Modified Ileal Conduit for Urinary Diversion After Radical Cystectomy: Perioperative and Oncological Outcomes

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Research Article

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Abstract

Background: To evaluate the surgical effects and oncological outcomes of modified ileal conduit (IC) after radical cystectomy (RC) for bladder cancer.

Methods: A single-centre cohort of 211 consecutive bladder cancer patients who underwent RC + modified IC from September 2012 to August 2019 were retrospectively studied. Demographic data, perioperative results, complications 30 and 90 days after surgery and oncological outcomes were recorded. Kaplan–Meier method was used to plot the stage-specific survival results. The 5-year recurrence-free survival (RFS and overall survival (OS) rate was calculated. Univariate and multivariate Cox regression analyses assessed the predictive risk factors on survival rate.

Results: Overall, 211 patients received modified IC after RC. The median operative time (OT) was 315 minutes (IQR, 260–375 minutes), and the median estimated blood loss (EBL) was 500 ml (IQR, 300–900 ml). There were a total of 103 (48.8%) complications. There were 35, 54, 11, and 2 cases of grade I, II, III, and IV complications, respectively; of which 89 cases were grade I and II, accounting for 87.3% of total cases. There were 38 cases of preoperative hydronephrosis and 22 cases of postoperative hydronephrosis. There were 19, 24, 108, 40, and 20 cases of PT0, T1, T2, T3, and T4, respectively, in postoperative pathological stages. The median lymphadenectomy was 14 (IQR, 6–18), and lymph node was found positive in 18 patients. The median follow-up time was 26 months (IQR, 13–43), with a total survival of 177 (83.9%), an RFS of 171 (81%), and 34 deaths. The estimated 5-year OS and RFS rates were 76.80% and 79.10%. Preoperative comorbidities, pathological stage, grade, and lymph node involvement were important influencing factors for OS, while preoperative comorbidities and high pathological grade were important influencing factors for RFS.

Conclusions: Modified IC after RC not only can achieve lower postoperative complications, especially the lower incidence of uretero-ileal anastomosis and stoma-related complications but can also achieve the established oncological outcomes of critical radical surgery.

1. Background

Bladder cancer is one of the most common malignant tumours in the urinary system, ranking the 9th among all malignant tumours in the world[1], and the 7th among male malignant tumours in the Chinese population[2]. About 20–30% of bladder cancer patients were diagnosed with muscular invasive bladder cancer (MIBC) at the initial consultation[3, 4]. Even in patients initially diagnosed with non-muscular invasive bladder cancer (NMIBC), 10–30% of patients progress to MIBC[5]. The overall incidence in China follows an upward trend compared to previous years[2, 6]. Radical cystectomy (RC) as a standard treatment for MIBC and high-risk NMIBC, such as in repeated recurrence and failure of Bacillus Callmette-Guerin (BCG) treatment, has been validated in open[7] and minimally invasive procedures[8–10]. RC is also recommended by current guidelines[11, 12]. However, RC involves a serious risk of urinary diversion (UD), making its choice as a preferred surgical method controversial. There are several types of UD techniques. Currently, the commonly used methods include orthotopic neobladder (ONB), ileal conduit (IC) and ureterocutaneostomy[12]. Currently, IC is the most widely used and applied diversion method in the world[13, 14]. In 1950, Bricker used the ileum as the output channel for UD[15]. Because of its good therapeutic effect, it has been widely promoted and utilised in clinical settings. The Bricker IC has also been regarded as the gold standard for incontinent UD[16]. The common complications of the classic Bricker IC are ureteral ileum anastomosis and stoma-related complications. It was reported that the incidence of ureter-ileal anastomosis-related complications was 2–14%, most of which occurred on the left side[17], which was an important cause of renal insufficiency during the postoperative course[18–21]. In the view of this fact, some scholars have made improvements on the IC, such as peritoneal externalisation of the IC[22], or pulling the input end of the IC under the mesosigmoid towards the left[23], all of which have yielded good perioperative results. However, there have been only a few reports of large cases or oncological outcomes of modified IC after RC so far. Since September 2012, our hospital has adopted a modified IC technique for UD after RC, which is similar to, but slightly different from the previously reported methods[22, 23], with a total number of 211 cases that had not been systematically evaluated or analysed. In this study, the data of patients undergoing modified IC after RC in our hospital for around 8 years were retrospectively analysed to evaluate the perioperative and oncological outcomes.

2. Methods

2.1 Patients

The medical records database of our institution has had an established electronic medical record homepage system since 2012. The database contains patient demographics, diagnosis, treatment (including surgery) and pathology information. It is a continuous database populated with data directly from the patient's electronic medical records and follow-up information. This system is also linked to electronic medical records, which can easily query all inpatient diagnosis and treatment information, under authorisation by the institution. After approval by the institutional review committee, all patients who underwent modified IC after radical cystectomy (RC+MIC) were reviewed between September 2012 and June 2019. Patients followed up for less than 6 months were excluded, except for those who died.

2.2 Surgical technique

During the study period, four teams of surgeons performed urinary tract reconstruction. An identical technique was adopted in all IC for UD. The steps taken were as follows:

Firstly, after RC and bilateral pelvic lymphadenectomy, an ileal segment was separated from the proximal ileocecal valve approximated 15–20 cm in length. As previously reported[23], the length of the IC was decided by the patient's abdominal condition and the small intestinal mesentery anatomy, ranging from 20 to 25 cm in length, which is slightly longer than the classical Bricker IC[15]. After continuity of the small intestine was restored, the ileal segment was washed with diluted iodophor to remove residual material in the small intestine.

Secondly, retroperitoneal placement of IC and uretero-ileal anastomosis were performed. At the level of the sacral promontory, behind the sigmoid mesocolon, a tunnel was obtusely dissociated. After closing the input end with 3-0 absorbable sutures, the proximal IC was pulled towards the left retroperitoneum without significant tension. At the intersection of the left IC and the left ureter, an 8-10-cm long redundant part of the ureteral stump was removed (Fig 1A). Then, the left ureter was anastomosed almost in situ to the ileum by end-to-side anastomosis, and a single J tube was placed inside the ureter-ileum as an internal stent for drainage. Moreover, the proximal IC was fixed to the left psoas major aponeurosis[24]. At the promontory of the sacrum, a retroperitoneal channel was separated towards the right (Fig 1B), and the outlet end of the conduit was passed from the retroperitoneum to the right side and led out from the prepositioned skin stoma. The right redundant ureter was resected the right ureter was anastomosed to the conduit in the same way, and a single J tube was placed inside for drainage Fig 1C). After removing the excess part, both ureters underwent almost in situ end-to-side uretero-ileum anastomosis, ensuring that the blood supply of the ureters would be good after the anastomosis.

Finally, ileal cutaneous stoma was constructed. A round stoma, about 3 cm in diameter, was made over the right abdominal wall area and the anterior and posterior sheaths of rectus abdominis around the stoma were sutured together. Next, the IC was drawn from the retroperitoneum and fixed to the rectus abdominis sheath. A papillary stoma was created at the output end of the IC, which was similar to a method previously reported[22, 25], leaving the papillary stoma partially exposed and protruding about 2–3 cm away from the skin (Fig 1D).

2.3 Follow-up

The patients were followed up every 3 months for the first year, every 6 months for the second year, and once yearly thereafter. Routine follow-up included: physical exam, serologic testing, and imaging examination, including electrolyte, creatinine, liver function test, and abdominal/pelvic ultrasonography. Chest X-ray and abdominal/pelvic CT were performed 6 months after surgery and then annually, as needed.

Follow-up data were obtained by reviewing medical records or by directly calling patients. Three of the authors (Zhang Yimu, Zhou Zhengyu, and Bai Jiyan) conducted the telephonic interviews. In addition, all complications, especially those related to ureteral-ileal anastomosis, were recorded in detail during follow-up. For patients followed up in other places, relevant records were obtained through telephone interviews.

2.4 Data collection

Demographic and preoperative variables were recorded as followed: age, gender, body mass index, smoking history, drinking history, Charlson comorbidity index, preoperative upper urinary tract collection system status, neoadjuvant chemotherapy, and bladder cancer surgery history (including partial cystectomy and TURBT).

The operation-related variables were written down as follows: operative time (OT), estimated intraoperative blood loss (EBL), intraoperative blood transfusion, postoperative first exhaust time (PFET), postoperative hospital stay (PHS), postoperative complications within 30 days, 90 days, and long-term complications. Long-term complications were defined as surgery-related complications encountered up to 90 days after operation. Postoperative uretero-ileal anastomosis-related complications, including postoperative urinary leakage and hydronephrosis, as well as stoma-related complications, including intestinal obstruction, intestinal leakage, parastomal hernia, and IC or stoma necrosis, were separately recorded.

Primary tumour invasion and lymph node involvement recorded in the pathological reports were classified according to the 2010 AJCC TNM staging system[26, 27]. If no cancer cells were found in postoperative pathological specimens, the staging was defined as T0, and the pathological grading referred to results of the preoperative cystoscopy biopsy or TURBT.

2.5 Statistical analysis

Continuous variables were recorded as median and interquartile ranges. Qualitative variables were reported as n (%). Survival times were defined as the time elapsed from procedure to the date of recurrence (RFS), or death (OS). Kaplan–Meier method was used to plot the stage-specific survival results. The 5-year survival rate was calculated, and the statistical significance among groups was evaluated by log-rank test. Univariate and multivariate Cox regression analyses were used to assess the predictive effects of comorbidities, tumour stage, grade, and lymph node status on survival rate. A two-sided P value of $\leq$0.05 was considered statistically significant. All statistical analyses were adopted with the IBM SPSS Statistics for Windows 10 ver. 25.0 (IBM Corp., Armonk, NY, USA).

3 Results

3.1 Patient demographic data

During the study period, of the 259 patients who underwent RC in our department, 211 (81.5%) underwent modified IC, 42 (16.2%) underwent ureterocutaneostomy, and 6 (2.3%) received orthotopic neobladder (ONB). Of the 211 patients who received IC, 136 (64.4%) underwent laparoscopic surgery and 75 (35.5%) underwent open surgery.

Of the 211 modified IC patients in this study, 183 were male and 28 were female. The demographic, perioperative and pathologic data are summarised and shown in Table 1. The median age of the patients was 61 years. Among them, 110 (52.1%) had a history of smoking and 31 (14.7%) had a history of alcoholism. Eighty-seven patients had comorbidities: 65 patients had hypertension, 27 patients had diabetes, and 63 patients had other comorbidities, including 16 patients with multiple system comorbidities. Seventy-seven (36.5%) had undergone bladder cancer surgery, including transurethral resection of bladder tumour(TURBT)with partial cystectomy, or multiple tumour resection. There were 15 cases with other system operation history, including 13 cases of abdominal open operation. Thirty-one patients received 2–3 courses of neoadjuvant chemotherapy.

Table 1
Baseline characteristics of patients (n = 211)

No. of patients	**211**
Sex,no.	
male	183(86.7%)
female	28(13.3%)
Median age (IQR), y	61(53–67)
Smoking history	110(52.1%)
History of alcoholism	31(14.7%)
comorbidity	87(41.2%)
Hypertension	65
Diabetes	27
Other comorbidities	63
Bladder cancer surgical history	77(36.5%)
Other surgical history	15
Abdominal and gastrointestinal surgical history	7
Other urological surgical history	3
History of hysterectomy	3
Orthopedic surgical History	2
Perioperative NAC	31(14.7%)

3.2 Hydronephrosis.

Hydronephrosis occurred preoperatively in 38 cases (17 cases of left hydronephrosis, 12 cases of right hydronephrosis, and 9 cases of bilateral hydronephrosis) and postoperatively in 22 cases (10 cases of left hydronephrosis, 4 cases of right hydronephrosis, and 8 cases of bilateral hydronephrosis). (shown in Supplemental Table 1 in the online version).

On comparison, preoperative hydronephrosis reduced or disappeared postoperatively in 22 cases, whereas postoperative hydronephrosis remained in 16 cases. Six patients without preoperative hydronephrosis developed postoperative hydronephrosis (5 cases on the left side, 1 case on the right side, and 1 case on both sides). In these 6 patients with postoperative hydronephrosis, renal function was normal or mildly abnormal by the last follow-up. The longest follow-up time was 83 months. By the end of our review, there were no cases of postoperative renal failure requiring dialysis.

3.3 Perioperative data

No intraoperative death or severe complications occurred during the period observed. The surgical and follow-up data are presented in Table 2. The median OT was 315 minutes (IQR,260–375 minutes)，with 342.5 minutes and 270 minutes for the LRC and ORC techniques, respectively. The median EBL was 500 ml (IQR，300–900 ml), with a median EBL for the LRC and ORC groups at 400 and 700 ml, respectively. The differences between OT and EBL were consistent with previous reports[28, 29]. A total of 96(45.5%) patients received a transfusion during the perioperative period. The median PFET was 4 days (IQR，3–5 days), and the median PHS was 16 days (IQR, 14–21 days).

Table 2
Perioperative results

Modalities, no.	
LRC + IC	136(64.5%)
ORC + IC	75(35.5%)
OT (median, IQR), min	315(260–375)
LRC group	342.5(280–450)
ORC group	270(210–320)
EBL (median, IQR), ml	500(300–900)
LRC group	400(240–560)
ORC group	700(450–1000)
Transfusions, no.	96(45.5%)
PFET (median, IQR), d	4(3–5)
PHS (median, IQR), d	16(14–21)

3.4 Complications

Postoperative complications were divided into 30-day, 90–day, and long-term postoperative complications. All of them were graded according to the Clavien–Dindo classification system[30] (Table 3) and the organ system classification[31](Supplemental Table 2 in the online version). A total of 102 (48.3%) postoperative complications were noted including 87 cases of complications within 30 days, 9 cases within 90 days, and 6 cases of long-term postoperative complications. Among these, 10 cases (4.7%) had IC-related complications and 11 cases (5.2%) had ureteral ileum anastomose-related complications according to the Clavien–Dindo classification system. Grade 1, 2, 3, and 4 complications were seen in 35, 54, 11, and 2 cases, respectively, of which 89 cases of grade 1 and 2 complications accounted for 87.3% of all complications. There were 11 patients with two or more simultaneous or successive complications, which were cured after comprehensive treatment.

Table 3
Surgical complications stratified by the Clavien classification system

Grade	Complication	No. of cases	Management
Early (≤ 30d after surgery)			
I	Incisional haematoma	1	Drainage
I	Wound fat liquefaction	8	Change the dressing and medication
I	Wound infection	12	Change the dressing and antibiotics
I	fever	7	Symptomatic treatment
II	Bowel ileus	7	Conservative
II	Delirium and agitation	2	Sedative
II	lymphatic leakage	11	Drainage and support therapy
II	Urinary leak	3	Stent drainage, antibiotics and supportive treatment
II	Pelvic infection	9	Two cases were treated with puncture and drainage, and 7 cases were treated with anti-infection
II	urinary tract infection	9	Antibiotics
II	pneumonia	4	Antibiotics
II	hydrothorax	2	Antibiotics and pleural puncture drainage
II	stress ulcer	1	Hemostasis and acid inhibition
IIIa	wound dehiscence	4	Suture with local anesthesia
	Small intestinal leakage	2	Reoperation
	Deep venous thrombosis	3	The thrombus filter was surgically installed
□a	Congestive heart failure	1	ICU monitoring and treatment
□b	multiple organ dysfunction	1	ICU monitoring and treatment
Late (> 30d after surgery)			

Grade	Complication	No. of cases	Management
I	hematuresis	2	Conservative
I	Mild hydronephrosis	5	observation
II	adhesive intestinal obstruction	3	Conservative
II	Recurrent urinary tract infection	3	Antibiotics
IIIa	hydronephrosis	1	One case of left hydronephrosis underwent percutaneous drainage
IIIb	Bowel ileus	1	A case of partial intestinal necrosis with intestinal obstruction was anastomosed after partial intestinal resection
Multiple complications		11	Comprehensive treatment

There were 25, 23, and 16 cases of wound, infection, and gastrointestinal system occupying the top three positions according to the classification of organ system,

3.5. Oncologic outcomes

The oncologic outcomes are shown in Table 4 and consist of the following: postoperative pathological staging, positive resection margin, positive lymph nodes, number of lymph nodes removed, median follow-up time, local recurrence or distant metastasis, RFS rate, and OS rate. There were 18, 23, 109, 40, and 21 patients with PT0, T1, T2, T3, and T4 stages, respectively. All patients with PT0 underwent TURBT before surgery. None of the patients had a positive surgical margin. Cases were divided into low- and high-grade urothelial carcinoma and non-urothelial carcinoma according to the WHO 2004 pathological classification method[32], with 47, 147, and 17 cases, respectively. Of the 211 patients analysed, the median lymph node resection count was 14 (IQR, 6–18), with 18(8.5%) patients having positive lymph node. There were 14 patients with local recurrence, 31 patients with distant metastasis, and 6 patients with both local recurrence and distant metastasis. The median follow-up time was 26 months (IQR, 13–43). A total of 177 patients (83.9%) survived, and 171 patients (81%) survived without recurrence.

Table 4 Oncologic outcomes

Postoperative pathological stage	
pT0	18(8.5%)
pT1	23(10.9%)
pT2	109(51.7%)
pT3	40(19.0%)
pT4	21(10%)
Positive surgical margin，n	0
Negative surgical margin，n	211
Postoperative pathological grade	
Low grade	47（22.3%）
High grade	147（69.7%）
Non-urothelial carcinoma	17（8.1%）
Lymph node involvement	
No positive lymph node	195（92.4%）
Positive lymph nodes	16（7.6%）
Lymph nodes removed (median, IQR)	14（6-18）
Recurrence or metastasis	40（19.0%）
Local recurrence	14（35%）
Distant metastasis	31（77.5%）
Local recurrence and distant metastasis coexist	6（15%）
Follow-up months (median, IQR)	26（13-43）
Overall survival，n	177（83.9%）
Recurrence-free survival，n	171（81%）
5-year RPS	79.10%
5-year OS	76.80%

Kaplan–Meier method was used to plot the stage-specific survival results (Fig. 2A-2B), and the 5-year RFS and OS rate were 79.10% and 76.80%, respectively. Log-rank test was used to evaluate the statistical significance among each group. Pathological stage (T4 vs. T0, P = 0.003; T4 vs. T1, P = 0.03; T4 vs. T2, P = 0.001; T3 vs. T0 = 0.032; T3 vs. T1 = 0.050), grade (low grade vs. high grade, P = 0.006; low grade vs. non-urethral epithelial carcinoma, P = 0.002), preoperative CCI (CCI = 0 vs. CCI ≥ 1, P = 0.000), and lymph node status (negative LN vs. positive LN, P = 0.000) had a significant influence on survival rate, while the influence of surgical method was negligible (Fig. 2C-2G). Univariate Cox regression analysis showed that preoperative comorbidities,pathological stage, grade, and lymph node involvement were the significant predictors of RFS and OS. Multivariate Cox regression analysis showed that preoperative comorbidities, pathological stage, grade, and lymph node involvement were important influencing factors for OS, while preoperative comorbidities and high pathological grade were important influencing factors for RFS, as shown in Supplemental Table 3 in the online version.

4. Discussion

RC combined with bilateral pelvic lymph node dissection (PLND), as the standard treatment for radical bladder cancer, has been validated clinically with multiple studies demonstrating similar oncologic results versus both open and minimally invasive procedures. However, the most important issue after RC is performing a proper UD or reconstruction as only when this link is completed, can the radical operation for bladder cancer be considered as over. Radical resection of bladder cancer combined with UD is considered as one of the most complex and difficult surgeries in the field of surgery due to the large amount of surgical trauma caused, the extensive resection needed, and the complexity of the surgical procedure, including resection and reconstruction, as well as the involvement of the intestinal tract. It is not difficult to infer therefore, that the rate of surgical complications is very high. The high complication rates in RC have been confirmed by many studies,with an overall complication rate of approximately 30–70%[29, 33]. A high incidence of complications is associated with urinary tract reconstruction or diversion, with a reported duct-related complication rate of up to 32.7%[34]. IC UD is currently the most widely used technique, accounting for the highest proportion of all UD surgeries[13, 14, 16].

The main problem with classic IC is in the placement of ileal segment and uretero-ileal anastomosis. With classic IC, the left ureter is widely dissociated and pulled towards the right side for anastomosis with ileum, increasing the potential risk for complications related to uretero-ileal anastomosis. This complication has also been reported by many other studies[18, 24]. To avoid such complications, many scholars have modified the Bricker IC. One method is to make the stoma extraperitoneal to avoid stomata-related complications. Another one is to pull IC from the posterior sigmoid colon towards the left side to reduce complications of left ureteral-ileal anastomosis. Combining the advantages of the two above procedures, we externalised the peritoneum of the stoma and pulled the input side of IC towards the left, significantly reducing the incidence of ileal conduit-related complications and ureteral-ileal anastomose-related complications. In this study, 103 cases (48.8%) had complications, including 16 cases (7.6%) of ileal conduit-related complications and 12 cases (5.7%) of ureteral anastomotic complications, which was lower than that reported in previous studies[18, 20, 24]. It is noteworthy that no cases of parastomal hernia were observed. Hussein et al.[35] reported that the incidence of parastomal hernia after RC and IC was as high as 20%, of which 15% patients required surgery. The absence of parastomal hernia in this study was mainly due to our modifications.

To reduce the complications associated with ostomy and ureteral-ileal anastomosis, to improve surgical safety, and to improve postoperative quality of life, we optimised and modified surgical procedures for UD after RC, with some parts completely changed. Based on an experience with 211 cases of modified IC over 8 years, we suggest the following: 1) If both ends cannot be taken into consideration, the outlet end of IC should be guaranteed first. Since IC enters the retroperitoneum from anterior sacrum, it needs a relatively long ileum and mesentery. Some obese patients, or people with short mesenteries, have difficulty taking care of both sides. After the peritoneal extraperitoneum of the IC, the position of uretero-ileal anastomosis should be preliminarily estimated under the condition that the exit is long enough. At this time, it may not be suitable to pull the left side of the IC towards the left ureter, but it can be as close to it as possible. That is, the position of uretero-ileal anastomosis can be slightly adjusted according to the specific length of the IC; 2) At the skin stoma, the aponeurosis of rectus abdominis should be sutured intermittently with 1 – 0 silk thread. The suture should be retained and used to fix the ileostomy. This can not only prevent the stoma from retraction or protrusion but can also prevent parastomal hernia. Extraperitoneal stoma, suture choice, and fixation of the outlet are the key techniques to avoid parastomal hernia; 3) Uretero-ileal anastomosis does not require anti-reflux. Continuous suture can be performed directly with 4 – 0 absorbable suture. The single J tubes were routinely placed inside as the stent for internal drainage, thus reducing the chance of urine leakage and anastomotic stenosis; 4) Under tension-free conditions, the maximum feasible amount of residual ureter should be removed to ensure a good blood supply to the remaining ureter, preventing lower ureter and anastomotic ischaemia, thereby reducing the occurrence of anastomotic stenosis and hydronephrosis.

To ensure negative surgical margins as far as possible, we had a wide range of resected area. Since Bricker IC does not need to consider the issue of urinary control, extended resection is feasible. The bladder was dissociated on both sides of the pelvic floor fascia and placed in the extraperitoneal space. The neurovascular bundle was generally not retained unless the patient requested it. After a cystectomy, the pelvic floor was almost skeletonized. In this study, none of the patients had a positive surgical margin. In addition, since IC was pulled towards the left retroperitoneum, the left ureteral stump was excised 8–10 cm, further ensuring a negative margin.

The ideal extent for lymph node dissection has not yet been determined. Some scholars reported that enlarged lymph node dissection yielded more lymph nodes and had a higher positive rate than standard lymph node dissection. In patients with lymph node positivity, the five-year recurrence-free survival rate after expanded lymph node dissection was significantly higher than that after localised lymph node dissection[36, 37]. However, a randomised phase 3 clinical trial involving 198 patients with extended lymph node dissection and 203 patients with limited lymph node dissection yielded the opposite result. The former had no significant advantage in terms of 5-year RFS,CSS and OS[38]. The current guidelines recommend a minimum of standard lymph node dissection, defined as the removal of lymphoid fat tissue below the bifurcation level of the iliac vessels. Guidelines also recommend that at least standard lymph node dissection should be performed, which is the removal of adipose tissue below the level of the iliac vascular bifurcation[12]. In this study, we used standard lymph node dissection. The median number of harvested lymph nodes was 14 (IQR, 6–18), and 16 (7.6%) patients were lymph node positive.

Although there is no consensus regarding the scope of lymph node resection, the impact of lymph node involvement on tumour prognosis is clear[39]. Patients with lymph node metastasis had worse RFS and OS than those without lymph node metastasis and that difference was statistically significant. Univariate and multivariate regression analyses further confirmed that lymph node positivity was an independent predictor of the prognosis in RC[8, 40, 41].

The prognosis of bladder cancer after radical resection has been verified via long-term clinical practice[7, 8, 42]. The introduction of minimally invasive surgery in the latest two decades, such as laparoscopic RC and robot-assisted RC for bladder cancer, has not only improved perioperative parameters, but has also achieved similar oncologic results as open surgery[43]. This has been further demonstrated in recent randomised clinical trials[9, 10, 28]. In our study, a modification of IC significantly reduced associated complications, especially those related to ureteral ileum anastomosis and the stoma. The tumour prognosis was also encouraging. Our study further confirmed that the most accurate predictors of tumour recurrence and death were the pathological stage of the primary tumour and regional lymph node status. Through univariate and multivariate regression analyses, the study also found that preoperative comorbidities had significant effects on RFS and OS, with poorer RFS and OS outcomes for patients with CCI $\geq$ 1. This was consistent with the poor physical status mentioned in the RAZOR trial as an important predictor of 36-month progression-free survival[29].

Minimally invasive treatment of tumours has become widely used in practice and it is most widely used in the field of urology. Minimally invasive surgery provides many important advantages, such as reducing intraoperative bleeding, accelerating recovery, shortening hospital stay and reducing wound complications[14, 29]. However, in addition to these perioperative advantages, there is scant evidence that these methods have better oncological outcomes, with outcomes still depending largely on the local tumour stage, the biological characteristics of the disease, and perhaps also on the surgeon's experience[9]. In fact, it is not difficult to speculate that, in a sense, minimally invasive surgery only achieves the same range of results as open surgery through less invasive methods, and in some aspects, with less resection under certain refined procedures, such as uterus preservation. In this study, there were 136 (64.5%) cases of minimally invasive surgery, compared with 75 (35.5%) cases of open surgery, RFS and OS were comparable, which was the same as previously reported results[9, 10, 28].

Currently, although the application of robotic surgery in large medical centres is accelerating around the world, its high cost hinders further popularisation. Although our hospital is a cancer treatment centre in central China, Da Vinci robotic surgery has started only recently. Therefore, it is reasonable to speculate that laparoscopic surgery will remain the main mode of minimally invasive surgery for the years to come. It is worth mentioning that open surgery is known for its relatively short operating time. For patients with a history of abdominal surgery, extensive intestinal adhesions, or cardiopulmonary diseases that do not allow long-term surgery with high CO_2 pressure in the abdominal cavity, open surgery will continue to play an irreplaceable role for quite a long time.

Since the current guidelines for bladder cancer in China are based on the 2010 TNM staging, which has not been updated, we refer to the seventh edition of the TNM staging system for clinical and pathological staging. The prognosis of patients with higher stages was significantly worse than that of patients with lower stage.

So far, although this is the largest single-centre study of modified IC after RC, it still has some inherent limitations. This study is retrospective in nature, making it prone to selection biases and differences in care. Inconsistent follow-up and lack of multicentre results also limit the wider applicability of this study. The OS and RFS of this study were higher than those reported before, which may be related to the relatively substantial number of patients who were lost to follow-up. In the past 20 years, China's economic and social development has been in a transitional period. Some patients, especially those in rural areas, have frequently changed their address and mobile phone number. Further, some patients living in remote areas may have not received regular follow-up, resulting in some mild complications not being recorded. In addition, under our country's current medical system, a three-level referral system is not yet complete. Further, patients can seek medical treatment anywhere, which poses challenges to follow-up. The number of complications may thus be less than the actual number of occurrences, and some may not have been recorded. We did not calculate the cancer-specific survival rate, mainly because a considerable number of patients died at home and the cause of death was unknown. However, except for a few deaths, the follow-up time was more than half a year, which showed that the complication reports within 180 days were accurate. Therefore, the results of the incidence of postoperative complications are reliable. However, most of the patients lost to follow-up were mainly concentrated before 2014,and these patients were lost to follow-up due to changes of their phone numbers and addresses. There were relatively few patients lost to follow-up after 2015, so the 3-year and 5-year RFS and OS were basically unaffected. In addition, the proportion of total patients lost to follow-up is still within the statistical range; therefore, the impact of loss to follow-up on survival rate is limited.

Conclusions

To the best of our knowledge, this is the largest single institution study of modified IC after RC to date. We evaluated the postoperative complications and oncological outcomes in detail. Modified IC after RC can not only reduce postoperative complications, especially the lower incidence of uretero-ileal anastomosis and stoma-related complications but can also achieve the established oncological outcomes of critical radical surgery. This requires longer-term follow-up and prospective randomised controlled studies for further verification.

Abbreviations

MIBC=muscle-invasive bladder cancer; NMIBC=nonmuscle-invasive bladder cancer; RC=Radical Cystectomy; BMI=body mass index; ORC=open radical cystectomy; LRC=laparoscopic radical cystectomy; IC= Ileal Conduit; RC+MIC=Radical Cystectomy and Modified Ileal Conduit; OS=overall survival; RFS=recurrence-free survival; CSS=cancer-specific survival. PLND=pelvic lymph node dissection;

OT=operative time; EBL=estimated blood loss; PFET= postoperative first exhaust time; PHS:=postoperative hospital stay; CT=computed tomography. MRI=magnetic resonance imaging. NAC=neoadjuvant chemotherapy ;CCI= Charlson's Comorbidity Index BCG = Bacillus Callmette-Guerin

Declarations

Ethics approval and consent to participate

The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study protocol conformed to the ethical guidelines of the 1975 Declaration of Helsinki and was approved by the ethics committee of Affiliated Cancer Hospital of Zhengzhou University (Zhengzhou, China). Written informed consent was obtained from all patients before receiving surgical therapy, according to the institutional guidelines.

Competing interests

All authors have completed the ICMJE uniform disclosure form. The authors have no conflicts of interest to declare.

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Authors' contributions

Yimu Zhang: Data analysis, conceptualisation, drafting the article, and critical revision of the article. **Jing Li**: Data analysis, conceptualisation, drafting the article, and critical revision of the article. **Jiyan Bai**: Data acquisition, data analysis, and critical revision of the article. **Zhengyu Zhou:** Data acquisition, data analysis, and critical revision of the article. **Pei Tian**: Conceptualisation and critical revision of the article. **Dong Yang**: Data acquisition, data analysis, and critical revision of the article. **Yan Ma**: Data acquisition and critical revision of the article. **Pengcheng Zhao**: Conceptualisation and critical revision of the article. **Chaohong He**: Data acquisition, conceptualisation, validation, supervision, and critical revision of the article. All authors have read and approved the final version of the article.

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Figures

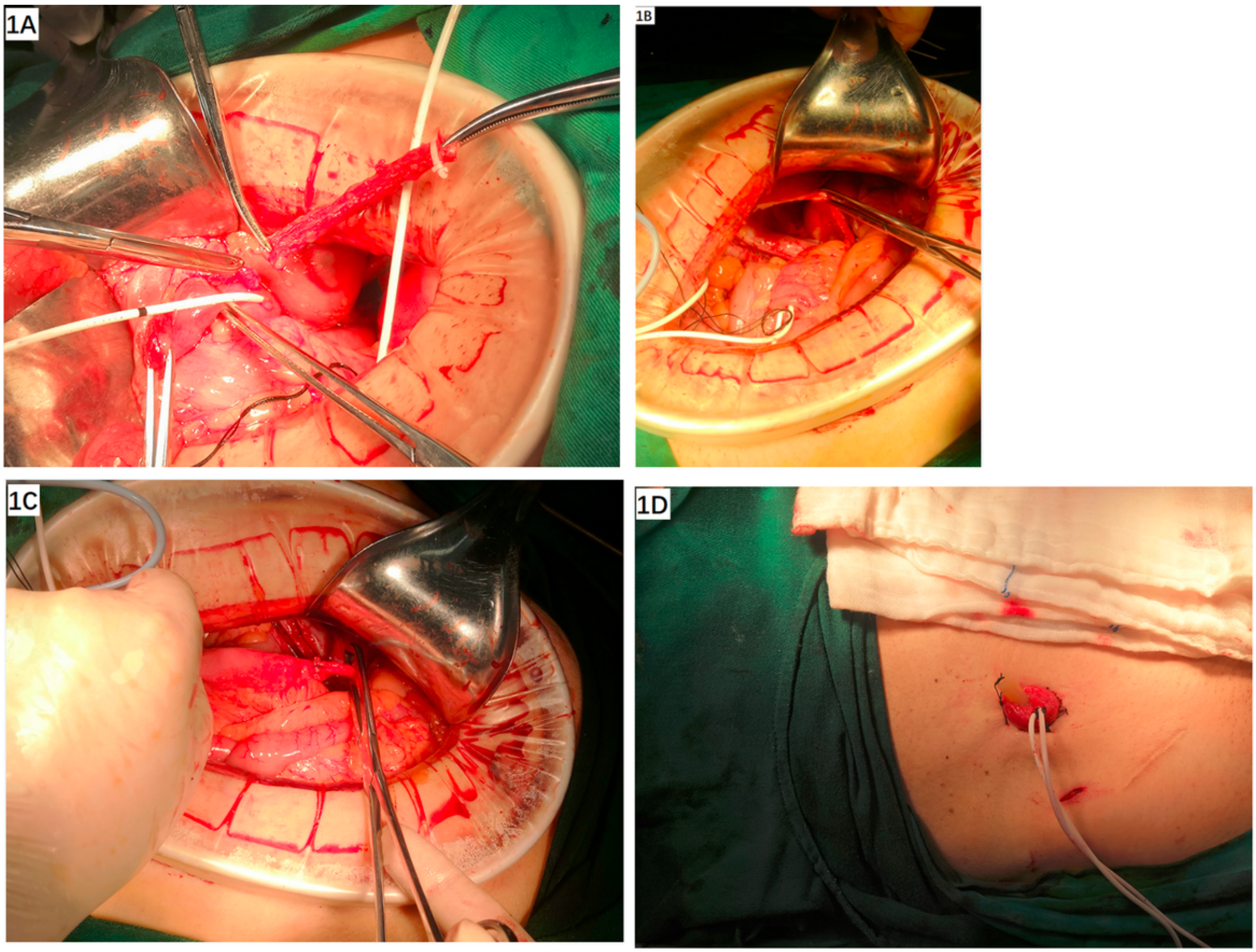

Figure 1

A: When ileal conduit (IC) was pulled under the sigmoid mesenteric to the left retroperitoneum, the redundant part of ureteral stump was removed at the intersection of the left ureter and the IC. B: A retroperitoneal channel is separated to the right. C: After the excision of the right ureter stump, the right ureter was anastomosed end-to-side with IC. D: The formed IC stoma is everted papillary.

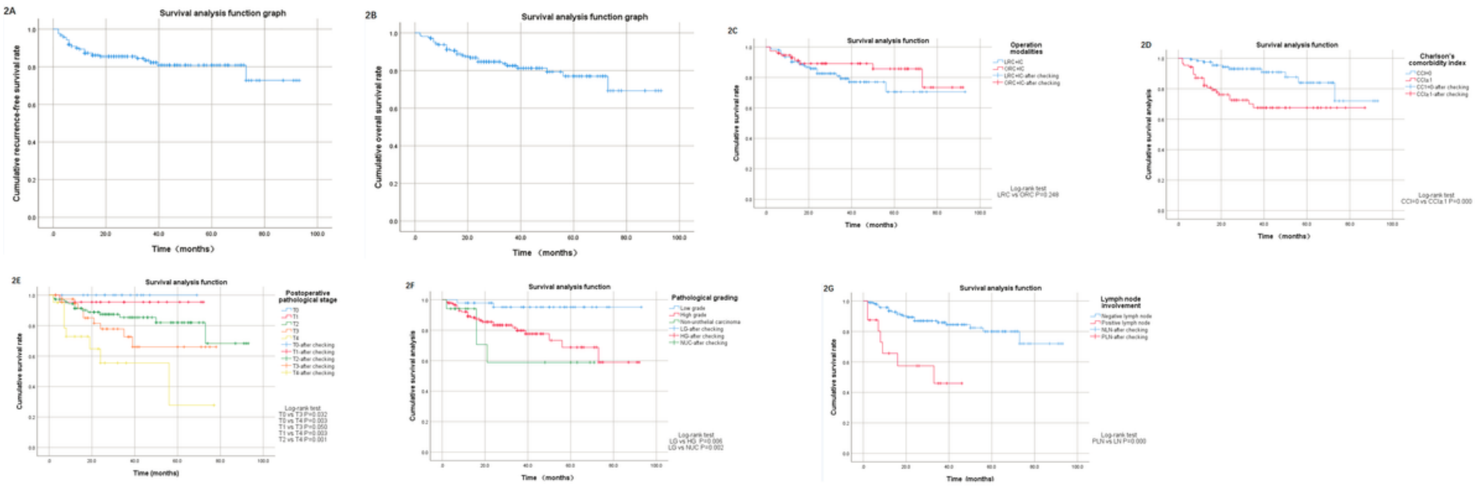

Figure 2

A: Kaplan-Meier curves for recurrence-free survival. B: Kaplan-Meier curves for overall survival. C: Kaplan-Meier curve and log-rank test stratified by operation modalities，there was no significant difference between laparoscopic surgery（LRC） and open surgery (ORC) (P = 0.248). D: Kaplan-Meier curve and log-rank test stratified by CCI, the survival rate of patients with CCI ≥ 1 was significantly lower than that of patients without comorbidity (P= 0.000). E: Kaplan-Meier curve and log-rank test stratified by pathologic stage, the higher the pathological stage, the worse the survival rate. F: Kaplan-Meier curve and log-rank test stratified by grade. As shown in figure F, the survival curve of low-grade urothelial carcinoma (LG) is significantly better than that of high-grade (HG) and non urothelial carcinoma (NUC). G: The survival curve of different lymph node status is shown in the figure 2G. Compared with the positive lymph node (PLN), the survival curve of the negative lymph node (NLN) is significantly better than that of the PLN(P=0.000).

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