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Modified transperitoneal versus retroperitoneal laparoscopic radical nephroureterectomy in the management of upper urinary tract urothelial carcinoma: Best practice in a single center with updated results

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Abstract

Objective: Radical nephroureterectomy remains the gold standard for the surgical treatment of upper urinary tract urothelial carcinoma (UTUC). Based on previous research, we prospectively compared the advantages of transperitoneal laparoscopic radical nephroureterectomy (TLNU) with a three-port technique in a single position versus retroperitoneal laparoscopic radical nephroureterectomy (RLNU).

Methods: We evaluated 48 patients diagnosed with UTUC at our institution from January 2015 to October 2019. The patients underwent either TLNU (n = 24) or RLNU (n = 24). We randomly assigned the patients to each technique group based on their body mass index because our experience has shown that the body mass index is the main interfering factor for this surgery. The baseline characteristics and perioperative outcomes were compared between the groups.

Results: We found no significant differences in the baseline characteristics, time until recovery of intestinal function, or postoperative hospital stay between the two groups. However, the TLNU group had a shorter operation time and better postoperative pain control than the RLNU group.

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Conclusion: Modified TLNU is associated with a shorter operative time and less severe postoperative pain compared with RLNU. Both techniques are safe and reliable with adequate management, and their therapeutic effects are comparable in other aspects.

Keywords
Transperitoneal, retroperitoneal, nephroureterectomy, upper urinary tract urothelial carcinoma, three-port technique, body mass index

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Introduction

Upper urinary tract urothelial carcinoma (UTUC) is a relatively rare tumor worldwide, accounting for about 10% of all kidney tumors and 5% of all urothelial carcinomas.[1,2] Statistically, UTUC accounts for 20% to 30% of all urothelial carcinomas in the Chinese population,[3] and the incidence of UTUC has been increasing in recent years.[2,4] In a previous study, we retrospectively compared the perioperative outcomes of transperitoneal laparoscopic radical nephroureterectomy (TLNU) versus retroperitoneal laparoscopic radical nephroureterectomy (RLNU) and found that the retroperitoneal approach was advantageous in terms of quicker bowel recovery and a shorter time to hospital discharge.[5]

Since that study, we have continued to find that TLNU has more advantages over RLNU, and we have further improved the surgical technique of TLNU. Today, TLNU is routinely carried out with a single-position three-port technique. This study was performed to examine the details of our single-position three-port TLNU technique and prospectively compare the perioperative outcomes of TLNU and RLNU.

Patients and methods

Patients

We prospectively enrolled patients with UTUC who underwent radical nephroureterectomy at the Second Xiangya Hospital of Central South University (Changsha, China) from January 2015 to October 2019. The patient characteristics included age, sex, body mass index (BMI), American Society of Anesthesiologists (ASA) score, tumor location, and tumor side. The inclusion criteria were treatment-naïve UTUC, no sign of any lymphatic or distant metastasis, no other primary tumors, no history of abdominal surgery, and a BMI of 18.5 to 23.9 kg/m^2. The exclusion criteria were pathologically confirmed non-urothelial carcinoma, performance of intraoperative lymph node dissection, obvious adhesions (such as intestinal adhesions or perirenal adhesions) found during surgery, a concomitant bladder tumor, medical comorbidity, and malnutrition or anemia. All TLNU and RLNU operations were performed by the same urologist. Considering the strict inclusion criteria of this study and the limited number of patients in our center, we randomly assigned the patients to each technique group based on their BMI status (as shown in Figure 1) because our experience has shown that the BMI is the main interfering factor for this surgery.

Preoperative evaluation

A blood panel and urinalysis were performed to exclude urinary and systemic infections as well as liver and kidney dysfunction. Cystoscopy was performed 1 day

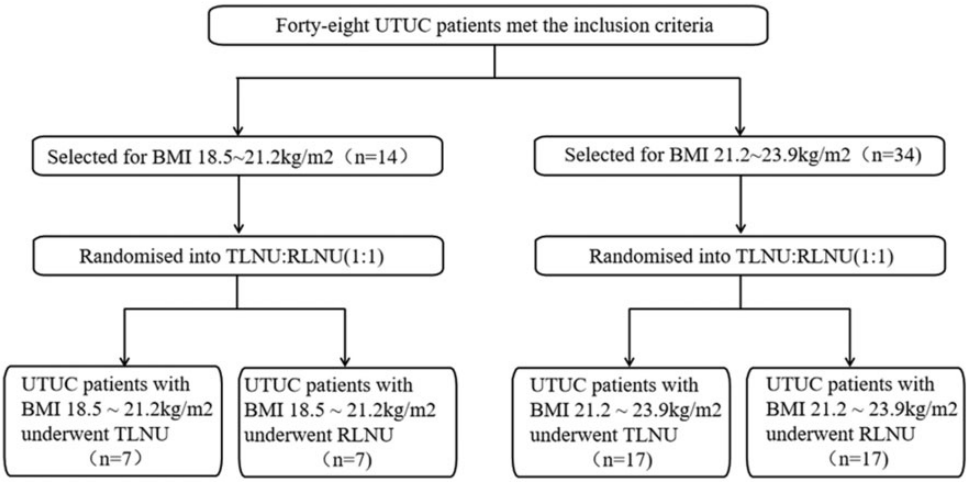

Figure 1. Flowchart showing the randomized enrollment of patients with UTUC. UTUC, upper urinary tract urothelial carcinoma; BMI, body mass index; TLNU, transperitoneal laparoscopic radical nephroureterectomy; RLNU, retroperitoneal laparoscopic radical nephroureterectomy.

before surgery to exclude bladder tumors, and a ureteral stent was placed in the contralateral ureter to mark the normal ureteral orifice. Chest radiographs were obtained to rule out lung metastasis and lung disease. Abdominal computed tomography or magnetic resonance imaging was performed to evaluate the primary lesion. Voided urine cytology was performed for all patients.

Postoperative treatment

The patients were asked to drink small, frequent amounts of water soon after recovery from anesthesia. A semi-liquid diet was begun 12 hours after surgery, and the patients were encouraged to chew gum to promote the recovery of intestinal function. Parecoxib sodium for injection was intravenously administered at 20 mg every 12 hours for 3 days. The patients were encouraged to begin early ambulation. The drainage tube was removed 3 days after surgery if there was no sign of leakage. The patients were discharged on postoperative day 4 if no complications had occurred.

The operation time was recorded immediately after the completion of surgery. Postoperative pain was assessed by a visual analog pain scale 1 day postoperatively before off-bed activity. The postoperative hospital stay and complications (assessed according to the Clavien–Dindo classification of surgical complications[6]) were recorded at discharge. The first follow-up was performed 1 month after surgery for early-stage recovery evaluation.

Surgical technique

TLNU. After administration of general anesthesia, the patient was positioned in a 45° lateral decubitus position contralaterally, and the operating table was rotated 30° toward the surgeon. Taking a left-sided lesion as an example, the surface projection of the ureterovesical junction was marked (mark X), a 10-mm trocar was placed 4 cm from the umbilicus at the umbilical level (Port A) for placement of the camera, and artificial pneumoperitoneum was established with carbon dioxide gas. A second 10-mm trocar and a third

12-mm trocar were then placed 8 cm from Port 1 and from each other cranially (Port B) and at the lesion side (Port C), respectively, ensuring that these three ports formed an equilateral triangle and that mark X lay on the bisector of angle Port B (as shown in Figure 2). Laparoscopic nephrectomy was performed at this position, but the ureter was left intact and dissected as distal as possible until it was technically inaccessible. Before further mobilization of the distal ureter, the ureter was ligated by a Hem-o-lok distal to the tumor site to prevent intraluminal tumor seeding (as shown in Figure 3).

The patient was then moved into the Trendelenburg position with a 30° slant angle toward the surgeon by rotating the operating table. Port B was now used for camera placement, and Ports A and C were used for the operation (as shown in Figure 4). There was no need to change the patient's position from lateral to supine.

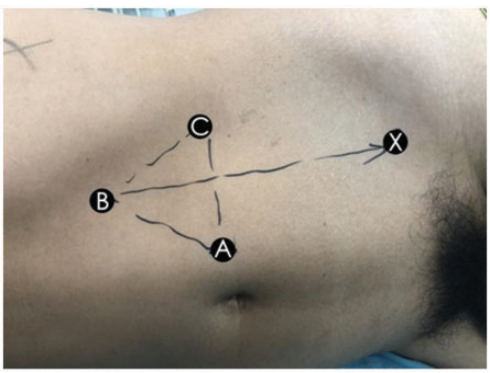

Figure 2. Surface projection of the ureterovesical junction was marked (mark X), a 10-mm trocar was placed 4 cm from the umbilicus at the umbilical level (Port A) for placement of the camera, and artificial pneumoperitoneum was established with carbon dioxide gas. A second 10-mm trocar and a third 12-mm trocar were then placed 8 cm from Port 1 and from each other cranially (Port B) and at the lesion side (Port C), respectively, ensuring that these three ports formed an equilateral triangle and that mark X lay on the bisector of angle Port B.

Figure 3. Laparoscopic nephrectomy was performed at this position, but the ureter was left intact and dissected as distal as possible until it was technically inaccessible. Before further mobilization of the distal ureter, the ureter was ligated by a Hem-o-lok distal to the tumor site to prevent intraluminal tumor seeding.

Figure 4. The patient was changed to the Trendelenburg position with a 30° slant angle toward the surgeon by rotating the operating table. Port B was then used for camera placement, and Ports A and C were used for the operation.

Secondary disinfection was also unnecessary. Before further dissection of the ureter, the bladder was filled with 100 mL of gemcitabine solution. The ureter was then dissected caudally until the ureterovesical junction was identified. Staying 1 cm from the ureterovesical junction, a cuff-shaped section of the bladder wall together with the distal ureter was resected, and the specimen was bagged immediately. The bladder was then closed and the pelvic cavity was reconstructed with running stitches. An incision of the appropriate size for specimen removal was made by enlarging Port A, a drainage tube was placed through Port C, and the wound was closed anatomically.

RLNU. The detailed surgical technique for RLNU was performed as described in our previous article.[6] Specifically, RLNU was first performed, but the ureter was left intact with the patient in the lateral decubitus position with overextension. The patient was then moved to the supine position, and a 6-cm oblique incision was made in the lower abdomen from McBurney's point. Open surgery for bladder cuff excision was performed, and the specimen was removed through the lower abdomen incision.

Statistical analysis

SPSS 21.0 software (IBM Corp., Armonk, NY, USA) was used for the statistical analysis. Statistical methods were tested by the t test and chi-squared test. Bilateral tests were used, and the difference was statistically significant when $P < 0.05$.

Ethics

Written informed consent was obtained from the patients and their families before the surgery. This study was approved by the Ethics Review Committee of the Second Xiangya Hospital of Central South University.

Results

We enrolled 48 patients from January 2015 to October 2019 (TLNU group, $n = 24$; RLNU group, $n = 24$). The patients comprised 28 men and 20 women. There were no significant differences between the two groups in any baseline characteristics: age, sex, BMI, ASA score, tumor side, or tumor location (Table 1).

The TLNU group had a shorter operation time and better postoperative pain control than the RLNU group ($P < 0.05$). However, there was no significant difference between the two groups in the time to recovery of intestinal function or the postoperative hospital stay (Table 2).

Two patients in each group developed postoperative complications, all of which were Clavien grade I or II. Specifically, two patients in the TLNU group and one patient in the RLNU group developed postoperative ileus (Clavien grade II), and one patient in the RLNU group developed subcutaneous emphysema (Clavien grade I) (Table 2).

Discussion

UTUC is more common in the Chinese population. This may be partially associated with certain adverse environmental factors in China, such as arsenic exposure in drinking water and the popularity of traditional Chinese medicine activities such as consumption of aristolochic acids containing herbs.[3,4] Compared with urothelial carcinoma of the bladder, UTUC is more likely to invade adjacent structures and has a higher recurrence rate because both the renal pelvis and the ureters are thin in texture.

The standard surgical treatment of UTUC is nephroureterectomy,[7] and clinical

Table 1. Patients' baseline characteristics.

Variables	Three-port TLNU	RLNU	P value
Patients	24	24	
Age, years	64.6 ± 13.3	63.9 ± 10.2	0.837
Sex			
Male	15 (62.5)	13 (54.2)	0.558
Female	9 (37.5)	11 (45.8)	
BMI, kg/m^2	21.9 ± 1.4	22.5 ± 1.3	0.209
ASA score			0.525
I	16 (66.7)	18 (75.0)	
II	8 (33.3)	6 (25.0)	
Tumor side			0.551
Left	14 (58.3)	16 (66.7)	
Right	10 (41.7)	8 (33.3)	
Tumor location			0.765
Pelvicalyceal	13 (54.2)	15 (62.5)	
Pelvicalyceal–ureteral	2 (8.3)	1 (4.2)	
Ureteral	9 (37.5)	8 (33.3)	

Data are presented as n, n (%), or mean ± standard deviation.
TLNU, transperitoneal laparoscopic radical nephroureterectomy; RLNU, retroperitoneal laparoscopic radical nephroureterectomy; BMI, body mass index; ASA, American Society of Anesthesiologists.

Table 2. Patients' perioperative outcomes.

Variables	TLNU	RLNU	P value
Patients	24	24	
Operating time, minutes	108.2 ± 11.2	126.5 ± 10.8	<0.001
Time from surgery to first bowel sound, days	2.4 ± 0.5	2.3 ± 0.5	0.514
Postoperative hospital stay, days	4.3 ± 0.9	4.1 ± 0.7	0.489
Visual analog pain scale score	2.0 ± 1.3	2.9 ± 1.4	0.025
Overall postoperative complications	2 (8.33)	2 (8.33)	
Clavien grade I	0 (0.00)	1 (4.17)	
Clavien grade II	2 (8.33)	1 (4.17)	

Data are presented as n, n (%), or mean ± standard deviation.
TLNU, transperitoneal laparoscopic radical nephroureterectomy; RLNU, retroperitoneal laparoscopic radical nephroureterectomy.

data have shown an equivalent oncologic outcome between open and microinvasive surgery.[8] With continuous improvement in techniques and instruments, microinvasive surgery has largely replaced open surgery as the most widely accepted approach for nephroureterectomy. In our previous study, we found that both the transperitoneal and retroperitoneal approaches were safe and effective for this surgery and that the retroperitoneal approach was associated with quicker bowel recovery and a shorter hospital stay.[5]

We have noticed that flank pain is a major problem for most patients who have undergone retroperitoneal surgery,

especially for patients with a heavier body weight. We attribute this flank pain to the following factors. The first is the flank incision by which the gross specimen is harvested. The cutting and suturing of the flank structure can cause acute pain soon after surgery because the flank muscle contracts either intentionally or involuntarily every time the patient moves his or her body. The second factor is the lateral decubitus position with overextension used during surgery. The patient's waist is under great pressure exerted by his or her own bodyweight throughout the surgery, which might cause fatigue or even injury not only to the flank muscle but also the lumbar vertebrae. This can result in chronic pain after surgery, and such pain is more serious for patients with a heavier body weight. The third factor contributing to flank pain is dissection of the retroperitoneal fat tissue. To create room to work in the retroperitoneal space, which is an anatomically latent space, the surgeon must first remove the retroperitoneal fat tissue. This procedure can be time- and labor-consuming in patients with a high body fat content and may cause wider tissue injury, resulting in greater postoperative pain.

Surgeons also often find the retroperitoneal approach to be difficult because they must operate from above. They must rotate their waist and elevate their arms higher throughout the surgery, which is fatiguing (as shown in Figure 5). In contrast, the transperitoneal approach is more comfortable for surgeons because they operate facing the patient, allowing them to sit while working (as shown in Figure 6).

With continuous refinement of surgical skills, transperitoneal surgery is performed more smoothly and quickly. The fat tissue does not need to be cleaned before the surgical procedure because the abdominal cavity is adequately large for this operation. The transperitoneal approach also provides a larger operating space and clearer anatomical landmarks, thus making it easier for surgeons to operate, minimizing the probability of accidental intraoperative injury, and shortening the operation time. More importantly, intraoperative patient repositioning, which is time-consuming, is not needed during transperitoneal surgery. However, it is necessary for retroperitoneal surgery. Full protection of the contralateral kidney function is particularly important for this surgery, and surgeons should be

Figure 5. The retroperitoneal approach is often difficult because the surgeon must operate from above. The surgeon must rotate their waist and elevate their arms higher throughout the surgery, which is fatiguing.

Figure 6. The transperitoneal approach is more comfortable for surgeons because they operate facing the patient, allowing them to sit while working.

very careful when incising the bladder and suturing the tissue to ensure that the contralateral ureteral orifice remains intact after surgery. Placement of a ureteral stent in the healthy side before surgery makes it much easier for surgeons to locate the contralateral ureteral orifice during surgery and thus saves time. We have replaced our previous four-port technique with our current three-port technique, and a fourth assisting port is now only occasionally needed in complicated cases.

The conception of enhanced recovery after surgery (ERAS) is widely accepted in multiple disciplines.[9,10] Based on our previous experience, a series of perioperative ERAS management protocols were adopted in the present study. Early tentative feeding and gum chewing effectively promoted the recovery of gastrointestinal function and thus ensured the supply of nutrition, which is crucial for wound healing. Additionally, regular postoperative analgesia and early removal of the drainage tube not only relieved the patient's pain, which was evident from the visual analog pain scale evaluation, but also facilitated early ambulation and allowed the patient to get out of bed, further promoting the overall recovery from surgery.

The overall postoperative complication rate in our study was 8.3%, and no Clavien grade III or IV complications occurred. This is an improvement over our previous report (19.1%).[5] We attribute the reduction in the complication rate to several factors. To minimize the objective bias and highlight the impact of the different surgical techniques on the patients' outcomes, we established strict inclusion and exclusion criteria and ensured that all patients were in relatively good clinical conditions. However, assessment of complications was limited by the small number of patients (only 48 patients were finally included in the study). Notably, our surgical proficiency and high standard for surgical details made the operation safer, and by continuous refinement of our surgical technique we further shortened the operation time and effectively reduced the intraoperative injury rate. Moreover, numerous studies have demonstrated that perioperative ERAS management facilitates gastrointestinal recovery and wound healing and can reduce the incidence of pulmonary infection and deep vein thrombosis.[9,11] By selective use of certain ERAS measurements, we have initially verified its effectiveness and safety for patients undergoing TLNU and RLNU, and we believe that our patients benefitted from these treatments.

Conclusion

Modified TLNU has the advantages of shortening the operative time and reducing postoperative pain compared with RLNU. Both techniques are safe and reliable with adequate management, and their therapeutic effects are comparable in other aspects.

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Availability of data and material

All data generated or analyzed during this study are included in this published article.

Author contribution

Ye K was responsible for the study concept, study design, and writing of the manuscript. Zhong Z was responsible for reviewing the article and proposing changes. Ren J, Xiao M, and Liu W collected and analyzed the data. Zhu L was responsible for the quality control of the data and algorithms. Xiong W was responsible for revision of the article and the study design. All authors read and approved the final manuscript.

Declaration of conflicting interest

Ye Kun, Zhong Zhaohui, Zhu Liang, Ren Jiannan, Xiao Ming, Liu Wentao, and Xiong Wei have no conflict of interest to declare.

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Supplemental material

Supplemental material for this article is available online.

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