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Article

Upper Urinary Tract Carcinoma: Does Tumor Location Matter?

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Abstract

Objective: to investigate the effect of tumor location on surgical and oncological outcomes in patients receiving robot-assisted radical nephroureterectomy (RANU) for upper urinary tract carcinoma (UTUC). **Methods:** a case-control study of 60 consecutive patients with UTUC who underwent RANU, no exclusions. Patients were divided into two groups based on tumor location: 20 patients (33%) with ureteral tumors (Group 1) and 40 patients (67%) with renal pelvis tumors (Group 2). Demographics, perioperative data, and pathology were analyzed. Cancer-specific survival (CSS) and overall survival (OS) were estimated using Kaplan–Meier and Cox regression analyses. **Results:** The rates of console time, blood transfusion, and complications were comparable in both groups. Group 1 had longer hospital stays (8.3 days vs. 7.5 days, p = 0.03) and higher readmission rates (20% vs. 5%, p = 0.07). In oncological outcomes, the T-stage distribution was similar. High-grade pathology was present in 72.5% of Group 2 and 50% of Group 1 (p = 0.04). All achieved R0 resection. Over a median 28-month follow-up, 5 patients experienced bladder recurrence (p = 0.5), and 7 (12%) developed distant metastases (p = 0.6). Cancer-specific death occurred in 5 patients, and 4 died from unrelated causes. The CSS and OS rates were 92% and 85%, respectively, with no significant differences between the groups (p = 0.7, p = 0.5). **Conclusion:** Our current research did not demonstrate that tumor location significantly affects postoperative surgical and oncological outcomes following RANU for UTUC. Additional studies are needed to explore the proposed hypothesis.

Keywords: upper urinary tract carcinoma (UTUC); RANU; tumor location

1. Introduction

Concerning oncological outcomes, ureteral tumors have been shown to exhibit significantly higher recurrence rates compared to tumors originating in the renal pelvicalyceal system [1]. In the analysis involving 637 patients across multiple institutions, Yafi et al. found that the location of ureteral tumors, especially when combined with the multifocal disease in the renal pelvis, acts as an independent prognostic factor for increased recurrence of disease and cancer-specific mortality [2]. Other authors reported that the ureteral location is associated with a shorter metastasis-free survival [3]. Additionally, multifocal presentation of ureteral tumors is a significant prognostic factor of the disease's progression-free survival [4]. Another study demonstrated a correlation between tumor location and the incidence of positive surgical margins [5]. Some series suggested that tumor locations within the lower ureter are associated with poorer oncological outcomes [6]. Moreover, two meta-analyses revealed a link between tumor location and intravesical recurrence [7,8]. However, Favaretto et al. found that tumor location did not predict bladder recurrence or cancer-specific survival [9]. Shibing et al. proved in their large multi-institutional cohort that tumor size over 3 cm

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correlated with worse recurrence-free, cancer-specific, and overall survival [10]. These findings were corroborated by subsequent case series [11]. Taken together, the majority of current literature suggests that ureteral tumor location is associated with poorer oncological outcomes. The present study evaluates the impact of tumor location on surgical and oncological outcomes in a contemporary cohort of patients who underwent robot-assisted nephroureterectomy (RANU), reflecting real-world clinical conditions.

2. Methods

Patients presenting with painless hematuria underwent a standardized diagnostic workup, including sonography, laboratory tests, and urethrocystoscopy. In cases where bladder cancer was excluded or located near the ureteral orifice, retrograde pyelography and renal pelvic urine cytology were performed. A CT scan with urinary phase was conducted for suspicious findings. If the diagnosis remained unclear, ureterorenoscopy (URS) with biopsy was carried out. Patients with signs of locally advanced or metastatic disease were counseled on neoadjuvant chemotherapy.

Based on tumor location, a total of 60 patients were divided into two groups: Group 1 included 18 patients with ureteral tumors and 2 with multifocal tumors, and Group 2 included 40 patients with renal pelvis tumors. Lymphadenectomy (LAD) was performed in high-risk cases: ipsilateral iliac nodes in ureteral tumors and hilar, paraaortic, and interaortocaval nodes in renal pelvis tumors. All patients underwent RANU between July 2019 and July 2024. Clinical and oncological variables—such as tumor size, multifocality, hydronephrosis, cytologic grade, concurrent bladder cancer, and smoking history—were prospectively collected in an institutional database and retrospectively analyzed. All surgeries were performed by a single experienced robotic surgeon (>2,500 robotic procedures) using the Da Vinci X® system (Intuitive Surgical, Sunnyvale, CA, USA).

Demographic and perioperative data were analyzed, and postoperative complications were classified according to the Clavien-Dindo classification [12]. Follow-ups were performed regularly according to EAU guidelines [13]. Data were collected and analyzed with SPSS® v29. Categorical variables were represented as frequencies, while continuous variables were presented as mean values. The Kolmogorov-Smirnov test was utilized to assess normal distribution. The independent T-test and Mann-Whitney U tests were applied to parametric and non-parametric variables for matched-pair analysis. A one-way ANOVA test was performed on parametric numeric variables, and the independent samples Kruskal-Wallis test was employed for non-parametric variables. Recurrence-free survival and CSS probabilities were estimated using Kaplan-Meier and Cox regression analyses. The research adhered to the ethical guidelines specified in the Declaration of Helsinki and received approval from the ethics committees of the Westfalen-Lippe Medical Association and the University of Muenster (2023-500-f-S).

3. Results

3.1. Baseline Parameters

The mean age of the patients was 70 years, and the mean BMI was 31 kg/m², with no significant differences between groups (p = 0.9 and 0.2, respectively; Table 1). Patients presented with multiple comorbidities; however, ASA scores were comparable across groups (p = 0.9). Anticoagulant use was more frequent in Group 1 (50%) than in Group 2 (30%) (p=0.03). According to EAU guidelines, 40% of Group 1 and 35% of Group 2 patients were classified as high-risk (p = 0.07). Preoperative histologic diagnosis was more commonly achieved in Group 1, with 35% having Ta and 15% T1 tumours. In contrast, only 15% of Group 2 patients had histologically confirmed carcinoma before surgery. Overall, 72% of patients underwent surgery based solely on clinical and radiological findings, a trend more pronounced in Group 2 (85%) compared to Group 1 (45%) (p = 0.002).

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Table 1. baseline characteristics and preoperative clinical and oncological parameters:.

UTUC	**Total (N=60)**	**Ureter N=20, 34%**	**Kidney pelvis N=40, 66%**	***p-Value***
Age (years), mean	70	70	71	0.9
BMI (kg/m²), mean	31	33	31	0.2
ASA-score				
1	16 (26,7)	5 (25)	11 (27)	
2	15 (25)	2 (10)	13(33)	0.9
3	29 (28)	13 (65)	16 (40)	
Risk Group according to EAU Guidelines	38	12 (60)	26 (65)	0.7
	22	8 (40)	14 (35)	
Preoperative Histology				
No Histology	43 (72)	9 (45)	34 (85)	
Tis	1 (1,6)	1 (5)	0	
Ta	12 (20)	7 (35)	5 (12)	*0.002*
T1	3 (5)	3 (15)	0	
T2	0	0	0	
T3	1 (1,6)	0	1 (3)	
Neoadjuvant Chemotherapy				0.2
cisplatin-Gemcitabine	2	0	2 (5)	
Anti-coagulation				
Aspirin	18	9 (45)	9 (22,5)	*0.03*
NOAC	6	3 (15)	3 (7,5)	
Bladder cuff				
No	10 (16)	4 (20)	6 (15)	0.6
yes	50 (84)	16 (80)	34 (85)	

Categorical data are presented as numbers %, UTUC: Upper Urinary Tract Urothelial Cell Carcinoma, BMI: body mass index, ASA: American Association of Anesthesiology Morbidity Score, EAU: European association for Urology, NOAC: New Oral Anticoagulants.

Table 2. intra- and postoperative results and oncological outcomes.

UTUC	**Total N=60**	**Ureter N=20, 34%**	**Kidney pelvis N=40, 66%**	**P-Value**
Console time (minute), mean (SD)	71	65	75	0.6
Pathological tumor stage, n (%)*				
Non muscle invasive (Tis-T1)	30 (50)	12 (60)	18 (45)	
Muscle invasive locally confined (T2)	10 (16)	4 (20)	6 (15)	0.2
Locally advanced (T3-4)	20 (33)	4 (20)	16 (40)	
Urothelial carcinoma grade*, n (%)				
0	3 (5)			
1	13 (22)	2 (10)	1 (2,5)	
2	5 (8)	7 (35)	6 (15)	0.04
3	39 (65)	1 (5)	4 (10)	
		10 (50)	29 (72,5)	
Postoperative Chemotherapy (yes. vs. none), n (%)	14 (23)			
cisplatin-Gemcitabine, n (%)	2 (3)	4 (20)	10 (25)	0.6
Initiation of CI therapy, n (%)			2 (5)	
Positive surgical margins (total), (%)	0	0	0	

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Number of Patients received LAD	22 (37)	8 (40)	14 (35)	0.7
Number of lymph nodes removed in patients, who received a lymphadenectomy, mean (SD)	10	8	11	0.7
Number of patients, who had a lymphadenectomy and had metastases among the total number of surgically treated patients	3 (14)	1 (12,5)	2 (14)	0.7
Length of hospitalization (days), mean	7,7	8,3	7,5	0.03
Transfusion rate, n (%)	5 (8)	2 (10)	3 (7,5)	0.7

Categorical data are presented as numbers %, UTUC: Upper Urinary Tract Urothelial Cell Carcinoma, RARC: robot-assisted radical cystectomy. SD: standard deviation, CI: Checkpoint inhibitor, * Grade according to WHO classification 1999 (Busch et al.)[20].

Table 3. complications, readmissions and oncological longterm outcomes.

		Total (n=60)	**Ureter N=20, 34%**	**Kidney pelvis N=40, 66%**	**P-value**
Total Complications		16 (26)	7	9	0.25
Minor	**CDC I**	4 (6,6)	1 (5)	3 (7,5)	
	CDC II	1 (1,6)	1 (5)		
Major	**CDC IIIa**	1 (1,6)		1 (2,5)	
	CDC III b	7 (12)	4 (20)	3 (7,5)	
	CDC VI	1 (1,6)	0	1 (2,5)	
	CDC V	2 (3,2)	1 (5)	1 (2,5)	
Readmissions		6 (10)	4 (20)	2 (5)	0.07
Bladder Recurrence		5 (8)	1 (5)	4 (10)	0.5
Distant metastasis		7 (12)	3 (15)	4 (10)	0.6
Cancer specific survival		55 (92)	18 (90)	37 (92.5)	0.7
Overall Survival		51 (85)	18 (90)	33 (82.5)	0.5

Categorical data are presented as numbers %, UTUC: Upper Urinary Tract Urothelial Cell Carcinoma, CD: Clavien-Dindo[12].

3.2. Intra- and Postoperative Data

Console time was, on average, 10 minutes longer in Group 2, although the difference between the Groups was not significant (p = 0.6). Group 1 patients had a significantly longer hospital stay compared to Group 2 (8.3 days vs. 7.5 days, p = 0.03). Overall, 50% of patients had non-muscle-invasive disease, and 33% had locally advanced tumors. Although T3–T4 tumors were more frequent in Group 2 (40%) than in Group 1 (20%), the difference was not statistically significant (p = 0.2). High-grade tumors were observed more often in Group 2 (72.5%) than in Group 1 (50%; p=0.04). Three patients had no malignancy in final pathology—1 following inductive chemotherapy preoperatively and 2 with prior Ta diagnoses. Adjuvant chemotherapy was administered to 14 patients (23%), and 2 patients received checkpoint inhibitors; no significant difference in adjuvant therapy was observed between groups (p = 0.6). All patients had negative surgical margins. LAD was performed in 37% of patients, with a mean of 10 lymph nodes removed, and there was no significant difference between groups (p = 0.7). Primary metastases were present in 14% of those who underwent LAD. Perioperative transfusions were required in 5 patients (8%), with an equal distribution between groups (p = 0.7). The overall 90-day postoperative complication rate was 26%, with 8% classified as minor and 18% as major complications requiring intervention. No significant difference was observed between the groups (p = 0.25). Major complications occurred in 4 patients (20%) in Group 1 and 5 patients (12.5%) in Group 2. Readmission within 90 days occurred in 20% of Group 1 patients compared to 5% in Group 2 (p = 0.07).

3.3. Oncological and Survival Outcomes

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Over an average follow-up period of 28 months, bladder recurrence was observed in 4 patients from Group 2 and 1 patient from Group 1 (p = 0.5). Distant metastases occurred in 7 patients (12%), with no significant difference between the groups (p = 0.6). Five patients died from cancer-related causes, whereas four deaths were due to cancer-unrelated reasons, including two perioperative fatalities due to multiorgan failure and cardiac decompensation. The CSS rates were 90% versus 92.5%, with no significant differences between groups (p = 0.7). The OS rates were 90% versus 82.5%, with no significant differences between groups (p = 0.5).

4. Discussion

Studies investigating tumor location, alongside other clinicopathologic factors influencing survival following RANU for UTUC, primarily focus on long-term outcomes and evaluate tumor location as a prognostic indicator of poorer survival [5,7,8]. However, the impact of tumor location on short-term surgical outcomes has not been thoroughly investigated.

The principal finding of our study is that tumor location (ureteral vs. renal pelvis) did not significantly affect short-term surgical or oncological outcomes following RANU for UTUC. Our observation aligns with findings from prior research [14]. In our cohort, 33% of patients were diagnosed with locally advanced (T3–T4) disease, with a higher incidence among those with renal pelvis tumors (40%) compared to ureteral tumors (20%). Favaretto et al. [9] conducted a retrospective study involving 234 patients and found that pathological stage and nodal status were the only independent predictors of disease recurrence. Tumor location, on the other hand, did not affect outcomes. Similarly, our study found no significant associations between tumor stage, location, or nodal status and oncological outcomes, likely due to the relatively short follow-up period of less than three years. No significant differences were observed in bladder recurrence, distant metastasis, or overall survival between the groups. The oncological outcomes within our cohort—comprising a bladder recurrence rate of 8%, a distant metastasis rate of 12%, and a cancer-specific survival rate of 92%—align with the findings documented in currently available literature [5,15]. This finding may, in part, be attributed to the relatively short median follow-up period of 28 months. Another possible explanation for the low recurrence rates observed in our cohort is the absence of positive surgical margins among all patients. This aligns with findings by Colin et al., who reported significantly lower 5-year CSS and metastasis-free survival in patients with positive surgical margins compared to those with negative margins (59.1% and 51.6% vs. 83.3% and 79.3%, respectively) [16].

Regarding perioperative outcomes and postoperative non-oncological metrics, patients with ureteral tumors undergoing RANU had a median console time 10 minutes shorter than those with renal pelvis tumors (65 vs. 75 minutes). Interestingly, our overall median operative time of 71 minutes is significantly lower than the durations reported in the systematic review by Stonier et al. [14] and other studies [17,18]. This shorter operative time likely results from avoiding robot redocking, as well as the efficiency and expertise of our surgical team.

In our study, the transfusion rate was 8%, consistent with earlier reports [17]. Notably, some patients had surgery after extended periods of gross hematuria and received transfusions because of existing comorbidities and to reduce perioperative risks.

Patients in Group 1 experienced longer hospital stays compared to those in Group 2 (8.3 vs. 7.5 days), exceeding durations reported in previous studies [17]. This longer stay may reflect local clinical practices, where patients are typically admitted the day before surgery and discharged only after the urinary catheter is removed. Additionally, many older patients often require more time for discharge planning and home care arrangements.

Our 90-day readmission rate of 10% corresponds with findings by Liedeberg et al. [18], who reported a rate of 8.2%. However, their reported major complication rate was markedly lower (1/146 patients) compared to ours (11/60 patients), despite similar baseline characteristics. This discrepancy may reflect the impact of the surgical learning curve in our setting, as well as methodological differences—specifically, the exclusion of 20 patients undergoing simultaneous cystectomy or other procedures in the Swedish series. In contrast, no exclusions were applied in our cohort. In our cohort,

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the 90-day postoperative mortality rate was 3% (2 patients), which is slightly higher than the rates reported in a recent meta-analysis comparing robotic and laparoscopic approaches [14,19]. However, the two deaths observed in our cohort were likely attributable to pre-existing patient vulnerabilities rather than the surgical technique or complications.

This study has several limitations. In addition to its retrospective design, small sample size, and relatively short follow-up period, we did not exclude patients with prior or simultaneous cystectomy, nor did we exclude those who underwent RANU in a palliative setting. While this approach reflects real-world conditions and enhances external validity, it might have introduced variability that influenced our results. Furthermore, the impact of chemotherapy or immunotherapy on survival was not evaluated, as it fell beyond the scope of this analysis. Lastly, a learning curve effect is evident, with higher complication rates observed earlier in the study period compared to lower rates toward the end.

5. Conclusions

In our single-center, retrospective study of patients undergoing robot-assisted nephroureterectomy for upper tract urothelial carcinoma, tumor location was not found to influence short-term surgical or oncological outcomes significantly. While ureteral tumors have previously been associated with poorer prognosis, our data did not confirm this association, potentially due to the limited follow-up period. The use of a standardized surgical technique may have contributed to the uniformly favorable outcomes observed across both groups. These findings underscore the need for larger, multicenter prospective studies with extended follow-up to assess better the prognostic significance of tumor location in upper tract urothelial carcinoma and to inform individualized treatment strategies.

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Clinical trial number: Not applicable.

Abbreviations

URS	ureterorenoscopy
EAU	European Association of urology
CDC	Clavien-Dindo Complication
UTUC	upper urinary tract carcinoma
RANU	robot-assisted radical nephroureterectomy
RARC	robot-assisted radical Cystectomy
LAD	Lymphadenectomy
LN	Lymph nodes
URS	ureterorenoscopy
AC	anticoagulation
ASA	American association of anesthesiology score
BMI	body mass index
Hgb	hemoglobin
PSM	positive surgical margins
CCS	cancer-specific survival
RFS	recurrence-free survival
OS	overall survival

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BR bladder recurrence

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