Upper Urinary Tract Transitional Cell Carcinoma and Lymph Node Involvement: Pre and Post Operative Outcomes

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INTRODUCTION

▪Upper urinary tract transitional cell carcinomas (UUT-TCC) comprise any malignancy arising from the renal pelvis to distal ureter. These cancers account for approximately 5-10% of all urothelial tumors. Two-thirds of cases are invasive with an estimated 5-year survival rate less than 50%. Pathologic staging, invasion into local structures, and lymph node involvement influence the overall survival rate. Lymph node dissection (LND) is associated with higher overall survival rates in UUT-TCC patients, likely by decreasing regional lymph node metastasis. Current literature suggests that removing eight to ten regional lymph nodes may improve survival. The outcomes of upper urinary tract malignancies (UTM) have significantly improved, however, no standard guidelines exist regarding the role of LND in UUT-TCC.

Objective

▪This analysis aims to investigate the impact of LND on outcomes in patients diagnosed with UUT-TCC.

METHOD

▪The American College of Surgeons National Surgical Quality Improvement Program (ACS NSQIP) is a Health Insurance Portability and Accountability Act (HIPAA) compliant data file containing patient cases from 706 participating hospital institutions. A total of 14,186 patients who underwent nephrectomy and nephroureterectomy were initially evaluated. Inclusion criteria included a postoperative diagnosis of UTM (n=923). The cohort was subgrouped to patients with LND. The groups were defined for patients with lymph node positive (LNP) (n=48) and lymph node negative (LNN) (n=255) on pathological staging. Patients without lymph nodes evaluated or unknown status were excluded. The two groups were then compared. Pearson's Chi-square test was performed for categorical variables, and t-test analysis for continuous variables. A univariate and multivariate analysis was performed with significant variables from the basic statistical analysis to predict independent factors. A Random forest model was also used. Statistical analysis was accepted at p<0.05.

Table 1. Patient Demographics and Post-Operative Outcomes and Variables, Lymph Node Positive vs Lymph Node Positive Patients

	Total Cohort		Lymph Node Positive		Lymph Node Negative		
	n = 303		n = 48 (15.8%)		n = 255 (84.2%)		
Patient Characteristics							
Mean Patient Age (SD)	70.12	10.32	70.22	13.45	70.10	9.68	P = 0.6
Height (in.) (SD)	66.82	4.01	65.96	4.00	66.98	4.00	P = 0.1
Weight (lbs.) (SD)	178.81	41.44	167.63	37.52	180.93	41.87	**P = 0.0**
Male Gender (%)	190	62.71%	25	52.08%	165	64.71%	P = 0.2
Non-Caucasian Race (%)	87	28.71%	10	20.83%	77	30.20%	P = 0.2
Ethnicity Hispanic (%)	8	2.64%	0	0.00%	8	3.14%	P = 0.3
Past Medical History /Co-morbidities							
Current Smoker (Within one year) (%)	51	16.83%	4	8.33%	47	18.43%	P = 0.1
Inpatient (%)	291	96.04%	48	100.00%	243	95.29%	P = 0.2
Transfer Status (Not Transferred - Admitted from Home) (%)	301	99.34%	48	100.00%	253	99.22%	P = 1.0
Functional Health Status Prior to Surgery (Independent) (%)	301	99.34%	48	100.00%	253	99.22%	P = 1.0
Prior Pelvic Surgery (%)	144	47.52%	25	52.08%	119	46.67%	P = 0.5
Prior Pelvic Radiation (%)	11	3.63%	1	2.08%	10	3.92%	P = 1.0
Chemo Within 90 days (%)	39	12.87%	7	14.58%	32	12.55%	P = 0.8
Perioperative Antibiotic Use (<72 hours) (%)	284	93.73%	47	97.92%	237	92.94%	P = 0.3
Mean Estimated Probability of Mortality (SD)	0.009	0.017	0.010	0.013	0.009	0.018	P = 0.5
Mean Estimated Probability of Morbidity (SD)	0.123	0.046	0.127	0.043	0.122	0.047	P = 0.4
Diabetes with Insulin Dependency (%)	24	7.92%	3	6.25%	21	8.24%	P = 0.7
Diabetes with Oral Agents (%)	50	16.50%	5	10.42%	45	17.65%	P = 0.3
Severe COPD (%)	20	6.60%	2	4.17%	18	7.06%	P = 0.7
HTN Requiring Meds (%)	179	59.08%	27	56.25%	152	59.61%	P = 0.7
Steroid Use for Chronic Conditions (%)	10	3.30%	3	6.25%	7	2.75%	P = 0.1
Dyspnea (%)	24	7.92%	2	4.17%	22	8.63%	P = 0.3
Malignancy Stage							
T0 (%)	13	4.30%	0	0.00%	13	5.10%	P = 0.2
T1 (T1a, T1b, T1c) (%)	92	30.40%	1	2.10%	91	35.70%	**P < 0.0**
T2 (T2a, T2b, T2c) (%)	38	12.50%	2	4.20%	36	14.10%	P = 0.0
T3 (T3a, T3b, T3c) (%)	126	41.60%	34	70.80%	92	36.10%	**P < 0.0**
T4 (%)	20	6.60%	11	22.90%	9	3.50%	**P < 0.0**
M0 (%)	147	48.50%	21	43.80%	126	49.40%	P = 0.5
M1 (%)	7	2.30%	4	8.30%	3	1.20%	**P = 0.0**
ASA Classification							
Class 1 (%)	1	0.30%	0	0.00%	1	0.40%	P = 1.0
Class 2 (%)	78	25.70%	11	22.90%	67	26.30%	P = 0.7
Class 3 (%)	202	66.70%	35	72.90%	167	65.50%	P = 0.4
Class 4 (%)	22	7.30%	2	4.20%	20	7.80%	P = 0.5
Operative Approach							
Planned Laparoscopic/Robotic (%)	200	66.01%	24	50.00%	176	69.02%	**P = 0.0**
Planned Open (%)	46	15.18%	13	27.08%	33	12.94%	**P = 0.0**
Unplanned Conversion to Open (%)	5	1.65%	0	0.00%	5	1.96%	P = 1.0
Outcome Variables							
Mean Operative Time (SD)	237.50	82.92	236.83	91.34	237.63	81.43	P = 0.9
Mean Length of Stay (SD)	4.31	4.91	5.06	4.18	4.16	5.03	P = 0.1
Mean Days from Operation to Discharge (SD)	3.93	3.72	4.58	3.18	3.80	3.80	P = 0.1
Mean Number of Nodes Evaluated (SD)	6.09	6.43	6.42	5.92	6.02	6.53	P = 0.6
Readmission (%)	22	7.26%	2	4.17%	20	7.84%	P = 0.5
Post Operative Complications							
Blood Transfusion (%)	31	10.23%	6	12.50%	25	9.80%	P = 0.6
Urinary Tract Infection (%)	21	6.93%	2	4.17%	19	7.45%	P = 0.5
Discharge to Home (%)	284	93.73%	43	89.58%	241	94.51%	P = 0.1
Prolonged Postop NPO or NGT Use (%)	16	5.28%	4	8.33%	12	4.71%	P = 0.2
Unplanned Reoperation Related to Principal Procedure (%)	8	2.64%	1	2.08%	7	2.75%	P = 1.0
Mortality (%)	2	0.66%	0	0.00%	2	0.78%	P = 1.0

Table 2. Univariate and Multivariate Analysis of Lymph Node Positive Patients

	Univariate Analysis		Multivariate Analysis	
	OR (95% CI)	P value	OR (95% CI)	P value
Weight (lbs.)	0.99 (0.98-1.00)	**0.042**	0.99 (0.98-1.00)	0.058
Operative Approach				
Planned Open	Referent		Referent	
Planned Laparoscopic/Robotic	0.35 (0.16-0.76)	**0.007**	0.37 (0.14-0.93)	**0.033**
T Malignancy Stage				
T1 (T1a, T1b, T1c)	Referent		Referent	
T2 (T2a, T2b, T2c)	5.06 (0.47-111)	0.191	5.35 (0.49-118)	0.180
T3 (T3a, T3b, T3c)	33.6 (7.02-604)	**<0.001**	35.5 (7.29-642)	**<0.001**
T4	111 (18.6-2157)	**<0.001**	94.5 (15.0-1874)	**<0.001**
M Malignancy Stage				
M1	7.64 (1.63-39.9)	**0.009**	2.29 (0.37-16.1)	0.369

Table 3. Patient Demographics and Post-Operative Outcomes and Variables, Patients with >8 Lymph Nodes Dissected vs ≤8 Lymph Nodes Dissected

	Total Cohort		>8 Lymph Nodes Dissected		≤8 Lymph Nodes Dissected		
	n = 303		n = 69 (22.77%)		n = 234 (77.23%)		
Patient Characteristics							
Mean Patient Age (SD)	70.12	10.32	68.93	10.39	70.46	10.30	P = 0.483
Height (in.) (SD)	66.82	4.01	66.47	3.68	66.93	4.10	**P = 0.384**
Weight (lbs.) (SD)	178.81	41.44	174.39	39.23	180.13	42.06	P = 0.297
Male Gender (%)	190	62.71%	43	62.32%	147	62.82%	P = 1.000
Non-Caucasian Race (%)	87	28.71%	24	34.78%	63	26.92%	P = 0.264
Ethnicity Hispanic (%)	8	2.64%	2	2.90%	6	2.56%	P = 1.000
Past Medical History /Co-morbidities							
Current Smoker (Within one year) (%)	51	16.83%	10	14.49%	41	17.52%	P = 0.683
Inpatient (%)	291	96.04%	68	98.55%	223	95.30%	P = 0.309
Prior Pelvic Surgery (%)	144	47.52%	35	50.72%	109	46.58%	P = 0.639
Prior Pelvic Radiation (%)	11	3.63%	3	4.35%	8	3.42%	P = 0.718
Chemo Within 90 days (%)	39	12.87%	11	15.94%	28	11.97%	P = 0.508
Perioperative Antibiotic Use (<72 hours) (%)	284	93.73%	65	94.20%	219	93.59%	P = 1.000
Mean Estimated Probability of Mortality (SD)	0.009	0.017	0.009	0.011	0.010	0.018	P = 0.585
Mean Estimated Probability of Morbidity (SD)	0.123	0.046	0.115	0.042	0.125	0.047	P = 0.088
Diabetes with Insulin Dependency (%)	24	7.92%	4	5.80%	20	8.55%	P = 0.624
Diabetes with Oral Agents (%)	50	16.50%	11	15.94%	39	16.67%	P = 1.000
Congestive Heart Failure (%)	3	0.99%	0	0.00%	3	1.28%	P = 1.000
Severe COPD (%)	20	6.60%	2	2.90%	18	7.69%	P = 0.267
HTN Requiring Meds (%)	179	59.08%	39	56.52%	140	59.83%	P = 0.725
Steroid Use for Chronic Conditions (%)	10	3.30%	1	1.45%	9	3.85%	P = 0.465
Dyspnea (%)	24	7.92%	5	7.25%	19	8.12%	P = 1.000
Malignancy Stage							
T0 (%)	1	0.33%	0	0.00%	1	0.43%	P = 1.000
T1 (T1a, T1b, T1c) (%)	78	25.74%	21	30.43%	57	24.36%	P = 0.391
T2 (T2a, T2b, T2c) (%)	202	66.67%	43	62.32%	159	67.95%	P = 0.468
T3 (T3a, T3b, T3c) (%)	22	7.26%	5	7.25%	17	7.26%	P = 1.000
T4 (%)	1	0.33%	0	0.00%	1	0.43%	P = 1.000
M0 (%)	78	25.74%	21	30.43%	57	24.36%	P = 0.391
M1 (%)	202	66.67%	43	62.32%	159	67.95%	P = 0.468
ASA Classification							
Class 1 (%)	13	4.29%	2	2.90%	11	4.70%	P = 0.756
Class 2 (%)	92	30.36%	19	27.54%	73	31.20%	P = 0.666
Class 3 (%)	38	12.54%	9	13.04%	29	12.39%	P = 1.000
Class 4 (%)	126	41.58%	30	43.48%	96	41.03%	P = 0.823
Operative Approach							
Planned Laparoscopic/Robotic (%)	200	66.01%	41	59.42%	159	67.95%	P = 0.242
Planned Open (%)	46	15.18%	17	24.64%	29	12.39%	**P = 0.021**
Unplanned Conversion to Open (%)	5	1.65%	1	1.45%	4	1.71%	P = 1.000
Outcome Variables							
Mean Operative Time (SD)	237.50	82.92	236.23	78.54	237.88	84.32	P = 0.881
Mean Length of Stay (SD)	4.31	4.91	4.62	4.42	4.21	5.05	P = 0.515
Mean Days from Operation to Discharge (SD)	3.93	3.72	4.43	4.33	3.78	3.51	P = 0.252
Mean Number of Nodes Evaluated (SD)	6.09	6.43	15.64	6.93	3.27	2.14	**P < 0.001**
Readmission (%)	22	7.26%	6	8.70%	16	6.84%	P = 0.796
Post Operative Complications							
Urinary Leak/Fistula (%)	4	1.32%	3	4.35%	1	0.43%	**P = 0.038**
Ureteral Obstruction (%)	5	1.65%	1	1.45%	4	1.71%	P = 1.000
Blood Transfusion (%)	31	10.23%	7	10.14%	24	10.26%	P = 1.000
Sepsis (%)	3	0.99%	2	2.90%	1	0.43%	P = 0.131
Urinary Tract Infection (%)	21	6.93%	2	2.90%	19	8.12%	P = 0.180
Acute Renal Failure (%)	2	0.66%	0	0.00%	2	0.85%	P = 1.000
Discharge to Home (%)	284	93.73%	66	95.65%	218	93.16%	P = 0.580
Prolonged Postop NPO or NGT Use (%)	16	5.28%	5	7.25%	11	4.70%	P = 0.373
Mortality (%)	2	0.66%	1	1.45%	1	0.43%	P = 0.404
Surgical Site Infection (SSI)							
Superficial SSI (%)	5	1.65%	0	0.00%	5	2.14%	P = 0.592
Organ Space SSI (%)	5	1.65%	2	2.90%	3	1.28%	P = 0.320

Table 4. Univariate and Multivariate Analysis of Patients with >8 Lymph Nodes Dissected vs ≤8 Lymph Nodes Dissected

	Univariate Analysis		Multivariate Analysis	
	OR (95% CI)	P value	OR (95% CI)	P value
Past Medical History /Co-morbidities				
Currently on Dialysis (Pre-op)	6.96 (0.66-151)	0.116	7.74 (0.68-176)	0.096
M Malignancy Stage				
M1	4.74 (1.02-24.5)	**0.045**	3.99 (0.74-23.1)	0.104
Operative Approach				
Planned Open	Referent		Referent	
Planned Laparoscopic/Robotic	0.44 (0.22-0.89)	**0.020**	0.52 (0.25-1.09)	0.077
Unplanned Conversion to Open	0.43 (0.02-3.18)	0.462	0.62 (0.03-4.99)	0.688
Post Operative Complications				
Urinary Leak/Fistula	10.59 (1.33-216)	0.042	19.4 (2.02-476)	**0.010**
Sepsis	6.96 (0.66-151)	0.116	23.6 (1.69-703)	**0.020**
Urinary Tract Infection	0.34 (0.05-1.20)	0.151	0.21 (0.02-0.93)	**0.038**
Pneumonia	2.61 (0.50-12.1)	0.216	1.72 (0.27-9.14)	0.539

Significant p values in bold. COPD = Chronic obstructive pulmonary disease, HTN = Hypertension, ASA = American Society of Anesthesiologists

RESULTS

▪The overall rate of lymph node involvement was 5.2% for 923 patients that underwent nephroureterectomy for UTM.
▪Among 303 patients with at least one lymph node evaluated, 48 (15.8%) were LNP.
▪On Chi-square and t-test analysis, the LNN group had higher pT1 staging and planned laparoscopy. The LNP group had higher pT3, pT4, and pM1 staging, and had more planned open procedures compared to the LNN group.
▪Postoperatively, there were no differences between the two groups including rate of lymphoceles or length of hospital stay (Table 1).
▪On multivariate analysis, pT3 (p=0.001) and pT4 (p<0.001) were associated with lymph node involvement.,
▪The LNP group was less likely to be planned laparoscopic/robotic compared to the LNN group (p=0.03).
▪The previously statistically significant difference in weight, pT1 staging, and pM1 staging were statistically insignificant on multivariable regression analysis.
▪No significant findings in patient characteristics, comorbid conditions, or disease staging/classification when looking at patients who had >8 or ≤8 lymph nodes dissected.

CONCLUSION

- Our study shows that pT3 and pT4 are independently associated with lymph node involvement.
- No differences in postoperative outcomes were seen on multivariable analysis including number of nodes evaluated, lymphocele occurrences, or length of hospital stay.
- Our data suggests that for patients with suspected pT3 or pT4 UUT-TCC, nephroureterectomy should be performed in conjunction with LND.

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