

Laparoscopic radical nephroureterectomy with only three trocars: Results of a prospective single centre study

Yazan Al Salhi^{1,2}, Andrea Fuschi^{1,2}, Alessia Martoccia¹, Gennaro Velotti¹, Paolo Pietro Suraci¹, Silvio Scalzo¹, Onofrio Antonio Rera¹, Alice Antonioni¹, Fabio Maria Valenzi¹, Giorgio Bozzini³, Antonio Carbone¹, Antonio Luigi Pastore¹

¹ Urology Unit, Department of Medico-Surgical Sciences and Biotechnologies, Faculty of Pharmacy and Medicine, Sapienza University of Rome, Latina, Italy;

² ICOT-Surgery, Orthopedics, Traumatology Institute, Latina, Italy;

³ Urology Unit, ASST Lariana, Como, Italy.

Summary

Introduction: Radical nephroureterectomy (RNU) with full bladder cuff excision is the gold standard for treatment of non-metastatic upper tract urothelial cancer (UTUC). We describe our technique of laparoscopic nephroureterectomy (LNU) with bladder cuff excision technique with modified port placement, reporting our long-term follow-up outcomes.

Methods: Patients affected by UTUC were prospectively enrolled and undergone to LNU. Perioperative outcomes, oncological data at 6, 12, 24 and 36 months after surgery, and all the surgical complications according to Clavien-Dindo classification were evaluated in all subjects.

Results: A total of 50 patients with UTUC underwent LNU, using this new technique without patient and port repositioning. The mean operative time was 168 minutes, estimated blood loss was 75 mL, mean length of hospital stay was 3 days. There were no intraoperative complications while four late complications occurred (two grade IIIb and two grade II according to Clavien-Dindo classification, incisional hernias and fever, respectively). Postoperative pathology was T1 in 12 patients, T2 in 17 patients, and T3 in 21 patients. Tumor grade was low in 12 patients and high in 38 patients.

Conclusions: In our study the described LNU technique was related to a significant reduction in terms of operative time and length of hospital stay, with a faster patients' recovery and no peri and postoperative complications. The long-term oncological outcomes were similar to data reported in literature.

KEY WORDS: Nephroureterectomy; Laparoscopy; Oncological outcomes; Hospital stay; Estimated blood loss.

Submitted 29 December 2021; Accepted 7 January 2022

INTRODUCTION

Upper tract urothelial carcinoma (UTUC) is rare, accounting for only 5-7% of all urothelial carcinoma cases, with a high frequency of both local and secondary bladder recurrence (1-2). Radical nephroureterectomy (RNU) with full bladder cuff excision is the gold standard for treatment of non-metastatic UTUC (3).

Laparoscopic nephroureterectomy (LNU) was firstly report-

ed by Clayman in 1991 (4) and several studies described, compared to the open technique, a minimized morbidity in terms of blood loss, perioperative pain, faster convalescence, and less perioperative complications (5, 6).

A recent meta-analysis and multicenter studies reported comparable oncologic results between the two surgical approaches (7-11). One of the most important surgical steps during LNU is the access to the distal ureter in order to perform the excision of the bladder cuff. Different techniques have been described regarding open, endoscopic or trans-vesical approach (12-14) but no one has been shown to be significantly better than the others. The ideal technique is represented, on one side, by removing of the specimen en bloc without spillage of tumor cells during the bladder cuff excision in respect of oncological criteria and, on the other side, by performing the entire procedure without patient and port repositioning to decrease operative time.

Herein, we describe our totally LNU with bladder cuff excision technique with modified port placement, which allows access to both kidney and ureterovesical junction without requiring patient repositioning.

MATERIALS AND METHODS

From January 2014 to June 2020, patients with diagnosis of UTUC, were prospectively enrolled and treated with LNU using our surgical technique performed by the same experienced surgeon (AC) at our University Department. The study was performed in accordance with the *Ethical Principles for Medical Research Involving Human Subjects* (World Medical Association, *The Declaration of Helsinki Principles*, 2000). The study was approved by the local ethical committee of Sapienza University Pharmacy and Medicine Faculty, Latina, Italy (DSBMC LT approval n. CE14/0924/2014 UROL). Written informed consent forms were obtained from all the patients before study enrollment. The patient demographic and clinic-pathologic data were prospectively collected and are summarized in Table 1. None of these patients had prior or concomitant bladder tumors and/or distant metastasis.

All tumors were staged based on the 2002 TNM classification of malignant tumors and were graded by the *World Health Organization classification* of 1998.

After the induction of general anesthesia, the patient is placed in a modified flank position (60° oblique position) with the lesion side up (the right side, e.g.) (Figure 1). The first port (12 mm port used for the 30 degrees camera) is placed by Hasson technique supraumbilical on the pararectal line at the caudal rim of the umbilicus. Peritoneal insufflation is established, and pneumoperitoneum is created by applying 12 mm Hg of CO₂ pressure. The second port is a 12 mm port placed on the paramedian line between the optical trocar and the costal arch. The third port is a 5 mm port placed in the midline between the *anterior superior iliac spine* (ASIS) and the umbilicus.

Figure 1.

Configuration of the three trocars positioning: A for 12 mm optical trocar, B for 12 mm right trocar, C for 5 mm left trocar.

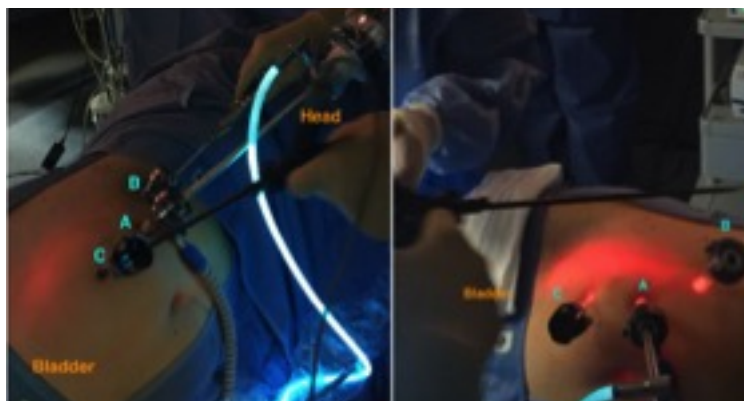
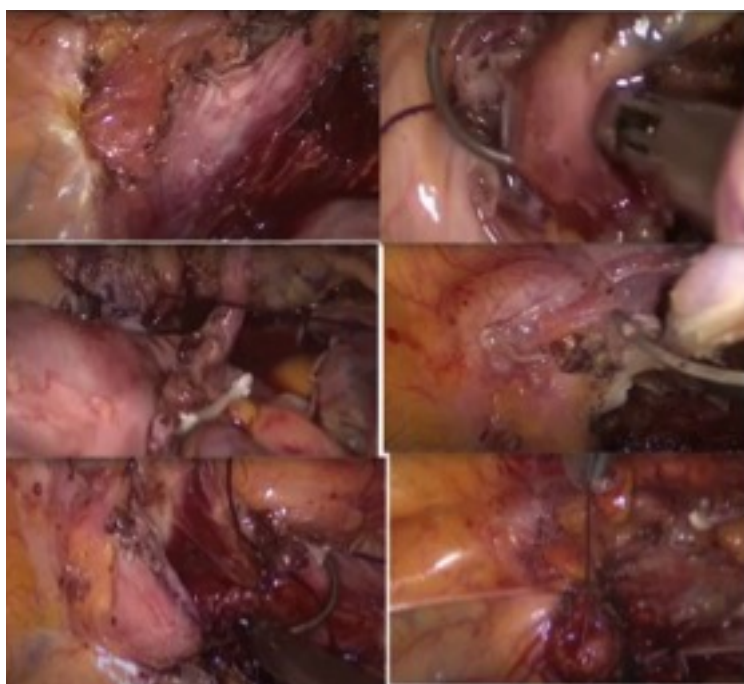


Figure 2.

Sequential surgical steps of bladder cuff excision, placement of stay suture and subsequent cystotomy.



Standard laparoscopic transperitoneal nephrectomy is performed with a radiofrequency device (*Ligasure™*, 5 mm Covidien®, U.S.) placed in the second port and a Johan forceps in the third port. First surgical time (nephrectomy) includes mobilization of the colon, ligation of the renal hilum and circumferential mobilization of the kidney, while leaving the ureter intact.

Retroperitoneal lymphadenectomy is performed in clinical indicated cases based on the preoperative CT scan, included the interaortocaval dissection plus hilar and pre-caval-paracaval-retrocaval regions for right-sided disease, and hilar with preaortic-paraortic-retroaortic tissues for left-sided disease.

During further mobilization, the ureter is clipped distal to the tumor site to prevent intraluminal tumor seeding.

By carefully dissecting the ureter over the iliac vessels down to the ureterovesical junction, the peritoneal covering overlying the dome of the bladder is incised and the detrusor muscle fibers are encountered. Using a combination of blunt and sharp dissection, the intramural ureter is separated from the surrounding detrusor muscle and down to the bladder mucosa.

Prior to complete detachment of the cuff, a 15 cm 3-0 barbed stay suture is placed at the superior margin of the planned cystotomy to provide traction during subsequent closure of the cystotomy. Bladder cuff is excised through monopolar scissors. At this point, after traction on the previously placed stay suture, the same barbed suture is used to close the first layer of the cystotomy. A second 3-0 barbed suture is then used to close a second imbricating layer (Figure 2). The bladder is checked to be water-tight by instilling 120 cc or more of irrigation via the Foley catheter. A perivesical drain is placed and the specimen is entrapped and extracted intact by low paramedian transverse abdominal incision in the ipsilateral lower quadrant of the abdomen.

Patients with bilateral tumor, tumor with node metastasis or bladder carcinoma, adenocarcinoma and squamous cell carcinoma, simultaneous pelvis tumor were excluded from the study.

RESULTS

A total of 50 patients (37 males, 13 females) underwent to LNU performed with our described technique. All cases were completed uneventfully without conversion to open surgery or patient repositioning. Mean age was 67 years old (range 58-83 years), mean BMI was 24.7 kg/m² (range 23.1-27.8). The mean operative time was 168 minutes (range: 132-215 min), estimated blood loss was 75 mL (range 50-125 mL), mean length of hospital stay was 3 days (range: 2-8 days). There were no intraoperative complications while four late complications occurred (two grade IIIb and two grade II according to Clavien-Dindo classification, incisional hernias, and fever respectively). No open conversion was required,

Table 1.
Patients' demographic and pathological characteristics.

N° patient		50
Mean age (range)		67 (58-83)
Sex	Males	37
	Females	13
BMI (range)		24.7 (23.1-27.8)
Side	Right	24
	Left	26
Tumor site	Renal pelvis	29
	Ureter	21
	Mean tumor size	3.3 (2.7 - 5.2)
TNM staging	pT1	12
	pT2	17
	pT3	21
Grade	Low grade	12
	High grade	38
Surgical margins	Negative	50
	Positive	0
Lymph node		3.4 (1-5)

and no blood transfusion needed. Regarding postoperative pathology (Table 1), 29 tumors were in the renal pelvis with a mean diameter of 3.9 cm (range: 3.1-5.2). The other twenty-one were localized as follows: 14 in the proximal ureter and the remaining 7 in the distal ureter, with a mean diameter of 2.9 cm (range: 2.7-3.2). There were no positive margins in any patients. Lymph node dissection was performed in 6 patients (16%) according to the pelvic and abdominal CT scan findings. Of those patients who underwent a lymph node dissection, the median lymph node count was 3.4 (range: 1-5). The pathologic stage was T1 in 12 patients, T2 in 17 patients, and T3 in 21 patients. The tumor grade was low in 12 patients and high in 38 patients. No concomitant carcinoma in situ was found. The median follow-up duration was 41 months (range: 9-62 months). At the first cystoscopy examination (3 months after surgery), we observed that the ureteral orifice of the affected side was absent in all the patients. No patients have presented with evidence of local or secondary bladder recurrence and none of the patients was shown to have stone formation at the routine postoperative follow-up cystoscopy. Moreover, at CT scan study (performed every 6 months for the first 24 months, and then yearly) no distant metastases were reported.

DISCUSSION

During the past twenty years, due to the widespread diffusion of laparoscopy and the development of new devices, LNU has become a feasible and safe mini-invasive procedure for the treatment of UTUC (15, 16). When compared to open RNU, LRN has shown overall remarkable benefits in terms of blood loss, perioperative pain, hospital stay and faster convalescence (17-19). Several minimally invasive surgical procedures have been described regarding nephroureterectomy, particularly focusing on distal ureterectomy and bladder cuff excision

management. It is still under debate which must be considered the optimal technique, with several approaches described such as traditional open trans vesical (stripping, detachment), endoscopic (transurethral resection of ureteral orifice, TUR) or laparoscopic extravesical.

Open excision, through a Gibson, low midline or Pfannestiel incision during LNU, is still the procedure of choice for ensuring the complete bladder cuff excision in terms of oncological principles, but its main drawback is the requirement of a larger incision in comparison to the one needed as the extraction site. TUR, known as "pluck" technique, can be used in patients with proximal tumor and absence of concomitant bladder disease (20, 21); it avoids the need for an extra incision with a shorter operative time compared with open excision (22). Several concerns about the chance of extravesical space tumor seeding have caused the sequential decreasing use of this technique (23). The stripping technique, using a ureteral catheter, can intussuscept the ureter into the bladder; then, the ureteral orifice is excised cystoscopically with a Collins knife (14).

This procedure is contraindicated in the presence of ureteral tumor because of the potential tumor seeding. The laparoscopic transvesical technique describes the placement of two transvesical laparoscopic ports and subsequently of an endoloop around the ureteral orifice, creating a closed urothelium with an en bloc removal of specimen. The disadvantages are represented by the difficult learning curve and the need for the patient repositioning for the nephrectomy surgical time (15).

Regarding pure laparoscopic techniques, the extravesical stapling technique has a shorter operative time and avoids incision into the urinary tract. However, this procedure has been associated with a higher risk of positive surgical margins and local recurrence due to the inadequate bladder cuff resection (24), as well as an increased risk of stone formation (25).

Recently, a new pure laparoscopic technique has been described, involving the use of a bulldog clamp applied distal to the tent shaped ureteral orifice and bladder cuff (26). The advantage of this approach is the en bloc removal without tumor spillage, however the use of the bulldog clamp does not ensure the direct visualization of the ureteral orifice and necessitates the addition of an extra port.

Regarding *robot assisted laparoscopic nephroureterectomy* (RALNU), Hemal *et al.* firstly described their technique for successful performance of robotic nephroureterectomy with bladder cuff excision, without patient repositioning and robot redocking (27). The authors concluded that all procedures were performed successfully without complications, and with excellent short-term oncological outcomes. Vecchia *et al.* in a systematic review and meta-analysis compared robotic nephroureterectomy with open, laparoscopic, and hand-assisted ones in over 87.000 patients; the authors highlight how the robotic approach offers advantages in terms of hospital stay, peri and post-operative complications, blood loss and transfusion compared to the open NU without compromising oncological outcomes; these advantages are on the other hand comparable between robotic and laparoscopic procedures (28, 29). Our technique is a simple modifica-

tion of the pure laparoscopic RNU placing the ports sites in a new more ergonomic and easier position in order to perform the distal ureterectomy and bladder cuff excision without the disadvantage of port or patient repositioning.

Dissection of the intramural part represents a difficult step of the RNU because of several risks during the excision of the bladder cuff, such as tumor spillage or contralateral ureteric orifice injury. However, the association between the laparoscopic magnified view and the use of laparoscopic instruments leads to a careful dissection under direct vision of the urothelium at risk away from the detrusor muscle.

We used this surgical technique for both proximal and distal ureteric tumor localization without reporting any injury of the tumor site during dissection, thanks to the combination of blunt and sharp dissection, separating the intramural ureter from the surrounding detrusor muscle and down to the bladder mucosa and utilizing cold scissors after placing the stay suture.

However, suturing during laparoscopy is not easy, but, in our technique, only two stitches are required in order to secure the bladder and ensuring the closure of the urinary tract during the whole procedure.

In the present study, we performed an en-bloc bladder cuff excision with clear surgical margins for all cases.

Shoma described the use of a purse-string suture in order to secure the bladder, but the author does not recommend this technique for distal ureter UTUC (30).

In the present study we treated 7 distal ureter UTUCs (14%) that did not show evidence of local and bladder recurrence at a mean follow-up of 38 months (range: 6-61 months).

Main limitations of the study included the small number of patients. Points of strength of the present investigation were the prospective study design, the long-term follow-up (38 months), all procedures performed by a single experienced surgeon, the inclusion of all localization sites of UTUCs (rarely reported in literature).

In our opinion, the improvement of this purely laparoscopic technique is to ensure the reduction of surgical trauma, hospital stay and estimated blood loss concurrently with the same oncologic outcomes.

CONCLUSIONS

In our study the described technique was related to a significant reduction in terms of operative time and length of hospital stay, with a faster patients' recovery and no peri and postoperative complications.

The technique enabled complete LNU without patient or port repositioning.

Our study reported successful operative and oncological outcomes with a long-term follow-up. Major limit of this technique is the need of an advanced laparoscopic skill, but the port setup presented gives maximum maneuverability and good visual field in both upper and lower urinary tract surgery without requirement of extra patient or port repositioning.

This technique appears to be safe and feasible; however, studies with longer follow-up periods and larger patient cohorts are required to confirm our findings.

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Correspondence

Yazan Al Salhi

yazan5585@gmail.com

Andrea Fuschi

andrea.fuschi@uniroma1.it

Alessia Martocchia

martocchia.alessia@gmail.com

Gennaro Velotti

gennaro.vel88@gmail.com

Paolo Pietro Suraci

spaolopietro@gmail.com

Silvio Scalzo

silvioscalzo@hotmail.it

Onofrio Antonio Rera

onofrioantonio.rera@uniroma1.it

Alice Antonioni

alice.antonioni@gmail.com

Fabio Maria Valenzi

fabiovalenzi@gmail.com

Giorgio Bozzini

gioboz@yahoo.it

Antonio Carbone

antonio.carbone@uniroma1.it

Antonio Luigi Pastore, MD (Corresponding Author)

antopast@hotmail.com

Urology Unit, Department of Medico-Surgical Sciences and Biotechnologies, Faculty of Pharmacy and Medicine, Sapienza University of Rome, 04100 Latina, Italy