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Original article

Nephron-sparing management (distal ureterectomy with reimplantation of ureter) for carcinoma of distal ureter: A single-center experience

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ABSTRACT

Objective: Radical nephroureterectomy with bladder-cuff excision has been the traditional treatment for upper tract urothelial carcinoma because of its high rate of recurrence. However, given the morbidity of nephrectomy and the risk of developing chronic kidney disease or dialysis-dependent renal failure, the nephron-sparing approach may be preferable in selected patients.

Materials and methods: A total of 118 patients who received unilateral distal ureterectomy with reimplantation at a single center in Taiwan were included, using surgical code numbers, from March 2006 to December 2014. A total of 82 patients were excluded due to nonmalignancy and 17 due to concomitant bladder cancer. Finally, 19 patients with primary, solitary, unilateral ureter lesions and confirmed to have ureter malignancy (urothelial carcinoma, $n = 18$; squamous cell carcinoma, $n = 1$) were included.

Results: Of the 19 patients (13 males and 6 females) included, the mean age was 69.3 ± 10.7 years. Tumor pathological staging was Tis ($n = 1$), Ta ($n = 3$), T1 ($n = 2$), T2 ($n = 6$), and T3 ($n = 5$). Histopathology grading was low grade ($n = 3$) and high grade ($n = 13$). No local recurrence was noted; nine patients had bladder recurrence (47.4%), three had distant metastasis (15.8%), and two had progression and finally underwent radical nephroureterectomy (10.5%). The mean time to bladder recurrence was 12.4 months (3–24 months); the mean follow-up time was 28.1 months (1–90 months). The 5-year overall survival rate was 73.7% (14/19); four patients were lost to follow-up, and one patient expired. The mean 5-year progression-free survival was 67.74%. The mean preoperative creatinine level was 1.61 mg/dL, and at 12 months after operation it was 1.56 mg/dL ($p = 0.95$).

Conclusion: In selected patients, distal ureterectomy with reimplantation, in our experience, is a feasible option for distal ureter tumor. Favorable postoperative outcomes with a low local recurrence rate, a low rate of progression to nephroureterectomy, and renal function preservation may prove the value of this modality and should be taken into consideration in suitable patients.

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1. Introduction

Comprising only 5% of all renal and urothelial tumors, upper tract urothelial carcinoma (UTUC) is a rare genitourinary malignancy.¹ For resectable tumors, radical nephroureterectomy (RNU) with bladder-cuff excision has been the gold standard treatment of choice. However, given the morbidity after nephrectomy and the risk of developing chronic kidney disease (CKD), cardiovascular

morbidity, or dialysis-dependent renal failure, a nephron-sparing approach may be preferable in selected patients.^{2,3} Nephron-sparing management (NSM) has been used for UTUC in patients with severely impaired renal function, solitary kidneys, bilateral synchronous tumors, or the necessity of platinum-based chemotherapy for future treatment.^{4,5}

According to the European Association of Urology (EAU) and National Comprehensive Cancer Network (NCCN) guidelines, segmental resection of the distal ureter could be an option for distal ureteral urothelial carcinomas (UCs) even in patients with high-grade, locally invasive distal ureteral UC, particularly for individuals with imperative indications.^{6,7}

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To our knowledge, it remains controversial whether NSM represents a valid alternative to standard RNU in selected patients, due to limited long-term oncological results of NSM for UTUC.

This study aimed to evaluate the oncological outcome in patients with distal ureteral carcinoma who were treated with NSM in a single center (Kaohsiung City, Taiwan). We retrospectively analyzed the oncological outcomes and changes in the renal function of patients with distal ureteral malignancy who underwent distal ureterectomy (DU) with reimplantation of the ureter.

2. Materials and methods

2.1. Study population

A total of 118 patients who received unilateral distal ureteral resection with reimplantation at a single center in Southern Taiwan from March 2006 to December 2014 were included. The exclusion criteria were aged < 18 years, concomitant bladder cancer, and a history of bladder cancer. Eighty-two patients were excluded due to nonmalignancy and 17 due to concomitant bladder cancer. Therefore, our final cohort included 19 patients with a primary, solitary, unilateral ureteric lesion confirmed as a ureteral malignancy (UC, $n = 18$; squamous cell carcinoma, $n = 1$) on final pathology. The preoperative evaluation included serum creatinine, renal echo, intravenous pyelography, computed tomography of the abdomen/pelvis or magnetic resonance imaging of the abdomen, magnetic resonance imaging of urography (MRU), and chest X-ray. Cystourethroscopy or ureteroscopy with tumor biopsy was not routinely performed, to avoid tumor cell spillage into the upper urinary tract. The tumor location and length can be evaluated using image studies such as intravenous pyelogram (IVP) and abdominal computed tomography. If the image study failed to evaluate the tumor location and length, we performed ureteroscopy for intraluminal evaluation. Some patients had a biopsy report at a previous hospital before the surgery; others had strong evidence of malignancy on image studies. As for resection length, the bulging tumor can be identified during the operation grossly, and the proximal and distal margins were sent for frozen section examination for confirmation that there was no malignancy.

2.2. Surgical procedures

All 19 patients received DU with reimplantation of the ureter using the Lich method, with psoas hitch bladder, direct ureteroneocystostomy, or Boari flap bladder. A frozen section of the proximal ureteral margin was examined during the operation and confirmed to be negative for malignancy. The indication for and extent of lymphadenectomy were considered by the surgeon. At a minimum, a lymphadenectomy was performed when lymphadenopathy was detected by imaging studies or during surgery.

2.3. Follow-up

Urine cytology, biochemical studies, including renal function and renal echo, were routinely performed every 3 months in the first 2 years and annually thereafter. Outcome measures were recurrence or distant metastasis, renal function preservation, time to recurrence, and overall survival.

2.4. Statistical analysis

Continuous parametric variables were reported as the mean value \pm standard deviation. The survival range was defined by the

time elapsed since the day of surgery and the last clinical evaluation or the patient's death. Survival curves were estimated using Kaplan–Meier curves. Analyses used SPSS version 18 (SPSS Statistics 18; IBM, Armonk, New York, United States). A p value < 0.05 was considered statistically significant.

3. Results

A total of 19 patients (13 males and 6 females) were included, and the mean age was 69.3 ± 10.7 years. Eleven patients received ureteral reimplantation by Lich method, four received psoas hitch bladder reimplantation, and four received Boari flap bladder reconstruction. Tumor pathological staging was T0 ($n = 1$), Ta ($n = 3$), Tis ($n = 1$), T1 ($n = 2$), T2 ($n = 6$), T3 ($n = 5$), and T4 ($n = 1$). The pT4 case had ureter tumor that invaded into the myometrium of the uterus. All had malignancy except one patient with pathology T0 who had endoscopic biopsy-proven malignancy before. The lesion might have been removed during the previous endoscopic biopsy procedure, and the patient had no further recurrence during the follow-up period. Histopathology grading was presented as follows: low grade, $n = 3$; high grade, $n = 13$. For the other three patients, the final pathology was pT0 in one patient and squamous cell carcinoma was found in another patient, which had no grading. The grading was not found in the remaining patient (Table 1). There were no local recurrences, but nine patients had bladder recurrence (47.4%), three had distant metastasis (15.8%), and two had progression and, ultimately, underwent RNU (10.5%). The mean time to bladder recurrence was 12.4 months (3–24 months) and the mean follow-up time was 28.1 months (1–90 months). The recurrence incidence was 66.7% (4/6) and distal metastasis incidence was 16.7% (1/6) for the Ta, T1, and Tis groups. The recurrence incidence was 50% (6/12) and distal metastasis incidence was 16.7% (2/12) for the T2, T3, and T4 groups. Furthermore, the recurrence incidence was 66.7% (2/3) and distal metastasis incidence was 33.3% (1/3) for the pathology low-grade group. The recurrence incidence was 61.5% (8/13) and distal metastasis incidence was 15.4% (2/13) for the pathology high-grade group. The 5-year overall survival rate was 73.7% (14/19); among them, four patients were lost to follow-up and one patient expired. The mean 5-year progression-free survival was 67.74% (Figure 1). The mean preoperative creatinine level was 1.61 mg/dL, and the postoperative creatinine level was 1.56 mg/dL at 12 months ($p = 0.95$). The Kaplan–Meier curves for bladder recurrence-free survival are displayed in Figure 2. The 5-year progression-free survival rate, stratified by stage, is presented in Figure 3. Owing to the limited cases, the relationship between stage and bladder recurrence incidence was not significant in this study.

Table 1
Patient characteristics ($n = 19$).

| | |
|--------------------------|----------------|
| Age (y) | 69.3 (46–82) |
| Sex (M:F) | 13:6 |
| Preop creatinine (mg/dL) | 1.61 (1.0–2.5) |
| Stage | |
| pT0 | 1 |
| pTa | 3 |
| pTis | 1 |
| pT1 | 2 |
| pT2 | 6 |
| pT3 | 5 |
| pT4 | 1 |
| Grade | |
| Low | 3 |
| High | 13 |
| Other | 2 |
| N/A | 1 |

N/A = not applicable.

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