Evaluation of two ureter sealing methods during radical nephroureterectomy

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ABSTRACT

Objective: 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 > 0.05). The peak intraluminal pressure (35.9 ± 7.6 cmH2O) during NFU was significantly lower than the BP (P < 0.05).

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

Keywords: Pluck technique, distal ureter and bladder cuff resection, electrocoagulation, thulium laser, bursting pressure, experimental porcine model
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 NFU with DUBC resection is the standard treatment for UTUC\(^3\). A large number of endourologic techniques have become promising alternatives to open distal ureter and bladder cuff (DUBC) resection\(^4\) during nephroureterectomy (NFU). However, the existing clinical trial evidence regarding their effectiveness and safety is inconclusive\(^5\). Keeley and Tolley\(^6\) reported a cystoscopic detachment of DUBC during laparoscopic NFU in 1998 that offered patients an additional benefits 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 break in the seal and result in tumor cell spillage. Are the electrocoagulation and laser methods effective in sealing the ureteral orifice? 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 compared 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. Ureteral orifice sealing

The sample size calculation followed the equation: \(N1=N2=2\left[\frac{(t_{\alpha/2}+t_{\beta})S}{\delta}\right]^2\). 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\(_2\)O; we sealed 3 human ureters by Tm-laser in vitro, and the burst pressure was 165.42 ± 12.50 cmH\(_2\)O. Therefore, the sample size was calculated to be 5.90.

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 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 bladder. The bilateral ureteral orifices were located, and two flexible cannulas were inserted into the bilateral orifices (Fig. 1A) and connected to the piezometer via the tri-way adapter (Fig. 1B). The orifices were secured using silk sutures to maintain hermetic. The simulated tumor was located at the level paralleling the lower pole of the kidney, and the proximal ureteral segment was ligated using silk sutures 0.5 cm distally to the renal pelvis (Fig. 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 (Fig. 1D). The baseline pressure was defined as the intraluminal pressure before surgical manipulation, and the intraluminal pressure was recorded at intervals of 3 s, when plucking the ureter, and at its maximum.

Statistical analyses
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’ tests were used if the variances were unequal. The burst pressure between the two groups was compared using a t-test. The comparison between the peak pressure and the burst pressure was performed by a t’ test. A P-value < 0.05 was considered statistically significant.

**RESULTS**
The BPs between the EC (104.3 ± 25.0 cmH\(_2\)O) and Tm-laser (74.8 ± 23.3 cmH\(_2\)O) groups were not significantly different (variances were equal, T=2.11, P=0.0606). The
mean intraluminal pressure fluctuated significantly during NFU, from $7.3 \pm 4.5$ cmH$_2$O when incising the subcutaneous tissue to $35.9 \pm 7.6$ cmH$_2$O when locating the simulated tumor and ligating the ureter (Table 1). In the Tm-laser group, the peak pressure was $35.9 \pm 7.6$ cmH$_2$O, which was significantly lower than the BP ($74.8 \pm 23.3$ cmH$_2$O), and the difference was statistically significant (variances were unequal, T=4.13, P =0.0090).

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), but the current clinical study data do not agree on to the relative risks 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 2 methods. We also found that the peak pressure was significantly lower than the 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 rather than in vivo. Besides, the experimental NFU were 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.

In conclusion, the sealing efficacies with electrocoagulation and Tm-laser of the ureteral orifice were similar, and the sealed ureteral orifice could withstand the pressure throughout the entire experimental NFU procedure.

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REFERENCES


Table 1. Intraluminal pressure over NFU.

<table>
<thead>
<tr>
<th>stage</th>
<th>Intraluminal pressure, cmH2O</th>
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</thead>
<tbody>
<tr>
<td>Incising the subcutaneous tissue</td>
<td>7.3 ± 4.5</td>
</tr>
<tr>
<td>Identifying the ureter</td>
<td>28.6 ± 8.2</td>
</tr>
<tr>
<td>Locating simulated tumor and ligating ureter</td>
<td>35.9 ± 7.6*</td>
</tr>
<tr>
<td>After ligating the ureter</td>
<td>33.1 ± 7.4</td>
</tr>
<tr>
<td>On mobilizing and ligating renal pedicle</td>
<td>30.0 ± 7.3</td>
</tr>
<tr>
<td>On dissecting the kidney</td>
<td>29.6 ± 9.1</td>
</tr>
<tr>
<td>Dissecting the ureter</td>
<td>35.0 ± 8.8</td>
</tr>
<tr>
<td>Plucking the ureter</td>
<td>33.1 ± 7.0</td>
</tr>
</tbody>
</table>

*: The peak pressure was during locating the simulated tumor
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.