Imperative Indications for Conservative Management of Upper Tract Transitional Cell Carcinoma

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Purpose: We report our experience with patients with imperative indications for endoscopic treatment for upper tract transitional cell carcinoma.

Materials and Methods: Between 1983 and 2004 we identified 37 patients with a solitary kidney, bilateral disease or preoperative creatinine greater than 2.0 mg/dl who underwent endoscopic treatment for localized upper tract transitional cell carcinoma. A retrospective chart review was performed.

Results: Of the 37 patients 32 had a solitary kidney, 3 had bilateral disease and 2 had preoperative creatinine greater than 2.0 mg/dl. Median age at diagnosis was 75 years (range 56 to 88). Bladder cytology was positive or atypical in 15 of 31 patients (48%). Tumors were grade 1 to 3 in 2, 13 and 7 patients, respectively, and diagnosed visually in 15. At a median followup of 2.7 years for survivors 23 patients (62%) had a total of 56 upper tract transitional cell carcinoma recurrences. Grade and stage progression occurred in 3 and 3 patients, respectively. Ten of the 23 patients who experienced upper tract recurrence died of transitional cell carcinoma. Overall kidney preservation was achieved in 24 of the 32 patients (75%) with a solitary kidney. At last followup 24 patients had died, including 11 (29.7%) of transitional cell carcinoma, at a median of 2.9 years. Cancer specific survival at 5 years for this cohort was 49.3%.

Conclusions: Our results indicate that upper tract tumor recurrence occurs in a majority of patients with imperative indications for endoscopic treatment, underscoring the need for frequent surveillance. While most kidneys can be preserved, cancer specific death is common.

Key Words: ureter; carcinoma, transitional cell; endoscopy; ureteral neoplasms; ureteroscopy

Nephroureterectomy with bladder cuff excision is the gold standard treatment for upper tract TCC due to the significant rate of multifocal ipsilateral tumors, risk of distal recurrence and low incidence of contralateral involvement.[1,2] However, when radical surgery would leave the patient functionally anephric, a nephron sparing approach is generally attempted. The advent of ureteroscopic instruments and small diameter, flexible laser fibers has made renal preserving endoscopic treatment feasible for upper tract TCC.[3] Traditionally endoscopic management of renal pelvis and ureteral TCC was reserved for patients with imperative indications, such as bilateral disease, renal insufficiency or solitary kidney.[4] Initial results from our institution and others have demonstrated favorable outcomes with low rates of local recurrence and death from disease.[3,5–10] However, long-term studies are lacking. We report our greater than 20-year experience with patients with imperative indications for endoscopic treatment for upper tract TCC.

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Study received Institutional Review Board approval.
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MATERIALS AND METHODS

After obtaining Institutional Review Board approval we identified 37 patients who underwent endoscopic treatment for localized upper tract TCC for imperative indications between 1983 and 2004. Imperative indications for endoscopy included solitary kidney, bilateral disease or preoperative creatinine greater than 2.0 mg/dl. A retrospective chart review was performed.

All patients underwent diagnostic evaluation using IVP, CT urogram or retrograde pyelography and urine cytology. Cytology results were determined from bladder and selective ureteral assessments. Criteria for exclusion from endoscopic treatment were tumor appearance too large for complete ablation or resection, as visualized on imaging or endoscopy. This decision was often based on surgeon experience. However, if a tumor completely filled the renal pelvis or multiple calices, it was considered unresectable.

The endoscopic techniques used at our institution for upper tract TCC were described previously.[5] We recently initiated the KTP laser at 20 W for tumor ablation after biopsy, as opposed to the Nd:YAG laser or cautery. Tumors were graded 1 to 3 according to the Broder classification and staged using the TNM system with an additional category of visual diagnosis only for tumors in which biopsy was not performed or an insufficient pathological specimen was obtained.

Followup evaluations were surgeon dependent. However, they were generally done every 3 to 4 months with IVP or CT

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urogram, cystoscopy and urine cytology for 2 years, and semiannually thereafter. Patients with any abnormal finding on any of these studies underwent further endoscopic examination. For most patients ureteroscopy was performed at each 3-month visit until tumor-free status was achieved and semiannually thereafter. Due to the referral nature of our clinic some patients elected surveillance by their local urologist and returned for yearly followup or if intervention was necessary. Contact was maintained through correspondence with the patients and local urologists.

Cancer specific, local recurrence-free and bladder recurrence-free survival was estimated using the Kaplan-Meier method. Associations with death from TCC, local recurrence and bladder recurrence were evaluated using Cox proportional hazards regression models and summarized with the risk ratio and 95% CI. Statistical analyses were performed using the SAS® software package. All tests were 2-sided with $p < 0.05$ considered statistically significant.

RESULTS

Patient and Treatment Demographics

Average patient age at diagnosis was 74 years (median 75, range 56 to 88). There were 32 males and 5 females. Table 1 lists the imperative indications. A history of bladder cancer was noted in 29 patients (78.4%), of whom 7 (24.1%) were treated with prior cystectomy. Table 2 lists the baseline features studied. Certain comorbidities were noted, including diabetes in 3 patients (8.1%), coronary artery disease in 9 (24.3%), chronic obstructive pulmonary disease in 11 (29.7%) and ASA score 3 or greater in 24 (68.6%).

Of the 35 cases in which IVP or retrograde pyelogram was performed 33 (94.3%) demonstrated a filling defect. CT urogram was performed in 11 cases, of which 8 (72.7%) had a filling defect, 1 (2.7%) was suspicious or high risk and 2 (5.4%) were without abnormalities. Of the 31 cases in which bladder cytology was performed 10 (32.3%) were positive for TCC, 5 (16.1%) were atypical and 16 (51.6%) were negative. Of the 5 cases in which upper tract selective cytology was performed 1 was positive, 2 were atypical and 2 were negative. Mean tumor size was 1.4 cm (median 1.0, range 0.3 to 3.8) (table 2). Upper tract TCC location was the renal pelvis in 24 patients (64.9%), ureter in 7 (18.9%), and renal pelvis and ureter in 6 (16.2%).

Conservative treatment consisted of ureteroscopic ablation in 26 patients (70.3%), percutaneous resection in 8 (21.6%) and the 2 approaches in 3 (8.1%). Tumor biopsy was successful in obtaining enough tissue for pathological evaluation in 22 patients (59.5%). We found no association between the incidence of successful biopsy and year of diagnosis (Wilcoxon rank sum test $p = 0.278$). Tumor management was achieved by resectoscope (percutaneous cases only) in 6 cases (16.2%), cautery ablation in 29 (78.4%) and laser ablation in 1 (2.7%). There were 8 acute complications (21.6%) and 5 late complications (13.5%), consisting of nonmalignant stricture disease (table 3). One patient was treated with mitomycin at endoscopy. Adjuvant postoperative BCG or mitomycin was administered by intravesical installation with ureteral stent reflux in 8 patients (21.6%), including 1 at endoscopy.

All 7 patients who previously underwent cystectomy had ileal conduit urinary diversion. Ureteroscopic surveillance

TABLE 1. *Imperative indications for endoscopic treatment of upper tract TCC*

Solitary Kidney	Bilat Disease	Creatinine Greater Than 2.0 mg/dl	No. Pts
No	No	Yes	2
No	Yes	No	3
Yes	No	Unknown	1
Yes	No	No	23
Yes	No	Yes	6
Yes	Yes	No	2*
Total			37

* Bilateral disease with 1 side treated with nephroureterectomy and the remaining solitary kidney treated endoscopically.

TABLE 2. *Baseline features in 37 patients with imperative indications for endoscopic treatment of upper tract TCC*

Feature	No. Pts (%)
Bladder Ca history	29 (78.4)
Bladder or selective cytology:	31
Neg	16 (51.6)
Atypical or pos	15 (48.4)
Tobacco use history	29 (78.4)
ASA score:	35
1	0
2	11 (31.4)
3	23 (65.7)
4	1 (2.9)
Presenting symptoms:	
Gross or microscopic hematuria	19 (51.4)
Flank pain	3 (8.1)
Incidental finding	6 (16.2)
Tumor size (cm):	
Less than 1.0	18 (48.7)
1.0	4 (10.8)
1.5	2 (5.4)
2.0	5 (13.5)
Greater than 2.0	8 (21.6)
Tumor grade:	
Visual	15 (40.5)
1	2 (5.4)
2	13 (35.1)
3	7 (18.9)
Tumor stage:	
Visual Ta	14 (37.8)
Ta	15 (40.5)
TIS	3 (8.1)
T1	4 (10.8)
T2	0
T3	1 (2.7)
Adjuvant BCG	5 (13.5)
Prior or subsequent cystectomy	10 (27.0)

TABLE 3. *Early and late complications following endoscopic treatment of upper tract TCC*

Complications	No. Pts (%)
Early:	
Bleeding	3 (8.1)*
Edema	1 (2.7)†
Fever	1 (2.7)
Infection	1 (2.7)
Perforation	1 (2.7)
Sepsis	1 (2.7)
Transfusion	1 (2.7)
Pneumothorax	0 (0.0)
Other	5 (13.5)
Late stricture	5 (13.5)

No patient had late tumor seeding, chest pain, gastrointestinal bleeding or acute renal failure.

* One patient required emergent nephrectomy for intractable bleeding.

† Required ureteral stent.