

Short Communication**Open surgical partial nephrectomy for upper tract urothelial carcinoma**

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Abbreviations & Acronyms

ATN = acute tubular necrosis
CCI = Charlson Comorbidity Index
eGFR = estimated glomerular filtration rate
ESRD = end-stage renal disease
NUx = nephroureterectomy
UTUC = upper tract urothelial carcinoma

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Abstract: We aimed to determine the ability of partial nephrectomy to prevent end-stage renal disease and tumor recurrence or progression in patients with upper tract urothelial carcinoma. Retrospectively, eight patients undergoing partial nephrectomy for upper tract urothelial carcinoma were identified and their medical records reviewed. All patients had imperative indications for nephron sparing, and diagnosis of upper tract urothelial carcinoma not adequately amenable to endoscopic management. Although three patients suffered acute tubular necrosis, only one required postoperative hemodialysis. During the follow-up period 25% (2/8) developed end-stage renal disease, including the one patient who had received postoperative hemodialysis. Recurrences occurred in five of seven patients with adequate oncological surveillance. Recurrences were successfully treated endoscopically in 80% (4/5) patients, and one patient had metastases. Of the eight patients, four have died. Death occurred 4 months, 1 year, 1.2 years and 3.5 years after partial nephrectomy. Of these patients, one succumbed to metastatic disease; the exact cause of death is unknown in the other three, but there was no documentation of metastatic cancer. The mean duration of follow up in the remaining four patients, all without evidence of metastatic urothelial cancer, is 71 months (range 22–108 months). In summary, partial nephrectomy for upper tract urothelial carcinoma in patients with imperative indications averts end-stage renal disease in most patients, and appears to be associated with acceptable disease-specific survival. Partial nephrectomy is a sparingly used option in patients with upper tract urothelial carcinoma refractory to endoscopic management who have imperative indications for nephron sparing.

Key words: kidney failure, kidney pelvis, nephrectomy.

Introduction

UTUC represents 5% of urothelial tumors.^{1,2} NUx is the standard treatment, but in some cases nephron sparing is indicated. Endoscopy is effective for low-grade, superficial disease, and in some more advanced tumors.^{3–6} If endoscopic treatment fails or is not possible, then the only way to spare nephrons is to carry out partial nephrectomy.^{7–10} The ability of open surgical partial nephrectomy to prevent ESRD and tumor recurrence or progression in patients with UTUC is not well-defined.

Methods

Eight patients undergoing open surgical partial nephrectomy for UTUC from March 1997 through May 2011 at The University of Michigan Health System, Ann Arbor, USA, by one of four attending urologists were identified. Through a combination of inspection of radiographs, palpation and intraoperative ultrasonography, the line of incision in the renal parenchyma was identified. After intravenous mannitol, the renal hilum was clamped and ice slush was applied. The renal tissue was incised, and the collecting systems in both the resected and remaining portions of the kidney were inspected, adding flexible nephroscopy if required. The collecting system and renal parenchyma were closed and the hilar clamp was removed.

The amount of parenchyma removed was estimated by the number of calyces excised. Each of the major calyces was counted as one-third of the renal parenchyma, except in case of heminephrectomy, in which case it was estimated that 50% was left remaining.

With institutional review board approval, medical records were retrospectively reviewed. The age-adjusted CCI, excluding the diagnosis of urothelial cancer, was calculated.¹¹ Postoperative complications were categorized using the modified Clavien system.¹² The eGFR was determined using the Modification of Diet in Renal Disease Study equation.¹³

Table 1 Characteristics of patients undergoing partial nephrectomy for UTUC

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6	Patient 7	Patient 8
Age at operation (years)	75	69	74	75	74	75	80	78
Sex	Male	Female	Female	Male	Male	Male	Male	Male
Body mass index	25.7	36.2	32.3	32.8	21.1	25.7	-	31
Diabetes mellitus					Yes			
Hypertension	Yes		Yes	Yes	Yes	Yes		Yes
Coronary artery disease			Yes	Yes	Yes	Yes		Yes
Tobacco use	Yes		Yes		Yes	Yes		
Pre-operative eGFR	45	90	72	72	34	79	44	16
CCI	3	3	6	4	7	6	6	3
Anatomically solitary kidney	Yes			Yes (horseshoe kidney)	Yes		Yes	
Unsuccessful endoscopic treatment		Yes		Yes		Yes		Yes
High volume UTUC recurrence	Yes				Yes		Yes	
Other indication for partial nephrectomy		Poor function contralateral kidney	Upper urinary tract duplication					Poor function contralateral kidney

Table 2 Tumor characteristics

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6	Patient 7	Patient 8
Location of tumor	Upper calyces	Upper calyces	Lower calyces into ureter	Renal pelvis of left moiety	Lower calyces	Upper calyces	Upper calyces	Upper and middle calyces
Tumor size (cm)	1.4	4	3.2	4	1.4	2.2	8	
pT stage	pTa	pT2	pT2b	Ta	T2	Ta	Ta	Tis
pN stage			Negative	Negative	Negative	Negative	Negative	
Grade	High	High	High	High	Low	Low	High	High
Other pathological findings		Angiolymphatic Invasion						

Bivariate comparisons of outcomes between groups were limited to two outcome levels per variable, using the Fisher's exact test.

Results

Table 1 contains the patient demographics. In the six men and two women, the mean age was 75 years. Overall, the patients had considerable medical comorbidities, with a mean CCI of 4.75. Of the patients, four had a solitary kidney, with three having undergone contralateral NUX for UTUC, and one having a congenitally solitary kidney. Endoscopic urothelial treatment had been carried out in seven patients. Endoscopy was unsuccessful in four patients; and in three patients, high-volume recurrence had followed initially successful endoscopic treatment. The one patient without prior endoscopic treatment had an UTUC lesion that was deemed most suitable for open surgery (2.5 cm proximal ureteral tumor subtending lower pole moiety of completely duplicated system). Tumor size ranged from 1.4 to 8 cm (mean 3.5 cm).

Tumor characteristics are listed in Table 2. All patients had confirmed urothelial cancer, high-grade in all but two. T stage was Ta in four, Tis in one and T2 in three patients. None had carcinoma *in situ*. All surgical margins were negative. None of the five patients undergoing regional lymphadenectomy had lymph node metastases.

The mean operative time was 238 ± 36 min (range 186–269). The mean ischemia time was 43 min (range 15–66 min). The mean estimated blood loss was 400 mL (range 150–850 mL). The mean duration of hospitalization was 7 days (range 3–9 days). Of the eight patients, seven experienced postoperative complications, with a mean Clavien score of 2.5 (range 0–4a), including ATN in three, surgical site infections in three, ileus in one, cerebral-vascular accident in one, seizures in one, upper tract obstruction in one and urine leak in one patient.

Table 3 shows renal function outcomes. The mean amount of renal parenchyma remaining was 58%. Mean follow up was 40 months (range 4–108 months). Of the patients, two progressed to ESRD after surgery. Of these two patients, one (patient 1, with 33% remaining parenchyma) had a serum creatinine of 4.1 mg/dL (compared with 1.8 mg/dL preoperatively) 1 year after surgery, but then developed acute renal failure and unrecoverable ESRD when an obstructing ureteral tumor later developed. The other patient (patient 5, with 66% remaining parenchyma), developed ATN postoperatively requiring temporary hemodialysis, initially recovered renal function, and then developed ESRD. No other patient required hemodialysis postoperatively. Eventual ESRD was not associated with the amount of remaining parenchyma ($P = 1.0$) or preoperative eGFR ($P = 0.43$), but it was associated with a postoperative event impacting renal function (ureteral obstruction in patient

Table 3 Renal function after partial nephrectomy for UTUC

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6	Patient 7	Patient 8
Renal ischemia time (min)	40	46	15	none	55	40	66	38
% parenchyma remaining	33%	66%	66%	50%	66%	66%	50%	66%
Preoperative eGFR	45	90	72	72	34	79	44	16
Serum creatinine levels (mg/dL)								
Pre-operative	1.8	1.0	1.2	1.2	2.3	1.1	1.8	4.4
1 day postoperative	3.2	1.0	1.0	1.3	3.1		4.7	
2 days postoperative	3.9	0.9	0.8	1.3	5.1		6.4	
3 days postoperative	4.3	1.0	0.9	1.4	4.7		5.5	
1 week postoperative	4.2	1.1	1.3	0.9	‡	1.4	6.2	4.2
1 month postoperative	3.4	1.2	0.9	1.0	3.9	0.9	2.0	
1 year postoperative	4.1	1.2		0.9	†	0.9		
Latest available	†	1.2	0.8	0.9		1.5		4.5
Weeks until latest available creatinine		52	41	374		451		97

†Permanent ESRD. ‡Temporary hemodialysis.

Table 4 Oncological outcome after partial nephrectomy for UTUC

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6	Patient 7	Patient 8
Months of follow up	14	22	12	84		108	4	42
Local recurrence	Ureter	Renal/bladder	Bladder	None		Ureter/bladder	None	Bladder
Metastases	Yes	No	No	No		No	No	No
Death from UTUC	Yes	No	No	No	No	No	No	No
Any death	Yes	No	Yes	No	No	No	Yes	Yes

1, and transient acute tubular necrosis requiring temporary hemodialysis in patient 5; $P = 0.04$).

Oncological follow up is summarized in Table 4. Of the eight patients, there is no information about cancer recurrence in one patient (patient 5). Of the remaining seven patients, two (29%) have had no recurrence of urothelial carcinoma, with follow up of 4 and 87 months (patients 7 and 4, respectively). Urothelial tumors recurred in the bladder in patient 3 9 months after surgery, and the last follow up was 12 months after surgery. There were 11 recurrences in the ureter and/or bladder in patient 6, beginning 15 months after partial nephrectomy and continuing to be detected at each follow up, with the last follow up 9 years after surgery. Patient 8 had three recurrences of urothelial cancer in the bladder, at 1, 3 and 6 months after partial nephrectomy, with the last follow up 39 months after surgery. Patient 1 had a ureteral recurrence 12 months after partial nephrectomy, and then subsequently developed lung metastases, so the ureteral recurrence was palliated with a ureteral stent until he succumbed to metastatic disease 2 years after surgery. Patient 2 developed multifocal unresectable recurrences in the bladder and renal pelvis at 11 months after surgery, and then underwent completion NUX after neo-adjuvant chemotherapy.

Of the eight patients, four have died. Death occurred 4 months, 1 year, 1.2 years and 3.5 years after partial nephrectomy. The exact cause of death was unknown in three patients, but there was no documentation of metastatic cancer. One patient succumbed to metastatic disease after 14 months. The mean duration of follow up in the remaining four patients, all

without evidence of metastatic urothelial cancer, was 71 months (range 22–108 months). Death from any cause was not associated with preoperative eGFR ($P = 0.49$) or ESRD ($P = 1.0$).

Discussion

Our institutional experience includes eight patients receiving open surgical partial nephrectomy due to UTUC. At the time of publication, three of eight patients (38%) remain alive and disease-free, with only one having died as a result of metastatic UTUC recurrence, and one is alive but undergoing neo-adjuvant chemotherapy.

Of our eight patients, two (25%) developed ESRD in the follow-up period. ESRD was associated with ATN, low percent of renal parenchyma remaining, and high Clavien score of IVa and IV. In the remaining five patients (71%) for whom follow-up data was available, hemodialysis was not required throughout the follow-up period. The successful avoidance of ESRD is notable, as ESRD has a significantly negative impact on survival and quality of life.^{14,15}

The 1-, 5- and 7-year survival for patients aged >65 years beginning dialysis has been reported as 81%, 30% and 15%, respectively.¹⁶ Munshi *et al.* showed that in patients aged >75 years, dialysis survival is even more truncated.¹⁷ The total 1-year survival for our series was seven out of eight (88%). Of the patients who were followed up for >3 years, three of the three (100%) were still alive.

In conclusion, partial nephrectomy for UTUC in patients with imperative indications results in a high rate of preventing

ESRD, and appears to be associated with acceptable disease-specific survival. In this small cohort, we could not identify any preoperative factors that were associated with the eventual onset of ESRD or death. Partial nephrectomy is a reasonable option in patients with UTUC refractory to endoscopic management who have imperative indications for nephron sparing.

Conflict of interest

None declared.

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