Long-Term Outcomes of Nephroureterectomy Versus Endoscopic Management for Upper Tract Urothelial Carcinoma

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Abbreviations and Acronyms

ASA = American Society of Anesthesiologists

BMI = body mass index

CCI = Charlson comorbidity index

ENDO = endoscopy

NUx = nephroureterectomy

UTUC = upper tract urothelial carcinoma

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Purpose: We compared outcomes in patients treated with nephroureterectomy vs nephron sparing endoscopic surgery for upper tract urothelial carcinoma.

Materials and Methods: Patients treated at our institution for upper tract urothelial carcinoma from 1996 to 2004 were monitored for upper tract and bladder recurrence, metastasis, and cancer specific and overall survival. Outcomes were compared between treatment groups by univariate and multivariate analyses based on pertinent pathological and demographic variables.

Results: Of 96 renal units 62 underwent immediate nephroureterectomy and 34 were managed endoscopically. Median followup in all survivors was 77 months. Overall nephroureterectomy and endoscopy complication rates were 29% and 9.3%, respectively. In patients with low grade tumors the 5-year metastasis-free survival rate after nephroureterectomy and endoscopy was 88% and 94%. The corresponding 5-year cancer specific and overall survival rates were 89% vs 100% and 72% vs 75%, respectively. Of endoscopic cases 84% had at least 1 ipsilateral recurrence. Multivariate analysis revealed that only tumor grade was significantly associated with metastasis-free survival while grade and body mass index correlated with cancer specific survival, and Charlson Comorbidity index and grade impacted overall survival. Treatment group was not associated with survival outcome.

Conclusions: When technically feasible and in select patients, endoscopic management provides cancer related and overall survival equivalent to that of nephroureterectomy in patients with low grade upper tract urothelial carcinoma at the cost of frequent re-treatments in many patients. Nephroureterectomy is standard treatment for high grade cancer when there is a normal contralateral kidney but endoscopy should be considered when there are imperative indications for nephron sparing.

Key Words: kidney; ureter; carcinoma, transitional cell; ureteroscopy; nephrostomy, percutaneous

Upper tract urothelial carcinoma accounts for only 5% of renal tumors and urothelial tumors.[1] Standard treatment is radical NUx with a bladder cuff. Originally done only in patients with imperative indications for nephron sparing,[2–5] ureteroscopic or percutaneous resection is now done in those with a normal contralateral kidney.[6] Groups at some high volume centers have produced 5-year survival curves comparing NUx and endoscopic management.[7,8]

In 2003[9] and 2005[10] we reported our results of endoscopic management and hand assisted laparoscopic NUx for UTUC with a mean followup of 15.8 months and a median followup

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of 25.0, respectively. We now update these 2 cohorts with a median followup exceeding 6 years in survivors and with additional data allowing stratification by tumor characteristics and patient comorbidity to inform the comparison of long-term outcomes.

MATERIALS AND METHODS

With institutional review board approval we identified 93 consecutive patients (96 renal units) with clinically localized UTUC treated with ENDO or hand assisted laparoscopic NUx at our institution from 1996 through 2004.

Endoscopy

Initial ureteroscopy was done in most cases.[9] UTUC was confirmed by biopsy in most cases with saline barbotage for cytology in the remainder. Tumors that could not be ablated by ureteroscopy were approached percutaneously with a 24Fr resectoscope and flexible nephroscope as needed.

After successful tumor ablation patients were counseled on ENDO vs NUx, considering UTUC grade, size and multifocality, overall patient medical condition and indications for nephron sparing, and estimated outcomes of each approach in regard to the need for additional procedures, recurrences, disease progression, and impact on renal function and quality of life. Patients electing immediate NUx were included in the NUx group. The ENDO group included only patients with complete endoscopic tumor resection and the intent to enter endoscopic surveillance, consisting of regular ureteroscopic examinations at variable intervals depending on tumor characteristics and recurrence patterns.[9] We attempted to treat recurrences by ureteroscopy but percutaneous nephroscopy was done as needed. At each recurrence the decision to perform endoscopic management vs NUx was reconsidered. When NUx was elected or the patient medical condition precluded NUx and we abandoned surveillance, treating only palliatively for symptomatic local recurrence, that patient was still included in the ENDO group.

Hand Assisted Laparoscopic NUx

A transperitoneal, hand assisted laparoscopic approach to NUx was used with distal ureteral management by various methods.[10] Flexible office cystoscopy was done 3 months later as the first bladder tumor surveillance with subsequent cystoscopies at variable intervals.

Systemic Surveillance

Systemic surveillance in each group consisted of abdominopelvic imaging with computerized tomography or magnetic resonance imaging, chest imaging with plain x-ray or computerized tomography, complete blood count and complete serum chemistry every 6 to 12 months depending on tumor characteristics.

Data Analysis

Tumor grade was assigned using the 1998 WHO classification. Endoscopic biopsy pathological staging was not attempted but NUx specimens were staged using the TMN system. We recorded all complications within 30 days of surgery and any complications directly related to the procedure. Major complications were those requiring significant postoperative intervention or hospital readmission. We recorded BMI, age, gender, ASA score and any prior bladder tumor. We calculated age adjusted CCI,[11] which for our analysis excluded urothelial carcinoma.

Cross-sectional imaging or chest radiography was done to determine metastasis-free survival. Cross-sectional imaging or ureteroscopy was required to assess for contralateral kidney occurrence. Cystoscopy was done to monitor bladder recurrence. In the ENDO group ipsilateral kidney recurrence was determined by ureteroscopy. For all surveillance methods the date of first documentation of recurrence defined the event time and the last pertinent surveillance date determined the censored time in patients without recurrence. For cancer specific and overall survival we contacted referring physicians, patients and families, and queried the Social Security Death Index and the University of Michigan Cancer Registry. Death from UTUC vs other causes could be determined in all except a few cases.

Statistical analysis was done using commercial software with $p < 0.05$ considered significant. To compare preoperative and intraoperative variables between groups we used the chi-square or Fisher exact test for categorical variables and the Mann-Whitney U test for continuous variables. Survival estimates were obtained from Kaplan-Meier survival curves. The log rank test was used to compare survival measurements between groups. We evaluated the impact of select variables on survival using proportional hazard regression models. Variables used for univariate analysis were tumor characteristics (size, extent, site and grade), history of bladder tumor, gender, BMI, age adjusted CCI group and treatment group. Patient age and ASA score were not included since they covaried with age adjusted CCI. After univariate analysis multivariate regression analysis was done using treatment group and any factors significant on univariate testing.

RESULTS

Of the 93 patients 1 had 2 renal units managed endoscopically and 2 had 1 renal unit in each treatment group. Thus, our study included a total of 96 renal units, including 62 managed by NUx and 34 managed endoscopically. Patients with NUx were healthier than those with ENDO with a lower mean ASA score and age adjusted CCI. Patients with NUx had worse tumor characteristics than those with ENDO in terms of more 2 cm or greater tumors and more high grade UTUC.

Of patients with ENDO 16 (47%) had imperative indications for nephron sparing, including bilateral disease, solitary kidney and chronic renal insufficiency. Only 3 of the 8 patients with high grade UTUC did not have imperative indications for endoscopic management. Patients treated with ENDO for nonimperative reasons had significantly lower age adjusted CCI than those with imperative indications, such that this measure of medical comorbidity in patients with nonimperative ENDO was sim-