

Surgical techniques and oncologic outcomes of pure transperitoneal laparoscopic radical nephroureterectomy for upper urinary tract urothelial carcinoma

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Abstract

Introduction: To discuss the clinical feasibility and oncologic outcomes of pure transperitoneal laparoscopic radical nephroureterectomy (LSRNU) for upper urinary tract urothelial carcinoma (UTUC).

Methods: Between July 2010 and December 2020, 115 patients were admitted to the hospital with a diagnosis of UTUC treated with pure LSRNU by one surgeon. A special laparoscopic bulldog clamp was placed at the bladder cuff before cutting and suturing. The clinical and follow-up data were preoperatively collected and analyzed. Overall survival (OS) and cancer-specific survival (CSS) were estimated by the Kaplan–Meier method.

Results All surgeries were completed uneventfully. The mean operative time was 145.69 minutes. The mean estimated blood loss was 56.61 ml. The mean removal time of the drain was 3.46 days. The mean time to liquid diet was 1.32 days, and the ambulation time was 1.50 days. All surgeries were effectively completed, and no case required open conversion. According to the Clavien–Dindo classification system, postoperative complications occurred in two patients (II, III). The mean length of postoperative hospital stay was 5.78 days. The median follow-up duration was 54.50 months. Recurrence in the bladder was 16.0% (15/94), compared with 4.6% (4/87) in the contralateral upper tract. The 5-year OS and CSS rates were 78.9% and 81.4%, respectively.

Conclusion Pure transperitoneal laparoscopic RNU is a safe and effective minimally invasive technology for the management of UTUC.

Introduction

Upper urinary tract urothelial carcinomas (UTUCs) are uncommon and account for only 5–10% of urothelial carcinomas[1]. Open radical nephroureterectomy (RNU) with bladder cuff excision is the standard treatment for UTUC, regardless of tumor location[2]. With the advancements of surgical instruments and laparoscopic techniques, laparoscopic RNU is also safe in experienced hands. There is a tendency towards equivalent clinical outcomes after laparoscopic or open surgery[3, 4]. Even after RNU, recurrence in the bladder occurs in 22–47% of UTUC patients[5], compared with 2–6% in the contralateral upper tract[6]. Five-year cancer-specific survival (CSS) rates are only 50–80%[7, 8].

At present, LSRNU is performed by laparoscopic nephrectomy and the management of the distal ureter by open excision or transurethral resection, and so on. Therefore, the conventional laparoscopic approach includes changing the position, disinfection, and drape once again. We innovatively adopted a pure laparoscopic procedure with a single position[9] of the RNU with bladder cuff excision. This approach is minimally invasive, avoids unnecessary operations, reduces infection risk and shortens the learning curve and operative time[10, 11]. We conducted this study to identify the oncological outcomes, including overall survival (OS) and cancer-specific survival (CSS), of pure transperitoneal LSRNU for UTUC.

Materials And Methods

Clinical materials

Between July 2010 and December 2020, 115 patients were admitted to the hospital with a diagnosis of UTUC treated with pure LSRNU by one surgeon. Lymph node dissection was conducted when lymph node metastasis was suspected in the preoperative evaluation or enlarged lymph nodes were found during surgery. We retrospectively collected demographic and perioperative data as well as follow-up data. Patients were assessed on preoperative imaging studies, such as chest X-ray, urinary ultrasound and computed tomography urography (CTU), were used routinely. None of these patients had concomitant bladder tumors. Tumors were pathologically staged based on the 2009 TNM classification of malignant tumors, and pathological grades were determined according to the 1973 World Health Organization (WHO) classifications. This study was approved by the Ethics Committee of Peking University First Hospital, and informed consent was obtained from all patients.

Surgical technique

Under general anesthesia, the patient was placed in the 45°~60° lateral position with the lesion side upside (take the left as an example). Access was achieved on the left midclavicular line at the subcostal margin using a Veress needle, and the abdominal ports were placed (Fig. 1a). The pneumoperitoneum pressure was maintained at 14 mmHg. A 12-mm trocar for the camera was placed 3 cm above the umbilicus, and the other 12-mm trocar was placed 3 cm below the umbilicus at the outer border of the left rectus abdominis. Then, another 12-mm trocar at the reverse McBurney point, as the main trocar, was used by the surgeon. A 5-mm trocar was placed along the Veress needle. If the lesion was on the right, the trocar was placed symmetrically. An additional 5-mm trocar for retraction of the liver was necessarily placed inferior to the xiphoid at the midline.

After mobilization of the colon, the renal pedicle was located through the gonadal veins and ureter. The renal hilum was fully dissociated, clipped and dissected with Endo-GIA, and the gonadal veins were dissected at the same time. Radical nephrectomy was performed by fully dissociating the affected kidney and retaining the ipsilateral adrenal gland. An additional 12-trocar was placed in the midline of the lower abdomen to dissect the distal ureter and bladder wall without position changes. The ureter was clipped distal to the tumor site by hem-o-lock to avoid tumor seeding. The ureter was further dissected carefully over the iliac vessels down to the detrusor muscle fibers of the ureterovesical junction (Fig. 1b). An intramural ureter and tent-shaped bladder cuff were formed with retraction of the bladder wall. A special laparoscopic bulldog clamp was innovatively used by our center[12] (Fig. 1c), which was placed at the bottom of the tent-shaped structure in case of urine spillage (Fig. 1d). Once the intramural ureter was separated from the surrounding detrusor muscle and down to the bladder mucosa, the intramural ureter and tent-shaped bladder mucosal cuff could be detected by retraction in the superior and lateral directions. A bladder cuff was incised, and closure was performed in a two-layer running manner using a barbed suture (Fig. 1e). After finishing the suture, the bulldog clamp was removed. Finally, the dissected specimen was extracted en bloc.

Postoperative management and follow-up

After the operation, patients received an urethral Foley catheter and pelvic drain. The urethral Foley catheters was removed within 1 week. The pelvic drain was usually removed when the output was < 50 mL after the operation. Scheduled follow-up occurred every three months for 1 year, every six months in the next 3 year, and annually after surgery by a definite telephone interview or clinical visit. Routine blood and urine tests, urine cytology, cystoscopy, and physical examination were performed at each visit. Imaging evaluations, including CT or MRI, were performed every six months for the first five years and then annually thereafter.

Statistical analysis

Statistical analysis was performed with SPSS software (IBM Corporation, Armonk, NY, USA, version 25.0). Categorical variables were shown as frequency. Parametric variables are shown as the mean \pm standard deviation ($m \pm s$). OS and CSS were estimated by the Kaplan–Meier method.

Results

The pathological characteristics of the patients are shown in Table 1. A total of 115 patients were included in the current study (58 males and 57 females). The mean age of patients was 68.9 years (range 35–88). The mean body mass index (BMI) was 24.6 kg/m², and the mean ASA was 2.2 (range 1–4). Pathologic analysis showed that 65 (56.5%) were G2 and 50 (43.5%) were G3. Staging revealed 52 (45.2%) patients with pTis-1, 38 (33.0%) with pT2, 24 (20.9%) with pT3, and 1 (0.9%) with pT4. There were more ureteral tumors (50.4%) than renal pelvis tumors (40.9%), and both accounted for 8.7%. 18 (15.7%) patients with multifocal tumors. Seven patients (6.1%) had positive lymph nodes, and one patient was found to have positive surgical margins. The surgical and oncological results are described in detail in Table 2. All surgeries were effectively completed, and no case required open conversion. The mean operative time was 145.69 minutes. The mean estimated blood loss was 56.61 ml. The mean drainage time was 3.46 days. The mean liquid diet time was 1.32 (1–4) days, and the ambulation time was 1.50 (1–5) days. The mean hospital stay was 5.78 days. According to the Clavien–Dindo classification system, two patients experienced a postoperative complication. One patient with symptoms of urine leakage (C-D II) disappeared completely by using antibiotics, and draining unobstructed quickly. The other patient with postoperative intestinal obstruction (C-D III) was treated by laparoscopic enterolysis. The mean length of postoperative hospital stay was 5.78 days.

Table 1
Pathological characteristics of patients.

No. of patients	115
Mean age (range)	68.9 (35–88)
BMI (kg/m ²)	24.6 ± 3.85
Sex	
Males	58 (50.4%)
Females	57 (49.6%)
Side	
Left	59 (51.3%)
Right	56 (48.7%)
Ureteroscopy	
Yes	23 (20%)
No	92 (80%)
ASA score	
1	11 (9.6%)
2	76 (66.1%)
3	26 (22.6%)
4	2 (1.7%)
Tumor site	
Renal pelvis	47 (40.9%)
Ureter	58 (50.4%)
Both	10 (8.7%)
Multifocality	
Yes	18 (15.7%)
No	97 (84.3%)
T stage, n (%)	
CIS, Ta, T1	52 (45.2%)
T2	38 (33.0%)

No. of patients	115
T3	24 (20.9%)
T4	1 (0.9%)
Grade, n (%)	
G1	0
G2	65 (56.5%)
G3	50 (43.5%)
Lymph node, n (%)	
N+	7 (6.1%)
N0 or Nx	108 (93.9%)
Surgical margins	
Negative	114
Positive	1

Table 2
Surgical details and perioperative data and follow-up data.

Parameter	data
Mean operative time, min	145.69 ± 50.60
Median estimated blood loss, ml,	56.61 ± 62.23
mean drain time, days,	3.46 ± 1.33
Liquid diet, days, range	1.32 (1–4)
Ambulation, days, range	1.50 (1–5)
postoperative length of stay, d	5.78 ± 3.77
Complication rate, Clavien-Dindo grade, n	II, 1; III, 1
Follow-up, n	102
Follow up time, months	54.50 ± 32.32
Bladder Recurrence	16.0%
Contralateral Recurrence	4.6%
5-year OS	78.9%
5-year CSS	81.4%

The median follow-up duration was 54.5 months. Among 115 patients, 13 patients were lost to follow-up, 27 patients died, and 20 of them died of the tumor. Recurrence in the bladder was 16.0% (15/94), compared with 4.6% (4/87) in the contralateral upper tract. The 5-year OS and CSS rates were 78.9% and 81.4%, respectively (Fig. 2). At the follow-up, cystoscopy (usually 3 months after surgery) showed that the affected side of the ureteral orifice disappeared (Fig. 3).

Discussion

Upper urinary tract urothelial carcinoma (UTUC) is a malignant tumour of the urologic system with a relatively low incidence and poor prognosis. In terms of the surgical approach, open RNU with bladder cuff excision is the gold standard treatment. However, with the advancements of surgical instruments and the development of laparoscopic techniques, laparoscopic RNU, as a more minimally invasive surgical approach, is gradually becoming mainstream for UTUC in experienced hands and can acquire similar oncological outcomes compared with open surgery[3, 4].

The traditional laparoscopic approach is performed with at least three trocar incisions and one large incision and. Many surgeons hesitate to use laparoscopic procedures for the distal ureter because the pelvic ureterovesical junction is deep, which subsequently converts to open bladder cuff excision with at least an 8 cm incision. Therefore, the traditional laparoscopic approach still causes significant surgical trauma,. To pursue more minimally invasive surgery, these procedures can be achieved with one incision just for removing specimens when pure LSRNU emerges[13].

What the essential procedure of RNU is the management of bladder cuff. As we all know, several techniques have been deemed to simplify the resection of distal ureter, including the pluck technique, intussusception, stripping, and transurethral resection of the intramural ureter. Although each technique has its strengths and weaknesses, till now none of these techniques has convincingly been displayed to be equal to complete bladder cuff excision[6, 14]. Additionally, the extravesical stapling technique is a pure laparoscopic approach, which has shorter operative time and keeps the urinary system closed to avoid tumor spread. Meanwhile, some literatures had shown higher incidences of positive surgical margins and local recurrence compared to other techniques of bladder cuff excision[15, 16]. Therefore, it is necessary optimize this pure laparoscopic technique to reduce surgical trauma and improve oncological outcomes.

Our technique is an innovative modification of pure LSRNU that highlights its advantages. First, the custom-made laparoscopic bulldog clamp helps the surgeon finish the en bloc removal of the complete distal ureter and bladder cuff, similar to the open technique, without opening the urinary tract to prevent tumor spillage. This conforms to the oncological principle because enough bladder cuff is guaranteed by the approach[12]. Second, by adding a trocar at the midline of the lower abdomen, surgeons are able to gain enough vision and perform precise bladder cuff excision with the patient remaining in the same position. The bulldog clamp accompanied by suturing rather than Endo-GIA with staples could prevent bladder stones from happening to a certain extent. Finally, this technique is not only a more minimally

invasive incision in the lower abdomen but also avoids unnecessary operations and in theory reduces the risk of infection without changing the position, disinfection or drape once again.

Several studies have demonstrated that a single dose of intravesical chemotherapy 2–10 days after surgery reduces bladder tumor recurrence[17]. Therefore, a single dose of intravesical chemotherapy was performed postoperatively. For the oncological outcomes, the Kaplan–Meier analyses showed that the 5-year OS and CSS of pure transperitoneal LSRNU were 78.9% and 81.4%, respectively. This study has relatively better outcomes than some traditional LSRUNs[18, 19]. It has been reported that recurrence in the bladder occurs in 22–47% of UTUC patients[5], compared with 2–6% in the contralateral upper tract[6]. Recurrence in the bladder was 16.0%, compared with 4.6% in the contralateral upper tract in our study. Therefore, excellent oncological outcomes are displayed by our techniques. This is the largest and longest follow-up study among pure LSRNU without patient repositioning for UTUC.

In addition, several authors have described pure robot-assisted RNU with good clinical outcomes[20]. If our technique could be adopted in robot-assisted surgery, it might decrease the difficulty of intracorporeal suturing. However, a high cost restricts the availability of robots in China.

There were several limitations in our study. First, the retrospective study was performed in a single medical center in China, which may cause a potential selection bias. A larger number of series and more extended follow-up periods are needed to confirm these results and achieve further evidence about the clinical effect of pure transperitoneal LSRNU for UTUC. We are optimistic that this initial report can serve as a foundation for developing optimal treatment for UTUC.

Conclusions

Pure transperitoneal LSRNU is an effective treatment for UTUC, with no change in body position to complete resection in the distal ureter and bladder wall section. It not only confers oncological principles but is also simple, safe, and feasible. Therefore, this technique possesses clinical practice value and is worth popularizing and utilizing. More trials and longer follow-up are needed for further confirmation.

Declarations

Ethics approval and consent to participate

The protocol of this research has been approved by the Ethics Committee of Peking University First Hospital, approval number (NO.2021130). All methods were performed in accordance with the Declaration of Helsinki. All patients have signed written informed consent.

Consent for publication

Not applicable.

Availability of data material

The datasets generated and/or analysed during the current study are not publicly available due to privacy or ethical restrictions but are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no conflicts of interest.

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Not applicable.

Authors' contributions

Conception and design: D Fang, XS Li; Administrative support: LQ Zhou; Provision of study material: CJ Zhang, YC Du; Data collection or management: WJ Zhu, C Meng; Data analysis: CR Xu, J Wang; Manuscript writing: CW Yuan.

Final approval of manuscript: All authors.

All authors have read and approved the manuscript.

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Figures

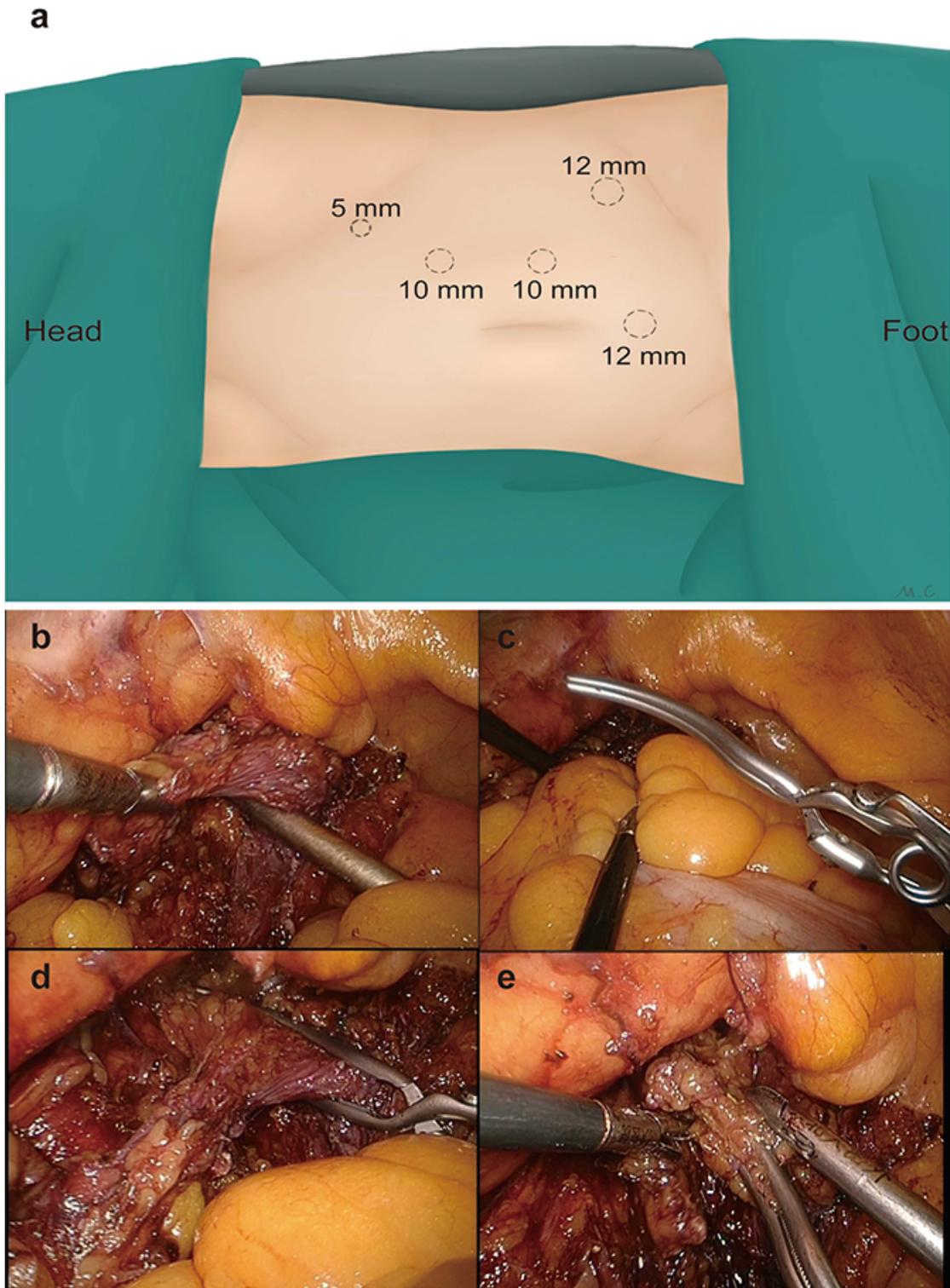


Figure 1

Description of pure transperitoneal LSRNU for UTUC. a. Operative position and trocar distribution. b. the distal of ureter. c. A bulldog clamp. d. A bulldog clamp was placed at the bottom of the tent-shaped structure. e. Bladder closure was performed in a two-layer running manner using a barbed suture.

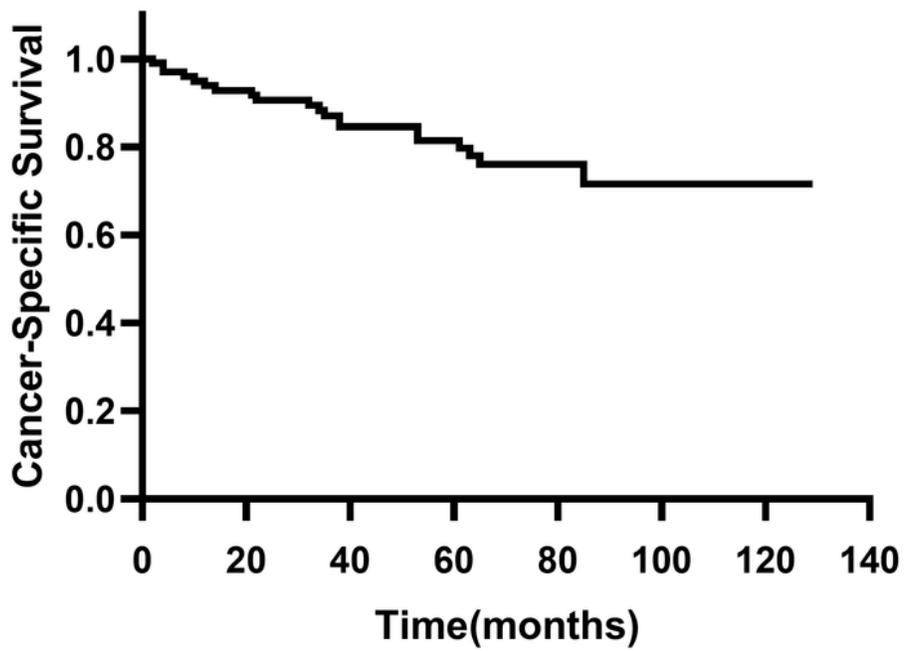
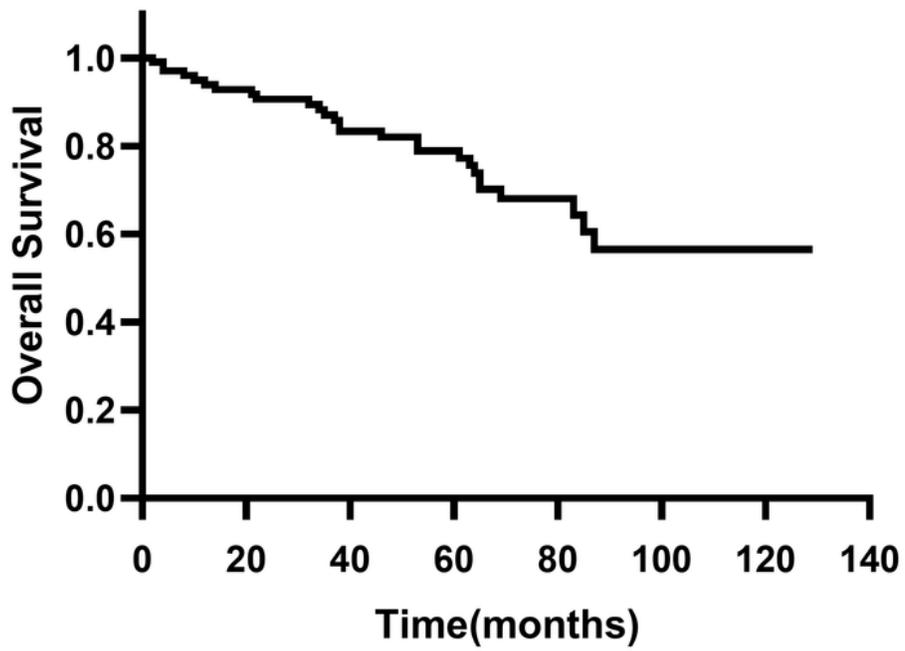


Figure 2

Estimated Kaplan-Meier overall survival and cancer-specific survival curve.

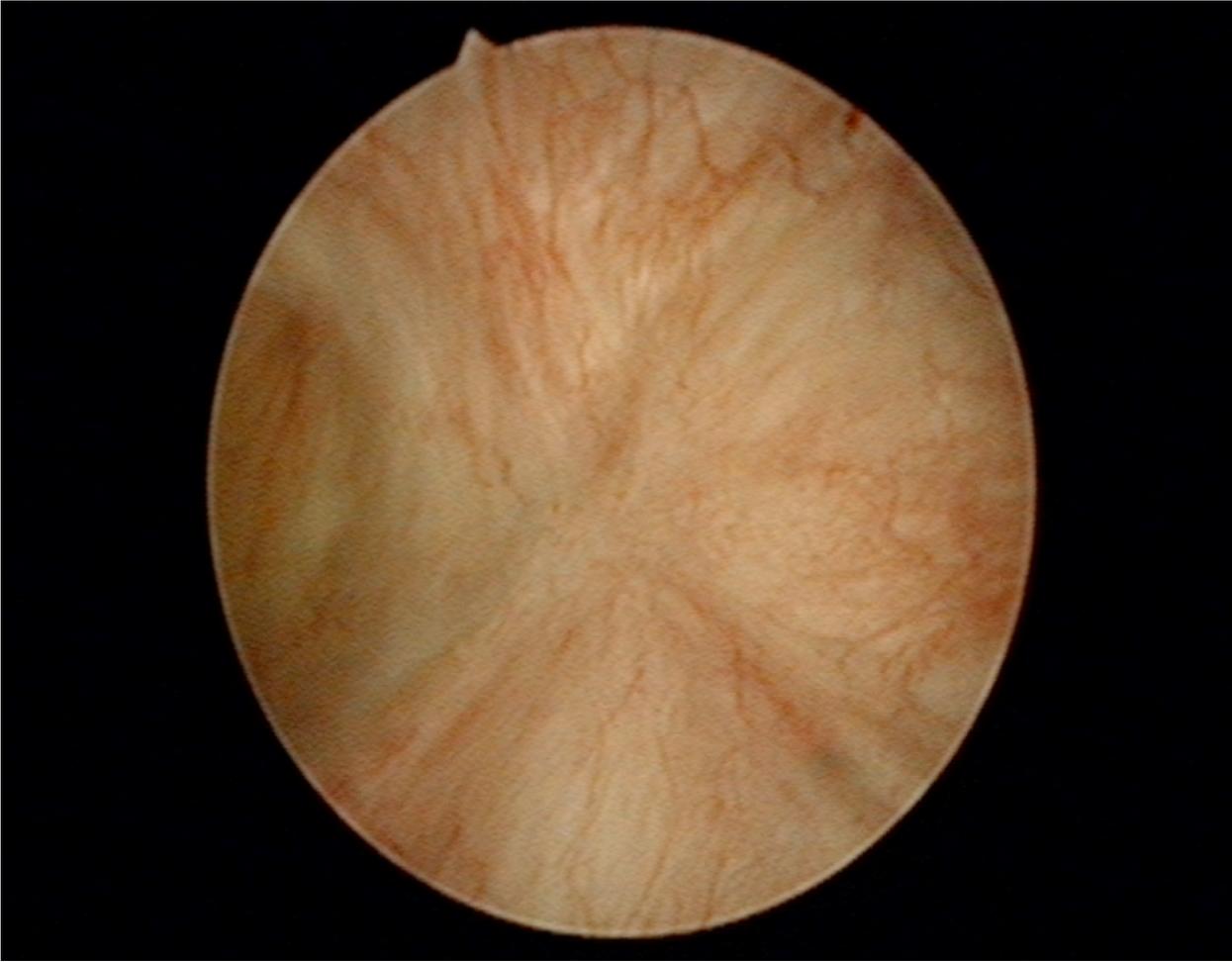


Figure 3

Postoperative cystoscopy showed that the ureteral orifice disappeared.