"Two-zone and Three-segment" Laparoscopic Radical Cystectomy vs Conventional Laparoscopic Radical Cystectomy for Male Patients With Bladder Urothelial Carcinoma: A Retrospective Analysis

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Purpose: The aim of this study was to introduce an advanced surgical technique for laparoscopic radical cystectomy (LRC), evaluate the perioperative outcome and compare it to that of conventional LRC (CLRC).

Materials and Methods: Between March 2018 and March 2020, sixty patients were divided into the "two-zone and three-segment" laparoscopic radical cystectomy (TTLRC) group or the CLRC group. Patient baseline characteristics, preoperative characteristics and postoperative complications were collected.

Results: The TTLRC technique was developed based on the pelvic anatomy of six formalin fixed male cadavers. None of the patient baseline characteristics, including ECOG-PS score, comorbidity, ASA score and Hb, were significantly different between the two groups ($p > 0.05$). There were significant differences in the operating time and estimated blood loss (total time: 3±0.2 vs 3.8 ± 0.4, $p < 0.001$; time to cystectomy and lymph node dissection: 1.7 ± 0.2 vs 2.2 ± 0.3, $p < 0.001$; estimated blood loss 182. 1± 18.8 vs 264.3 ± 27.4, $p < 0.001$). Although there were no differences in late complications, early complications were significantly different between the two groups ($p = 0.033$). No statistically significant differences were found between the two groups in other outcomes ($p > 0.05$).

Conclusion: The TTLRC technique achieves a clearer surgical field, has a shorter operating time and produces less blood loss than CLRC. It is safe and feasible for urologists to perform this improved LRC procedure.

Keywords: laparoscopic radical cystectomy; bladder cancer; outcome; complication; surgical technique

INTRODUCTION

Bladder cancer (BCa) is the 10th most common malignancy according to the latest global cancer statistics, with an estimated 549,000 new cases and 199,000 deaths occurring per year[1]. Approximately 25% of patients with primary BCa have been diagnosed with muscle invasive bladder cancer (MIBC), and approximately 10-30% of non-muscle invasive bladder cancer (NMIBC) can progress to MIBC[2,3]. Accordingly, the treatment of BCa is of great importance for urologists.

Radical cystectomy (RC) with extended pelvic lymphadenectomy is the guideline-recommended treatment for high-risk NMIBC and MIBC[4,5]. Open RC (ORC) is considered one of the most invasive surgeries in urology and has serious perioperative complications[6,7]. Following rapid technical advances, laparoscopic radical cystectomy (LRC) has been widely accepted because of its minimal invasiveness, lower blood loss, and shorter hospital stay, while yielding equivalent or better outcomes for patients relative to ORC[8-10]. Furthermore, one of the most important advantages of LRC is the lower incidence of postoperative ileus, which is the most frequent complication after cystectomy and a common reason for longer hospital stays[11]. LRC also achieves better hemostasis due to pneumoperitoneum and precise visibility when performing the technique. However, the technical procedure for LRC is complicated, and the surgeon should have an excellent understanding of the pelvic anatomy. LRC is still a challenge due to the longer operation time and the need to establish pneumoperitoneum, especially for elderly or higher BMI patients[12]. It is difficult to perform surgical manipulations in the insufficient operative space. Thus, it is important to understand the pelvic anatomy precisely and improve the surgical procedure to decrease the incidence of complications and operating time in LRC.

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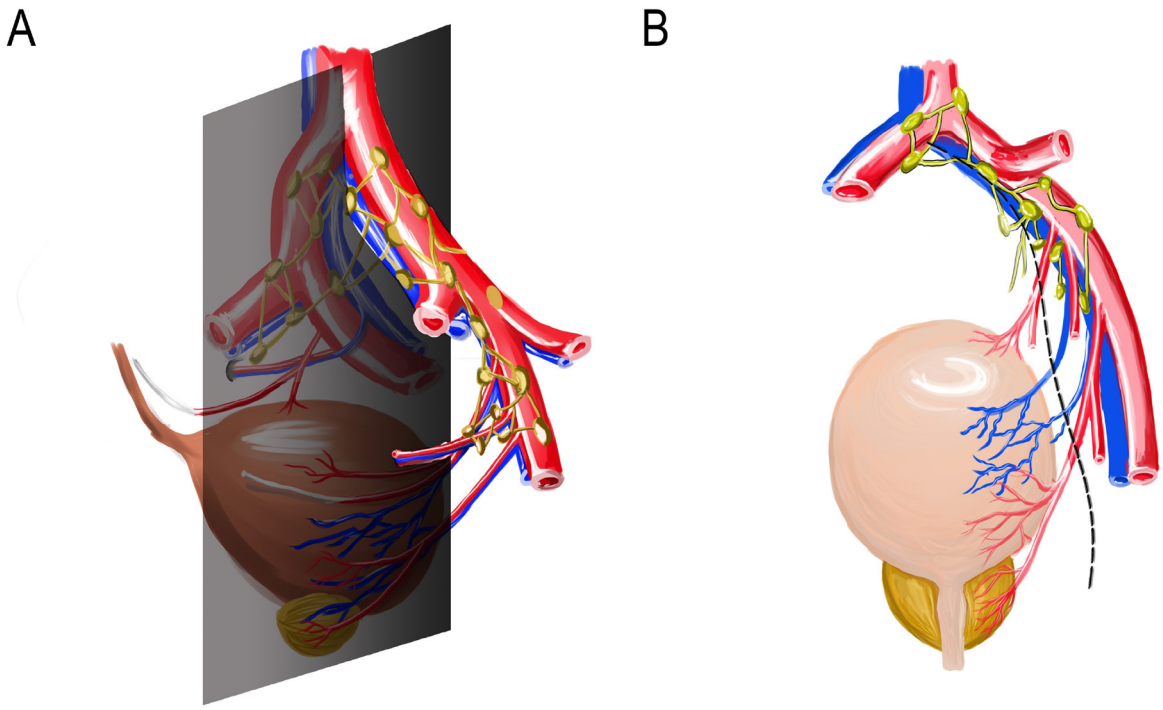

Figure 1. Schematic model of "two-zone and three-segment" laparoscopic radical cystectomy. **(A)** Lateral view. **(B)** Anterior view.

Herein, we performed an advanced surgery technique for LRC based on our pelvic anatomy research, named "two-zone and three-segment" laparoscopic radical cystectomy (TTLRC). We conducted a retrospective analysis to evaluate the efficiency and safety of TTLRC and compare it to conventional LRC (CLRC).

MATERIALS AND METHODS

Patients

Patients who met the following conditions were excluded from this study: (1) any distant metastases; (2) auto-

Table 1. Patient Demographics and Tumor Characteristics

Variables	Total (n=60)	TTLRC (n=29)	CLRC (n=31)	*P*-value
Age, year (mean ± SD) [a]	64.7 ± 10.9	65.3 ± 11.9	64.1 ± 10.0	0.668
History of smoking, n (%)	20 (33.3)	10 (34.5)	10 (32.3)	0.536
BMI (kg/m2) (mean ± SD) [b]	24.1 ± 3.3	24.0 ± 3.3	24.1 ± 3.3	0.777
ECOG-PS score, n (%)				0.281
0	56 (93.3)	26 (89.7)	30 (96.8)	
≥1	4 (6.7)	3 (10.3)	1 (3.2)	
Comorbidity, n (%)				0.881
Hypertension	19 (31.7)	8 (27.6)	11 (35.5)	
Diabetes mellitus	14 (23.3)	7 (24.1)	7 (22.6)	
Coronary artery disease	10 (16.7)	6 (20.7)	4 (12.9)	
Chronic obstructive pulmonary disease	7 (11.7)	3 (10.3)	4 (12.9)	
Others	3 (5.0)	1 (3.4)	2 (6.5)	
ASA score, n (%)				0.538
1-2	53 (88.3)	26 (89.7)	27 (87.1)	
3	7 (11.7)	3 (10.3)	4 (12.9)	
Hb (g/L) b	122 ± 7.1	122.3 ± 7.0	121.6 ± 7.2	0.880
Clinical stage, n (%)				0.538
NMIBC	16 (26.7)	8 (27.6)	8 (25.8)	
MIBC	44 (73.3)	21 (72.4)	23 (74.2)	
Clinical tumor grade, n (%)		0.586		
Low	8 (13.3)	4 (13.8)	4 (12.9)	
High	48 (80.0)	24 (82.6)	24 (77.4)	
Squamous cell carcinoma	2 (3.3)	0 (0)	2 (6.5)	
Adenocarcinoma	2 (3.3)	1 (3.4)	1 (3.2)	

Abbreviations: TTLRC, "Two-zone and Three-segment" Laparoscopic Radical Cystectomy; CLRC, Conventional Laparoscopic Radical Cystectomy; SD, Standard Deviation; BMI, Body Mass Index; ECOG-PS, Eastern Cooperative Oncology Group performance Status; Hb, Hemoglobin; NMIBC, Non-Muscle Invasive Bladder Cancer; MIBC, Muscle Invasive Bladder Cancer

[a] These variables were compared by independent samples t-test

[b] These variables were compared by Mann-Whitney test

Table 2. Perioperative characteristics.

Variables	Total (n=60)	TTLRC (n=29)	CLRC (n=31)	*P*-value
Operating time, hours (mean±SD)				
Total timea	3.4 ± 0.5	3.0 ± 0.2	3.8 ± 0.4	< 0.001
Time to cystectomy and lymph node dissectiona	1.9 ± 0.4	1.7 ± 0.2	2.2 ± 0.3	< 0.001
EBL, ml (mean±SD) [a]	224.6 ± 47.6	182.1 ± 18.8	264.3 ± 27.4	< 0.001
Pelvic lymph node dissection, n (%)		0.538		
Standard	53 (88.3)	26 (89.7)	27 (87.1)	
Extended	7 (11.7)	3 (10.3)	4 (22.9)	
Urinary diversion type, n (%)		0.424		
Ureterocutaneostomy4	8 (80.0)	24 (82.8)	24 (77.4)	
Ileal conduit	12 (20.0)	5 (17.2)	7 (22.6)	
Transfusion, n (%)	8 (13.3)	2 (6.9)	6 (19.4)	0.15
Time to ambulation, day, median (range)	2 (2-4)	2 (2-4)	2 (2-4)	0.764
Time to oral intake, day, median (range)	3 (2-5)	2 (2-4)	3 (2-5)	0.409
Time to flatus, day, median (range)	2 (2-4)	2 (2-4)	2 (2-4)	0.803
Hospital stay after surgery, day, median (range)	5 (4-9)	5 (4-6)	7 (4-9)	< 0.001

Abbreviations: TTLRC, "Two-zone and Three-segment" Laparoscopic Radical Cystectomy; CLRC, Conventional Laparoscopic Radical Cystectomy; SD, Standard Deviation; EBL, Estimated Blood Loss; min, Minute
[a] These variables were compared by Mann-Whitney test

immune disease; (3) cancer in other systems; (4) American Society of Anesthesiology (ASA) grade > 3; (5) clinical stage T4; (6) previous pelvic radiotherapy; and (7) severe cardiopulmonary dysfunction preventing surgical tolerance. This retrospective analysis included the clinicopathologic and follow-up data of 60 patients with high-risk NMIBC, MIBC or other types of BCa in Qilu Hospital of Shandong University from March 2018 to March 2020. All patients were divided into 2 groups; 29 patients in the TTLRC group and 31 in the CLRC group. None of the patients had neoadjuvant chemotherapy or radiotherapy. Patients with lymph node-positive disease or locally advanced disease were treated with adjuvant chemotherapy. This study was approved by the Institutional Ethics Committee of the Qilu Hospital of Shandong University. Written informed consent was obtained from all the patients in this study.

All patients underwent routine laboratory tests, echocardiography, lung function tests, chest radiographs, computerized tomography (CT), magnetic resonance imaging (MRI), urinary cytology and / or cystoscopy with tissue biopsy. All operations and perioperative management were performed by the same laparoscopic surgical team. All three surgeons (BK, XZ and DQ) in this study are well-experienced in performing LRC. BK performed 18 and 16, XZ performed 7 and 9, and DQ performed 4 and 6 TTLRC and CLRC procedures, respectively.

Conventional laparoscopic radical cystectomy

The basic procedures were performed as reported by Campbell-Walsh Urology[13]. The patient was placed in a dorsal supine position with a 15 - 25° Trendelenburg position after general anesthesia. A five-port fan-shaped approach was used. The camera port was placed just above the umbilicus after establishment of pneumoperitoneum and the remaining four ports were placed in a fan shape. Standard lymphadenectomy was first conducted after releasing the ureter. Then, the posterior wall of the bladder was separated. The lateral ligaments of the bladder were dissected (**Figure 1A**). The anterior plane was then established distally toward the prostate (**Figure 1B**). The attachments of the prostatic apex to the pelvic floor were released, and the urethral catheter was removed. After dissection of the Santorini venous plexus, the urethra was dissected. After laparoscopic cystectomy, urinary diversion, was performed with procedures such as the Bricker operation of ureterocutaneostomy according to the patient's preference. "Two-zone and three-segment" laparoscopic radical

Table 3. Pathological characteristics.

Variables	Total (n=60)	TTLRC (n=29)	CLRC (n=31)	*P*-value
pT stage, n (%)	0.631			
Cis	2 (3.3)	1 (3.4)	1 (3.2)	
Ta/T1	7 (11.7)	3 (10.3)	4 (12.9)	
T2	26 (43.3)	10 (34.5)	16 (51.6)	
T3	16 (26.7)	10 (34.5)	6 (19.4)	
T4	9 (15.0)	5 (17.2)	4 (12.9)	
Pathological tumor grade, n (%)				0.327
Low	11 (18.3)	4 (13.9)	7 (22.6)	
High	44 (73.3)	24 (82.8)	20 (64.5)	
Squamous cell carcinoma	2 (3.3)	0 (0)	2 (6.5)	
Adenocarcinoma	3 (5.0)	1 (3.4)	2 (6.5)	
Concomitant Cis, n (%)	5 (8.3)	3 (10.3)	2 (6.5)	0.666
pN stage, n (%)				0.608
pN0	52 (86.7)	25 (86.2)	27 (87.1)	
pN+	8 (13.3)	4 (13.8)	4 (12.9)	

Abbreviations: TTLRC, "Two-zone and Three-segment" Laparoscopic Radical Cystectomy; CLRC, Conventional Laparoscopic Radical Cystectomy; CIS, Carcinoma in Situ

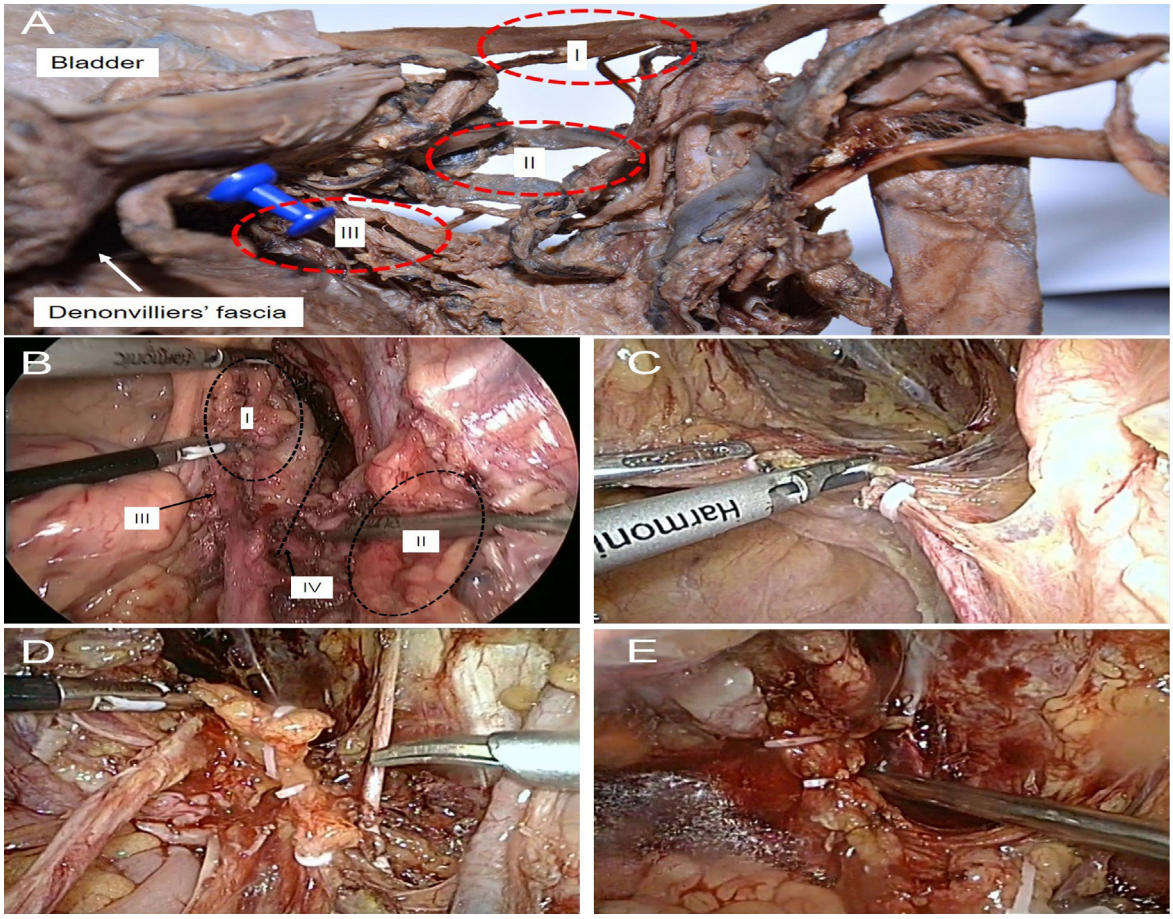

Figure 2. The "two-zone and three-segment" laparoscopic radical cystectomy techinique. **(A)** Anatomical picture of the lateral vascular pedicles of the bladder, which consists of three segments: I, the superior bladder artery segment; II, the bladder vein segment; and III, the inferior bladder artery segment. **(B)** Laparoscopic image showing the two zones: I, the lateral vascular bladder pedicle zone; and II, the lymph node dissection zone. III represents the umbilical artery, and IV represents the umbilical artery lateral plane, which was the boundary between the two zones. **(C)** Dissecting the superior bladder artery segment. **(D)** Dissecting the bladder vein segment. **(E)** Dissecting the inferior bladder artery segment.

cystectomy

The "two-zone and three-segment" laparoscopic radical cystectomy technique was developed based on the pelvic anatomy. Six formalin-fixed male cadavers, which were provided by the Institute of Anatomy, Shandong University, were used to conduct anatomical studies.

According to the anatomical characteristics of the lateral vascular pedicles of the bladder, we defined 3 segments: the superior bladder artery segment, the bladder vein segment, and the inferior bladder artery segment (**Figure 2A**). The inferior bladder artery segment is also called the prostatic vascular pedicle segment.

"Two-zone and three-segment" laparoscopic radical cystectomy was performed as follows. The umbilical artery was first identified after releasing the ureter. The umbilical artery lateral plane was established distally toward the pelvic floor, an important procedure of this technique. On the interior side of the plane was the "lateral vascular pedicles of bladder" zone, while on the opposite side of the plane was the "lymph node dissection" zone (**Figure 2B**). Standard pelvic lymphadenectomy was performed in the areas of the common, external and internal iliac arteries and the obturator. The superior bladder artery segment and the bladder vein segment were dissected (**Figure 2C-D**). Mobilization of the posterior wall of the bladder was performed. Then, the inferior bladder artery segment was dissected. The next steps were the same as in the conventional methods.

Demographic parameters and follow-up

The following demographic parameters were recorded and analyzed by clinical researchers with no association with the operations (JF and SZ): preoperative baseline clinicopathological and laboratory data, such as age, gender, history of smoking, BMI, clinical tumor stage, and hemoglobin, were obtained from the electronic medical records. Perioperative data, including operation time, estimated blood loss (EBL), blood transfusion, urinary diversion method, time to ambulation, time to bowel recovery, time to oral intake and hospital stay, and oncologic data, including pathologic tumor stage, grade and lymph node metastasis status, were also assessed. Operation time was defined as the duration of anesthesia from the beginning to the end. Pathological T stages were uniformly adjusted according to the 2009 TNM classification as approved by the Union Internationale Contre le Cancer (7th edition), and tumor grade was assessed based on the 2004 World Health Organization (WHO) classification guidelines[2,4].

Table 4. Complications characteristics by Clavien-Dindo classification.

Variables	Total (n = 60)	TTLRC (n = 29)	CLRC (n = 31)	Clavien-Dindo classification	*P*-value
Early complications (≤ 30 day), n (%)					0.033
Paralytic ileus	8 (13.3)	2 (6.9)	6 (19.4)	I	
Anemia	7 (11.7)	2 (6.9)	5 (16.1)	II	
Hypokalemia	4 (6.7)	2 (6.9)	2 (6.5)	II	
Urinary tract infection	3 (5.0)	1 (3.4)	2 (6.5)	II	
Blood transfusions	2 (3.3)	1 (3.4)	1 (3.2)	II	
Entorrhagia	4 (6.7)	2 (6.9)	2 (6.5)	III	
Rectal injury	4 (6.7)	1 (3.4)	3 (9.7)	III	
Acute coronary syndrome	3 (5.0)	1 (3.4)	2 (6.5)	IV	
Heart failure	2 (3.3)	1 (3.4)	1 (3.2)	IV	
Late complications (31-90 day), n (%)					0.729
Hydronephrosis	4 (6.7)	2 (6.9)	2 (6.5)	I	
Pyelonephritis	3 (5.0)	1 (3.4)	2 (6.5)	II	
Urinary tract infection	5 (8.3)	2 (6.9)	3 (9.7)	II	
Pneumonia	5 (8.3)	2 (6.9)	3 (9.7)	II	
Deep venous thrombosis	1 (1.7)	1 (3.4)	0 (0.0)	II	
Ureteral stricture	2 (3.3)	1 (3.4)	1 (3.2)	III	
Urolithiasis	3 (5.0)	2 (6.9)	1 (3.2)	III	
Renal failure	2 (3.3)	1 (3.4)	1 (3.2)	III	
Death	1 (1.7)	0 (0.0)	1 (3.2)	V	

Postoperative complications were recorded and categorized using the modified Clavien-Dindo classification complications system introduced by Dindo D et al.[14], which includs five groups and two subgroups. Complications were classified as early complications (within 30 days) and late complications (31-90 days).

Common comorbidities were also recorded in detail, including hypertension, diabetes mellitus, coronary artery disease, chronic obstructive pulmonary disease and other chronic diseases.

Patients were followed postoperatively at least every 3–4 months for the first 2 years, biannually for the next three years, and annually thereafter. Postoperative complication data were obtained by either chart review or telephone contact follow-up.

This research complied with the guidelines for human studies and the research was conducted ethically in accordance with the World Medical Association's Declaration of Helsinki. The research was approved by Ethics Committee of Shandong University Qilu Hospital. Approved number: KYLL-2020-264

Statistical analysis

Statistical analysis was conducted using the Statistical Package for Social Science (SPSS for Windows, version 23.0, SPSS Inc., Chicago, IL) software. Quantitative data are shown as the mean ± SD, and categorical data are presented as the frequency (%). Pearson's chi square test or Fisher's exact test was used to evaluate the differences between categorical variables, student's t test (meet the normality of distribution and homogeneity) and Mann-Whitney test (meet the nonparametric test) were used for continuous variables in this study. Two-sided P values of less than 0.05 were considered statistically significant.

RESULTS

Patient characteristics

The baseline characteristics are shown in Table 1. Of the 63 patients who underwent LRC at our institution from March 2018 to March 2020, 3 patients were excluded because of exclusion criteria. The mean (SD) age of the total patients was 64.7 (10.9), and among the 60 patients, 20 (33.3%) had a history of smoking. The mean (SD) body mass index (BMI) was 24.1 (3.3). Sixteen patients (26.7%) were clinically diagnosed with NMIBC, and 44 (73.3%) were clinically diagnosed with MIBC. A low tumor grade was found in 8 patients (13.3%), and a high tumor grade was found in 48 (80.0%). The median (lower quartile, upper quartile) duration of follow-up was 26 (19.75, 31.25). None of the patient clinical characteristics, including ECOG-PS score, comorbidity, ASA score and Hb, were significantly different between the TTLRC and CLRC groups ($P > .05$).

Perioperative characteristics

The perioperative characteristics of the two groups are shown in Table 2. The operating time of the TTLRC group was significantly shorter than that of the CLRC group (total time: 3.0 ± 0.2 vs 3.8 ± 0.4, $P < .001$; time to cystectomy and lymph node dissection: 1.7 ± 0.2 vs 2.2 ± 0.3, $P < .001$). Additionally, the EBL of the TTLRC group was significantly lower than that of the CLRC group (182.1 ± 18.8 vs 264.3 ± 27.4). Fifty-three patients (88.3%) underwent standard pelvic lymph node dissection, and 7 (11.7%) underwent extended pelvic lymph node dissection. Forty-eight patients (80.0%) underwent LRC with ureterocutaneostomy and 12 (20.0%) underwent LRC with ileal conduits. Moreover, except for hospital stay after surgery, there were no significant differences between the two groups in the transfusion rate, time to ambulation, time to oral intake or time to flatus.

The pathological characteristics of the patients are shown in Table 3. Both the TTLRC and CLRC groups included one patient with CIS each, and 5 patients were found to have concomitant CIS, 3 and 2 in the TTLRC and CLRC groups, respectively. No significant differences were found in pathological T stage, tumor grade or N stage ($P > .05$).

Postoperative complications

The early and late postoperative complications of the two groups are shown in **Table 4**. During the follow-up period, only one death occurred in both groups. According to the Clavien-Dindo classification of postoperative

complications, thirty-seven patients (61.7%) experienced early complications. Eight and 16 minor (I-II) complications and 5 and 8 major (III-IV) complications were observed in the TTLRC and CLRC groups, respectively. The common complications were paralytic ileus and anemia. There was a significant significance between the two groups in early complications (I-II vs III-IV, $P = .033$), not in late complications (I-II vs III-IV, $P = .729$).

DISCUSSION

Radical cystectomy is one of the most difficult urological surgeries, and the LRC procedure is difficult to master and technically challenging. Most patients with BCa are elderly males whose pelvis is narrow, which could increase the difficulties of surgery. The present study is the first paper comparing TTLRC and CLRC in male patients. These operations were performed by the same laparoscopic surgical team, including three surgeons, in a single center.

We used 6 male cadavers to conduct pelvic anatomical research and developed the improved TTLRC technique. There were variations in the superior vesical artery segment among the cadavers. Most superior vesical arteries are derived from the umbilical artery, and a few are derived from the internal iliac artery directly. Therefore, it is important to expose bladder-associated vessels, such as the superior vesical artery, umbilical artery, and obturator artery. It is also important for experienced surgeons to learn the anatomy from cadavers. A more detailed evaluation of anatomy has allowed a better understanding of the variability of vessels, prevents disruption of vessels, and helps guide the operational procedure. In the TTLRC group, the bladder vein segment, including the many branches derived from the bladder vein and part of the large veins, was the most common bleeding site in LRC surgery. A LigaSure or endovascular gastrointestinal anastomosis (Endo-GIA) stapler was used to rapidly dissect this segment to shorten the operating time. Moreover, for male patients who desire retention of erectile function, we should avoid thermal damage to preserve the neurovascular bundles (NVBs), which is another important step for the patients.

Tong et al. reported the anterior approach LRC could modify the laparoscopic visualization and enlarge the working space. This procedure also reduces the operation time and EBL without causing substantial differences in perioperative complications[15]. Additionally, compared with CLRC, the extraperitoneal LRC technique resulted in a shorter time to flatus and time to liquid intake but had no benefit on operation time[16]. In the present study, the TTLRC group showed benefits in early complications and perioperative outcome, including operating time, time to cystectomy and lymph node dissection and EBL. From our study, there were several surgical benefits for the TTLRC group. First, we divided the surgical location into two zones to dissect the vessels and lymph nodes separately, which improved visualization of the anatomical hierarchies. Moreover, for patients of older age or moderate comorbidity status, a modified surgery in which only the bladder was dissected while the lymph nodes were left intact was conducted to shorten the operating time and further reduce the risk of surgery. Last, we defined the male bladder-associated region, and systematically introduced a surgical procedure that could be useful for laparoscopic-naive urologists.

Urinary diversion approaches can be divided into ureterocutaneostomy, ileal conduit and orthotopic neobladder. In addition, most of the complications are related to the use of the bowel. Ureterocutaneostomy is the simplest form of diversion and has a lower complication rate[17]. Here, the incidence of ileus was lower in patients who underwent ureterocutaneostomy than in those described in other studies[18]. Ureterocutaneostomy was performed in more patients in the TTLRC group, which might be a potential factor influencing the shorter operation time. Furthermore, extended lymph node dissection and ileal conduit diversion were performed more often in the CLRC group, which also might have affected the operation time.

There are a few limitations in this study. First, patients were recruited from a single center in this study, which could have caused selection bias. Second, the sample size was small, and future studies should include an enlarged sample size. Third, this is a retrospective study, not a randomized controlled trial, which is needed to improve the power in drawing a definitive conclusion in a future study. Last, a comparison of the long-term clinical outcomes between TTLRC and CLRC should be collected and analyzed in future studies.

CONCLUSIONS

In conclusion, we studied the pelvic anatomy based on cadavers, and defined the zones and segments used for surgery to develop the “two-zone and three-segment” LRC procedure, whose outcomes were compared with conventional LRC. Compared with CLRC, TTLRC has several advantages, including a clearer surgical field, a shorter operating time and less blood loss. It is safe and feasible for urologists to perform this improved LRC procedure.

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CONFLICTS OF INTEREST

The authors have declared that no conflicts of interest exist.

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