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Technical Modification of Terminal Ureter During Total Transperitoneal Laparoscopic Nephroureterectomy for Upper Urinary Tract Urothelial Carcinoma

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Cover letter

Dear Editors:

We would like to submit the enclosed manuscript entitled " **Technical Modification of Treating The Terminal Ureter During Total Transperitoneal Laparoscopic Nephroureterectomy for Upper Urinary Tract Urothelial Carcinoma**", which we wish to be considered for publication in "JOVE". No conflict of interest exits in the submission of this manuscript, and manuscript is approved by all authors for publication.

I would like to declare on behalf of my co-authors that the work described was original research that has not been published previously, and not under consideration for publication elsewhere, in whole or in part. All the authors listed have approved the manuscript that is enclosed.

In this work, we evaluated **a novel technique in Total Transperitoneal Laparoscopic Nephroureterectomy which was feasible and facilitated in the procedure**. I hope this paper is suitable for "JOVE".

We deeply appreciate your consideration of our manuscript, and we look forward to receiving comments from the reviewers. If you have any queries, please don't hesitate to contact me at the address below.

We hope that this article can to be "in-press" at 10/20/2019

Thank you and best regards.

Yours sincerely,
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TITLE:

Technical Modification of the Terminal Ureter During Total Transperitoneal Laparoscopic Nephroureterectomy for Upper Urinary Tract Urothelial Carcinoma

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KEYWORDS:

total transperitoneal, laparoscopic surgery, nephroureterectomy, renal pelvis carcinoma, ureteral carcinoma, ureteral terminal

SUMMARY:

Here, we present a protocol to increase the surgical field of view and reduce the difficulty of total transperitoneal laparoscopic nephroureterectomy surgery by precutting the umbilical ligament before treating the terminal ureter.

ABSTRACT:

Upper tract urothelial carcinoma (UTUC) accounts for 5%–10% of all urothelial tumors. Radical nephroureterectomy is the standard treatment procedure. At present, different choices still exist for treating the ureteral end during laparoscopic ureteral bladder sleeve resection. Our center has adopted a new method for treating the ureteral end. This new method can increase the operating space and reduce the difficulty of the surgery compared with current methods.

INTRODUCTION:

Radical nephroureterectomy is a standard procedure for treating upper tract urothelial carcinoma (UTUC)[1]. Traditional open surgery requires two large incisions in the lower abdomen, which is associated with a large amount of trauma and many complications[2]. With the rapid development of minimally invasive techniques in urology, laparoscopic surgery has been gradually applied in many research studies. Laparoscopic surgery is identical to open surgery in treating the tumors, so the traditional surgical methods have gradually been replaced by laparoscopic surgery[3].

In laparoscopic surgery, treatment of the terminal ureter has been an area of focus and a known difficulty of the surgery. At present, different choices exist for treating the ureteral end in laparoscopic nephroureterectomy. However, reductions in the difficulty of the surgery and the amount of trauma has not been possible[4,5].

After years of exploration, our center has improved and adopted a new method for the treatment of the terminal ureter: precutting the medial umbilical fold not only increases the operating space but also reduces the difficulty of the surgery and minimizes extra trauma to the patient.

PROTOCOL:

All methods described here have been approved by the ethics committee of the Beijing Hospital. Indications and contraindications for surgery are according to the European Association of Urology guidelines for upper urinary tract urothelial cell carcinoma.

1. Instruments for operation

1.1. Ensure the availability of the laparoscopic imaging system, images of the pneumoperitoneum, and ultrasonic scalpel.

2. Preparation for operation

2.1. Prepare the patient with a bowel cleansing before the operation. Have the anesthesiologist perform an anesthesia risk assessment of the patient prior to surgery. Have patients taking aspirin before surgery stop taking it.

2.2. Prepare the skin around the surgical site.

2.3. Preoperatively administer an intravenous antibiotic 30 min before the operation to all patients. Use cefuroxime sodium 1.5 g with 100 mL of 0.9% sodium chloride solution.

2.4. Before administering general anesthesia, lay the patient down on the operating table.

2.5. After general anesthesia, place the healthy side of the patient in a 60° recline at the waist, so the patient is in a V-shaped position on the operating table.

3. Procedure

3.1. Place trocars (see **Figure 1**).

3.1.1. Begin the operation with the patient in the right lateral position.

3.1.2. Establish pneumoperitoneum by inserting a pneumoperitoneal needle using the Veress method. Maintain the pneumoperitoneum pressure at 14 mmHg.

3.1.3. Implant a trocar at the umbilical level near the outer edge of the left rectus abdominis muscle. Then, insert the laparoscope.

3.1.4. Place the other trocars.

3.2. Treat the kidney and upper and middle ureters.

3.2.1. Rotate the operating bed axially so that the patient is in an ~80°–90° lateral position.

NOTE: This position allows for the intestines to fall to the side, which better exposes the renal hilum for treatment.

3.2.2. Dissect the peritoneum on the affected side and fully release the colon downwards.

3.2.3. Free and clamp the ureter at the distal end of the tumor with a vascular closure clip and then dislodge upwards along the ureter until reaching the renal hilum level.

3.2.4. Treat the renal artery and renal vein successively and completely free the kidney.

3.2.5. Free the ureter to the external vascular level.

3.3. Treat the terminal ureter.

3.3.1. Rotate the operating bed axially so that the patient is in a 50° lateral position.

NOTE: This position is optimal for surgery inside the pelvic area and avoids having the surgeon operate in a position that is too low.

3.3.2. Open the anterior peritoneum of the ureter with an ultrasonic scalpel and after crossing the iliac vessels, identify the umbilical medial iliac crest, where the umbilical artery is located[6] (**Figure 2**).

3.3.3. Cut the medial iliac crest so that the artery can reach the outside of the bladder (**Figure 3**).

3.3.4. Clamp and cut the distal end of the vascular structure as is the norm. Free the bladder until the ureter enters the bladder.

3.3.5. Cut the entire layer of the bladder wall at the upper side of the ureteral junction. Suture the full layer of the bladder with 3-0 absorbable thread to indicate and provide traction to see the normal bladder mucosa[5,7].

3.3.6. Remove the ureteral bladder wall segment and part of the bladder mucosa with a scalpel. While making the incision, completely suture the bladder wall with absorbable lines (**Figure 4**).

3.4. Take out the specimen.

3.4.1. Load the surgical specimen into the specimen bag.

3.4.2. According to the conditions, extend the incision for cannula A and take out the specimen.

3.4.3. Layer off each incision.

3.5. Postoperative care

3.5.1. Let the patient lay in bed for approximately 1 h postoperatively in the care unit until he or she completely wakes up from anesthesia.

3.5.2. Meanwhile, monitor the patient and ensure that oxygen is available during this time.

3.5.3. When the patient completely wakes up, return the patient to the ward. Pay attention to the color and volume of the urine and abdominal drainage. Pay attention to the presence of any abdominal signs and symptoms (e.g., stomachache and peritoneal irritation).

REPRESENTATIVE RESULTS:

In total, 87 patients underwent surgery without difficulties, and there were no open surgeries. The average age of the patients was 67.25 ± 9.90 years. Within this group, there were 47 cases of renal pelvic cancer, 10 cases of pelvic cancer with ureteral cancer, and 30 cases of ureteral cancer (10 cases of upper ureteral cancer, 9 cases of middle ureteral cancer, and 11 cases of lower ureteral cancer). In total, 49 cancers were on the left side and 38 cancers were on the right side. The average tumor diameter was 3.24 ± 1.47 cm, and the average operation time was 162.50 ± 45.64 min. The volume of intraoperative blood loss was 113.33 ± 59.74 mL. No patients required perioperative blood transfusions. On average, the drainage tubes were in place for 4.56 ± 1.12 days, and the catheters were in place for 5.63 ± 2.17 days. The surgical specimens were positive. The postoperative pathological stages ranged from T1N0M0 to T4N0M0 (T1 = 24 cases, T2 = 19 cases, T3 = 37 cases, T4 = 7 cases). No complications occurred during the operation, although two patients had complications after the operation (i.e., infection). After treatment, the patients were discharged. All patients underwent routine intravesical instillation. Urinary pathology tests, cystoscopy and imaging examinations were performed in regular outpatient

clinics. The follow-up time was 1–44 months, and the median follow-up time was 13 months. Eight patients had postoperative tumor recurrence, all of which were bladder recurrence (**Table 1** and **Table 2**).

FIGURE AND TABLE LEGENDS:

Figure 1: Trocar position. (**A**) Position of the trocar on the right side. (**B**) Position of the trocar on the left side. (a) The umbilical level of the affected side, close to the lateral edge of the rectus abdominis (viewed with a mirror). (b) Under the affected part of the midline of the clavicle (operating hole). (c) The front side of the affected side intersects with the umbilical level. The operator uses his or her hand to treat the kidney. The operator uses his or her hand to treat the lower part of the ureter. (d) The midline of the clavicle and the midpoint of the inguinal ligament are on the same longitudinal line as the clavicle. A triangular relationship exists with the umbilical level and cannula A when treating the lower segment of the ureter. (e) Under the xiphoid while lifting the liver.

Figure 2: Treatment of the umbilical ligament (exposure). Diagram (**A**) and image (**B**).

Figure 3: Treatment of the umbilical ligament (cut). The umbilical ligament is like a curtain that completely blocks the end of the ureter and the side of the bladder. After the peritoneum of the free umbilical ligament is cut, the umbilical ligament can be well exposed and directly treated. Diagram (**A**) and image (**B**).

Figure 4: Treatment of the lower ureter. After the end of the ureter is closed, the entire layer of the bladder was cut, and the full layer of the bladder was sutured with 3-0 absorbable thread as an indicator and for traction. If the ureteral end and the bladder sleeve mucosa are not completely disconnected, the bladder incision is exactly sutured under direct vision. Diagram (**A**) and image (**B**).

Table 1: Perioperative data of 87 patients with UTUC who underwent total transperitoneal laparoscopic nephroureterectomy. Data are shown as mean ± SD; UTUC = upper tract urothelial carcinoma; SD = Standard deviation.

Table 2: Postoperative pathological stage.

DISCUSSION:

A traditional open renal ureter resection and bladder cuff-like resection mostly involve upper and lower incisions, which require changing positions and disinfecting the surgical towels twice. The operation time is long, and the amount of trauma is large. Laparoscopic renal ureter and bladder sleeve resection have been gradually adopted by urologists since minimally invasive surgery techniques have been widely used in urology[8]. The methods for laparoscopic nephroureterectomy and radical resection of ureteral cancer are not the same in all medical centers. The main differences are in the approach and the distal ureteral treatment. At present, hospitals in China have adopted open surgery or transurethral distal ureterectomy. In recent years, complete laparoscopic techniques have been used to treat upper urinary tract urothelial

tumors[9]. The biggest advantage of the method used in this study is that it does not require position changes or complete removal of the upper urinary tract urothelial cells. This tumor treatment technique reduces the overall time needed for surgery and anesthesia[10], reduces the risk of local tumor implantation[11], simplifies the operation, reduces the difficulty of the surgery, and facilitates promotion of this technique[12].

Compared with other treatments for upper urinary tract urothelial tumors, the techniques used in this study have the following characteristics: Traditional laparoscopic surgery is mainly used to treat the renal and upper ureter. During distal ureter and bladder sleeve resection, an incision in the lower abdominal oblique muscles is made, or transurethral distal ureterectomy is used. Transurethral ureteral resection first requires that the patient be placed in the lateral position, thus, the ureteral opening is not clearly visible once the entire layer of the bladder is cut open. Before blocking the affected ureter, the continued outflow of urine with tumor cells may increase the chance of extra bladder implantation, which is not ideal to prevent tumors[13]. A complete laparoscopic kidney, ureter, and bladder sleeve resection was performed. After completely freeing the kidney, we continued to free the distal end of the ureter to the level of the external iliac vessels. The medial umbilical artery travels from the outside of the surgical field to view to the inside, like a curtain obstructing the end of the ureter and the outside of the bladder. After cutting the medial iliac crest, the artery can reach the outside of the bladder. Then, the end of the ureter falls towards the inner side, increasing the operation space. The nondominant hand of the surgeon does not need to be used to retract the medial iliac crest. Before the distal ureter and bladder were treated, the umbilical artery was disconnected, and the curtain blocking the visual field was opened and fully exposed to increase the operation space, which helps the surgeon and reduces the risk of injury to the surrounding tissues[14]. The technique in this study was superior to traditional laparoscopic kidney, ureter, and bladder sleeve resection in terms of operative time, intraoperative blood loss, urinary catheter indwelling time, length of postoperative hospital stay, and postoperative complications[15].

In summary, this complete laparoscopic renal ureteral bladder resection and modified ureteral endpoint treatment is a safe and effective minimally invasive treatment method for upper urinary tract urothelial tumors compared to other ureteral treatment methods. The surgical procedure is simpler, the end of the ureter is treated under direct vision of the laparoscope, and the bladder incision is sutured reliably.

ACKNOWLEDGMENTS:

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DISCLOSURES:

The authors have nothing to disclose.

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Figure 1

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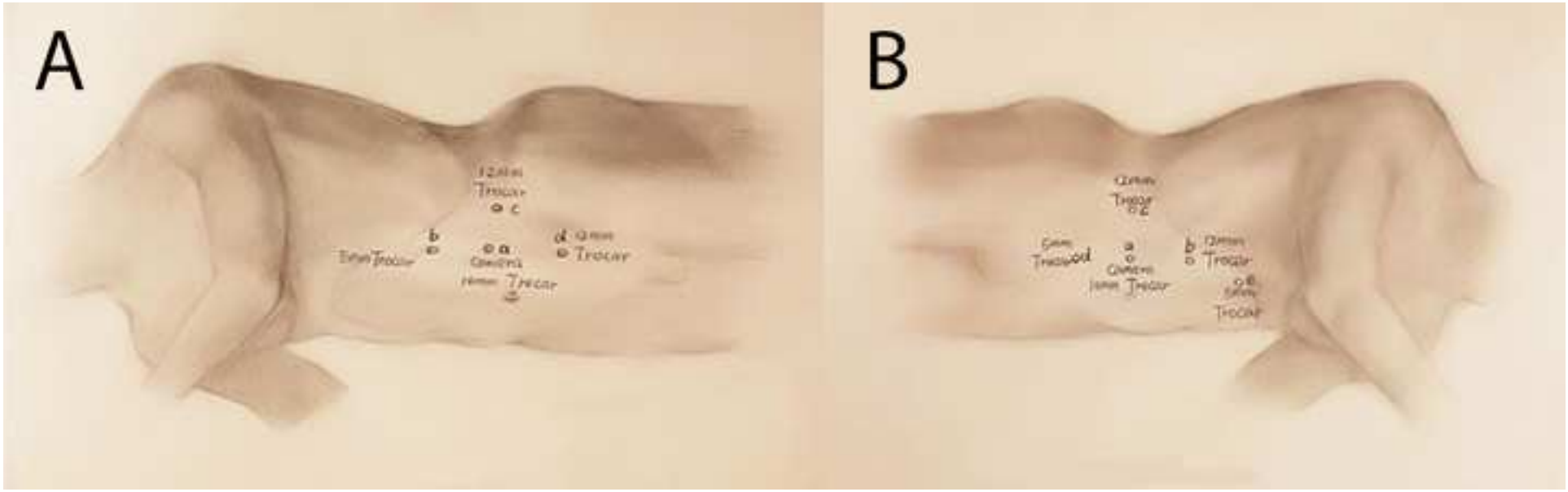

Figure 2

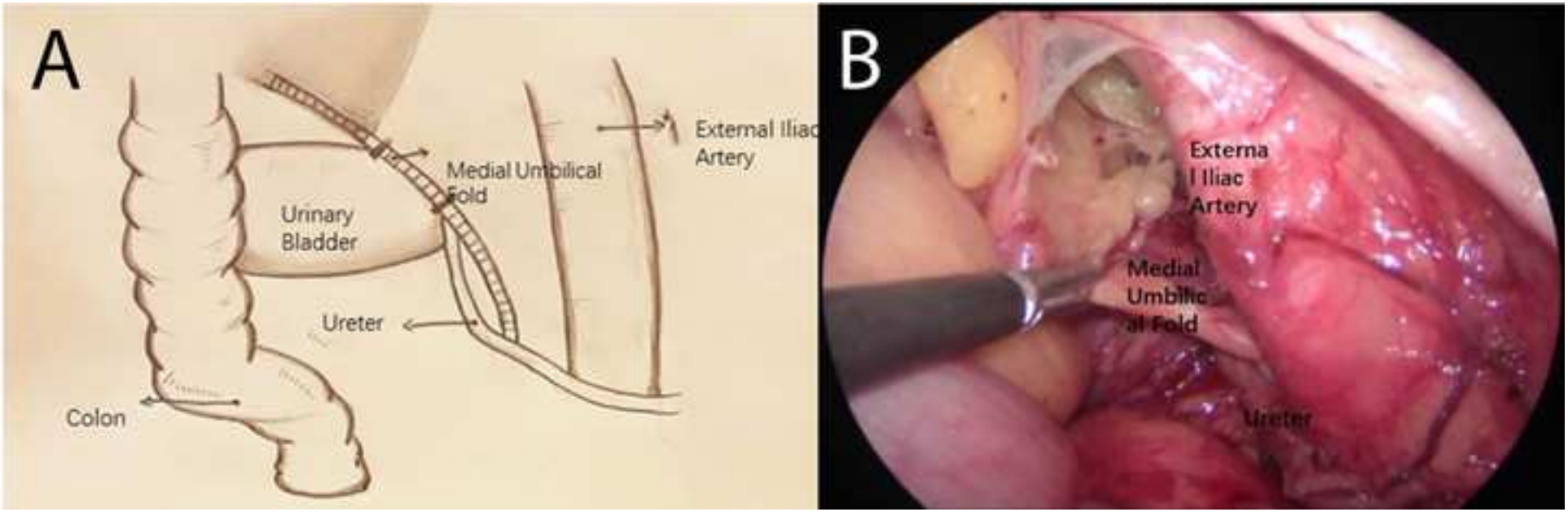

Figure 3

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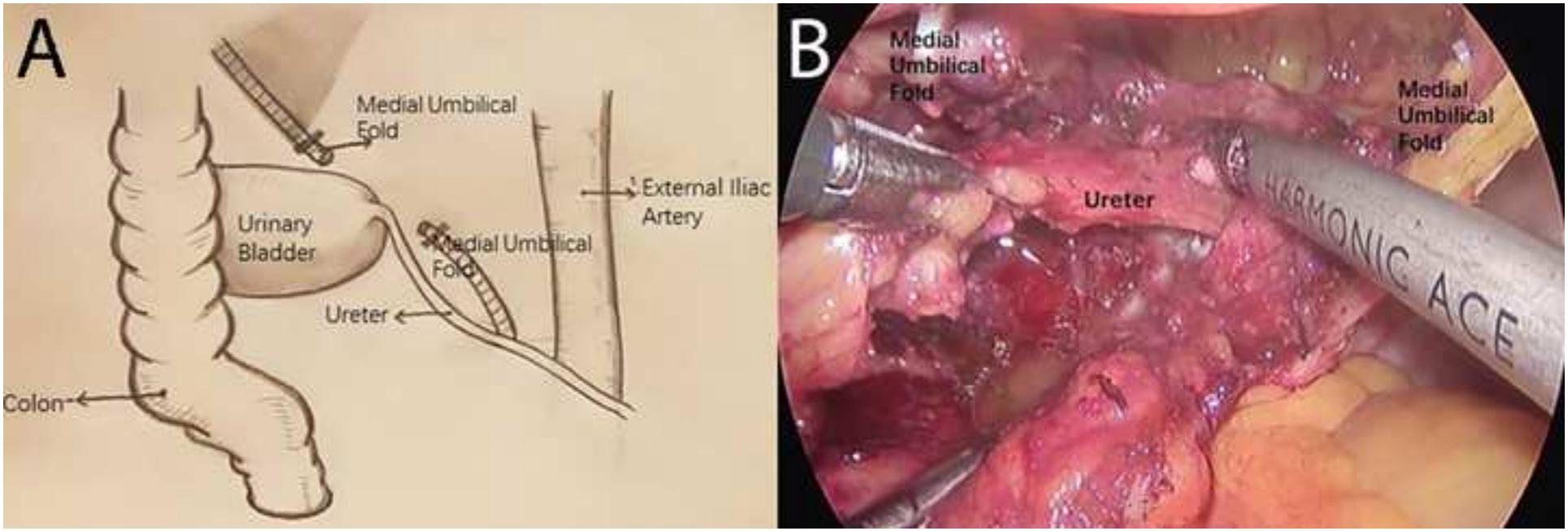

Figure 4

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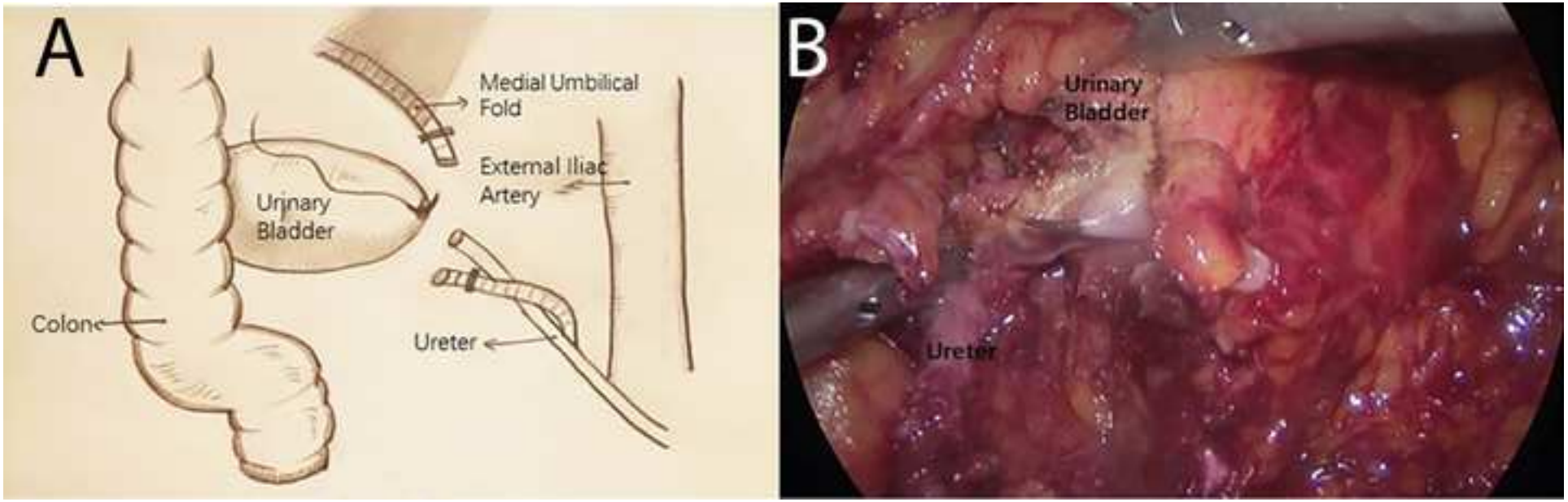

Table 1

Parameters	Data
Age (years)	67.25 ± 9.90
Renal pelvic carcinoma	47
Renal pelvic carcinoma and ureteral cancer	10
Ureteral cancer	30
Upper ureteral cancer	10
Middle ureteral cancer	9
Terminal ureteral cancer	11
Left tumors	49
Right tumors	38
Tumor diameter	3.24 ± 1.47
Operative time (min)	162.50 ± 45.64
Bleeding (mL)	113.33 ± 59.74
Blood transfusion rate (%)	0
Drainage duration (days)	4.56 ± 1.12
Catheter duration (days)	5.63 ± 2.17
Intraoperative complications	0
Postoperative complications	2
Positive rate of surgical margin(%)	0
Median follow-up time (months)	13
Tumor recurrence	8

Table 2

T	N		M	Number
	1	0	0	24
	2	0	0	19
	3	0	0	37
	4	0	0	7

Table of Materials

Click here to access/download;Table of Materials;Table of Materials.xlsx

Name of Material/ Equipment	Company	Catalog Number
Laparoscopic imaging system	STORZ	
Pneumoperitoneum	STORZ	
Ultrasonic scalpel	Johnson	
Vascular closure clip	Hem-o-Lock	

Comments/Description

Addresses Each of The Editorial And Peer Review Comments

Dear Editors and Reviewers,

Thank you for your letter and for the editorial comments and reviewers' comments concerning our manuscript. These comments are all valuable and very helpful for revising and improving our paper , as well as the important guiding significance to our research. We have studied the comments carefully and have made correction as required , which we hope that we will meet with approval. Revised portion are marked in red in the manuscript.

Yours sincerely
Chunlong Fu

Editorial comments:

General:

1. Please take this opportunity to thoroughly proofread the manuscript to ensure that there are no spelling or grammar issues.

I have proofread the manuscript and ensured that there are no spelling or grammar issues in the manuscript.

2. Please include email addresses for all authors in the manuscript.

I have added all authors' emai address in the manuscript.

3. Please rephrase the Summary to clearly describe the protocol and its applications in complete sentences between 10 and 50 words: "Here, we present a protocol to …"

I have revised the manuscript as required.

4. To avoid the appearance of being an advertisement, please remove commercial language (e.g., Hem-o-Lock) from your manuscript.

- Please use generic terms instead
- All commercial products should be sufficiently referenced in the Table of Materials and Reagents instead.

I have used generic terms instead of commercial language

Protocol:

1. Please include pre-operation procedures, e.g., patient selection.

I have added patient selection in pre-operation.

2. Please ensure there is enough detail in the Protocol.

- Please ensure you answer the "how" question, i.e., how is the step performed?
- Alternatively, add references to published material specifying how to perform the protocol action.
- If revisions cause a step to have more than 2-3 actions and 4 sentences per step,

please split into separate steps or substeps.
I have revised the manuscript as required and added related references in the manuscript.

Figures and Tables:
1. Please remove the embedded figures and tables from the manuscript.
I have remove the embedded figures and tables
2. Please include one image file per figure, with all panels for each figure combines (3 files in total).
I have uploaded files as required
3. Please label figure panels as 'A', 'B', etc., not 'Figure 1-1', etc.
I have revised the manuscript as required
4. Please include one file per Table (2 in total), uploaded as 'Table's (separate from the Table of Materials; there will be an option in Editorial Manager).
I have uploaded files as required

Discussion:
1. Please include critical steps in this procedure.
I have added critical steps in this procedure as required
References:
1. Please do not abbreviate journal titles.
I have revised the references as required

Table of Materials:
1. Please include a Table of Materials with information on all materials and equipment used, especially those mentioned in the Protocol.
I have provided all of information on all materials and equipment used in the tables

Reviewers' comments:
Reviewer #1:
Manuscript Summary:.
Different technique for closing the bladder has been introduced. I only wanna have a video in order to understand better if possible.

Dear Reviewer , I have uploaded the video which can help us to describe the procedure of treating of the distal ureter and bladder cuff excision.

Reviewer #2:
Manuscript Summary:
This is an interesting topic.
However, due to lack of a comparison with other similar works, it is not clear how this paper will advance the field. Moreover, the novelty of the technique described by the Authors is not clarified. Cutting the umbilical ligament can hardly be considered as a new method. Thus, I would suggest the Authors to present their numerous material as

a pure laparoscopic nephroureterectomy with technical modification of the distal ureter and bladder cuff excision.

Dear Reviewer , I have took ‘ Technical Modification of Treating The Terminal Ureter ’ as the title of the manuscript according to your suggestion.

For the following reasons , it is our firm conviction that this paper will advance in the field.
Firstly, cutting the umbilical ligament technique before treating the terminal ureter can greatly increase the surgical room and reduce the difficulty of surgery. Especially for beginners, the learning curve can be shortened very quickly. Secondly , Some operators may cut the umbilical ligament when the terminal ureter is difficult to expose, but cutting the umbilical ligament is used as a routine step in the process of treating lower ureter in our hospital . And cutting the umbilical ligament reduce surgery time and surgical complications .Thirdly , cutting the umbilical ligament, this method of treating the lower ureter has not been reported in the literature.

Besides ,I also have uploaded the video which can help us to describe the procedure of treating of the distal ureter and bladder cuff excision.

Addresses Each of The Editorial Comments

Dear Editors ,

Thank you for your letter and for the editorial comments concerning our manuscript. These comments are all valuable and very helpful for revising and improving our paper , as well as the important guiding significance to our research. We have studied the comments carefully and have made correction as required , which we hope that we will meet with approval. Revised portion are marked in red in the manuscript.

Yours sincerely
Chunlong Fu

Editorial comments:

1. Protocol 3.1: “Introduce the operation of the patient…” is unclear; also, there is nothing about placing trocars in this section. Please clarify.
I have revised the manuscript as required.

2. 3.5.3: What ‘abdominal signs and symptoms’ are usually seen?
The patient mainly was paid attention to the color and volume of the patient's urethra and drainage after operation. Only patients with severe bladder anastomosis or intestinal injury during operation will have abdominal symptoms and signs, which usually does not occur.
I have revised the manuscript as required.

3. Figure panels are still in separate files; please combine them so that there is one image file for figure 1 (as opposed to two currently), one image for Figure 2, etc. We will not be able to combine panels for you.
I have revised the manuscript and pictures as required.

4. Please relabel panels-it should be Figure 1A and B; Figure 2 A and B, etc. (and labeled as such in the manuscript, not as Figure A, B, etc.).
I have revised the manuscript as required.