Perioperative Outcomes of Open Extra-peritoneal Versus Laparoscopic Radical Cystoprostatectomy: A single Center Comparative Study

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Purpose: To compare 90-day perioperative complications and pathological outcomes between laparoscopic radical cystectomy (LRC) and extraperitoneal radical cystectomy (EORC) approaches.

Materials and Methods: All operations were performed in a single high-volume tertiary referral center by the same surgical team. Males ≥ 18 years with pre-cystectomy clinical T1–T3 disease and having undergone an ileal conduit were included. Exclusion criteria included patients with inflammatory bowel disease, previous pelvic and/or abdominal irradiation, neo-adjuvant chemotherapy, and/or clinical T4 disease. Perioperative outcomes such as operative time, estimated blood loss, transfusion rate, hospital stay, and 90-day complications were evaluated. The recovery duration of regular bowel activity, mean stool passage and ileus rates were recorded.

Results: A total of 221 patients met the inclusion criteria(81 LRC and 130 EORC). Demographics and preoperative parameters were comparable. Intraoperative estimated blood loss favored LRC by a median of 450 mL (200-900) (P = .021) vs. a median of 700 mL (300-2900) for EORC. The transfusion rate did not differ between the two groups; %14.8 (N = 12) for the LRC and %20.8 (N = 27) for EORC (P = .37). The median hospital stay was 9 (4-49) days for EORC and 8 (4-29) days for LRC (P = .011). The need for analgesics to control pain through an epidural catheter was higher for EORC (P = .042). There was no difference in overall complication rates (P = .47).

Conclusion: Although LRC appears to have a slight advantage over EORC, both techniques yield satisfactory results in regard to ileus rates and 90-day perioperative complications.

Keywords: laparoscopic cystectomy; open extra-peritoneal cystectomy; perioperative complications

INTRODUCTION

Open radical cystectomy (ORC) remains the gold standard of care for patients with muscle-invasive organ-confined bladder cancer, providing efficacy in local control and long-term disease-free survival[1,2]. Laparoscopic cystectomy (LRC) and robot-assisted radical cystectomy (RARC) have acquired popularity over the years as minimally invasive surgical techniques. These techniques were deemed advantageous for their reduced morbidity and accelerated convalescence[3], resulting in comparable oncologic outcomes. LRC and RARC are characterised by reduced blood loss and postoperative pain and have emerged as minimally invasive modalities that substantially enhance the recovery of intestinal function[4,5]. However, high costs still make surgical robots unavailable in most institutions. On the other hand, laparoscopic surgery has a steep learning curve that hinders its wide use worldwide. Therefore, ORC is still the treatment of choice despite its high complication rates[6]. To reduce morbidity, surgeons have sought modifications to the surgical technique for ORC. Kulkarni et al. introduced the extraperitoneal RC technique in 1999 to reach lower morbidity rates with this approach[7]. Afterwards, other researchers published studies comparing the conventional and extraperitoneal techniques favouring the extraperitoneal approach regarding complications. These studies especially mention the superiority of the extraperitoneal technique in terms of gastrointestinal complications[8,9]. However, there is still a paucity of literature investigating the outcomes of minimally invasive techniques and extraperitoneal radical cystectomy (EORC). Only limited studies compared the minimally invasive RC approaches, and the EORC in literature, and only one study with a low patient number confronted LRC with EORC[10,11]. Most of these studies did not use standardised methods for reporting perioperative complications. We use the Martin criteria for reporting perioperative complications[12]. We published our perioperative outcomes of EORC previously. Nowadays, LRC and EORC techniques are performed routinely in our clinic. The current study aimed to compare LRC and EORC approaches to 90-day perioperative complications and pathological outcomes.

MATERIALS AND METHODS

From 2016 to 2022, a retrospective study of male patients with clinical T1-3 disease who underwent LRC

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Table 1. Patient Characteristics and Pathological Outcomes

	LRC	EORC	*P* value
Patient number	81	130	
Age, median (IQR)	63 (59-68)	65 (58-70.25)	0.34
BMI, median (IQR)	25.1(22,1-27,67)	25.5 (23.11-27,47)	0.63
Charlson's score, median, (IQR)	4 (2-8)	4 (2-8)	0.147
Operating time, minutes, median (IQR)	280 (220-340)	240(218.75-300)	0.069
Hospitalisation time, day, median (IQR)	8 (6-11)	9 (7-14)	0.011*
Estimated blood loss, ml, median (IQR)	450 (305-500)	700 (560-782.5)	0.021
Pathological stage, N(%)			0.24
pT1/Ta/Tcis	14 (17.5)	27 (20.8)	
pT2	25 (31.25)	26 (20)	
pT3	27 (33.75)	45 (34.6)	
pT4	14 (17.5)	30 (23.1)	
Pathological lymph node, N(%) status N+			0.62
N0	64(79)	106 (71.5)	
N1	17(21)	24(18.5)	
Clavien-Dindo classification, N(%)			0.47
Minor 1–2	36(45)	63(48.5)	0.32
Major 3≤	9(11.1)	17(13.1)	0.83
Opioid dosage (µg)	8 (7,4-8,3)	10.2 (8,4-10,4)	0.042*

BMI = body mass index; §Grade 0 = no complications, Grade 1 = complications needing only oral medications or bedside intervention; Grade 2 = complications needing only intravenous medications, total parenteral nutrition, or blood transfusion; Grade 3 = complications needing interventional radiology, therapeutic endoscopy, intubation, angiography or surgery; Grade 4 = complications causing residual and lasting disability requiring major rehabilitation or organ resection; Grade 5 = complications causing death.

or EORC with IC diversion was conducted in our institution. The Review Board approved the study of our institution. Each technique, LRC or EORC, was performed by the same surgical team in the same institution who were highly proficient in open oncologic surgery or laparoscopy. In light of the study's retrospective design, signed consent was obtained from the patients. Data from the patients were retrieved from our institution's prospectively owned electronic database for bladder cancer. Exclusion criteria included patients with inflammatory bowel disease, previous pelvic and/or abdominal irradiation, neo-adjuvant chemotherapy and/or clinical T4 disease. Any patient who underwent orthotopic neobladder or uretercutanostomi was excluded from providing a homogenous study population. Beacause of the retrospective design of the study a specific matching procedure was not used. Fast-track surgery programmes did not include any patients. The same postoperative pathway was applied to all patients. Preoperative parameters included age, gender, body mass index (BMI), Charlson's comorbidity index, history of abdominal surgery, disease stage, tumour grade,

Table 2. Surgical outcomes and perioperative complications.

	LRC, N(%)	EORC,N(%)	*P* value	Odds ratio (95%CI)
Overall early complications (first 90 postoperative days)				
Gastrointestinal complications	13	23	0.75	1.124 (0.534-2.368)
Ileus	6	10		
Constipation	4	6		
Diarrhoea	3	7		
Intestinal bleeding	0	0		
Infection	15	20	0.66	0.8 (0.848-1.093)
Urinary tract infection	12	20		
Fever unknown origin	5	4		
Pyelonephritis	1	1		
Gastroenteritis	1	1		
Urosepsis	1	3		
Wound	4	18	0.039*	
Wound infection/seroma	4	16		3.094 (1.008-9.487)
Wound dehiscence/evisceration	0	2		
Genitourinary	2	1		
Renal failure	2	1		
Cardiac	3	5		
Arrhythmia	1	2		
Myocardial infarction	0	1		
Syncope/hypotension	2	2		
Pulmonary	6	6	0.34	0.605 (0.188-1.944)
Pneumonia	1	1		
Respiratory distress	1	1		
Pleural effusion	2	1		
Atelectasis	3	3		
Bleeding needing transfusion	12	27	0.36	1.507 (0.715-3.176)
Thromboembolic events	3	4		
Deep venous thrombosis	2	2		
Pulmonary embolism	1	2		
Neurological	0	1		
Delirium/agitato	0	1		

Table 3. Comparison of Gastrointestinal Symptoms and Ileus Rates

	LRC	EORC	*P* value, Odds ratio (95%CI)
Recovery of Bowel Function, days, median (IQR)	3 (3-4)	3(3–5)	*P* = 0.41
Passage of Stool, day, median (IQR)	4 (4-5)	4(4-6)	*P* = 0.48
Ileus Rates, N(%)	6	10	*P* = 0.85, 0.96 (0.33-2.75)

and type of bowel preparation. Perioperative outcomes as operative time (OT) (defined as skin incision to skin closure), estimated blood loss (EBL), transfusion rates (TR), and hospital stay (HS) were evaluated. The single steps of the procedure as trocar placement time, cystectomy time, and duration of bowels to the atmosphere, were also recorded. According to the modified version of the original Clavien-Dindo grading system, all complications occurring within the first 90 days were recorded and categorised. Grades 3 to 5 indicate major complications, while grades 0 to 2 indicate minor or no complications[13]. The Martin criteria were used to classify perioperative complications[12]. The recovery duration of regular bowel activity and mean stool passage was recorded. Paralytic ileus was defined as persistent postoperative abdominal pain including vomiting and nausea, the need for interruption of oral nutrition and intravenous fluid support and/or nasogastric tube placement, or oral intolerance by postoperative day 4, leading to fasting with or without the need for antiemetics or nasogastric tube placement[2].

The EORC process was carried out as previously reported[8]. The LRC was performed employing the technique described by Guillotreau[14]. The surgical specimen was extracted through a minor sub-umbilical median incision. The ureter was reconstructed and reimplanted through a sub-umbilical mini-laparotomy. Extended lymphadenectomy was conducted in every case. On the first postoperative day, routine monitoring was carried out in the interdisciplinary ICU. Afterwards, the patients were followed-up and treated according to our standardised cystectomy pathways. Following the surgical procedure, intravenous patient-controlled analgesia (PCA) was delivered to all patients for the purpose of pain management. The PCA-administered opioid dose was quantified as the quantity of fentanyl administered per kilogramme of body weight. Daily clinical follow-up and laboratory monitoring were carried out in a standard manner. The third-month consultations included a series of medical procedures, namely a physical examination, urine culture, blood tests, and abdominopelvic computed tomography.

Data were analysed using Statistical Package for Social Science (SPSS) program for statistical analysis (version 23). Categorical variables were described using frequency and percentage of rows and percentage of columns. The categorical data were compared using Pearson's $\chi 2$-test was used. Continuous data with normal distribution were compared using the independent samples t-test. Shapiro–Wilk test's test was used to define the normal distribution. Mann-Whitney U test was utilised for non-normal distributions. Two-sided tests were used, and the significance level was set at $P < .05$.

RESULTS

A total of 221 patients met the inclusion criteria (81 LRC and 130 EORC). The mean age of our study population was 64 (59-70). The two groups had corresponding demographic data, including age range, prior abdominal surgery, comorbidity status, and disease stage (**Table 1**). The mean OT was longer in the LRC group than in the EORC group median 280 (220-340 IQR) minutes vs 240 (218.75-300 IQR) minutes, respectively; $P = 0.068$). Intraoperative EBL favoured the LRC group by a median of 450 ml (305-500 IQR) $P = 0.021$); it was a median of 700 mL (560-782.5 IQR) for EORC. However, TR did not differ between the two groups; it was %14.8 (N = 12) for the LRC and %20.8 (N = 27) for EORC ($P = 0.37$). The median HS was 9 (7-14 IQR) days for EORC and 8 (7,4-8.3 IQR) days for LRC ($P = .011$). The need for analgesics to control pain through an epidural catheter was higher for EORC ($P = .042$). The median duration of the abdominal cavity exposure to the atmosphere during the operation was 68 (56-104) for LRC and 73 (59–103) for EORC ($P = 0.25$). Concerning the 90-day overall perioperative complication rate, no statistically significant difference was defined between the two groups. Overall, 176 complications were determined in 125 (59.2%) of the 211 patients. Of these, 80 (N = 61.5%) developed in the EORC, whereas 45 (N = 58.75%) complications occurred in the LRC group ($P = .47$). Comparing the two techniques regarding minor and major complications, no statistically significant difference was determined ($P = .32$ and $P = .83$, respectively). The incidence of major and minor complications were 48.5% (N = 63) and 13.1% (N = 17) for EORC and 45% (N = 36) and 11.1% (N = 9) for LRC, respectively. Gastrointestinal and wound healing disorders were the most common complications after surgery. Ileus was the most frequent GIS complication among the two groups. Neither method experienced significantly more GIS problems than the other ($P = .75$). The time of recovery for function and time for the passage of stool yielded no difference ($P = .36$ and $P = .23$, respectively). No patient required re-intervention due to obstructive ileus. Of note, the incidence of wound complications was higher in the EORC. Four patients (4.9%) in LRC experienced a wound infection, compared to 18 (13.84%) in the EORC group. Two patients of the EORC group required surgery due to wound dehiscence. Local subcutaneous emphysema in LRC recovered during hospitalisation in two patients. Multivariate analysis revealed the Charlson index as the only predictor of overall complication rate (**Table 4**).The median number of lymph nodes retrieved for LRC and EORC was 19 (17-22 IQR) and 18.5 (17-22 IQR), respectively ($P = .83$). Lymphoceles did not occur in both groups. Twenty-four (18.46%) patients in the EORC group and 17 (21%) in the LRC group exhibited lymph node positivity ($P = .78$). All three patients received adjuvant chemotherapy following surgery. One patient in either group had a positive surgical margin.

DISCUSSION

Radical cystoprostatectomy is certainly the most challenging urological surgery, regardless of the technical

Table 4. Factors Associated with the Occurrence of Perioperative Complications Using Multivariate Analysis.

	Odds Ratio	95% CI	*P* value
OperativeTechnique	1.405	.787-2.509	0.25
Charlson's score	1.303	1.068-1.589	.009
BMI	.975	.903-1.053	.517
Age	1.001	.970-1.032	.968

method used. The trans-peritoneal ORC is notorious for having a high incidence of postoperative complications[14]. Due to this, there is greater interest, particularly in minimally invasive surgical approaches as well as a necessity for developing less morbid open techniques at institutions without access to such technology in the last years.

In this context, Kulkarni et al. introduced the EORC for the first time in 1999, and then studies of other investigators followed. Kulkarni aimed to decrease complications, especially GIS complications with the EORC technique[7]. In open EORC the peritoneal and extraperitoneal cavities can be divided in suturing the peritoneum to the base of the ileal loop mesentery at the end of the operation. In consequence, this maneuver precludes exposure of the intestines to lymphatic secretions or the potential urinary escape. Moreover, it mitigates the formation of adhesion bonds within the peritoneal cavity, thereby reducing the likelihood of complications. However, the EORC is criticised for its oncologic safety because of leaving the peritoneum overlying the bladder. Patients who qualify for this procedure are still a matter of debate. This is primarily due to the absence of studies, the small number of patients included, and the paucity of randomised trials[10,15-18]. Zhu et al. evaluated the characteristics of patients suitable for the extra-peritoneal approach. These authors concluded that patients with T2-T4 stage, positive lymph nodes, or non-urothelial histologies were not good candidates for peritoneum preservation[18]. To assess the oncologic effects of EORC, ex vivo biopsies of the peritoneum overlying the bladder were obtained from 136 cystectomy specimens. With the primary aim of oncological safety, we did not preserve the peritoneal overlying the posterior bladder wall. However, we think a lack of both the EORC and LRC performed in our clinic is that we did not apply the bilateral reperitonealization of the dorsolateral pelvic walls described by Roth et al. Surgically induced inflammatory reactions between the small intestine and the deperitonealized pelvic wall will result in small bowel palsy, ileus, or constipation. The readoption of the autologous peritoneal flaps is reported to lower gastrointestinal complications and the requirement for peridural anaesthetics while respecting oncological principles[19]. An advantageous aspect of the open EPRC technique is that the peritoneal layers are sutured to the base of the ileal loop mesentery at the end of the operation, effectively dividing the peritoneal and extraperitoneal cavities. Consequently, subsequent to the operation, there will be no exposure of the intestines to lymphatic secretions or the potential urinary escape. Moreover, it mitigates the formation of adhesion bonds within the peritoneal cavity, thereby reducing the likelihood of complications that may result. Given the significant advancements in urological laparoscopy over the last several decades, LRC has become a popular minimally invasive therapy for MIBC. Patients with organ-confined, non-bulky bladder cancer, a manageable age, a reasonable BMI, and minimal morbidity were the most frequently chosen for LRC[20]. Consequently, rapid recovery, decreased TR, and other problems may be noted compared to ORC. Our surgeons employed the same selection criteria for both techniques. In our dataset, only two patients were converted to open due to bulky disease. Lymphadenectomy with many nodes is a mainstay of oncological outcomes and is also considered an index of surgical quality[21-22]. On the other hand, it should be noted that the reported lymph node count is affected by the pathologist's thoroughness in searching for lymph nodes and by the method used to submit the sample for pathological investigation[23]. The EORC approach may constitute a disadvantage for lymph node dissection. However, previous studies determined no difference in lymph node numbers compared to conventional ORC[8,9]. As stated in prior research, our investigation did not identify any variations in removed lymph nodes between the groups[18]. The number of lymph nodes with prognostic value is around 15[21]. The median number of extracted lymph nodes among our patients was 19, which is acceptable. The incidence of positive surgical margins was reasonable. Unfortunately, the long-term oncologic results of our patients were not evaluated.

Gastrointestinal complications are the most common adverse effects of cystectomy, affecting approximately 35% of patients[6]. Complications associated with GIS are a significant cause of extended hospitalization[24]. Increased exposure of the intestines to the atmosphere and intestinal manipulation during surgery for clearing the operative field during the surgery are reasons for these complications[16]. Abdominal surgery that triggers a spinal reflex arc and widespread sympathetic hyperactivity decreases gastrointestinal motility[25]. Other contributory factors are using analgesics and anaesthesia for peritoneal inflammation resulting from the procedure. Gum chewing, drugs that target the peripheral m-opioid receptor, fast-track regimens, and other conservative measures have all been tried to lower the incidence of gastrointestinal problems following RC[15,26,27]. However, the actual surgery has a far higher impact on the onset and progression of POI. Laparoscopy enables a prompt resumption of oral feeding due to its ability to minimise manipulation of the digestive loops and reduce postoperative opioid consumption[28]. There were no differences concerning GIS complications between the two groups in our study. In both groups, bowel exposure to the atmosphere and tactile manipulation of abdominal contents is lower compared to conventional ORC[9,10]. Concordant with our results Zao et al. defined no difference in postoperative ileus rates between LRC and EORC[12]. The paralytic POI rate in EORC and LRC was likewise acceptable compared to previous research[8,9]. Compared with the standard ORC series, we obtained lower ileus rates with EORC and LRC[6,8,14]. At least, the ileus rate for LRC was consistent with previous research[19,28]. None of the patients required surgical reintervention due to ileus. Recovery of Bowel Function and time for passage of stool were similar between the two techniques in our series. As it is known, laparoscopy allows earlier return to oral feeding as it reduces manipulation of the digestive loops[28]. Conversely, Zao et al. revealed no difference in the interval of flatus and liquid intake[11]. In two further investigations comparing transperitoneal LRC with extraperitoneal LRC,

the authors found that extraperitoneal LRC resulted in decreased incidence of gastrointestinal problems and ileus[29,30].

One of the most common problems in RC is wound-related complications. LRC patients had a lower rate of wound complications than EORC patients. In EORC, prolonged abdominal wall retraction might result in wound infection or evisceration. The manipulation of the abdomen wall is minimal during LRC. In the LRC, we did not find any evidence of evisceration. The requirement for analgesics is another topic of discussion. Prolonged abdominal retraction and longer incisions during ORC were mentioned as the cause of analgesic requirements[31]. Less postoperative pain and a reduced need for narcotic analgesics may be related to a shorter recovery period and, in addition to blood loss, provide an additional reason for early discharge. Our results revealed a lower analgesic requirement for LRC. Similar to our findings, previous studies[20,31] reported less need for analgesics for LRC compared to conventional RC. However, Zhao et al. found no difference in analgesic requirement between LRC and EORC[11]. Consistent with prior studies comparing minimally invasive surgery to ORC, the LRC group in our study experienced less blood loss and lower TR[20,28,31]. This results from the technique being more delicate and exact, the pneumoperitoneum, and the excellent visibility of magnification. It should be emphasised that the EORC approach appears to have no impact on blood loss, similar to the findings of prior studies[9,17].

As stated in previous studies, the OT was longer for LRC[20]. LRC patients were discharged earlier than EORC patients. Lower EBL and TR in LRC, which presumably lead to a shorter recovery time, maybe a factor in early discharge. Reduced wound problems with LRC may also contribute to shorter HS. The HS varies around different countries. This can be attributed to the financial aspects of the respective healthcare systems. As a result, it is difficult to compare with previous studies in terms of hospital duration[9,20,28,31]. In our opinion, the overall HS is relatively high in the current study. This is because, unlike in Western nations, healthcare providers outside of hospitals are unavailable in our country. Moreover, a significant proportion of patients are referred from rural regions within our nation, where the ability to effectively address issues may be limited within state-operated healthcare facilities. The Enhanced Recovery After Surgery protocol was not followed in our patients, which also accounts for the increased HS.

The overall early complication rates observed in our study were relatively high. Nonetheless, it was consistent with prior ORC investigations that utilised standardised reporting techniques[2-6]. In a multicenter research with 503 patients, the LRC complication rate was reported to be 54%, which also corresponds well with our data[32]. Tang et al. concluded that LRC appears to be a safe, feasible, and minimally invasive alternative to ORC with fewer complications[20]. Noteworthy, our research showed that the complications for EORC and LRC were comparable. Similarly, Zhao et al. observed no difference in complications between EORC and LRC[11]. We performed LRC with total extracorporeal urinary diversion. The advantage of LRC appeared to be with radical cystoprostatectomy and not with urinary diversion. Despite our surgeons having advanced laparoscopic suturing skills and experience, laparoscopic suturing during intracorporeal diversion is challenging, demanding, and associated with prolonged OT. This might negate the benefit provided by laparoscopic surgery. Besides decreasing OT, extracorporeal diversion allows for more secure anastomosis. We perform the ileal conduit through a 4-6 cm incision where the specimen is extracted. The diversion can be conducted without any abdominal wall traction.

Ultimately, whereas LRC and open EP cystectomy provide comparable outcomes, it is crucial to emphasise that the learning curve for laparoscopy is significantly steeper in comparison to open robotic surgery. Furthermore, the use of laparoscopy in the pelvic region is not as prevalent. It is ergonomically challenging for both the surgeon and the assistant, and robotic surgery has the greatest advantage over conventional laparoscopy in the pelvic region.

Several limitations should be considered in relation to this study. First, the patients in the study were not randomly assigned, and selection bias may have affected the results. There may also be susceptibility to information bias in data insertion and collection. A prospective, randomised study design would yield more reliable results. While acknowledging the potential influence of surgeon bias on the outcomes, we have taken measures to mitigate this effect. Specifically, we have ensured that the surgical teams participating in the experiment had surpassed their learning curve for cystectomy and that a standardised pathway was consistently used to all patients. The re-adaptation of the dorsolateral peritoneal layer might contribute to a more favourable postoperative outcome. This should be stated as another weakness of the study. Most high volume centres use Enhanced Recovery After Surgery protocols as postoperative pathway. Our postoperative pathway is not commonly used anymore.

CONCLUSIONS

Despite the reality that LRC was related to a longer OT, patients with LRC may experience less blood loss, a shorter HS, less TR, lower wound-related complications and a lower necessity for narcotic analgesics. In our experience, EORC resulted in POI and 90-day complications similar to that of LRC despite the factors favouring LRC. Although LRC appears to have a slight advantage over EORC, both techniques yield satisfactory outcomes.

SUMMARY

There is limited research about minimally invasive radical cystectomy confronting extraperitoneal radical cystectomy in terms of outcomes. Most of these studies did not use standardised methods for reporting perioperative complications. Although LRC appears to have a slight advantage over EORC, both techniques yield satisfactory results in regard to ileus rates and 90-day perioperative complications.

CONFLICT OF INTEREST

The authors report no conflict of interest.

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