

Original article

Preoperative pyuria predicts advanced pathologic tumor stage and worse survival in patients with urothelial carcinoma of the upper urinary tract treated by radical nephroureterectomy

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Received 5 January 2016; received in revised form 10 March 2016; accepted 23 April 2016

Abstract

Objectives: To investigate the association of preoperative pyuria with pathologic features and oncologic outcomes in patients with urothelial carcinoma of the upper urinary tract (UTUC) treated by radical nephroureterectomy (RNU).

Material and methods: A cohort of 176 patients treated with RNU from January 2001 to December 2014 were retrospectively reviewed. Logistic regression and survival analysis methodology was used to investigate the association of preoperative pyuria with clinicopathologic outcomes.

Results: Among this cohort, 36 (20.5%) presented with preoperative pyuria. Logistic regression revealed that pyuria was significantly associated with advanced pT stage ($P = 0.001$). During a median follow-up of 41 months (interquartile range: 22–60), 65 (37%) patients died, including 54 (31%) from UTUC. Overall survival rates at 3 year and 5 years in patients with pyuria were significantly lower than those in patients without pyuria (62.3% and 36.1% vs. 78.4% and 65.3%, respectively; $P = 0.004$). Also, cancer-specific survival rates at 3 year and 5 years in patients with pyuria were significantly lower than in patients without pyuria (65.7% and 50% vs. 80% and 67.6%, respectively; $P = 0.016$). Furthermore, in the multivariate analysis, after incorporating only preoperative factors, pyuria was found to be an independent predictor of overall survival and cancer-specific survival ($P = 0.005$ and $P = 0.028$, respectively).

Conclusions: Preoperative pyuria among UTUC patients underwent RNU was significantly associated with advanced pathologic tumor stage and worse survival. Our data suggested that pyuria as a prognostic predictor could be valuable in preoperative risk stratification and guiding better therapeutic approaches, but further validation in a larger population is needed. © 2016 Elsevier Inc. All rights reserved.

Keywords: Upper tract urothelial carcinoma; Preoperative pyuria; Survival; Radical nephroureterectomy

1. Introduction

Upper tract urothelial carcinoma (UTUC) is relatively uncommon, representing only 5% to 10% of urothelial tumors. Arising from the urinary urothelium, pyelocaliceal tumors are approximately twice as common as ureteral tumors [1,2]. Though low-risk cases can also be treated by radical nephroureterectomy (RNU), this therapy remains the

standard of care for high-risk UTUC with a bladder cuff excision [2]. Owing to tumor aggressivity and progression, the prognosis for UTUC after radical surgery still remains unsatisfactory, especially in advanced tumor stage [3,4]. Uncovering efficient prognostic predictors would benefit patients with this malignancy.

Currently, there have been series of studies published to explore prognostic factors for UTUC. Overall, postoperative factors mainly focus on pathologic parameters, including tumor stage, grade, lymph node invasion (LNI), and lymphovascular invasion (LVI). And promising preoperative factors are mostly derived from comorbidity (e.g., hydronephrosis and previous or synchronous bladder

This article does not contain any studies with animals performed by any of the authors. Informed consent was obtained from all individual participants included in the study.

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tumor) and serum inflammatory biomarkers [5,6]. However, data are still scarce concerning urine prognostic factors. Identifying urine prognostic predictors would allow a better therapeutic approach for UTUC.

Previous reports have proved that the presence of inflammation is associated with oncogenesis and tumor progression [7–9]. As one well-known marker of urinary inflammation, preoperative pyuria was found to be an independent predictor of recurrence and progression for non-muscle-invasive bladder cancer (NMIBC) [10,11]. Given the similarity between UTUC and bladder cancer, we ascertain whether pyuria could also play a predictive role in UTUC. Thus, the present study aims to investigate the association between preoperative pyuria and pathologic features, and to evaluate pyuria as a prognostic factor in patients with UTUC treated after RNU.

2. Material and methods

2.1. Patients selection

After institutional review board approval, we retrospectively reviewed data of 258 patients with upper tract tumors at our institution between January 2001 and December 2014. After excluding those patients who had nonurothelial cancer ($n = 10$), conservative surgery ($n = 32$), previous or concomitant radical cystectomy ($n = 14$), metastatic diseases ($n = 2$), active infections ($n = 2$), or incomplete medical data ($n = 26$), a total of 176 UTUC patients who underwent RNU were finally enrolled into this study. All these eligible patients were treated by surgeons according to the standard criteria for RNU, that is, extrafascial dissection of the kidney with the entire length of ureter and adjacent segment of the bladder cuff. The hilar and regional lymph nodes adjacent to the ipsilateral great vessel were generally resected if palpable intraoperatively or enlarged on preoperative axial imaging. Extended lymphadenectomy (paracaval, retrocaval, interaortocaval, para-aortic, ipsilateral common, external and internal iliac, obturator, and presacral LN) was not routinely performed. In addition, patients with previous or synchronous NMIBC were all treated by transurethral resection. Respectively, 27 (15%) and 4 (2%) cases were administered with adjuvant chemotherapy and radiotherapy, the majority of whom were in advanced TNM stage (stage III or IV).

2.2. Clinicopathologic variables evaluation

All specimens were histologically confirmed to be urothelial carcinomas by genitourinary pathologists. Clinicopathological variables including age, sex, tumor side, size and location (renal pelvic, ureteral, and multifocal tumors), previous or synchronous NMIBC, primary tumor stage (pT) and grade (2009 TNM classification and the 1973 World Health Organization grade [2]), LN status, LVI,

presence of preoperative hydronephrosis, adjuvant chemotherapy or radiotherapy, and surgery type (open or laparoscopic) were collected for individuals. LN status was determined by pathological assessment of retrieved lymph nodes after surgery and LVI was defined as the presence of tumor cells within an endothelium-lined space without underlying muscular walls. Multifocality was defined as synchronous presence of 2 or more pathologically confirmed macroscopic tumors in the upper urinary tract. In addition, preoperative hydronephrosis was determined by radiographic techniques such as computed tomography, magnetic resonance imaging, or ultrasonography.

Urine analysis and culture was performed before any tumor manipulation, such as cystoscopy, ureteroscopy, or RNU. Pyuria was defined as ≥ 10 white blood cells (WBCs) per high power field of urine, because this cutoff value was usually used for diagnosis of urinary tract infection [12].

2.3. Postoperative assessment

All patients were generally followed every 3 months for the first year after surgery, then every 6 months from the second through to the fifth years and annually thereafter. Routine surveillance protocol included cystoscopy and blood or urine tests. Urinary cytology, elective bone scans, abdominal or chest computed tomography, and magnetic resonance imaging were performed if clinically indicated.

2.4. Statistical methods

Comparisons of clinicopathologic features between groups were performed using χ^2 tests for categorical variables and Kruskal-Wallis tests for continuous variables. The cause of death was determined by the treating physicians, chart review corroborated, telephone interview, or death certificates alone. Using the Kaplan-Meier method, overall survival (OS) and cancer-specific survival (CSS) were estimated from the time of RNU to event. Survival was compared between patients with or without pyuria with the log-rank test. Logistic regression and Cox proportional hazard models were used to evaluate risk factors of pathologic parameters and oncologic outcomes. Only those variables that were univariately significant were entered into the multivariate Cox analysis. All reported P values are 2-sided and statistical significance was set at $P < 0.05$. Statistical analysis was performed using PASW version 18.0 statistical software (IBM Corp, Somers, NY).

3. Results

The clinicopathologic features of all the patients grouped by preoperative pyuria are summarized in Table 1. As depicted, the average age was 70 year (interquartile range: 62–77) and the median follow-up time was 41 months

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