Comparison of Open and Laparoscopic Radical Cystectomy for Bladder Cancer: Safety and Early Oncological Results

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ABSTRACT

Objectives: To evaluate perioperative and postoperative morbidity and functional results of laparoscopic radical cystectomy (LRC) in a single-site cohort of patients by comparing it with standard open radical cystectomy (ORC).

Materials and methods: A prospective analysis was performed in 42 muscle invasive and locally advanced bladder cancer (BCa) patients who underwent radical cystectomy (RC) between February 2012 and March 2014 in N.N. Petrov Research Institute of Oncology, Saint Petersburg, Russia. The final cohort included 21 ORC and 21 LRC patients. The average patients’ age was 64 (38 to 81) years, which did not differ between the groups. The pathological stage was similar in the LRC and ORC groups. Multivariable logistic and median regression was performed to evaluate the operating time, perioperative, and postoperative complications (30-day and 90-day) according to Clavien classification, readmission rates, and length of stay (LOS) – both totally and in ICU.

Results: The operating time during LRC was longer than that of ORC (398 vs 243 minutes respectively). Despite that, there was no statistically significant difference of the type of surgery on intraoperative complications – 14.3% in the ORC group and 4.7% in the LRC patients. The major complication rates (Clavien grade ≥3; 23.8 vs 19.4%) were similar between the groups. However, LRC had four times lower rate of minor complications (Clavien grade 1 and 2) compared to ORC (4.7 vs 19.0%). Laparoscopic radical cystectomy had a significantly shorter LOS (27.8 vs 22.6 days in the ORC and LRC groups respectively), but no significant differences in ICU stay existed (5.1 vs 2.1 days). Morbidity was presented by one patient in each group (average rate 5.8%). The common transfusion rate during and after surgical intervention was 19.6% and was higher in the ORC group (33.3 vs 4.7% in LRC); additionally, intraoperative bleeding was lower after laparoscopic cystectomy – the average volume of blood loss was 285 mL in LRC and 577 mL during ORC. Depending on the timing of complications, there were 30-day complications in 19 patients (37.2%) and 90 days in 27 patients (52.9%). The greatest difference was observed between the grades of gastrointestinal complications (foremost, ileus) with significantly better outcomes in the LRC patients – 14.2% compared to 47.6% in ORC.

Conclusion: We have found that LRC is safe and associated with lower blood loss, reduced postoperative ileus, and lower LOS compared with ORC. Using a population-based cohort, we have found that laparoscopic surgery for bladder cancer reduced minor complications (mainly due to lower bleeding and gastrointestinal complication rate) and had no impact on major complications.

Keywords: Bladder cancer, Complications, Ileal neobladder, Radical cystectomy.

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INTRODUCTION

Despite significant improvements in perioperative complications during last decades, radical cystectomy (RC) in patients with bladder cancer (BCa) is thought to be a major operative procedure with potential for substantial morbidity and mortality.1,2

Due to a widespread use of the laparoscopic technique, minimally invasive RC and intestinal urinary reconstruction is becoming more and more common. This technique has some benefits in terms of duration of hospitalization with probably reduced morbidity of the procedure.3-5 Among these techniques, laparoscopic radical cystectomy (LRC) has been demonstrated to be feasible, safe, and provides operative and functional advantages. Besides, minimally invasive approach could increase the number of patients eligible for adjuvant chemotherapy.6 Despite that, technical difficulties and high cost of the procedure have hampered its widespread adoption. Recently, Smith et al7 have showed that only 3% of surgeons performed purely intracorporeal urinary diversion. Moreover, despite significant improvement in mortality rates (from 2.4–15.0% in early series to 0–3.9% in recent reports), early complication rates were not reduced noticeably and still remain as high as 11 to 68%.8

In this study, we report the results of treatment of patients with BCa in terms of safety (30-day and 90-day complication rate) and immediate oncological results after LRC with complete intracorporeal ileal urinary diversion in 21 patients, by comparing them with the similar number of patients treated with open radical cystectomy (ORC).
MATERIALS AND METHODS

Between January 2012 and March 2014, 42 convective patients underwent RC at our institution as initial treatment for muscle invasive or locally advanced BCa, with no evidence of distant metastasis. Among these patients, 21 underwent LRC (group 1) and 21 ORC (group 2). The study protocol was approved by the institutional review board of N.N. Petrov Research Institute of Oncology. Pretreatment characteristics of patients are presented in Table 1. Preoperative evaluation was conducted according to the current European Association of Urology (EAU) guidelines. Patients with previous radiation therapy and/or radiotherapy were excluded from the study. Among all patients, in 2 (3.9%) of them cystectomy was performed due to non-muscle invasive bladder cancer (NMIBC), refractory to the intravesical BCG therapy. Preparation to the cystectomy included interintestinal preparation. Open radical cystectomy and diversion was performed.

The postoperative care included no use of the nasogastric tube, early activation (1 day postoperatively), and early feeding (2 to 3 days postoperatively) of the patient. Removal of the abdominal drain was made when the output was <100 mL/day. The ureteral stents were removed 10 to 14 days postoperatively.

Intraoperative, postoperative 30- and 90-day complications were assessed according to the modified Clavien–Dindo classification. Pursuant to the patient protocol, the operation time, bleeding volume, and blood transfusion rates were checked and analyzed. In the early postoperative period, we assessed the impact of the surgery type on duration of hospitalization (totally and in ICU), intestinal and urinary complications separately in the 30- and 90-day periods, readmission and reoperation rates. All patients were eligible for a minimum 90-day follow-up. The follow-up data were collected from a patient survey 1 month after cystectomy and once per 3 months thereafter. Patients with positive surgical margins were managed in an adjuvant setting.

Differences in proportions and means were tested using a two-sided t-test. The value of p < 0.05 was accepted as statistically significant in rejecting the null hypothesis (no difference in proportions/means).

RESULTS

Intraoperative and Pathomorphological Data

The operative data are summarized in Table 2. The average operating time was higher in the LRC group when assessed totally (368 vs 263 minutes) and separately in the extirpative (143 vs 118 minutes) and reconstructive (225 vs 145 minutes) steps, in laparoscopic and open surgery respectively (p = 0.04). Among intraoperative complications, the most serious one was damaging of the major blood vessels – one case in each group (due to intracorporeal sutures). The most frequent complication was bleeding (grade 2) which required blood transfusion seven times higher (33.3 vs 4.7%) in the ORC group (p = 0.02). No intraoperative mortality was observed.

None of the cases required conversion to open cystectomy. The median hospitalization duration was 12.6 and 21.1 days, which largely depended on (1) Perioperative comorbidity and (2) the day of removal of urethral stents.

The main intestinal function recovery criteria – median time to regular diet and to stool – were 4.3 and 4.4 days in the LRC group, and 6.2 and 7.5 days in the ORC group (p-value < 0.05 between the groups in both cases).

<table>
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<tr>
<th>Table 1: Pretreatment patient characteristics</th>
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<tr>
<td><strong>Variable</strong></td>
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<td>Age (y) (average, IQR)</td>
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<td>Clinical tumor stage, n (%)</td>
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<td>cT1</td>
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<td>cT3-4</td>
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<td>Sex:</td>
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<td>Female, n (%)</td>
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<tr>
<td>BMI, kg/m²</td>
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<td>Previous surgery, n (%)</td>
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LRC: Laparoscopic radical cystectomy; ORC: Open radical cystectomy; IQR: Interquartile range

<table>
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<tr>
<th>Table 2: Operative data</th>
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<tr>
<td><strong>Variable</strong></td>
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<tr>
<td>Total operative time, min</td>
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<td>Extirpative component time, min</td>
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<td>Reconstructive component time, min</td>
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<td>Estimated blood loss, mL</td>
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<td>Transfusion rate, %</td>
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<td>Time to regular diet, days</td>
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<td>Length of ICU stay, days</td>
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<td>Time of hospital stay, days</td>
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LRC: Laparoscopic radical cystectomy; ORC: Open radical cystectomy; ICU: Intensive care unit
The pathologic data are presented in Table 3. None of the patients had concomitant incidental prostate cancer; all tumors were transitional cell carcinomas. The number of cases with carcinoma in situ was not assessed. The positive surgical margin rate was similar in both groups (9.5%). These 4 (2 in both groups) patients, as well as 11 (5 and 6 in the LRC and ORC groups respectively) patients with positive lymph nodes, received adjuvant chemotherapy. All pathological data did not differ significantly between the groups.

**Early Postoperative Period**

In any grade, the 30-day complication rate was 35.7% (15 patients) – 47.6 and 23.8% in the ORC and LRC groups respectively (p = 0.05). In 23 (54.8%) patients 90-day complications were observed – 14 (66.7%) and 9 (42.9%) after open and laparoscopic RC respectively (p = 0.04). In each group 30-day mortality occurred in 1 patient (p = 0.6). Distribution of patients according to the grade of complications and time of their development is presented in Table 4, and according to the type of event and treatment strategy in Table 5.

Reoperation was performed in 4 (19.0%) and 2 (9.0%) of the patients in the ORC [anastomotic ureteroileal urinary leakage in one patient, pelvic abscess in one patient, and intestinal anastomotic failure (leakage or ileus) in three patients] and LRC (one patient both in anastomotic ureteroileal urinary leakage and intestinal anastomotic leakage) groups respectively (p = 0.65). No cases of conversion to open surgery and no perioperative mortalities were reported.

We did not find significant difference between the groups in neither intraoperative (p = 0.7) nor 30-day (p = 0.55) complications with grade 3 and more.

Three patients (14.3%) in the ORC group and 2 (9.5%) in the LRC group required repeated hospitalization in 90 days after initial surgery (p = 0.65). The reason was grade 3 complications – acute upper urinary tract infection (one patient in each group), ileal obstruction (one patient in each group), and pelvic abscess (one patient in the ORC group).

**DISCUSSION**

Historically, RC has been associated with the highest risk of morbidity and mortality compared to all other major urologic procedures, particularly in the more elderly population. Standardized reports on complications after RC using the validated Clavien reporting system reveal disappointingly high complication and mortality rates – from 26 to 64% and 1 to 7% respectively.13-16

Until recently, there has been a dearth in standardized reporting of complications after RC. Only 2% of reports (73 open series and 36 minimally invasive series) from 1995 to 2005 met at least nine of the critical reporting elements in surgical outcomes according to Donat.17

A lot of studies demonstrated the unmet need for treatment of MIBC in terms of safety and efficacy. The purpose of introduction of the minimally invasive approach was to improve operative, pathological, and short-term clinical outcomes to the open approach. According to recent data, LRC suggests that operative
results include lower intraoperative blood loss, earlier return to bowel function, less pain, and quicker postoperative convalescence. However, complication reports may be limited by reporting and selection bias for healthier patients. Moreover, the difficulty in obtaining data on complications results from a lack of consistency in reporting complications.

One of the limiting factors of laparoscopic cystectomy is its labor intensity and duration. Indeed, recent data show an increased treatment time compared to open surgery. In our study, the duration of LRC was 1.6 times greater than ORC. However, when analyzing the entire series of laparoscopic surgery, a significant decrease was found in this indicator up to 1.3 times in the last 10 transactions compared to the first 10, which means that we gain experience. In other words, we find that LRC takes longer to do than open procedure but results in better functional outcomes with reduced blood loss, transfusion rate, shorter length of stay in hospital, and fewer complication rates. According to the recent literature, nearly 40% of this patient cohort experienced at least one readmission within 90 days following RC. No differences in age, gender, race, or stage were observed between patients who did vs did not undergo the ER. Gastrointestinal, wound, and deep vein thrombosis complications were most commonly documented with readmission within 30 days. Genitourinary, neurologic, and cardiac complications were more common in those with later readmissions. Stimson et al showed that the readmission rates were as high as 27%, with bowel, urinary, and infectious complications being the most common reasons. The transfusion rate in one series was appr. 66%, with an average estimated blood loss of 1 l for 1,142 consecutive ORCs. Our experience shows that in accordance with the mentioned studies, when comparing LRC and ORC, the results favor the use of the laparoscopic approach. Other important characteristics are the number of days in ICU and duration of hospitalization. There was no significant difference between these items (p = 0.53).

According to the Clivend’s clinic data, which has the greatest experience in minimally invasive RC with intracorporeal urinary diversion, this technique of intestinal substitution is significantly better than the extracorporeal one in terms of better intestinal function recovery. Other complication rates were comparable between both groups. Totally, despite significant improvements in armamentarium and surgical technique, the complication rate after minimally invasive RC remains high. In the largest series, the 30-day complication rate is about 60 to 65%, and in 90 days complications occurred in nearly 80%. Among all patients with 90-day complications, 80% had grade 1 and 2 according to Clavien system. The results of our study suggest benefits of the minimally invasive approach.

Several studies showed survival impairment after intraoperative blood transfusion. Thus, the transfusion rate could be potentially important for patients due to its hypothetically immunosuppressive effect. According to the literature, blood loss in open, laparoscopic, and robotic RC is about 700 to 1500, 250 to 790, and 22 to 460 respectively. The same authors showed lower blood transfusion rate for minimally invasive RC [5 to 20% and 1 to 4% in LRC and robot-assisted RC (RARC) respectively] compared to the open procedure (14 to 40%). Our study showed higher (compared to the literature data) blood loss during ORC, probably due to a lower number of patients. However, in the literature we found similar results with blood loss reduction due to reducing invasiveness of intervention.

Another significant problem related to radical bladder surgery consists in gastrointestinal complications. Intraoperative rectal wall damage occurred at a relatively low rate – about 0.2% (up to 4% according to some data). The same rate (0.2 to 2%) was noted for large blood vessels damaging both in LRC and ORC. Such intraoperative adverse events (Table 2) were associated with locally advanced tumors and did not depend on the type of surgery (ORC or LRC).

With the minimally invasive approach, patients with ileal conduit urinary diversion had a decreased risk of complications compared to continent urinary diversions. Totally, the 90-day perioperative mortality rate was 5.3%. According to our data, the most clinically significant event (in terms of hospital and ICU readmission rates, repeated surgery) was gastrointestinal complications, particularly, ileus. This event has the greatest differences among the patients after LRC (14.2%) and ORC (47.6%). Recent studies showed that postoperative ileus happened in 23, 3, and 8% of patients after open, laparoscopic, and robotic cystectomy respectively. However, many studies used different definition of this event. Ramirez et al in the recent review found 21 articles with a clear definition of postoperative ileus. The most frequent one was absence of flatulence, stool on the 5th or 6th postoperative day; postoperative nausea and vomiting which required to stop enteral feeding and to start intravenous feeding and/or nasogastrointestinal intubation on the 5th or 6th postoperative day; absence of intestinal movement on the 5th postoperative day; intestinal movement impairment which lead to prolonged hospitalization. Recovery of the bowel function and/or removal of the gastric tube and/or inability of oral food intake after 5 postoperative days were the criteria for establishment of dynamic intestinal obstruction (ileus) in our study. According to these, we
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suspected ileus in 38 and 4.7% of patients in the I and II groups respectively. Suspicion of mechanical obstruction was an indication for repeated surgery – revision of the abdominal cavity. This was performed in seven (13.7%) cases. In the study conducted by Chang et al, postoperative ileus was the most common cause for prolonged hospital stay after cystectomy. Our data support this position, making aware of the modern trends and standards for management of patients, which include, for example, minimizing the traumatic mechanical intraoperative effects on the intestine, which distinguishes the technique of laparoscopic cystectomy using the open method. The study made some changes in the technique of the operation and, predominantly, LRC. So, in the first 10 patients, ureteralileal anastomosis (UIA) formation was performed with interrupted sutures and holding the left ureter through the mesentery of the sigmoid colon, and in the next 4 to 5 cystectomies nodal sutures were made, and the left ureter was thrown over the sigmoid colon. This led to a significant decrease in the intestinal phase time from 250 to 200 minutes. Furthermore, there was a trend to reduce frequency in the formation of anastomotic strictures and, as a consequence, hydronephrosis (4% for the first 10 operations and 1% subsequently) with the absence of anastomosis defect (gap) developed (1 case in both groups).

Lymphocele and chyloperitoneum were more common than LRC (6.4%), whereas no differences were observed between ORC and RARC – about 2%.[15] In our results, the frequency of such complications did not differ among the groups.

Urinary fistula developed in about 1% after ORC, LRC, and RARC. The incidence of UIA was higher after LRC in several studies – up to 15%, while after ORC and RARC the rate was 1.5 to 10%.[5,23,29] According to some assumptions, the risk factor for this complication is excessive dissection of the urethra formation by extravaginal anastomosis. However, in a recent study represented by Anderson et al, the difference in frequency of UIA stricture formation between ORC and LRC was not significant, despite some differences (8.5 and 12.6% respectively, p > 0.05), and decreases with improvement of surgical technique.

In terms of oncological results, in recent meta-analysis Fonseka et al showed that LRC provides better outcomes than ORC and similar to RARC. Totally, talking about early oncological results, we must reflect several factors: Surgical margins, the number of removed and positive lymph nodes. Data from the International Laparoscopic Cystectomy Registry (ILCR) demonstrate a soft-tissue surgical margins (STSMs) rate of 2%. Advancing T stage, positive lymph nodes, and increasing age were independently associated with a higher likelihood of STSMs, while the number of cases and institution volume were not found to be predictive. For every increase in pathological T stage above T2, there was a five times higher chance for positive STSM (p < 0.001). In a series of 121 patients, Snow-Lisy et al reported a positive STSM rate of 6.6%. In patients with large tumors and/or suspected extravesical disease, wide dissection of the perivesical tissue is recommended to reduce STSM rates. We found positive surgical margin in two cases in both groups – 9.5% (p > 0.05).

The same absence of difference was noted regarding the lymph nodes – the average number of totally removed (15 and 16 in the LRC and ORC groups respectively) and the amount of positive nodes (5 and 6 in the LRC and ORC groups respectively). The 2004 consensus study by Herr et al targeted at standardizing outcomes of surgical treatment for invasive bladder cancer and identified 15 lymph nodes as the minimal acceptable yield for this surgery. Generally, this rule matches all studies mentioned in this analysis.

Unfortunately, due to a short period of follow-up, we cannot provide survival analysis for our cohorts. However, several recent studies showed similar recurrence-free, cancer-specific, and overall survival after minimally invasive and open cystectomy. MD Anderson’s low-risk cohort of MIBC showed a 5-year DSS of 81%; the same statistic published by Hautmann et al for all-comers cT2-cT4a Nx was 71%.

The major limitations of our study are retrospective analysis, low number of patients in groups, single-center experience, lack of long-term oncological results, and possible biases. However, there are few studies comparing LRC and ORC, particularly with totally intracorporeal urinary diversion.

CONCLUSION

Laparoscopic cystectomy is a safe radical treatment of bladder cancer associated with reduced blood loss, lower incidence of early postoperative complications (including dynamic ileus), leading to a reduction in duration of hospitalization and good early functional results. However, to be recognized as a standard treatment, it requires more prospective data on safety of laparoscopic cystectomy, functional, oncological results, and cost-effectiveness. Moreover, for complete evaluation of LRC effectiveness and its adequate comparison with the open procedure, it is necessary to obtain long-term oncological results.

REFERENCES


