

Original article

The effect of tumor location on prognosis in patients with primary ureteral urothelial carcinoma[☆]

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Abstract

Objectives: To investigate the association of tumor location on oncological outcomes in patients treated with radical nephroureterectomy (RNU) for primary ureteral urothelial carcinoma (UC).

Materials and methods: From January 1990 to December 2007, 127 patients with primary solitary ureteral UC who underwent RNU at our institution were included. The patients were divided into 3 groups based on tumor location—proximal, middle, or distal ureter. Patients' medical records were reviewed retrospectively. The clinicopathologic data and oncologic outcomes were compared among the groups.

Results: Of the 127 patients, 40 (31.5%) had tumors in the proximal ureter, 40 (31.5%) in the middle ureter, and 47 (37.0%) in the distal ureter. Patients with distal ureteral UC were more likely to undergo open procedures to manage the bladder cuff ($P = 0.005$). Other clinical and histopathologic variables were not different among the 3 groups. Comparing the proximal, middle, or distal ureteral UC, bladder recurrence developed in, respectively, 25.0%, 25.0%, and 21.3% cases ($P = 0.892$); local retroperitoneal recurrence in 2.5%, 12.5%, and 4.3% ($P = 0.141$); contralateral recurrence in 0%, 0%, and 4.3% ($P = 0.177$); and distant metastasis in 17.5%, 10.0%, and 4.3% ($P = 0.147$). Recurrence-free and cancer-specific survival among the 3 groups were not different ($P = 0.781$ and 0.192, respectively).

Conclusions: Tumor location cannot be used to predict oncologic outcomes in patients treated with RNU for primary ureteral UC. Therefore, clinical decisions or follow-up protocol should not differ among patients with primary proximal, middle, or distal ureteral UC. © 2013 Elsevier Inc. All rights reserved.

Keywords: Nephroureterectomy; Prognosis; Recurrence; Ureter; Urothelial carcinoma

1. Introduction

Upper tract urothelial carcinoma (UTUC) is a rare disease that accounts for approximately 5%–10% of all renal tumors and 5% of all urothelial carcinomas. Ureteral tumors

are even rarer than renal pelvis tumors, and account for only about 25% of UTUCs [1,2]. Although nephroureterectomy with ipsilateral bladder cuff excision (radical nephroureterectomy, [RNU]) is considered the standard management for ureteral urothelial carcinoma (UC), nephron-sparing surgery may be an alternative treatment modality in selected cases [1–3]. According to the National Comprehensive Cancer Network (NCCN) guidelines, ureteral tumor locations may affect the primary treatment protocols (e.g., segmental ureterectomy should be reserved for individuals with low-

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grade middle ureteral lesions and for individuals with distal ureteral tumors [3]).

The pathologic stage of the primary tumor, lymph node status, the presence of distant metastases, and tumor grade are the important prognostic factors for UTUC [1,2,4,5]. However, the primary tumor location (renal pelvis vs. ureter) represents a controversial risk factor. Some authors have reported worse outcomes for ureteral UC than for renal pelvic UC [6]. In contrast, other investigators have found that tumor location did not have a differential effect on cancer recurrence and survival [7,8]. Although the NCCN guidelines suggest that ureteral tumor location is an important criterion when deciding therapy, to the best of our knowledge, no previous studies have clarified the impact of its location on prognosis in patient treated with RNU.

Because of the low incidence of UTUCs, most studies include UC of the ureter and the renal pelvis together when analyzing clinical outcomes. In Taiwan, an unusually high incidence of UTUC has been reported, with ureteral tumors accounting for more than 50% of all UTUCs [4,5,9]. Thus, in this population, analysis of prognostic predictors by using a large cohort of patients is possible. In this study, we aimed to elucidate the effect of tumor location on prognosis in patients with primary ureteral UC managed by RNU.

2. Materials and methods

This study was approved by the institutional review board. From January 1990 to December 2007, 282 patients with ureteral tumor were treated by RNU at our institution. Of these 282 patients, 271 (96.1%) had UC, 3 (1.1%) had squamous cell carcinoma, 1 (0.4%) had adenocarcinoma, 1 (0.4%) had metastatic signet ring cell carcinoma, 1 (0.4%) had metastatic buccal squamous cell carcinoma, and 5 (1.8%) had nonmalignant disease. All patients enrolled in this study were diagnosed with primary ureteral UC. Of the 271 patients with UC, 118 were excluded from the study, namely 80 with synchronous renal pelvic and ureteral tumors, 26 with concurrent bladder tumor, 12 with multifocal ureteral tumors, 9 with previous urinary bladder tumors, 4 with bilateral synchronous UTUC, and 13 with incomplete medical data. The remaining 127 patients who underwent RNU for primary solitary ureteral UC were included in this study. Regional lymph nodes dissection was performed in patients with enlarged nodes on preoperative imaging or intraoperative examination. None of the patients received preoperative chemotherapy or radiation therapy. In all, 20 patients who had cancer progression received adjuvant chemotherapy.

The clinicopathologic data were recorded retrospectively. Pathologic staging (pT) was based on the 2002 TNM staging system, and tumors were graded according to the 1998 WHO classification. The patients were divided into 3 groups based on tumor location (proximal, middle, or distal ureter). The middle ureter was defined as the segment of the ureter overlying the sacroiliac joint; the proximal ureter was

defined as the segment above the joint, and the distal ureter as the segment below. Postoperative follow-up consisted of a history, physical examination, urinalysis, urine cytology, routine blood work, chest radiography, abdominal ultrasonography, intravenous urography, and abdominal computed tomography. Cystoscopy was performed every 3 months for the first 2 years, every 6 months for the next 2 years, and annually thereafter. Intravenous urography or contrast-enhanced computerized tomography was obtained annually during the follow-up visit or when clinically indicated.

The predictive value of the clinicopathologic prognostic factors was analyzed with respect to the cancer-specific and recurrence-free survival rates. Recurrence-free survival was calculated as the time interval between nephroureterectomy and the date of the first documented clinical recurrence in the local tumor bed, lymph nodes, or contralateral upper urinary tract or distant metastasis. Bladder recurrences were not considered in the analysis of recurrence-free survival rate. Cancer-specific survival was defined as the time interval between the initial date of presentation and the endpoints, including death or censoring.

Statistical analyses were performed using the statistical software SPSS ver. 17.0 (SPSS, Inc., Chicago, IL). The percentage frequencies of the 3 groups were compared by using χ^2 analysis. Univariate and multivariate analyses were performed using the Kaplan-Meier method with the log rank test and Cox proportional hazards regression model. For all statistical analyses, $P < 0.05$ was considered statistically significant.

3. Results

We analyzed 59 male and 68 female patients whose mean age was 66.3 ± 10.6 years (range 25–87), with a median follow-up period of 40 months (range 2–186). The patients' clinicopathologic characteristics are listed in Table 1. The stage distribution of ureteral UC in this cohort was 45.7% pTa/Tis/T1, 23.6% pT2, 26. % pT3, and 4.7% pT4. Among the patients, 54.3% had high-grade urothelial tumors, and 15.7% received adjuvant chemotherapy. At follow-up, there were 23 (18.1%) cancer-related deaths and 9 (7.1%) deaths from other causes. At the time of analysis, 95 patients (74.8%) were alive.

Overall, 40 (31.5%) tumors were located in the proximal ureter, 40 (31.5%) in the middle ureter, and 47 (37.0%) in the distal ureter. Median follow-up period for the proximal, middle, and distal groups was 39.5 (range 2–185), 38 (range 2–180), and 43 (range 8–186) months, respectively ($P = 0.609$). A comparison of the 3 groups showed that there were no differences in age, gender distribution, smoking status, clinical presentations, tumor side, tumor size, type of nephroureterectomy, stage, grade, lymph node status, and adjuvant chemotherapy. Most (89.4%) of the patients with distal ureteral UC underwent open surgery to manage the bladder cuff ($P = 0.007$).

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