each group, and a wide variation in patient comorbidities. Looking to the future the ERAS protocol is becoming increasingly popular and we would look to incorporating this in our approach. In addition, perioperative chemotherapy (neoadjuvant and adjuvant), which may impact survival outcomes, would be incorporated into a future study.

Conclusions

Our study demonstrated that LRC is comparable to ORC for management of bladder cancer as regards long-term oncological outcomes with no measurable negative impact. LRC is therefore an alternative option for muscle invasive bladder cancer treatment. It is safe, effective, and feasible. However, further large and long-term comparative studies are recommended to support our results.

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Conflict of Interest

The authors declare no conflict of interest.

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