

Original Article

Three-port retroperitoneal laparoscopic complete nephroureterectomy with bladder-cuff resection for treatment of upper urinary tract malignant tumors

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Abstract: Aim: To explore the surgical safety, efficacy and curative effects of the modified three-port retroperitoneal laparoscopic completely nephroureterectomy with bladder-cuff resection surgery in treatment of upper urinary tract urothelial carcinoma. Methods: Cancer patients received either modified three-port surgery or traditional laparoscopic operation were retrospectively selected from January 2015 to December 2017. The baseline information and safety profiles of operative procedures were collected. Cystoscopy was performed on all patients 10-14 days after operation. The urine test and cystoscopy were reviewed every 3 months after operation, and the abdominal computed tomography was reviewed every 6 months. Results: A total of 46 patients were included, of which 28 were managed with three-port retroperitoneal laparoscopic completely nephroureterectomy with bladder-cuff resection (modified method), while another 18 cases adopted retroperitoneal laparoscopy combined with the open lower abdominal incision (traditional method). The baseline information was comparable between the two groups. Operations of both groups were successfully completed without serious operative complications. Compared with the traditional method, the modified three-port method has shorter operation time (268 min vs 180 min, $p=0.002$) and less intraoperative blood loss (70 mL vs 225 mL, $p=0.001$). Besides, in the same period, no recurrence was found in the modified three-port group, whereas five cases recurred in the retroperitoneal laparoscopy combined with radical operation of ureteral carcinoma with lower abdominal incision, including one case of urinary tract recurrence and one case of intravesical recurrence. Conclusion: The modified three-port method is a safe, convenient and effective way of operation to manage upper urinary tract carcinoma.

Keywords: Laparoscopy, nephroureterectomy, retroperitoneal space, urinary tract cancer, urothelial carcinoma

Introduction

Urothelial carcinoma is one of the most common malignant tumors, of which the upper urinary tract urothelial carcinoma (UTUC), including renal pelvis carcinoma and ureteral cancer, accounts for 5-10% of this type of cancer [1]. The gold standard surgical treatment for upper urinary tract urothelial carcinoma is open radical nephroureterectomy and bladder-cuff resection with the ureteral orifice [2]. Laparoscopic nephroureterectomy was proposed by Clayman in 1991 [3]. Currently, laparoscopic surgery is popularized by its advantages such as minimal invasion, less bleeding, and faster recovery, and also the comparable long-term effects as open surgery. The procedure has gradually replaced open surgery and become

the major surgical method for upper urinary tract tumors.

However, traditional laparoscopic nephroureterectomy is divided into two phases: laparoscopic nephrectomy and proximal ureterectomy, and open excision of the distal ureter and bladder-cuff resection [4]. This surgical procedure not only requires changes in body position of the patient during the operation, prolonging the duration of operation, but also increases the risk of tumor metastasis as the extravasation of urine containing tumor cells may occur in the process of removing the ureter. Therefore, it has become the focus of urologists to reduce the patient's intraoperative position changes, and mitigate the risk of metastasis in the course of implantation so as to ensure safer

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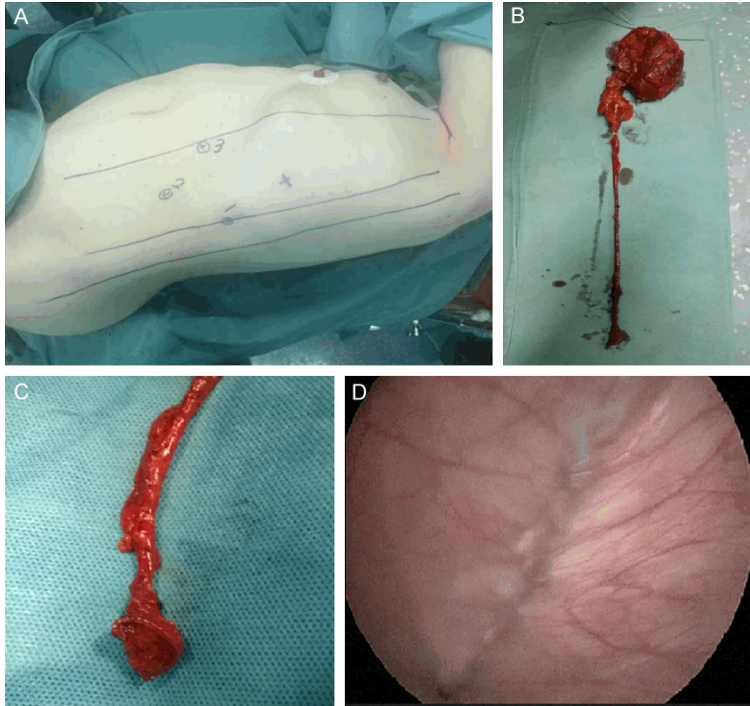


Figure 1. A: Operation position and distribution of the three portal sites for radical resection of upper urinary tract cancer by three-port retroperitoneal laparoscopic completely nephroureterectomy with bladder-cuff resection. (The first point was the intersection between the costal margin and the vertical line 2 cm away from the posterior part of anterior superior iliac spine. The second point was 2 cm away from the intersection between the anterior axillary line and the vertical line 2.5 cm away from the anterior part of anterior superior iliac spine. The third point was marked through horizontal extension of 9 cm toward the ventral side from the first point. An isosceles triangle was presented finally following the determination of the above three points). B: Full length of the ureter via surgical resection. C: A close-up image of the cuff of the bladder by surgical excision. D: No stone formation in suture under cystoscopy 6 months after the operation.

and more efficient laparoscopic nephroureterectomy. These procedures facilitate access to better and long-term postoperative treatment effects for patients with UTUC.

This study aims to explore the surgical safety, efficacy and curative effects of our three-port retroperitoneal laparoscopic complete nephroureterectomy with bladder-cuff resection surgery in treatment of upper urinary tract urothelial carcinoma. Therefore, an analytical comparison was made in the study between 28 cases treated with three-port retroperitoneal laparoscopic completely nephroureterectomy with bladder-cuff resection for localized upper urinary tract carcinoma and 18 cases managed with retroperitoneal laparoscopy combined with the open lower abdominal incision for radical treatment of ureteral carcinoma from

January 2015 to December 2017 from several aspects such as the convenience, safety, and short-term efficacy of the operation.

Patients and methods

Patients

This study was a single-center retrospective study. From January 2015 to December 2017, a total of 46 patients postoperatively or preoperatively diagnosed with UTUC were included, of which 28 were managed with three-port retroperitoneal laparoscopic complete nephroureterectomy with bladder-cuff resection (modified method), while another 18 cases adopted retroperitoneal laparoscopy combined with the open lower abdominal incision (traditional method) for radical treatment of ureteral carcinoma. All patients did not receive anti-tumor therapy before surgery and all involved in this study gave their informed consent. This study was approved by the Institutional Ethics Committee of our hospital.

Surgical procedures of three-port retroperitoneal laparoscopic completely nephroureterectomy with bladder-cuff resection

All cases underwent operations under general anesthesia. The patient was kept at a 30-degree tilt position from the contralateral side to the dorsal side, while holding a head-down and feet-down position, heightening of the waist bridge, and fully extending the affected side of the waist. The operative position and distribution of the three portal sites are shown in **Figure 1A**. Perirenal fascia was exposed and separated subsequently from the dorsal side of the kidney using an ultrasonic knife. Renal hilum was dissociated bluntly using a suction apparatus from the posterior part of the kidney. The renal artery and vein were cut off after detaching and clipping through Hem-o-lok. Ureter was found

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Table 1. Patients' clinicopathologic characteristics stratified by surgical procedure

| Total | Surgical procedure | | p Value | |
|--------------------------|--------------------|--------------------|-------------|-------|
| | Modified method | Traditional method | | |
| Gender, n (%) | | | | |
| Male | 27 | 17 (62.96%) | 10 (37.04%) | 0.057 |
| Female | 19 | 11 (57.89%) | 8 (42.10%) | 0.259 |
| Age (yr) | | | | |
| Median | 73 | 75.5 | 71.5 | 0.149 |
| Laterality, n (%) | | | | |
| Right | 23 | 11 (47.83%) | 12 (52.17%) | 0.768 |
| Left | 23 | 17 (73.91%) | 6 (26.09%) | 0.001 |
| Tumor Location, n (%) | | | | |
| Renal Pelvis | 12 | 8 (66.67%) | 4 (33.33%) | 0.110 |
| Ureter | 34 | 20 (58.82%) | 14 (41.18%) | 0.146 |
| Tumor Grade, n (%) | | | | |
| G3 | 35 | 21 (60%) | 14 (40%) | 0.094 |
| G1-2 | 10 | 7 (70%) | 3 (30%) | 0.089 |
| pT Stage, n (%) | | | | |
| pTa/Tis | 9 | 6 (66.67%) | 3 (33.33%) | 0.173 |
| pT1 | 10 | 6 (60%) | 4 (40%) | 0.328 |
| pT2 | 11 | 6 (54.55%) | 5 (45.45%) | 0.500 |
| pT3 | 12 | 8 (66.67%) | 4 (33.33%) | 0.110 |
| pT4 | 3 | 2 (66.67%) | 1 (33.33%) | 0.500 |
| pN classification, n (%) | | | | |
| N0 | 35 | 21 (60%) | 14 (40%) | 0.094 |
| N1 | 2 | 0 (0%) | 2 (100%) | 0.167 |
| N2 | 1 | 0 (0%) | 1 (100%) | 0.500 |
| Nx | 5 | 5 (100%) | 0 (0%) | 0.004 |

along the surface of the psoas major muscle. The upper segment of the ureter was clipped with Hem-o-lok without cut off, followed by dissociation toward the distal end of the ureter. The lens was turned so that the second screen (Attached monitoring screen) of the foot side could be visible to the surgeon. The ureter was kept on detaching to the inner segment of the bladder wall to expose the part of the bulge. The ureter and partial bladder wall were cut off using an Endo-GIA vascular stapler under laparoscope (30 mm, blue). Complete general specimen (**Figure 1B**) of renal ureter was extracted through enlarged casing inserted incision (12 mm) under the ribbed edge. Visual inspection was performed to confirm whether the distal end of the ureter and the part via bladder-cuff excision were removed completely or not. A close-up image of the Cuff of the bladder by surgical excision was shown in **Figure 1C**. The incision was sutured after successful hemosta-

sis and placement of a retroperitoneal drainage tube.

Safety and postoperative follow-up

Cystoscopy was performed on all patients 10-14 days after operation to determine whether the bladder tissue around the ureteral orifice was adequately removed and whether there was any bladder stump fistula. The urine routine test, urine cytology and cystoscopy were reviewed every 3 months after operation, and the abdominal CT was reviewed every 6 months. No stone was formed in suture under cystoscopy 6 months after operation (**Figure 1D**).

Statistical methods

The clinicopathological features of the two groups (modified method and traditional method) were compared with the X^2 test for categorical variables and the Kruskal Wallis test for

continuous variables. The postoperative survival rate was assessed by Kaplan Meier, and the logarithmic rank test was used for comparison between groups. The analysis of tumor prognosis mainly included tumor cause-specific survival (CSS) rates, recurrence-free survival (RFS) rates, and metastasis-free survival (MFS) rates. All test were bilateral, with $p < 0.05$ indicating a significant statistical difference. Statistical analysis was carried out by the statistical software package SPSS 22.0 (IBM Corp., Somers, NY, USA).

Results

Baseline information of patients

The baseline clinicopathological features of all patients are summarized in **Table 1**. No significant difference in the baseline information was observed between patients who underwent

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Table 2. Comparison of safety profile based on surgical procedure

| Total | Surgical procedure | | | p Value |
|-------------------------------------------------|--------------------|--------------------|------------|---------|
| | Modified method | Traditional method | | |
| Operative time, median | 225 min | 180 min | 268 min | 0.002 |
| Intraoperative blood loss, median | 110 mL | 70 mL | 225 mL | 0.001 |
| Indwelling time of drainage tube, median | 5 d | 4 d | 6 d | 0.072 |
| Length of stay in hospital, median | 20.5 d | 17.5 d | 22.5 d | 0.195 |
| Incidence of intraoperative complication, n (%) | 5 (10.87%) | 1 (3.57%) | 4 (22.22%) | 0.047 |
| Incidence of perioperative complications, n (%) | 2 (4.35%) | 0 (0%) | 2 (11.11%) | 0.148 |
| Postoperative recurrence, n (%) | 5 (10.87%) | 0 (0%) | 5 (27.78%) | 0.004 |

the modified three-port method and those treated with traditional method. Among them, 1 case died ten months after surgery due to acute cerebral hemorrhage and 1 case died of unexplained renal failure three months after the operation.

Safety of operation

Information including the operation duration, intraoperative blood loss, average length of hospital stays, and intraoperative complications of the two groups are summarized in **Table 2**. The median operative duration of the modified group was 180 minutes and that of the traditional group was 268 minutes. The difference was statistically significant as the operative duration of the modified method was obviously shorter than that of the traditional method. The intraoperative blood loss was 70 mL in the modified three-port method and 225 mL in the traditional method. Statistically significant differences were observed as the modified method caused less blood loss than the traditional operation. The incidence of intraoperative complications was 3.57% and 22.22% for the modified and traditional method, respectively, showing obvious statistical difference. Specifically, one case with three-port method developed a rupture of peritoneum, while 4 cases of peritoneal rupture occurred in the traditional group. Among patients treated with the traditional method, one had 1500 ml blood loss during the operation due to dense adhesion and unclear anatomy in renal hilum, and was then treated with Endo-GIA vascular stapler until the renal hilum was disconnected. Another developed iliac vein rupture with 1500 ml blood loss and was subsequently given vascular suture to stop bleeding.

During the perioperative period, no patients were found with complications including intesti-

nal obstruction, secondary bleeding, incisional infection, or intestinal fistula.

Comparison of short-term curative effect

In general, no patients had tumor-related deaths due to the relatively short period of follow-up, and two patients died of other causes.

During the follow-up period, none of the twenty-eight patients had recurrence in the modified three-port method group. While in the traditional group, no tumor relapse was observed except that one was found with recurrence around the primary lesion, one with retroperitoneal lymph node metastasis four months after surgery, one with bladder tumor six months after treatment, one with urethral tumor eleven months after the surgery, and one with renal hilar lymph node a year after the operation.

Discussion

For patients with normal contralateral kidney function and no metastatic diseases, nephroureterectomy and bladder-cuff resection remains the gold standard for UTUC. The methods for bladder-cuff resection vary considerably since views on the therapeutic role and the removal degree of lymph node resection are divergent. Based on oncologic results, different methods for excision of distal ureter with bladder-cuff for UTUC during radical nephroureterectomy (RNU) were evaluated. It has been revealed in a retrospective analysis by Xylinas et al. in which 2,681 patients who were treated with RNU underwent excision of distal ureter with bladder-cuff with transvesical, or extravesical, or endoscopic methods that there was no difference in oncologic results in terms of CSS, RFS, and OS among these three types of bladder-cuff resections [5]. A prospective randomized study which compared open RNU and lapa-

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roscopic nephroureterectomy (LNU) has reported that the LNU group has better perioperative outcomes, less blood loss, and shorter hospital stay than the open RNU group. Although it has been suggested that patients with locally advanced diseases may benefit from open surgery, the oncological outcomes of organ-limited disease in both groups were found to be similar during the median follow-up of 44 months [6]. Several studies have also shown that the multi-mode approach is beneficial to improve the prognosis of patients with locally advanced diseases [7], as is discussed below.

Currently, radical laparoscopic nephrectomy has multiple operative approaches, including the common Bishoff method of laparoscopy combined with open surgery [8]. In 1999, a complex radical laparoscopic nephroureterectomy was reported by Gill et al. [9, 10]. In their report, the patient in a lithotomy position received a bladder puncture via the lower abdomen, two 5-mm cannulae were then implanted immediately, one with grasping forceps and the other with lasso. A transurethral catheterization of ureter was further performed with cystoscope by another surgeon, followed by an electro-excision to dissociate the intravesical segment of ureter by 3-4 cm under the assistant of the transvesical grasping forceps. Afterwards, the distal isolated segment was captured by lasso and was soon tightened up. The entire ureter wall was free from the bladder. This method can effectively prevent the extravasation of urine in the upper urinary tract, but urine containing tumor cells in the bladder may still leak into the abdominopelvic cavity, resulting in the spread of the tumor. In addition, changes of patients' position were involved during the operation, resulting in significant complicated preoperative preparation with certain risks. In China, the most commonly used surgical procedure is laparoscopic nephrectomy combined with transurethral electro-resection of bladder mucosa surrounding the bladder orifice [11-13]. Similar to the operation reported by Gill et al., this procedure also required intraoperative change of body position. To be specific, patients received ureter catheterization via a cystoscope in a lithotomy position, followed by a separation of the inner segment of ureter wall from bladder by ring-shaped electric resection. The end of the free ureter was pushed outward and the laparoscopic nephroureterectomy was performed

after changing the position of the patient. Therefore, the operation also has the risk of tumor dissemination and safety risk. In order to solve the problems existing in the above surgical procedures, McDougall et al. [14] performed a sleeve resection of the bladder tissue around the ureteral orifice in 10 patients with an Endo-GIA vascular stapler, in combination with the closure of the stump at the time of resection to avoid extravasation of urine containing tumor cells in bladder. No postoperative tumor dissemination occurred in 10 patients. A follow-up study by Chandhoke et al. [15] on this procedure also confirmed that no exposure of anastomotic nail or stone formation were observed under cystoscopy 3-9 months after the operation.

In the present study, three-port retroperitoneal laparoscopic completely nephroureterectomy with bladder-cuff resection was adopted for treatment. Perirenal fascia was exposed and then separated from the dorsal side of the kidney using an ultrasonic knife. With dissociation of renal hilum bluntly using suction apparatus from the posterior part of kidney, renal artery and vein were cut off after detaching and clipping through Hem-o-lok. Then, the upper segment of the ureter was clipped with Hem-o-lok without cut off, followed by dissociation toward the distal end of the ureter. Furthermore, the ureter and partial bladder wall were cut off using Endo-GIA vascular stapler under laparoscope (30 mm). Complete general specimen of renal ureter was extracted through enlarged casing-inserted incision (12 mm) under the ribbed edge. In this operation, there was no requirement to change the position of the patient, leading to improvement in the complicated preoperative preparation and reduction of the safety risk of patients significantly. In addition, Hem-o-lok was used first to locate and clip the upper ureter at the beginning of location, and then the bladder incision was closed with an Endo-GIA vascular stapler to prevent the extravasation of tumor-containing urine. Finally, the operation was completed by laparoscopy, with smaller trauma and less intraoperative bleeding. Additionally, the apparatus and equipment used in the surgery were the same as traditional laparoscopic nephrectomy, which not only reduce patients' pain but also maintain the financial burden.

In addition, in order to reduce the risk of tumor spread and grafting, complete organ removal

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was also implemented in our study, and the original laparoscopic radical nephrectomy was developed to laparoscopic nephroureterectomy. Unlike the previous direct removal of kidney that carried tumor tissues, the whole affected kidney was placed into a sac via an incision of about three inches in length. The sac was made up of well-sealed plastic and two non-malleable nylon layers which was strong and durable [16]. In the laboratory, the sac wrapped outside was intact under laparoscope in the process of cutting the whole kidney at high speed, which was further confirmed by our clinical trial.

In this study, the operations of two groups of patients were successfully completed without serious operative complications, all of which were safe and reliable. Compared with the traditional method, the modified three-port method had a shorter operation time and less intraoperative blood loss. Furthermore, in the same period, no recurrence was found in the modified three-port group, whereas five cases recurred in the retroperitoneal laparoscopy combined with radical operation of ureteral carcinoma with lower abdominal incision, including one case of urinary tract recurrence and one case of intravesical recurrence. It has been suggested that the modified three-port method is more convenient and safer, and it may have a good effect on preventing the recurrence of UTUC in patients.

Conclusion

In conclusion, for patients with malignant tumor of upper urinary tract, the modified three-port method is a safe, convenient, and effective way of operation based on our experience. In theory, it can effectively prevent the leakage of urine and reduce the incidence of local recurrence in such as the urethra or the bladder.

Acknowledgements

This study was approved by the Institutional Ethics Committee of Aerospace Center Hospital and had been performed in accordance with the ethical standards as laid down in the 1964 Declaration of Helsinki and its later ethical standards. All patients involved in this study gave their informed consents.

Disclosure of conflict of interest

None.

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References

- [1] Vikram R, Sandler CM, Ng CS. Imaging and staging of transitional cell carcinoma: part 2, upper urinary tract. *AJR Am J Roentgenol* 2009; 192: 1488-1493.
- [2] Mandalapu RS, Matin SF. Contemporary evaluation and management of upper tract urothelial cancer. *Urology* 2016; 94: 17-23.
- [3] Clayman RV, Kavoussi LR, Figenschau RS, Chandhoke PS, Albala DM. Laparoscopic nephroureterectomy: initial clinical case report. *J Laparoendosc Surg* 1991; 1: 343-9.
- [4] Yao L, Yang K, Li X, Zhang Z, Zhang C, Gong K, Xi Z, He Z, Zhou L. Comparison between completely and traditionally retroperitoneoscopic nephroureterectomy for upper tract urothelial cancer. *World J Surg Oncol* 2016; 14: 171.
- [5] Xylinas E, Rink M, Cha EK, Clozel T, Lee RK, Fajkovic H, Comploj E, Novara G, Margulis V, Raman JD, Lotan Y, Kassouf W, Fritsche HM, Weizer A, Martinez-Salamanca JI, Matsumoto K, Zigeuner R, Pycha A, Scherr DS, Seitz C, Walton T, Trinh QD, Karakiewicz PI, Matin S, Montorsi F, Zerbib M, Shariat SF; Upper Tract Urothelial Carcinoma Collaboration. Impact of distal ureter management on oncologic outcomes following radical nephroureterectomy for upper tract urothelial carcinoma. *Eur Urol* 2014; 65: 210-217.
- [6] Simone G, Papalia R, Guaglianone S, Ferriero M, Leonardo C, Forastiere E, Gallucci M. Laparoscopic versus open nephroureterectomy: perioperative and oncologic outcomes from a randomised prospective study. *Eur Urol* 2009; 56: 520-526.
- [7] Seisen T, Granger B, Colin P, Leon P, Utard G, Renard-Penna R, Comperat E, Mozer P, Cussenot O, Shariat SF, Rouprêt M. A systematic review and meta-analysis of clinicopathologic factors linked to Intravesical recurrence after radical nephroureterectomy to treat upper tract urothelial carcinoma. *Eur Urol* 2015; 67: 1122-1133.
- [8] Bishoff JT, Kavoussi LR. *Ahas of laparoscopic retroperitoneal surgery* M I. Philadelphia: WB Saunders 2000: 130-136.
- [9] Gill IS, Soble JJ, Miller SD, Sung GT. A novel technique for management of the en bloc bladder-cuff and distal ureter during laparoscopic nephmureterectomy. *J Urol* 1999; 161: 430-434.

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- [10] Gill IS, Sung GT, Hobart MG, Savage SJ, Meraney AM, Schweizer DK, Klein EA, Novick AC. Laparoscopic radical nephroureterectomy for upper tract transitional cell carcinoma: the Cleveland Clinic experience. *J Urol* 2000; 164: 1513-1522.
- [11] Men QL, Liu JZ, Luo XH, et al. Effect of laparoscopic radical resection of renal pelvic carcinoma combined with electric resection. *Journal of Clinical Medicine in Practice* 2016; 20: 138-139.
- [12] Zhang SY, Jin TX. Retroperitoneal laparoscopic radical resection of renal pelvic carcinoma: a clinical analysis of 38 cases. *Journal of Jilin Medical College* 2016; 37: 28-30.
- [13] Wang JT, Zhang CH, Yu SQ, et al. Retroperitoneal laparoscopic nephrectomy combined with transurethral electrocoagulation for upper urinary tract urothelial carcinoma: a prospective clinical controlled study. *Chinese Journal of Urology* 2014; 35: 905-908.
- [14] McDougall EM, Clayman RV, Elashry O. Laparoscopic nephroureterectomy for upper tract transitional cell cancer: the washington university experience. *J Urol* 1995; 154: 975-9; discussion 979-80.
- [15] Chandhoke PS, Clayman RV, Kerbl K, Figenschau RS, McDougall EM, Kavoussi LR, Stone AM. Laparoscopic ureterectomy: initial clinical experience. *J Urol* 1993; 149: 992-997.
- [16] Urban DA, Kerbl K, McDougall EM, Stone AM, Fadden PT, Clayman RV. Organ entrapment and renal morcellation: permeability studies. *J Urol* 1993; 150: 1792.