

A Retrospective Study Comparing Surgical and Early Oncological Outcomes between Intracorporeal and Extracorporeal Ileal Conduit after Laparoscopic Radical Cystectomy from a Single Center

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Abstract

Background: Robot-assisted/laparoscopic intracorporeal ileal conduit (ICIC) has been reported in many experienced centers. Whether laparoscopic ICIC is superior to extracorporeal ileal conduit (ECIC) and whether laparoscopic ICIC should be promoted is still controversial. The aim of the study was to compare surgical and early oncological outcomes between patients undergoing laparoscopic radical cystectomy (LRC) with ICIC and ECIC.

Methods: From January 2011 to June 2016, a total of 45 patients with bladder cancer underwent LRC with ileal conduit at our department, of whom 20 patients underwent LRC with ECIC and 25 patients underwent LRC with ICIC. Data of each patient's characteristics, surgical outcomes, and short-term oncological outcomes were collected and analyzed.

Results: LRC with ileal conduit was performed successfully on all 45 patients. There were no significant differences in patients' characteristics, mean total operative time, and mean estimated blood loss between the ICIC and ECIC groups. Median time of flatus and oral intake was shorter in the ICIC group compared with the ECIC group (3 vs. 5 days, $P = 0.035$; 4 vs. 5 days, $P = 0.002$). The complications rates did not show significant difference between the two groups within the first 90 days postoperatively ($P = 0.538$). Cancer staging showed 45% of patients in the ECIC group and 36% in the ICIC group had a pathologic stage of T3 or T4, and 50% of patients in the ECIC group and 44% in the ICIC group had a pathologic stage of N1 or N1+. Kaplan–Meier analysis showed no significant difference in overall survival at 24 months (60% vs. 62%, $P = 0.857$) between the ECIC and ICIC groups.

Conclusions: ICIC after LRC may be successful with the benefits of faster recovery time. No significant difference was found in complications and oncological outcomes between ICIC and ECIC. However, larger series with longer follow-up are needed to validate this procedure.

Key words: Ileal Conduit; Laparoscopy; Urinary Bladder Cancer

INTRODUCTION

Radical cystectomy with pelvic lymph node dissection is considered to be the standard treatment for muscle-invasive bladder cancer.^[1] Laparoscopic radical cystectomy (LRC) is considered to be a safe and feasible alternative to open radical cystectomy with fewer overall complications, reliable pathologic and oncologic efficacy, and shorter recovery time.^[2] Conventionally, extracorporeal construction of urinary diversion following LRC is performed in the majority of medical centers because the procedure is complex and time consuming.

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Robot-assisted/laparoscopic intracorporeal ileal conduit (ICIC) has been reported in many experienced centers since the procedure was initially described in 2000 by Gill *et al.*^[3] Recently, ICIC is mostly performed with the robot-assisted laparoscopic approach, and those studies demonstrated that intracorporeal urinary diversion can be accomplished safely, with comparable outcomes to open urinary diversion.^[4-7] However, the conventional laparoscopic approach has seldom been reported. Furthermore, comparison studies evaluating the benefits of laparoscopic ICIC versus extracorporeal ileal conduit (ECIC) are even limited in the English literature.^[4] Hence, whether laparoscopic ICIC is superior to ECIC and whether laparoscopic ICIC should be promoted is still controversial. This article aimed to compare perioperative complications and short-term oncologic outcomes of ICIC and ECIC following LRC.

METHODS

Ethical approval

As the retrospective study and data analysis was performed anonymously, this study was exempt from the ethical approval and informed consent from patients.

Patients

From January 2011 to June 2016, a total of 45 patients with bladder cancer who underwent LRC with ileal conduit at our department by one surgeon with high volume surgical experience in LRC were retrospectively analyzed in this study, of whom 20 patients underwent LRC with ECIC from January 2011 to January 2014 while 25 patients underwent LRC with ICIC from February 2014 to June 2016. The indications for surgery included (1) muscle-invasive bladder cancer, (2) T1G3 or high-risk and recurrent superficial bladder cancer, and (3) extensive non-muscle-invasive bladder cancer that could not be controlled by transurethral resection and intravesical therapy. All patients were examined by pelvic magnetic resonance (MRI) or enhanced computed tomography examination before operation. Ileal conduit was considered after evaluation of the patients' tumor status, general condition, and intention. Postoperative complications were analyzed according to the Clavien–Dindo classification.^[8] Perioperative, postoperative complications and oncologic outcomes were compared. After discharge, patients were followed up at 2 weeks, 3, 6, and 12 months, and then yearly.

Surgical technique

After general anesthesia, patients were placed in a dorsal supine position with a 30° Trendelenburg position [Figure 1]. Five to six trocars were introduced. The first 10-mm trocar for the camera was placed at the upper level of the umbilicus. Two 12-mm trocars were placed at the right and left lateral rectus line 1 cm below the umbilicus and two 5-mm trocars were placed 2–3 cm superior and medial to the anterior superior iliac spines on each side. An additional 12-mm trocar was placed 1 cm cranial to the pubic symphysis in the middle line for Endo-GIA for ICIC. LRC was then performed using the same technique as that reported previously.^[9]

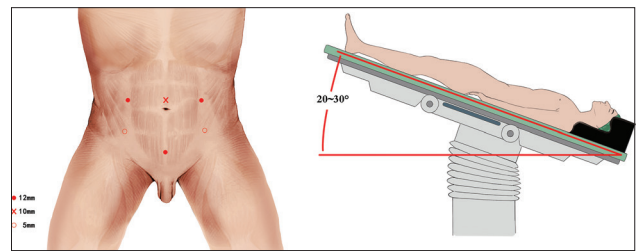


Figure 1: Trocar placement and patient position.

Extended pelvic lymph node dissection involved removal of nodal tissue cranially up to the aortic bifurcation, including the internal iliac, presacral, obturator fossa, and external iliac and common iliac nodes. Then, lymph nodes of different position were marked and put into the Endo-Catch bag. The left ureter is tunneled under the sigmoid mesentery to the right side.

For ECIC, all ports were removed and the Endo-Catch bag was removed via a midline laparotomy below the umbilicus approximate 10–15 cm. The previously mobilized ureters were brought out through the incision. The clips were removed from the dilated ureters. Both ureters were spatulated for approximately 3 cm, and Mono-J ureteric stents (6F) were inserted in both ureters. Through the skin incision, the ileum was extracted from the peritoneal cavity. An ileal segment 15 cm long was isolated 30 cm proximal to the ileocecum. The ileal side-to-side reanastomosis was performed cranially to the ileal conduit using 80-mm stapler and 4-0 Vicryl was used for the closure of the mesenteric defect to prevent internal hernia. Then, the ureters were anastomosed with the proximal end of ileal conduit end-to-end with 4-0 Vicryl. A circular disc of skin at the right 12-mm port was excised, and the conduit brought out through extraperitoneal space was fixed with fascia and skin. After a drain was placed, the incisions were closed.

For ICIC, a 15–20 cm ileum segment was identified approximately 30 cm away from the ileocecum. A 60-mm Endo-GIA stapler was used to divide the bowel lumen on both sides of the conduit. The continuity of the small bowel was restored using the Endo-GIA with a 60-mm stapler, positioning the distal and proximal end of the ileum side to side with the antimesentery parts facing each other. The open end was then closed with transverse firing of the Endo-GIA stapler [Supplementary Video 1]. Before performing ureter-ileal conduit anastomosis, the distal end of the conduit was pulled out through predesigned stoma site. The posterior wall of the distal ureters was continuously sutured with the posterior wall of the proximal end of the ileal conduit (4-0 Vicryl) [Supplementary Video 2]. After single J ureteric stents were inserted into the ureters and renal pelvis, the anterior wall of ureters was sutured continuously with the proximal ileal conduit. For male patients, the specimen bag was taken out through a small abdominal incision by extending the 12-mm port 3 cm above the pubic symphysis. For female patients, the specimen bag was taken out through the vagina.

Statistical analysis

Mean values with standard deviations were computed and reported for continuous data in normal distribution. Nonnormally distributed continuous data were described by median and interquartile range. An independent Student's *t*-test or Mann–Whitney U-test was used for comparison of normally distributed or nonnormally distributed continuous variables, respectively. Categorical variables were compared with Chi-square test. Kaplan–Meier analysis was used to calculate survival probabilities, and differences in survival were compared using log-rank test analysis. Cox regression analysis was performed to determine which variables were independent predictors of oncological outcomes (age, neoadjuvant history, positive lymph node, T stage, surgical method). All $P < 0.05$ were considered statistically significant. Statistical analysis was performed using STATA v12 (StataCorp LLC, College Station, Texas, USA).

RESULTS

The characteristics of patients are shown in Table 1. There was no significant difference between the ECIC and ICIC groups in mean age, sex distribution, BMI, and American Society of Anesthesiologists score. Neoadjuvant chemotherapy was administered in 5 patients in the ECIC group and 7 in the ICIC group, and the difference was not statistically significant ($\chi^2 = 3.802$, $P = 0.821$).

There was no significant difference between the two groups in terms of mean operative time, mean EBL, transfusion rate, and needing ICU after surgery [Table 2]. For ECIC, the mean operative time was 339 min, while for ICIC, the operative mean time was 329 min. The median EBL was both 200 ml for ECIC and ICIC. Three patients in the ICIC group and two patients in ECIC group required intraoperative blood transfusion.

The two groups were significantly different in terms of time to flatus, time of intake of liquid diet, and length of hospital stay after surgery [Table 2]. The median time of flatus was 3 days for ICIC and 5 days for ECIC and the median time of intake of liquid diet was 4 days for ICIC and 5 days for ECIC. The median hospital stay after surgery was 11 days for ICIC and 17 days for ECIC.

The complications rates did not show significant difference between the two groups within the first

90 days postoperatively ($P = 0.538$). In the ECIC group, 13 patients (65%) experienced at least one complication of any grade within 90 days of surgery and 12 of these patients (60%) experienced a minor complication (Grade 1–2). Similarly, there were 12 patients (48%) in the ICIC group who experienced at least one complication of any grade, 11 (44%) of whom experienced a minor complication. The major complications (Grade 3–5) occurred in one patient from each of the ECIC (5%) and ICIC (4%) groups. The patient in the ECIC group died on postoperative day 60 because of acute myocardial infarction and the patient in the ICIC group, who had 4 years' medical history of heart stent implantation, died on postoperative day 11 because of atrial fibrillation. A total of 49 complications were recorded within the first 90 days postoperatively [Table 3]. The most common complications in ICIC were anemia and UTI, while pain syndrome and gastrointestinal complication were most common in ECIC.

One patient in each group showed a positive surgical margin, and 45% of patients in the ECIC group and 36% in the ICIC group had pathologic stage T3 or T4, and 50% of patients in the ECIC group and 44% in the ICIC group had pathologic stage N1 or N1+. The mean number of lymph nodes harvested was 14 for ECIC and 18 for ICIC ($t = 1.255$, $P = 0.216$). The lymph node density (total number of positive lymph nodes/total number removed) was 12.6% in the ECIC group and 13.4% in the ICIC group ($\chi^2 = 0.092$, $P = 0.762$) [Table 2].

The mean follow-up time was 37 and 18 months for ECIC and ICIC groups, respectively. Seven (35%) patients in ECIC group and 4 (16%) patients in ICIC group suffered cancer metastasis, while no patient experienced local recurrence. Kaplan–Meier analysis showed no significant difference in overall survival (OS) rate at 24 months (60% vs. 62%, $P = 0.857$) between the ECIC and ICIC groups [Figure 2]. Cox analysis showed that surgical approach was not significantly associated with OS (hazard ratio [HR] = 0.91, $P = 0.859$, 95% confidence interval [CI] 0.34–2.44). T stage was significant predictor for OS (HR = 1.92, $P = 0.017$, 95% CI 1.12–3.29).

DISCUSSION

LRC with intracorporeal urinary diversion is a technically challenging procedure that requires extensive operative

Table 1: Characteristics of patients with bladder cancer who underwent LRC with ileal conduit

Variables	Intracorporeal (n = 25)	Extracorporeal (n = 20)	Statistics	P
Age (mean ± SD), years	63 ± 10	65 ± 8	0.360*	0.720
Male, n (%)	18 (72)	17 (85)	1.118†	0.290
BMI (mean ± SD), kg/m ²	24 ± 3	26 ± 3	1.750*	0.087
Neoadjuvant chemotherapy, n (%)	7 (28)	5 (25)	3.802†	0.821
ASA score, n				
1–2	22	19	Fisher	0.617
3	3	1		

**t* values; † χ^2 values. BMI: Body mass index; ASA: American Society of Anesthesiologists; LRC: Laparoscopic radical cystectomy; SD: Standard deviation.

Table 2: Surgical outcomes and follow-up data of patients with bladder cancer who underwent LRC with ileal conduit

Variables	Intracorporeal (n = 25)	Extracorporeal (n = 20)	Statistics	P
Operative time (mean ± SD), min	329 ± 97	339 ± 51	0.335*	0.739
EBL (median [IQR]), ml	200 (100–300)	200 (100–225)	0.012†	0.991
Transfusion, n (%)	3 (12)	2 (10)	0.045‡	0.831
ICU after surgery, n (%)	3 (12)	1 (5)	0.710‡	0.400
Time of flatus (median [IQR]), days	3 (2–4)	5 (3–5)	2.109†	0.035
Time of intake of liquid diet (median [IQR]), days	4 (3–5)	5 (5–6)	3.092†	0.002
Time of ambulation (median [IQR]), days	2 (2–2)	2 (2–2)	0.195†	0.845
Length of hospital stay after surgery (median [IQR]), days	11 (8–12)	17 (15–22)	4.639†	<0.001
90-day complication rates, n (%)			Fisher	0.538
None	13 (52)	7 (35)		
Minor (I–II)	11 (44)	12 (60)		
Major (III–V)	1 (4)	1 (5)		
Lymph node yield (mean ± SD), n	18 ± 10	14 ± 8	1.255*	0.216
Lymph node positive patients, n (%)	11 (44)	10 (50)	0.161‡	0.688
Lymph node density, %	13.4	12.6	0.092‡	0.762
Positive surgical margin, n (%)	1 (4)	1 (5)		1.000
Pathologic stage (pT0-T4), n (%)			Fisher	0.568
Tis	2 (8)	1 (5)		
T0	0	2 (10)		
T1	8 (32)	4 (20)		
T2	6 (24)	4 (20)		
T3	6 (24)	4 (20)		
T4	3 (12)	5 (25)		
Pathologic stage (pN0-T4), n (%)			Fisher	0.620
N0	14 (56)	10 (50)		
N1	3 (12)	5 (25)		
N2	5 (20)	4 (20)		
N3	3 (12)	1 (5)		
Follow-up time (mean ± SD), months	18 ± 23	37 ± 9	3.843*	<0.001
Recurrence, n (%)	0	0		
Metastasis, n (%)	4 (16)	7 (35)	2.172‡	0.141
The 2-year rate of overall survival, %	62	60	Fisher	0.857

**t* values; †*Z* values; ‡ χ^2 values. IQR: Interquartile range; EBL: Estimated blood loss; LRC: Laparoscopic radical cystectomy; ICU: Intensive Care Unit; SD: Standard deviation.

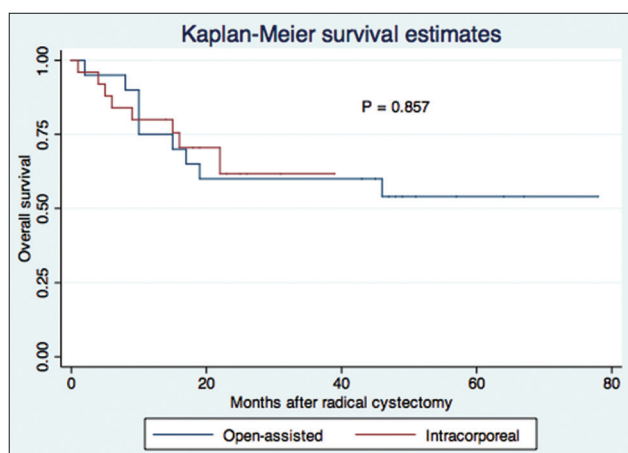


Figure 2: Kaplan–Meier survival estimates between open-assisted group and intracorporeal groups.

experience and patience. The procedure has seldom been reported since the first 2 cases presented by Gill *et al.*^[3] In the present study, surgical outcomes and follow-up data were compared between laparoscopic intracorporeal and ECIC after

LRC. The results of the study suggest that surgical complications and short-term oncological outcomes are comparable between the two groups. However, ICIC can be accomplished with the benefits of faster recovery of gastrointestinal function and shorter hospital stay compared to ECIC.

Haber *et al.*^[10] retrospectively evaluated outcomes of LRC with ICIC (*n* = 8) and ECIC (*n* = 18) 10 years ago. The complete laparoscopic approach was associated with longer operative time (8.0 h vs. 5.4 h, *P* < 0.001), blood loss (650 ml vs. 300 ml, *P* = 0.02), time to ambulation (5.5 d vs. 3.0 d, *P* = 0.02), and postoperative complications (87% vs. 28%, *P* = 0.004), suggesting that the open-assisted laparoscopic approach is technically more efficient and associated with a quicker recovery and decreased complication rates. The learning curve was steep for LRC with ICIC, which can be overcome with increasing a surgeon's experience. In our study, the mean operative time of ICIC is 329 min compared to 339 min for ECIC, which is acceptable in comparison with robot-assisted radical cystectomy with ICIC. Azzouni *et al.*^[16] reported their first 100 robot-assisted radical cystectomy with

Table 3: Complications by Clavien grade recorded among the 45 patients with bladder cancer who underwent LRC with ileal conduit within the first 90 days postoperatively

Group	Clavien grade	Within 90 days complication (n)	Treatment
Intracorporeal	1	Fever (1)	Antipyretics plus antimicrobials
		Pain syndrome (2)	Analgesics
		UTI (3)	Antibiotics
		Anemia (4)	Observation
		Vomit (2)	Antiemetic
	2	Ileus (1)	Conservative
		Deep venous thrombosis (1)	Anticoagulation
		Hypoproteinemia (1)	Human albumin injection
	5	Myocardial infarction (1)	Conservative
Extracorporeal	1	Anemia (6)	Observation
		UTI (3)	Antibiotics
		Pain syndrome (7)	Analgesics
		Gastrospasm (1)	Antispasmodic
		Vomit (6)	Antiemetic
		Fever (1)	Antipyretics
		Wound infection (1)	Conservative
	2	Incisional hernia (1)	Conservative
		Ileus (2)	Conservative
		Anemia (2)	Transfusion
	5	Deep venous thrombosis (1)	Anticoagulation
	5	Myocardial infarction (1)	Conservative

UTI: Urinary tract infection; LRC: Laparoscopic radical cystectomy.

ICIC, and the median overall operative time was 353 min. In the present study, a three-dimensional laparoscopic system was utilized in the procedure of LRC and ICIC and ileal conduit was constructed manually in the procedure of LRC and ECIC, which might explain the reason that the mean operative time of ICIC was shorter than ECIC.

In the current study, the time of flatus and oral intake is shorter in the ICIC group. Many studies did not mention the time of flatus and oral intake after ICIC.^[4,6] No significant difference was seen between LRC with ICIC and ECIC in regard to oral intake time (3 days vs. 3 days, $P = 0.22$) in Haber's study.^[10] Pyun *et al.*^[11] compared the perioperative outcomes of intracorporeal urinary diversion with those of extracorporeal urinary diversion following robot-assisted radical cystectomy, indicating that the time to flatus is also comparable (72.1 h vs. 71.9 h, $P = 0.979$). Increasing evidence from colorectal surgery indicates that minimally invasive surgery and enhanced recovery programs can reduce surgical morbidity and length of stay. Enhanced recovery programs are now recognized as an important component of surgical management for radical cystectomy.^[12] Since 2014, we began to adopt partial enhanced recovery programs for radical cystectomy. That may be one reason that time of flatus and oral intake in ICIC group is faster than ECIC group in our study.

Azzouni *et al.*^[6] reported that 81 patients (overall complication rate: 81%) had a postoperative complication in the first 90 days, of whom 15 patients had a high-grade complication (high-grade complication rate: 15%).

A total of 164 complications were recorded and the most common complication was urinary tract infection. Ahmed *et al.*^[4] compared the perioperative outcomes of 935 patients undergoing extracorporeal urinary diversion and intracorporeal urinary diversion following robot-assisted radical cystectomy, and the 90 days complication rate was not significant between the two groups (41% vs. 49%, $P = 0.05$); however, gastrointestinal complications were significantly lower in the intracorporeal group. Similarly, gastrointestinal complications were more common in the ECIC group in our study.

Data on oncological outcomes of ICIC are limited as the technique has not been widely adopted because of its technical challenges. Tyrirtzis *et al.*^[13] and Desai *et al.*^[14] reported a 24-month OS of 88.9% and 82.0%, respectively, in their iRARC series. Tan *et al.*^[15] found no significant difference in OS at 24 months between open radical cystectomy and robotic-assisted radical cystectomy with intracorporeal urinary diversion (73.5% vs. 83.8%, $P = 0.277$). We also identified no difference between ICIC and ECIC in OS at 24 months. However, the OS at 24 months in our study is lower. Fifty percent of pathologic lymph node in ECIC and 44% patients in ICIC were positive. A small portion of patients in both groups received neoadjuvant chemotherapy, which might be the reason of lower OS at 24 months.

This study had several limitations. First, the sample size was relatively small; thus, it was difficult to reach a definitive

conclusion. Second, this was a comparative study of nonrandomized patients. Selection bias may have existed and influenced the results. Third, our study had a relatively short follow-up period. Fourth, we did not compare the cost and pain score of the two methods. Finally, only OS rate was applied to evaluate oncological outcome, which may not be enough to evaluate oncological outcome of bladder cancer.

In conclusion, ICIC can be accomplished with the benefits of faster recovery of gastrointestinal function and shorter hospital stay compared to ECIC without compromising complications and oncological outcomes. However, larger series with longer follow-up are needed to validate the procedure.

Supplementary information is linked to the online version of the paper on the Chinese Medical Journal website.

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Conflicts of interest

There are no conflicts of interest.

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回顾比较单中心腹腔镜根治性膀胱切除体腔内回肠通道与体腔外回肠通道手术结果及短期肿瘤疗效

摘要

背景：目前一些大的医疗中心报道了腹腔镜下/机器人辅助根治性膀胱切除+体腔内回肠通道术。腹腔镜下根治性膀胱切除+体腔内回肠通道术是否优于传统体腔外回肠通道术尚没有定论。本研究的目的是比较腹腔镜下根治性膀胱切除之后体腔内回肠通道术与体腔外回肠通道术手术结果及短期肿瘤疗效。

方法：从2011年1月到2016年6月，共有45位膀胱癌患者接受了腹腔镜下根治性膀胱切除加回肠通道术，其中前20位患者接受了体腔外回肠通道术，后25位患者接受了体腔内回肠通道术。收集并统计分析患者的一般资料、手术结果数据及短期肿瘤随访结果。

结果：所有45例手术均顺利完成。两组患者的一般资料、总手术时间及出血量无统计学差异。体腔内回肠通道组术后排气时间及恢复流食时间均明显缩短（3 vs. 5 天, $P = 0.035$; 4 vs. 5 天, $P = 0.002$ ）。术后90天内并发症未见明显差异（ $P = 0.538$ ）。在体腔外回肠通道组中，45%的患者病理分期为T3及以上，50%的患者存在淋巴结转移；而体腔内回肠通道组共36%患者在T3及以上，44%患者存在淋巴结转移。Kaplan-Meier分析显示两组术后24月总生存率无明显差异（60% vs. 61.7%, $P = 0.857$ ）。

结论：腹腔镜下根治性膀胱切除后体腔内回肠通道术可能会加快术后肠道功能恢复，在术后并发症及短期肿瘤疗效方面没有明显差异。然而此研究结论需要大样本长期随访临床试验进一步验证。