Evaluation of Two Ureter Sealing Methods During Radical Nephroureterectomy

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Purpose: To investigate the safety of electrocoagulation and thulium laser (Tm-laser) sealing methods of distal ureter resection during radical nephroureterectomy (NFU) in a porcine model.

Methods: 9 pigs were used in the study: 6 were used to measure the bursting pressure (BP) and 3 were used to measure the highest pressure during NFU. Twelve ureters were to measure BP after being sealed by electrocoagulation or Tm-laser (n = 6, each). Six experimental NFUs were performed in 3 pigs to measure the intraluminal pressure of all procedures.

Results: The mean BP in the electrocoagulation group (104.3 ± 25.0 cmH2O) was similar to that of the Tm-laser group (74.8 ± 23.3 cmH2O, $P > .05$). The peak intraluminal pressure (35.9 ± 7.6 cmH_2O) during NFU was significantly lower than the BP ($P < .05$).

Conclusion: The effectiveness of the sealing was confirmed using both electrocoagulation and Tm-laser during NFU.

Keywords: bursting pressure; distal ureter and bladder cuff resection electrocoagulation; experimental porcine model; Pluck technique; thulium laser

INTRODUCTION

Upper tract urothelial carcinoma (UTUC) is a relatively uncommon disease that accounts for 5–7% of all renal tumors and 5–10% of all urothelial tumors, with an estimated annual incidence of 1–2 cases per 100,000[(1)]. UTUC is encountered in approximately 25% of ureteral cancer cases and is subject to a high risk of local recurrence that ranges from 30% to 75%[(2)]. Radical nephroureterectomy (NFU) with distal ureter and bladder cuff (DUBC) resection is the standard treatment for UTUC [(3)]. A large number of endourologic techniques have become promising alternatives to open DUBC resection[(4)] during NFU. However, existing clinical trial evidence regarding their effectiveness and safety is inconclusive[(5)]. In 1998, Keeley and Tolley[(6)] reported a cystoscopic detachment of DUBC during laparoscopic NFU that offered patients an additional benefit of a minimally invasive technique. However, it is related to a high potential for local relapse, which is hypothesized to be because of local tumor cell spillage[(7)]. Oncological safety concerns arise from nonmechanically sealed ureteral openings[(8)]. It may be that the high intraluminal pressure during the NFU after endoscopic manipulation could lead to a breakage in the seal and result in tumor cell spillage. Thus, the effectiveness of electrocoagulation and laser methods in sealing the ureteral orifice is controversial.

As the pressure to the DUBC cannot be measured during NFU in patients, we designed a porcine NFU model to measure the peak pressure to the DUBC and com-

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Table 1. Intraluminal pressure over NFU.

Stage	Intraluminal pressure, cmH_2O
Incising the subcutaneous tissue	7.3 ± 4.5
Identifying the ureter	28.6 ± 8.2
Locating simulated tumor and ligating ureter	35.9 ± 7.6*
After ligating the ureter	33.1 ± 7.4
On mobilizing and ligating renal pedicle	30.0 ± 7.3
On dissecting the kidney	29.6 ± 9.1
Dissecting the ureter	35.0 ± 8.8
Plucking the ureter	33.1 ± 7.0

* The peak pressure was during locating the simulated tumor

pared it to the bursting pressure (BP) of the ureteral openings that were sealed by either electrocoagulation (EC) or a Tm-laser.

MATERIALS AND METHODS

Laboratory animals

The Institutional Animal Research Committee at the Sixth People's Hospital of Shanghai Municipality approved the study protocol (SCXK[SH]2007-0013). Nine Shanghai white pigs, each weighing 60 ± 5 kg, were purchased from Shanghai Nanhui Special Farm (license GB/T 8473-1987). Six pigs were used to determine the BP of the sealed ureters, and 3 pigs underwent experimental NFU.

Sample Size

The sample size calculation followed the equation: $N1=N2=2[(t_{\alpha/2}+t_{\beta})S/\delta]^2$. We defined $\alpha = 0.05$, and $1-\beta = 0.2$. According to a Chinese article, we found that the human ureteral sealing pressure was 192.25 ± 14.27 cmH_2O; we sealed 3 human ureters by Tm-laser in vitro, and the burst pressure was 165.42 ± 12.50 cmH_2O. Therefore, the sample size was calculated to be 5.90.

Study Design

Six pigs were euthanized to harvest ureter specimens (n = 12). These specimens were equally and randomly divided into EC and Tm-laser groups. For the EC group, the distal ureteral segment was placed into a metal container full of 5% mannitol, to the bottom of which an electrode pad was attached. The ureteral orifice was sealed under direct vision using an electrosurgical hook (LISA Laser Products OHG, Katlenburg-Lindau, Germany) at 45 W for 8-10 s.

For the Tm-laser group, the distal ureteral segment was placed into a metal container full of normal saline. A medical Tm-laser system (wavelength, 2.01 μm; maximum output power, 110 W; LISA Laser Products OHG, Katlenburg-Lindau, Germany) was used for laser coagulation in the continuous-wave mode. The ureteral orifice was sealed under direct vision using a 550-μm end-firing PercuFib fiber (LISA Laser Products OHG, Katlenburg-Lindau, Germany) at a set power of 70 W for 5-7 s.

Measurement of BP

The BP limit of the ureteral orifice after sealing was performed as previously described[1]. For real-time monitoring of the intraluminal dynamic pressure, a 5-cm segment of the excised distal ureter was transected, and the stump was connected to a tri-way adapter, which was also connected to a piezometer (Y-50, Wuxi, China) and a 20-mL syringe. The distal ureteral segment was continuously perfused with saline containing methylene blue (Baxter, Suzhou, China) via the syringe at a flow rate of 0.1 mL/s. The BP was defined as the

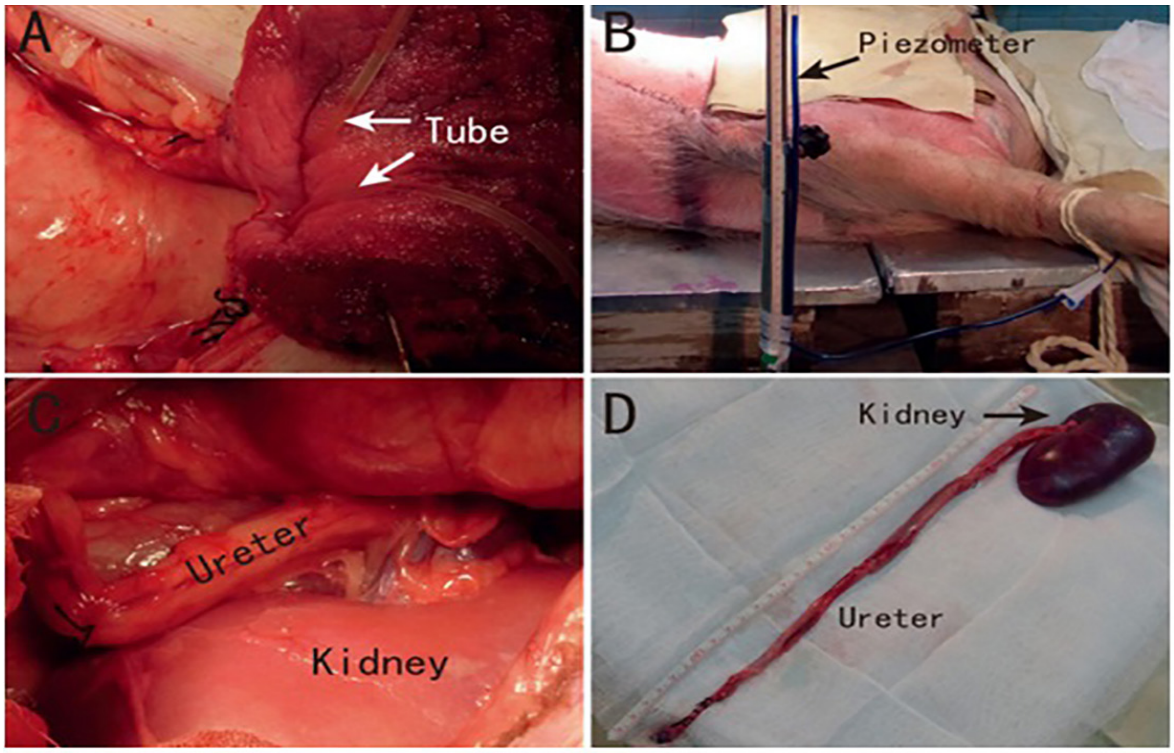

Figure 1. Key stages of the experimental NFU: **(A)** cannulation of bilateral ureteral orifices; **(B)** connection to the piezometer via the tri-way adapter; **(C)** location of the simulated tumor and ligation of the ureter; and **(D)** en bloc resection of the ureter and the kidney.

intraluminal pressure at the time that the blue-stained saline leaked from the sealed orifice, which was the primary experimental outcome.

Experimental NFU

The experimental NFU was performed. Under general anesthesia, the animal was placed in a supine position, and a lower median abdominal incision was made to expose the bladder. The bilateral ureteral orifices were located, and two flexible cannulas were inserted into the bilateral orifices (**Figure 1A**) and connected to the piezometer via the tri-way adapter (**Figure 1B**). The orifices were secured using silk sutures to maintain hermetic. The simulated tumor was located at the level paralleling the lower polar of the kidney, and the proximal ureteral segment was ligated using silk sutures 0.5 cm distally to the renal pelvis (**Figure 1C**). The ureter and kidney were moved to the level of the renal pedicle, and the renal vessels were securely ligated. The ureter was plucked, and the piezometer was disconnected to remove the NFU specimen en bloc (**Figure 1D**). The baseline pressure was defined as the intraluminal pressure before surgical manipulation, and the intraluminal pressure was recorded at intervals of 3s, when plucking the ureter, and at its maximum.

Statistical analysis

SAS v8.02 software (SAS, Cary, NC, USA) was used for statistical analyses. All continuous data are expressed as the mean ± standard deviation. A normality test was performed, and the measurement data that conformed to normal distributions were analyzed by t-tests to determine if the variances were equal, and T-test was used if the variances were unequal. The burst pressure between the two groups and the comparison between the peak pressure and the burst pressure was evaluated using *t*-test. *P*-value < 0.05 was considered statistically significant.

RESULTS

The BPs between the EC (104.3 ± 25.0 cmH_2O) and Tm-laser (74.8 ± 23.3 cmH2O) groups were not significantly different (variances were equal, T=2.11, *P* = .0606). During NFU, the mean intraluminal pressure fluctuated significantly from 7.3 ± 4.5 cmH2O when incising the subcutaneous tissue to 35.9 ± 7.6 cmH2O when locating the simulated tumor and ligating the ureter (**Table 1**). In the Tm-laser group, the peak pressure was 35.9 ± 7.6 cmH_2O, which was significantly lower than the BP (74.8 ± 23.3 cmH_2O) and the difference was statistically significant (variances were unequal, T = 4.13, *P* = .009).

DISCUSSION

Radical NFU with DUBC resection is the standard treatment for UTUC[3]. The DUBC are sealed by either electrocoagulation or a thulium laser (Tm-laser) before NFU to prevent the dissemination of tumor cells along the urinary tract[1,9]. These two sealing methods have been shown to have comparable perioperative and oncological outcomes[9], which were consistent with our previous research[1]. DUBC resection is an effective and safe procedure in terms of disease recurrence and overall survival[10]. Compared with open resection, the endoscopic management of DUBC resection significantly shortens the operative time[11], reduces intraoperative bleeding, and expedites postoperative recovery [9]. However, intraoperative tumor cell seeding is a risk factor for local recurrence[12-14]. Current clinical studies do not agree on the relative risk of urine spillage and tumor cell seeding between the pluck technique and open resection method[15]. Is the sealing pressure safe for preventing urine spillage and tumor cell seeding?

Our porcine biomechanical study was designed to assess whether the intraluminal pressure would exceed the BP of the ureteral orifice when sealed by either electrocoagulation or Tm-laser. We found that the burst pressures between the EC and Tm-laser groups were not significantly different, indicating that the sealing effectiveness was equal between the two methods. We also found that the peak pressure was significantly lower than BP during NFU. The intraluminal pressure at each stage of the experimental NFU was well below the BP of the ureteral orifices, regardless of the sealing technique. Therefore, it is very unlikely that intraoperative manipulation in NFU will burst the sealed ureteral orifice and result in tumor cell spillage.

This study was limited in that the BP was measured ex vivo rather than in vivo. Besides, the experimental NFU was performed on pigs, whose urinary system anatomy differs from that of humans to some extent. Finally, no actual oncological safety test was conducted, and tumor cell spillage might occur even in the absence of bursting the sealed urethral openings.

CONCLUSIONS

In conclusion, the efficacy of electrocoagulation and Tm-laser methods in sealing the ureteral orifice was similar, and the sealed ureteral orifice could withstand the pressure throughout the entire experimental NFU procedure.

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