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## What is the cost of maintaining a kidney in upper-tract transitional-cell carcinoma? An objective analysis of cost and survival.

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## **Clinical Science: First Prize**

# What Is the Cost of Maintaining a Kidney in Upper-Tract Transitional-Cell Carcinoma? An Objective Analysis of Cost and Survival

Raymond W. Pak, M.D., Eric J. Moskowitz, and Demetrius H. Bagley, M.D.

### **Abstract**

**Background and Purpose:** For many years, the gold standard in upper urinary tract transitional-cell carcinoma (UT-TCC) management has been nephroureterectomy with excision of the bladder cuff. Advances in endourologic instrumentation have allowed urologists to manage this malignancy. The feasibility and success of conservative measures for UT-TCC have been widely published, but there has not been an objective cost analysis performed to date. Our goal was to examine the direct costs of renal-sparing conservative measures *v* nephroureterectomy and subsequent chronic kidney disease (CKD) or end-stage renal disease (ESRD). Secondary analysis includes a discussion of survival and quality-of-life issues for both treatment cohorts.

**Patients and Methods:** Retrospective review of a cohort of patients treated at our institution with renal-sparing ureteroscopic management of UT-TCC who were followed for a minimum of 2 years. The costs per case were based on equipment, anesthesia, surgeon fees, pathologic evaluation fees, and hospital stay. ESRD and CKD costs were estimated based on published reports.

**Results:** From 1996 to 2006, 254 patients were evaluated and treated for UT-TCC at our institution. A cohort of 57 patients was examined who had a minimum follow-up period of 2 years. Renal preservation in our series approached 81%, with cancer-specific survival of 94.7%. Assuming a worst-case scenario of a solitary kidney with recurrences at each follow-up for 5 years *v* nephroureterectomy and dialysis for the same period, an estimated \$252,272 U.S. dollars would be saved. This savings would cover the expenses of five cadaveric renal transplantations.

**Conclusions:** Conservative endoscopic management of UT-TCC in our experience should be the gold standard management for low-grade and superficial-stage disease. From a cost perspective, renal-sparing UT-TCC management is effective in reducing ESRD health care expenses.

### **Introduction**

UPPER URINARY TRACT transitional-cell carcinoma (UT-TCC) is relatively rare and accounts for no more than 5% of all urothelial tumors and less than 10% of renal tumors.<sup>1</sup> For many years, the gold standard in UT-TCC management has been radical nephroureterectomy with excision of the bladder cuff.<sup>2</sup> Advancements in endourologic instrument technology have allowed urologists to manage this malignancy without radical extirpation of the affected kidney and ureter. Current practice patterns reveal that there is no consensus on the

management of UT-TCC; however, minimally invasive conservative measures are preferred.<sup>3</sup>

Many nephroureterectomies are performed yearly in the United States when, in contrast, most UT-TCC is low grade and superficial.<sup>4</sup> This discordance is difficult to understand when one considers the strong arguments for renal preservation in the management of small renal tumors.<sup>5</sup>

The feasibility and success of conservative measures for UT-TCC have been widely published, but there has not been an objective cost analysis performed to date, despite many cost analyses for other urologic conditions.<sup>6–8</sup> In the era of

cost-effective management, we should understand the costs to preserve a kidney in the setting of UT-TCC, especially in patients with imperative indications (bilateral UT-TCC, a solitary kidney, and preexisting renal insufficiency). End-stage renal disease (ESRD) accounts for a large percentage of health care spending in the elderly.<sup>9</sup> Moreover, survival and quality of life when receiving dialysis can be severely diminished.<sup>9-10</sup>

Our goal was to examine the direct costs of renal-sparing conservative measures *v* radical nephroureterectomy and subsequent chronic kidney disease (CKD) or ESRD. Secondary analysis includes a discussion of survival and quality-of-life issues for both treatment cohorts.

## Patients and Methods

We conducted a retrospective review of a selected cohort of patients who were treated at Thomas Jefferson Hospital with conservative renal-sparing ureteroscopic management of UT-TCC and who were followed for a minimum of 2 years. The data were analyzed to determine recurrence rates, progression, renal preservation, and survival. Patients with high-grade disease and/or unresectable disease were offered laparoscopic radical nephroureterectomy with excision of the bladder cuff. The costs per case were based on equipment, anesthesia time, surgeon fees, pathologic evaluation fees, and hospital stay. Additional costs of follow-up office and imaging visits were collected as well.

A standardized protocol was used with regard to upper-tract surveillance, which included retrograde pyelography and ureteroscopy at 3-month intervals from last recurrence and extended to 6 months for negative surveillance. Urine cytologic evaluation and imaging was performed at each follow-up office visit.

Global costs for arteriovenous fistula formation, continuous hemodialysis, and medical management of CKD were estimated based on published 2007 cost reports.<sup>9</sup> UT-TCC survival and recurrence data and quality-of-life estimates when receiving dialysis were collected from published papers found on Medline. Cost analysis only included events related to UT-TCC and excluded bladder tumor encounters for all

TABLE 1. PATIENT CHARACTERISTICS

Number of patients	57
Mean age (years)	65.6
Mean follow-up months (range)	53 (24-146)
Mean number of procedures	10.1
Number with solitary kidney	8
Recurrence rate	89.5%
Mean recurrences per patient	5.5
Renal preservation	80.7%
Overall survival	93%
Cancer-specific survival	94.7%

groups. All costs were calculated based on data for U.S. dollars (USD).

## Results

From 1996 to 2006, 254 patients were evaluated and treated for UT-TCC at our institution. A cohort of 57 patients was examined who had a minimum follow-up period of 2 years. The average number of procedures per patient was 10.1 with a range of 5 to 41. The patient demographics and treatment results are summarized in Table 1. A total of eight patients had a solitary renal unit at presentation. Renal preservation in our series approached 81%, with cancer-specific survival of 94.7%.

### Cost analysis

Our algorithm for patients in whom UT-TCC was diagnosed is outlined in Figure 1. The direct costs incurred at Thomas Jefferson Hospital were calculated for ureteroscopic laser treatment, diagnostic ureteroscopy, laparoscopic nephroureterectomy with bladder cuff, and dialysis vascular access formation (Table 2). Estimates for cadaveric renal transplantation were based on available published data.<sup>11</sup> The cost to maintain a kidney was calculated per annum and projected over a period of 5 years against other treatment options (Table 3, Table 4, Fig. 2).

FIG. 1. Treatment algorithm for upper tract TCC.

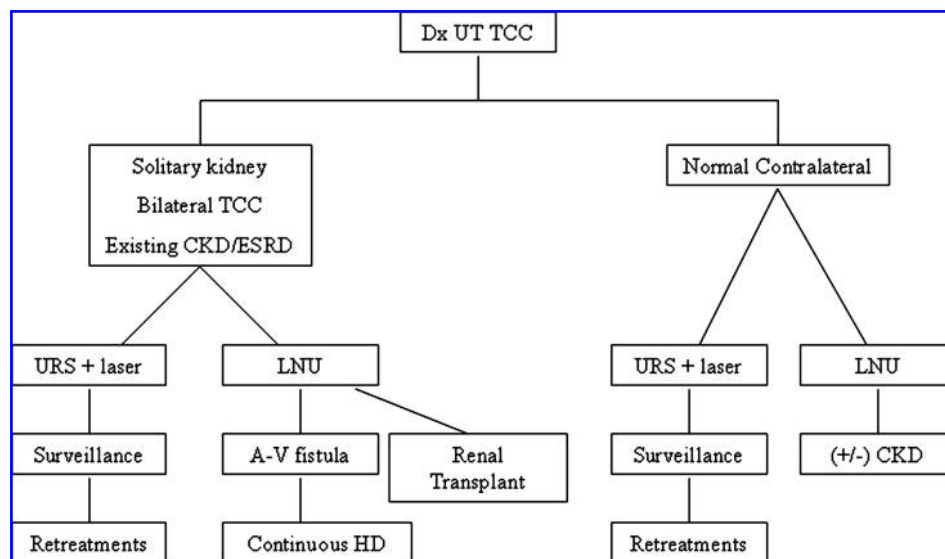


TABLE 2. COSTS OF EACH TREATMENT MODALITY

Cost variables	Cost			
	Ureteroscopic laser ablation	Diagnostic ureteroscopy	Laparoscopic nephroureterectomy	AV fistula placement
Operating room costs, supplies	1,589	856	3,678	
Anesthesia professional fees	825	525	1,725	
Surgeon professional fees	2,200	1,580	7,100	
Pathology fees	656	N/A	882	
Room, nursing costs	N/A	N/A	8,379	
Total perioperative costs	5,270	2,961	21,764	14,592

AV = arteriovenous; N/A = not available.

A best-case scenario for an initial treatment and no recurrences yielded an initial cost of \$5,270 for ureteroscopic laser treatment followed by a negative surveillance visit at 3 months with subsequent negative surveillance visits that occurred every 6 months, which cost \$7,181 annually. A worst-case scenario had UT-TCC recurrence at each follow-up visit, an initial ureteroscopic laser ablation treatment that cost \$5,270, followed by re-treatment visits every 3 months costing a total of \$20,634 in the first 12 months and \$26,864 each subsequent year. This scenario comprises the most aggressive treatment algorithm reserved for patients with imperative indications for renal preservation.

Most patients will fall between these two extremes of estimated 5-year costs for renal preservation in the setting of UT-TCC management. The estimated cost of a recurrence per year is \$18,980 USD and adds an additional outpatient hospital visit per year. Therefore, at our institution, with an average recurrence rate of 5.5 recurrences per patient over a mean follow-up period of 53 months, our average cost to maintain a kidney is \$117,890 USD.

Under the most-costly scenario, an initial nephroureterectomy cost of \$21,764 is followed by a one-time cost of \$14,592 for arteriovenous fistula placement and then \$69,758 annually for maintenance hemodialysis. Over an estimated 5-year projection, this cost rises to \$385,146.

### Survival analysis

The overall survival for our cohort of 57 patients was 93% with a cancer-specific survival of 94.7%. Renal preservation was 80.7% in our series. The cancer-specific survival for patients treated with a solitary kidney was 75% (2/8). Four patients were alive at the time of analysis with metastatic TCC and were undergoing medical therapy.

A review of selected UT-TCC series using conservative management was examined for survival data and is summarized in Table 5.<sup>12-17</sup> Cancer-specific survival rates ranged from 49.3% to 100% in the selected series. Renal preservation rates ranged from 70% to 80%.

In contrast, survival data for ESRD and hemodialysis are not very impressive. Table 6 summarizes the age-based survival rates for patients on chronic hemodialysis over 1, 3, 5, and 10 years.<sup>9</sup>

### Discussion

The challenge of conservative management of UT-TCC is that it requires advanced endoscopic skills, expensive equipment, and compliant patients willing to undergo multiple procedures. In this analysis, the measure of cost was used to objectively compare the conservative management of UT-TCC against nonrenal-sparing measures.

TABLE 3. ANNUAL COST OF SURVEILLANCE/RE-TREATMENT POST-URETEROSCOPIC (URS) LASER ABLATION

Cost variables	Cost (\$)	
	Surveillance and re-treatment at each follow-up visit	Surveillance only at each follow-up visit
Ureteroscopic laser ablation	5,270	0
Diagnostic Ureteroscopy	0	2,961
Imaging		
CT urography	See original fax rest of column	0
Intravenous urography	661	See original fax rest of column
TCC marker studies:		
Cytology	299	299
Total surveillance/re-treatment costs per visit	6,230	3,260
Number of annual follow-up visits	4	2
Sub-total annual surveillance/re-treatment costs	24,920	6,520
Once-yearly imaging:		
CT urography	1,944	N/A
Intravenous urography	N/A	661
Net total annual surveillance/re-treatment costs	26,864	7,181

TABLE 4. FIVE-YEAR PROJECTED COSTS AFTER RADICAL VERSUS RENAL PRESERVING MANAGEMENT

Months since initial treatment	Total Cost (\$)				
	URS laser ablation with surveillance and retreatment	URS laser ablation with surveillance only	LNU + CKD	LNU + AV fistula placement + hemodialysis	LNU + kidney transplantation
0	6,230	6,230	21,764	36,356	69,226
12	26,864	13,411	42,548	106,114	86,499
24	53,728	20,592	63,332	175,872	103,772
36	80,592	27,773	84,116	245,630	121,045
48	107,456	34,954	104,900	315,388	138,318
60	134,320	41,474	125,684	385,146	155,591
Annual cost of CKD = (\$1,294 + \$438) × 12 = \$20,784 (US Renal Data 2007 Report)				20,784	
Annual cost of HD = \$69,758 (US Renal Data 2007 Report)				69,758	
Cost of kidney transplant = \$47,462 (Saidi) <sup>11</sup>				47,462	
Annual cost of maintaining kidney transplant = \$17,273 (US Renal Data 2007 Report)				17,273	

URS = ureteroscopic; LNU = laparoscopic nephroureterectomy; CKD = chronic kidney disease; AV = arteriovenous; HD = hemodialysis.

Recent data suggest increased risks for renal insufficiency in patients who underwent radical nephrectomy for renal cortical tumors, supporting the importance of renal preservation.<sup>18</sup> The argument for conservative measures in the setting of a solitary kidney, bilateral UT-TCC, and preexisting CKD are not difficult to make when considering the alternative options. This study, however, highlights the importance of renal preservation in patients who were considered elective candidates for conservative (normal contralateral kidney) management. Moreover, there are data to suggest that higher grade tumors develop in patients with ESRD or CKD and UT-TCC and that these patients subsequently fare worse.<sup>19</sup> This fact may be further reflected in our series as well as that of the Mayo clinic.<sup>14</sup>

In patients with imperative indications for renal preservation, the cost savings over a 5-year period range from 3-fold to

almost 10-fold when compared with the ESRD and hemodialysis cohort. In addition, the overall survival of conservatively treated patients is much higher compared with age-based survival statistics in patients receiving hemodialysis. Survival rates on chronic hemodialysis for a 70-year-old patient with ESRD are 70.6%, 38.8%, and 19.2%, respectively, at 1, 3, and 5 years. In contrast, the worst reported cancer-specific and overall survival for conservative UT-TCC management was 49.3% and 35%, respectively, for a cohort with an average age of 74 years with 35 months of follow-up.<sup>14</sup>

Assuming a worst-case scenario of a solitary kidney with recurrences at each follow-up for 5 years *v* nephroureterectomy and dialysis for the same period, an estimated \$252,272 USD would be saved, not to mention improved quality of life and overall survival. These savings would cover the expenses of five cadaveric renal transplantations.

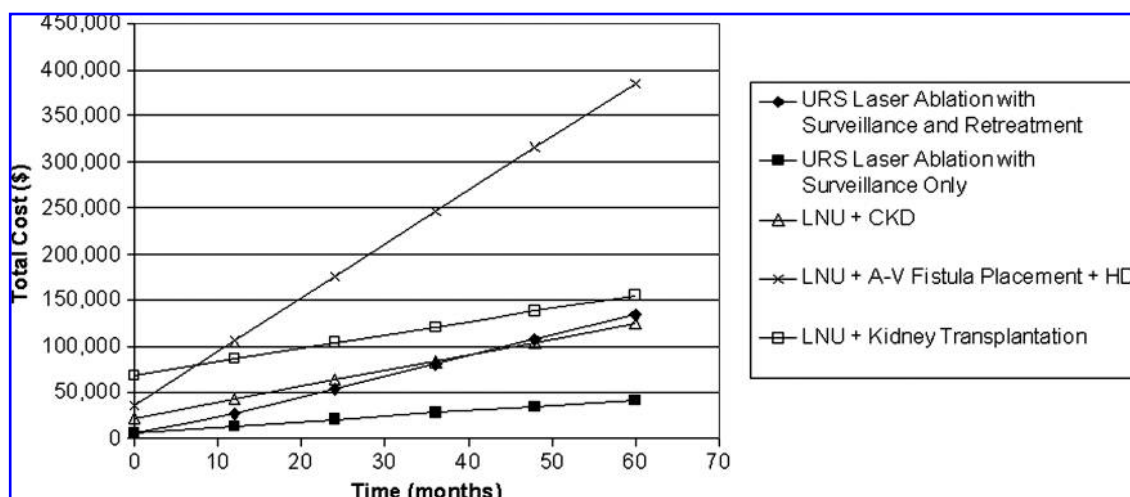


FIG. 2. Projected cost over 5 years.

TABLE 5. RECENTLY PUBLISHED DATA ON CONSERVATIVE MANAGEMENT OF UPPER-TRACT TRANSITIONAL CELL CARCINOMA

Author	Year	Institution	N	Age (years)	Cancer-specific survival %	Overall survival	Renal preservation	Follow-up (months)
Deligne <sup>15</sup>	2002	Lyon, France	61	66	84	77	81	40
Iborra <sup>16</sup>	2003	Valencia, Spain	54	62	87.1	62.9	77.7	85
Milner <sup>17</sup>	2006	Loyola, Chicago	10	70	70	70	80	33
Sowter <sup>12</sup>	2007	Edinburgh, UK	40	65	100	80	70.7	41.6
Krambeck <sup>14</sup>	2007	Mayo Clinic, Minnesota	37	74	49.3	35	75	35
Thompson <sup>13</sup>	2008	Mayo Clinic, Minnesota	83	71	89	58	67	55.2

Real-world costs are difficult to calculate, especially when you include loss of productivity, morbidity, etc; therefore, this cost analysis is very conservative and underestimates the real cost of preserving a kidney in the setting of UT-TCC.

The issue of quality of life in UT-TCC has never been examined. Performing a MEDLINE search using quality of life and TCC revealed only eight reports regarding bladder TCC and urinary diversions. Using the Medical Outcomes Study Short-Form 36-item survey (SF-36), investigators found that patients with superficial bladder TCC who were undergoing repeated transurethral resections had general health perceptions lower than normal cohorts; however, in patients who were undergoing multiple procedures, the quality-of-life scores for all other domains improved with four or more transurethral resection procedures.<sup>20</sup>

This is our best estimate of UT-TCC quality of life. In contrast, a similar MEDLINE search using the terms quality of life and dialysis yielded 1087 published reports. Quality-of-life evaluations in ESRD hemodialysis patients have revealed that patients would give up one-quarter to one-half of their remaining life expectancy in current health if the sacrifice would allow them to have perfect health for a shorter time.<sup>21</sup>

**Conclusions**

Conservative endoscopic management of UT-TCC in our experience should be the gold standard for low-grade and superficial-stage disease. Not only is cancer-specific and overall survival excellent, but also recurrences and progression are manageable and oncologically acceptable. From a cost perspective, renal-sparing UT-TCC management is effective in reducing ESRD health care expenses.

**Disclosure Statement**

No competing financial interests exist.

TABLE 6. END-STAGE RENAL DISEASE SURVIVAL BASED ON AGE AND YEARS ON DIALYSIS

Age (years)	ESRD survival probabilities*			
	1 year (%)	3 years	5 years (%)	10 years (%)
50–59	86.1	65.4	48.3	21.7
60–64	82.3	57.1	37.2	11.3
65–69	77.7	49.3	29	6
70–79	70.6	38.8	19.2	2.6
80+	60.6	25.5	8.5	0.8

\*Based on 2007 US Renal Data System Report.<sup>9</sup>  
ESRD = end-stage renal disease.

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#### **Abbreviations Used**

CKD = chronic kidney disease

ESRD = end-stage renal disease

UT-TCC = upper-tract transitional-cell carcinoma

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