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Independent prognostic factors for initial intravesical recurrence after laparoscopic nephroureterectomy for upper urinary tract urothelial carcinoma

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Abstract

Objective: To elucidate clinicopathologic independent prognostic factors for intravesical recurrence after laparoscopic nephroureterectomy for primary upper urinary tract urothelial carcinoma (UUT-UC).

Methods and materials: This study included 212 consecutive patients clinically diagnosed as localized UUT-UC and treated by retroperitoneal laparoscopic nephroureterectomy between January 2002 and October 2010, after exclusion of those with a previous or concurrent history of bladder cancer. The clinicopathologic features, risk factors, and intravesical recurrence–free survival were analyzed using the Kaplan-Meier method. Univariate and multivariate analyses by Cox proportional hazards regression model was used to identify independent risk factors for intravesical tumor recurrence.

Results: Of the patients, 64/212 (30.2%) developed subsequent intravesical recurrence during a median follow-up period of 39 months (range 7–78 months). Among them, 56/64 (87.5%) developed recurrent bladder cancer within 2 years after the surgery for UUT-UC, and the median interval between surgery and intravesical recurrence was 14 months (range 7–51 months). Multifocal tumors, renal insufficiency, and immunosuppression were determined as risk factors for intravesical recurrence by univariate analysis. However, by multivariate analyses, multifocality (hazard ratio = 2.060, $P = 0.006$) and immunosuppression (hazard ratio = 1.915, $P = 0.037$) were identified as independent predictors for the development of recurrent bladder cancer.

Conclusions: The incidence of intravesical recurrence after laparoscopic nephroureterectomy for UUT-UC is high, and most subsequent bladder cancers recur within 2 years after surgery. Tumor multifocality and immunosuppression are significant independent risk factors in developing initial intravesical recurrence after laparoscopic surgery for primary UUT-UC.

Keywords: Laparoscopic surgery; Transitional cell carcinoma; Bladder cancer; Recurrence; Immunosuppression

1. Introduction

Upper urinary tract urothelial carcinoma (UUT-UC) is relatively uncommon, accounting for 5% to 7% of all renal tumors, and approximately 5% of all urothelial tumors [1]. Although radical nephroureterectomy is considered the mainstay for the treatment for UUT-UC before metastasis, the urothelial cancer often develops recurrence in the bladder after surgery. As 15% to 50% of patients who undergo nephroureterectomy have been reported to experience postoperative intravesical recurrence during the follow-up period [2], studies attempted to identify the clinicopathologic risk factors for predicting the initial intravesical recurrence in patients with UUT-UC, which showed controversial outcomes.

In recent years, laparoscopic radical nephroureterectomy (LRNU) has become a viable alternative strategy for conventional open surgery at many institutions worldwide. This change of therapeutic modality may influence the outcomes of surgical treatment for UUT-UC, and affect the subsequent intravesical recurrence. However, most previous studies included a relatively small number of patients who underwent pure laparoscopic procedures for UUT-UC.

In this study, we retrospectively reviewed data from a total of 212 consecutive patients who were treated by LRNU and assessed the clinicopathologic features as risk factors for initial postoperative intravesical recurrence.

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2. Methods and materials

A review of the clinical records of our institute identified 267 consecutive patients who underwent LRNU with curative intent for primary UUT-UC without any suspicious metastasis between January 2002 and October 2010. Numbers of patients excluded from this study were 12 with a previous history of bladder cancer, 6 with concomitant bladder cancer, 5 with a nonrecurrent follow-up period less than 1 year, and 32 with prophylactic intravesical chemotherapy, leaving a cohort of 212 patients retrospectively available for evaluation.

The median age of the 212 patients was 66.5 years (range 31–84). As one of the largest kidney transplantation centers in China, 35 patients with end-stage renal disease (primary chronic glomerulonephritis except one patient with aristolochic acid nephropathy) underwent renal transplantation and received immunosuppressive medication (cyclosporin A, mycophenolate mofetil, and prednisone) before the diagnosis of UUT-UC, and the others in this study were not in immunosuppression status during the follow-up. Each patient was evaluated before operation with blood tests, urine cytology, serum creatinine, chest x-ray, and abdominopelvic computerized tomography. By using abbreviated Modification of Diet in Renal Disease formula, the patient's estimated glomerular filtration rate was calculated [3]. Based on the area of the primary lesion, tumor locations were divided into either renal pelvis or ureter, and no tumor involved both renal pelvis and ureter in our study. The focality of UUT-UC was classified as either a single site or multiple sites. In the cases with multiple tumors, the pathologic characteristics were identified with the highest stage and grade, the largest size of the tumors.

Of 212 patients, combined with retroperitoneal LRNU, 124 received open ipsilateral distal ureterectomy with excision of the bladder cuff, and 88 received transurethral resection of the ureteral orifice as the management for distal ureters within 2 weeks after their diagnosis. As neoadjuvant topical or systemic chemotherapy has not been adopted in general urologic practice in China, no patient received this treatment. Regional lymph nodes dissection was performed in 91/212 patients (42.9%), as clinical and intraoperative status determined whether the lymph nodes around the ipsilateral great vessels should be removed. Resected specimens were pathologically staged using the 2009 International Union Against Cancer TNM classification. Because tumors with low malignant potential were not found, the urothelial carcinoma was pathologically graded into 2 groups: low grade and high grade, according to the 2004 World Health Organization classification. The pathologic T stage included 31 cases of pTa, 81 cases of pT1, 74 cases of pT2, 25 cases of pT3, and 1 case of pT4. Additionally, 20 pN1 cases were found. Adjuvant chemotherapy was not recommended for patients except in 8/212 (3.8%) administered with platinum-based regimen within 3 months after surgery.

The follow-up of all patients was carried out as follows: serum creatinine test and surveillance cystoscopy every 3 months for the first 2 years after LRNU, then every 6 months for the next 2 years, and annually thereafter; abdominopelvic computerized tomography and chest radiography every 6 months for the first 2 years and annually thereafter. The lesion suspected of intravesical recurrence was removed by transurethral resection or radical cystectomy, and was diagnosed pathologically. The end point of this study was defined as the initial recurrence of urothelial carcinoma in the bladder.

Clinicopathologic features of patients were evaluated. Qualitative variables were compared by the chi-square test and quantitative variables by the Student t-test. The intravesical recurrence–free survival data were analyzed by the Kaplan-Meier method with the log rank test. For univariate and multivariate analyses, the Cox proportional hazards model was used to determine the contribution of clinicopathologic factors to the bladder tumor–free survival rates. All probability (P) values were 2 sided and P values <0.05 were considered as statistical significance. All statistical analyses were performed with SPSS 13.0 software (Statistical Product and Service Solutions, SPSS Inc, Chicago, IL).

3. Results

The median follow-up after LRNU was 39 months (range 7–78 months). Of the 212 patients included, 11 (5.2%) died of metastatic urothelial cancer and 28 (13.2%) died of other diseases before any presentation of developing intravesical recurrence. Renal insufficiency (estimated glomerular filtration rate <60 ml per minute per 1.73 m^2) was found in 29 patients before or within their postoperative follow-up, and 15 among them underwent renal transplantation and received immunosuppressive medication during the follow-up, including 1 recipient who stopped the immunosuppresant therapy because renal allograft lost function 52 months after LRNU, and 8 months before the end of follow-up without intravesical recurrence. At the time of analysis, 64/212 (30.2%) developed recurrent bladder cancer, and the median interval between surgery and intravesical recurrence was 14 months (range 7–51 months); and 87.5% patients (56/64) developed recurrent bladder cancer within 2 years after LRNU. Transurethral resections were performed for the patients with initial recurrent bladder cancer, except 2 patients who underwent radical cystectomy. The pathologic stage and grade of the initial intravesical recurrence distribution was as follows: 23 pTa, 37 pT1, 3 pT2, 1 pT3, 5 papillary urothelial neoplasia of low malignant potential, 32 low-grade tumors, and 27 high-grade tumors.

Table 1 compared clinicopathologic characteristics between patients with and without intravesical recurrence after LRNU. Seventeen parameters were subjected to