

Laparoscopic versus open radical cystectomy in the treatment of locally advanced T3 and T4 bladder cancer: Perioperative and Mid-term oncological outcomes

Sinan Çelen¹ , Onur Kaygısız² , Hakan Vuruşkan² , İsmet Yavaşcaoğlu² 

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ABSTRACT

Objective: In this study, we aim to compare the perioperative and midterm oncological outcomes in patients with advanced bladder cancer and those who had laparoscopic radical cystectomy (LRC) and open radical cystectomy (ORC).

Material and methods: We retrospectively reviewed medical records of patients who underwent LRC or ORC in a single center between 2008 and 2014 with a pathological diagnosis of pT3 and pT4 bladder cancer. Thirty-five and 39 patients were included in the study as part of the LRC and ORC groups, respectively.

Results: There was no statistically significant difference between the two groups in terms of disease-free survival (LRC, 39.8±4.86 months; ORC, 45.47±8.92 months, P=0.896). Average estimated blood loss and length of hospitalization were significantly less in the LRC group. The overall survival rates of patients at 1, 2, and 3 years were 73%, 46%, and 46% in the ORC group and 78%, 65%, and 40% in the LRC group, respectively, and there was no statistically significant difference between the two groups. One patient in the ORC group experienced rectal injury in the form of a serosal tear, which was repaired primarily without any postoperative sequelae. There were no conversions in the laparoscopic group. Similarly, in 1 patient, rectal serosal tear was repaired preoperatively.

Conclusion: Our study showed that LRC provides midterm oncological outcomes similar to ORC in the treatment of locally advanced T3 and T4 bladder cancer. However, long-term oncological and functional outcomes are required.

Keywords: Bladder; bladder cancer; bladder neoplasms; cystectomy; laparoscopy; locally advanced; urinary diversion.

ORCID IDs of the authors:

S.Ç. 0000-0003-4309-2323;
O.K. 0000-0002-9790-7295;
H.V. 0000-0002-3917-4847;
İ.Y. 0000-0002-1788-1997.

¹Department of Urology,
Pamukkale University School
of Medicine Hospital, Denizli,
Turkey

²Department of Urology,
Uludağ University School of
Medicine Hospital, Bursa,
Turkey

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Corresponding Author:
Sinan Çelen
E-mail:
sinancelen@hotmail.com

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Introduction

Open radical cystectomy (ORC) with pelvic lymphadenectomy is the gold standard treatment for muscle-invasive bladder cancer and recurrent, high-grade, superficial or organ-confined disease. However, significant morbidity is associated with conventional radical cystectomy in 20%–50% of patients.^[1,2] With the advent of surgical techniques and the enhancement of equipment and laparoscopy, a new surgical option, i.e., laparoscopic radical cystectomy (LRC), has been developed for the treatment of bladder cancer.^[3,4] Laparoscopic surgery significantly reduces bleeding, analgesic require-

ments, and length of hospitalization, and it provides similar oncological outcomes to open surgery.^[5-7] However previous studies included a small number of patients with all pathological stages. In many comparative studies, selection biases were observed. Theoretically, laparoscopy seems to be more applicable and safer in the treatment of low-stage bladder cancer; however, there have been concerns about the use of LRC in the treatment of locally advanced T3 and T4 bladder cancer because of the limited evidence in the literature. In this study, we aim to compare the perioperative and midterm oncological outcomes of LRC and ORC in patients with advanced-stage bladder cancer.

Material and methods

Ethics committee approval was received for this study from the ethics committee of Uludag University (17.03.2015/2015-7-10). The clinical and oncological data of patients who underwent LRC or ORC in our center between 2008 and 2014 were collected retrospectively from medical records. Direct telephone surveys were conducted for the patient whose current survival data were not available in their medical records. Patients with a pathological stage T3–T4 or N0–3 bladder cancer were included in this study.

Patients who had contraindications for the Trendelenburg position, clinical stage T4 or M1, and extensive abdominal surgery, and who underwent previous pelvic radiation were excluded from the study. Those patients whose follow-up was shorter than 3 months, those who underwent ileal neobladder reconstruction, and those with metachronous carcinoma were excluded from the study as well. After establishing the exclusion criteria, 35 and 39 patients were included in the LRC and ORC groups, respectively. The clinical and oncological data were collected from their medical charts. Missing data were obtained from the patient or family members through telephone. Patients were followed up with serial clinical examinations every 3 months and chest X-ray and abdominal computerized tomography every 6 months.

Surgical technique

Radical cystectomy, pelvic lymphadenectomy, and ileal conduit urinary diversion were performed in all patients. Noncontinent transileal ureterostomy was performed using Bricker's technique. A midline incision of 6–10 cm was created to remove the specimen, and ileal conduit urinary diversion surgery was carried out. The urinary diversion was reconstructed extracorporeally. All procedures were performed by three experienced

surgeons using the same surgical principles and strictly adhering to the technique. Concurrent total urethrectomy was performed in patients with a positive margin of the urethra, involvement of the bladder neck or prostatic urethra, or presence of carcinoma *in situ*. Standard lymph node dissection was performed in all patients. Adjuvant chemotherapy was given to patients based on the intensity of their physical activity and health status. Postoperative complications were assessed using the Clavien Grading System.

Statistical analysis

Data were expressed as the mean±standard deviation. An overall survival, cancer-specific survival, and recurrence-free survival were estimated using the Kaplan–Meier method and log-rank test. Survival rates were compared using the log-rank test. A *p*-value <0.05 was considered statistically significant. Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS Inc.; Chicago, IL, USA) Version 11.0 software package.

Results

Table 1 shows patients' demographic, preoperative, intraoperative, and postoperative data. Age, sex, body mass index (BMI), American Society of Anesthesiologists (ASA) score, clinical stage, preoperative Bacillus Calmette–Guerin (BCG) treatment status, neoadjuvant chemotherapy, estimated blood loss, median operative time, median hospitalization period, and median time of oral intake were compared between the two groups. The mean age of the LRC group was significantly lower than that of the ORC group, and the total blood loss was significantly lower in the LRC group.

Table 2 shows the histopathological details; a total of 74% of all patients had transitional cell carcinoma, and 26% of all patients had other types of pathologies. There was no significant difference between the two groups in terms of histopathological data. Table 3 shows the oncological outcomes. The number of patients with primary prostatic adenocarcinoma was 5 (14.3%) in the LRC group and 9 (23.1%) in the ORC group.

When further divided into subgroups, urothelial carcinoma was found in 33 (94.3%) and 26 (66.7%) of patients in the LRC and ORC groups, respectively. Squamous differentiation or the sarcomatoid type was found in 2 (5.7%) and 13 (33.3%) patients in the LRC and ORC groups, respectively (*p*=0.003). The outcomes of the adjuvant treatments were analyzed in two categories, which are the chemotherapy and chemotherapy plus radiotherapy, and no statistically significant difference between the groups (*p*=0.121) in terms of recurrence and/or metastasis was observed.

Main Points:

- Laparoscopic cystectomy significantly reduces bleeding, postoperative pain, and length of hospitalization, and it provides similar oncological outcomes to open surgery.
- Theoretically, laparoscopy seems to be more applicable and safer in the treatment of low-stage bladder cancer; however, there have been concerns about the use of LRC in the treatment of locally advanced T3 and T4 bladder cancer because of the limited evidence in the literature.
- We have found that both procedures have similar outcomes in terms of intraoperative, early postoperative, and midterm follow-up results
- LRC patient series are still small, and average follow-up periods are short. Furthermore, its applicability in local advanced bladder cancer is still contradictive.

Table 1. Demographic and preoperative, perioperative, and postoperative data for laparoscopic and open radical cystectomy groups

		LRC	ORC	p
Number of patients		35	39	
Median age (min–max) years		61 (50–80)	67 (48–91)	0.019
Median BMI (min–max) (kg/m ²)		25.34 (20.09–38.46)	26.81 (17.31–35.03)	0.127
No. men/women	Men	31 (88.6%)	30 (76.9%)	0.189
	Women	4 (11.4%)	9 (23.1%)	
ASA score	1	16 (45.7%)	13 (33.3%)	0.665
	2	18 (51.4%)	25 (64.1%)	
	3	1 (2.9%)	1 (2.6%)	
Clinical stage (%)				
	2	15 (42.9%)	14 (35.9%)	
	3	20 (57.1%)	25 (64.1%)	
Preoperative BCG		2 (5.7%)	4 (10.35%)	1
Neoadjuvant chemotherapy		1	7	0.136
Number of patients				
Median estimated blood loss (mL) (min–max)		200 (100–1200)	300 (100–900)	0.024
Blood transfusion (number of units) (min–max)		1 (0–11)	1 (0–5)	0.457
Median operative time (mins) (min–max)		330 (180–630)	300 (120–480)	0.259
Median hospital stay (days) (min–max)		11 (6–21) (days)	12 (8–34) (days)	0.329
Median time to oral intake (days) (min–max)		3 (1–8)	3 (2–8)	0.234
LRC: laparoscopic radical cystectomy; ORC: open radical cystectomy; ASA: American Society of Anesthesiologists; BCG: Bacillus Calmette–Guérin; BMI: body mass index				

There was no statistically significant difference between the two groups in terms of disease-free survival (LRC, 39.8±4.86; ORC, 45.47±8.92; p=0.896). The average estimated blood loss and length of hospitalization were significantly less in the LRC group. The overall survival rates of patients at 1, 2, and 3 years were 73%, 46%, and 46% in the ORC group and 78%, 65%, and 40% in the LRC group, respectively, and there was no statistically significant difference between the two groups (Figures 1 and 2).

Table 4 shows the postoperative complications. One patient in the ORC group experienced rectal injury in the form of a serosal tear, which was repaired primarily without any postoperative sequelae. There were no conversions in the laparoscopic group.

Discussion

While ORC is the gold standard in the treatment of muscle-invasive bladder cancer, it is not without complications. Even when it is performed by experienced surgeons, complications may occur, which may be due to a long incision, abdominal wall retraction,

and fluid loss.^[8] Therefore, urologists have recently inclined to less invasive procedures with the goal of minimizing complications. As a result of this effort, robotic and laparoscopic surgery has been performed increasingly globally.^[9,10] Previous studies have reported the advantages of LRC over ORC, such as less bleeding, shorter hospitalization, early recovery of bowel function, less postoperative analgesic requirement, and better cosmetic results.^[6,11,12] The aim of our study is to compare the preoperative, postoperative, and midterm oncological outcomes of LRC and ORC in advanced-stage bladder tumors. We have found that both procedures have similar outcomes in terms of intraoperative, early postoperative, and midterm follow-up results. The only difference was less intraoperative bleeding observed in the LRC group. In our study, there was no difference between both groups in terms of BMI, gender, ASA score, preoperative clinical stage, preoperative BCG treatment, and neoadjuvant chemotherapy. The only difference was the age which was higher in the ORC group. We thought that the primary reason for this was the higher risk of anesthesia for laparoscopy in elderly patients, which diverts these patients to open surgery. Second reason was the retrospective design of the study, which was one of the limitations. Neoadjuvant treatment was higher in the ORC group although the difference was

Table 2. Histopathological details

	LRC	ORC	p
Number of Patients			
pT3	23	26	
pT4	12	13	
Number of pN classification			
pN0	26	24	
pN1	3	6	
pN2	6	9	
Number of positive surgical margins	5 (14.3%)	8 (20.5%)	0.482
Number of positive pN	8 (22.9%)	16 (41%)	0.096
Median extended pN (min-max)	12 (3%-30%)	10 (2%-25%)	0.238
pT3aN0	15 (42.9%)	17 (43.6%)	0.778
pT3aN1	2 (5.7%)	4 (10.3%)	
pT3aN2	4 (11.4%)	5 (12.8%)	
pT3bN0	2 (5.7%)	0 (0%)	
pT4N0	9 (25.7%)	7 (17.9%)	
pT4N1	1 (2.9%)	2 (5.1%)	
pT4N2	2 (5.7%)	4 (10.3%)	
Urothelial carcinoma	33 (94.3%)	26 (66.7%)	
Others	2 (5.7%)	13 (33.3%)	
Number of primary prostatic adenocarcinoma	5 (14.3%)	9 (23.1%)	0.335

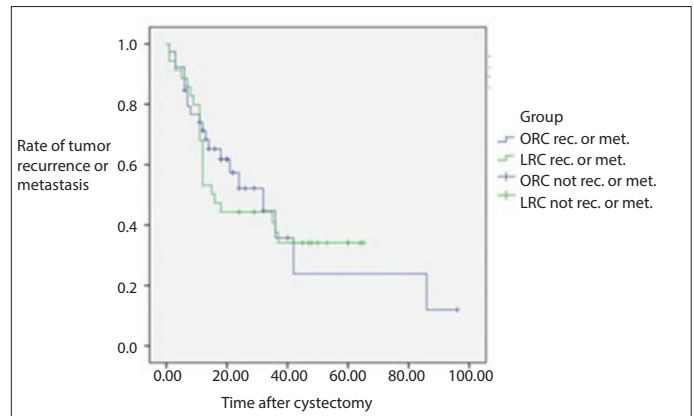
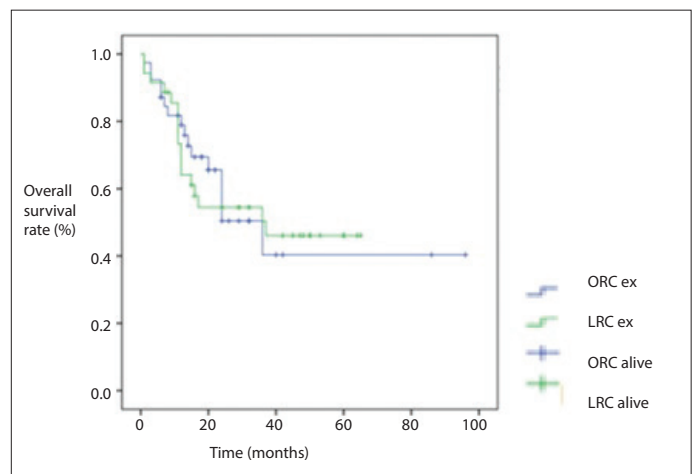
pN: lenf node; LRC: laparoscopic radical cystectomy; ORC: open radical cystectomy

Table 3. Oncological outcomes

	LRC (%)	ORC (%)	p
Number of local recurrence (%)	5.7	2.6	p>0.05
Number of metastases (%)	34.3	30.8	
Adjuvant chemotherapy (%)	62.9	71.8	0.121
Adjuvant chemotherapy and radiotherapy (%)	11.4	0	

LRC: laparoscopic radical cystectomy; ORC: open radical cystectomy

not statistically significant. Because this was a retrospective study, and pathological classification was done according to postoperative examination of the specimens, we think that more invasive tumors based on the preoperative assessment might be directed to open surgery with the assumption that laparoscopy could not be technically feasible. Several published studies comparing ORC and LRC in patients with bladder cancer have found that the postoperative parameters.^[6,12-14] In our study, we could not find any significant difference between the two groups with regard to al-

**Figure 1. Rate of tumor recurrence or metastasis****Figure 2. Overall survival rate****Table 4. Complications**

	LRC	ORC
Incisional hernia	0	1
Evisceration	2	1
Wound infections	3	7
Rectal injury	0	1
Intestinal obstruction	1	1
Uretero-intestinal strictures	1	1

LRC: laparoscopic radical cystectomy; ORC: open radical cystectomy

most all compared parameters; however, the blood loss rate was found to be significantly lower in the LRC group although the transfusion rate was similar. Orthotopic diversions were excluded to form a homogeneous group. A positive surgical margin is the most important risk factor for local recurrence.^[15,16] Rates of positive surgical margins in the LRC series range from 0% to 7.4%. Haber et al.^[17] reported this rate as 2%. However, pathological

stages were not exactly stated in this publication. In addition, this ratio was <1% in the large ORC series. In our study, rates of positive surgical margins were 14 (3%) and 20 (5%) in the LRC and ORC groups, respectively. No statistically significant difference was observed, which may be due to a low case load. Lymph node positivity was also significantly lower in the LRC series than in the open series. This rate was 22%–24% in the large ORC series and 10%–15% in the LRC series.^[18-20] Unfortunately, although the number of lymph nodes received was greater in the LRC group, the lymph node positivity was greater in the ORC group in our study. Overall survival and tumor recurrence or metastasis were not different between the groups. The median time from surgery to metastasis in the ORC series was ≤ 12 months.^[18-20] From this point of view, it could be seen that LRC series have a very low metastatic rate; however, this is because the follow-up time of the LRC series is <12 months. The ratio of patients developing metastasis in the ORC series ranged from 22% to 35%; whereas the ratio of patients developing metastasis in the LRC series ranged from 5% to 15%. This shows similarity between the rate of metastasis development and the rate of patients with organ-confined disease in the ORC series. Considering the above stated, inconsistencies are noted between the ORC series and LRC series in the pathological stage, surgical border positivity, lymph node involvement, metastatic patient rate, and local recurrence rate. These serious differences in patient groups make the comparison of survival insufficient. These incompatibilities can be attributed to several cases, and the most important of them is likely to be systematic errors in patient selection. In the article of Hautmann et al.,^[21] these discrepancies were examined in detail, and it was emphasized that no patient should lay on the line by the way that the patient had a radical cystectomy to be performed in accordance with the oncological surgical rules of the single treatment option. It is stated that the advantages of LRC in the perioperative period should be balanced with oncological success, and it is stated that the deterioration in the parameters that is frequently lethal, such as surgical border positiveness, cannot be accepted at all. While the pathological stage distribution is similar to the standard ORC cohort, parameters such as the lymph node positivity are compatible with organ-confined disease, and these were connected to selection bias. Until the figures in the LRC series become comparable to ORC, it was emphasized that the standard procedure for invasive bladder tumors was ORC and that LRC should still be considered an experimental approach.

Our study has several limitations. Because of the surgical nature of the trial, blinding could not be performed. Cases in our study were relatively small (i.e., <40), and another limitation was the relatively short follow-up time. But due to lack of randomization, data were hardly suitable. Procedures were performed by 3 experienced surgeons, but all surgeons had extensive experience on cystectomy. Another limitation was the lack of cost analyses. Although advanced technologies for bladder cancer man-

agement appear to be more costly, a recent study reported that LRC had lower costs compared with ORC, but there were no statistically significant differences.^[22] Furthermore, enhanced recovery after surgery (ERAS) protocols aim to improve surgical outcomes by reducing variation in perioperative best practices. However, among published studies, results show a striking variation in the effect of ERAS pathways on perioperative outcomes after cystectomy; however, we did not do ERAS protocols.

In conclusion, LRC seems superior to ORC in terms of surgical parameters. Although LRC's complication rate is similar with that of ORC's, it provides less postoperative pain, better cosmetic results, early bowel function recovery, earlier ambulation, and lower surgical morbidity rate. It has not been shown yet that the success of LRC in cancer control is equal to ORC. Although midterm results are promising in published series, in comparison with ORC series, incongruities are particularly noticeable in terms of pathological outcomes. This makes it difficult to compare LRC and ORC results. LRC patient series are still small, and average follow-up periods are short. Furthermore, its applicability in local advanced bladder cancer is still contradictive. Carefully designed further randomized studies, taking into account all clinical T3 bladder cancer cases, are needed to evaluate oncological efficacy for more advanced disease.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Uludag University (17.03.2015/2015-7-10).

Informed Consent: Written informed consent was obtained from patients who participated in this study.

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