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JU Insight

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Study Need and Importance: Upper tract urothelial carcinoma (UTUC) is a rare malignancy, representing only 5%−10% of urothelial carcinomas. Despite its incidence, this malignancy is typically diagnosed at a high stage with 30% of patients presenting with lymph node metastasis. Utility of lymph node dissection (LND) during nephroureterectomy on oncologic outcomes in UTUC is not well defined. In this study, we sought to evaluate the impact of LND on prognosis, survival and oncologic outcomes in a multi-institutional cohort of patients with UTUC.

What We Found: In our study, we found that lymphadenectomy in patients undergoing robotic nephroureterectomy with lymph node positive disease does not improve 2-year overall (p <0.001), cancer-specific (p <0.001) or recurrence-free (p <0.001) survival outcomes. However, LND can provide important prognostic information for further characterization, staging and treatment of tumors before or after surgical resection. Furthermore, we found that large (OR 1.14, p=0.001) and high-grade (OR 11.74, p=0.015) tumors were more likely to have lymph node metastasis on diagnosis. Lastly, we observed that patients with clinical node negative disease may benefit from extended node dissection. Patients with clinical node negative disease who had dissection of 10 or more lymph nodes showed improved 2-year recurrence-free survival (p=0.043) compared to those with node negative disease and fewer than 10 nodes dissected, and patients with no node dissection (see Figure).

Limitations: Our multi-institutional study is limited by lack of a standardized dissection template and central pathological review, which may limit the accuracy of lymph node yield. However, surgeries were performed by experienced urologists at centers of excellence.

Interpretation for Patient Care: Overall, our data point to refinement of selection criteria for LND in UTUC. Our study shows that in patients with large tumors and high-grade disease, LND may be deferred due to high likelihood of lymph node metastasis. Additionally, in patients with clinical node-negative disease, extended LND may provide a significant survival benefit.

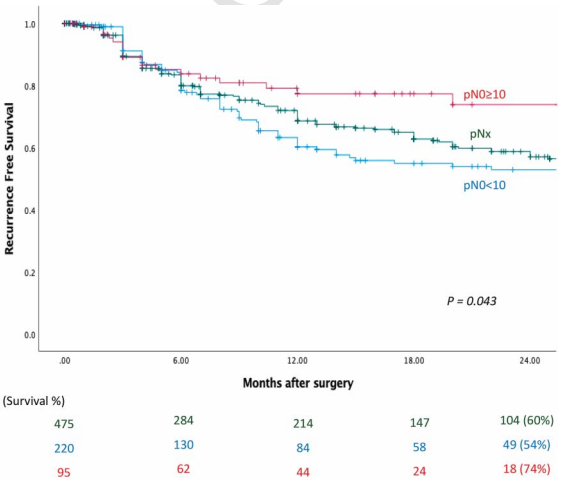

Figure. Kaplan-Meier analysis comparing patients who did not undergo LND (*pNx*), and patients who underwent LND with negative (*pN0*) and positive (*pN+*) nodes for recurrence-free survival outcomes.

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Outcomes of Lymph Node Dissection in Nephroureterectomy in the Treatment of Upper Tract Urothelial Carcinoma: Analysis of the ROBUUST Registry

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Purpose: We sought to evaluate outcomes of lymph node dissection (LND) in patients with upper tract urothelial carcinoma.

Materials and Methods: We performed a multicenter retrospective analysis utilizing the ROBUUST (for RObotic surgery for Upper Tract Urothelial Cancer Study) registry for patients who did not undergo LND (pNx), LND with negative lymph nodes (pN0) and LND with positive nodes (pN+). Primary and secondary outcomes were overall survival (OS) and recurrence-free survival (RFS). Multivariable analyses evaluated predictors of outcomes and pathological node positivity. Kaplan-Meier analyses (KMAs) compared survival outcomes.

Results: A total of 877 patients were analyzed (LND performed in 358 [40.8%]/pN+ in 73 [8.3%]). Median nodes obtained were 10.2 for pN+ and 9.8 for pN0. Multivariable analyses noted increasing age (OR 1.1, p <0.001), pN+ (OR 3.1, p <0.001) and pathological stage pTis/3/4 (OR 3.4, p <0.001) as predictors for all-cause mortality. Clinical high-grade tumors (OR 11.74, p=0.015) and increasing tumor size (OR 1.14, p=0.001) were predictive for lymph node positivity. KMAs for pNx, pN0

ABBREVIATIONS and Acronyms

BMI = body mass index
CSS = cancer-specific survival
EBL = estimated blood loss
KMA = Kaplan-Meier analysis
LN = lymph node
LND = lymph node dissection
MVA = multivariable analysis
OS = overall survival
pN+ = patients who underwent lymph node dissection with positive nodes
pN0 = patients who underwent lymph node dissection with negative nodes
pNx = patients who did not undergo lymph node dissection
RFS = recurrence-free survival
UC = urothelial carcinoma
UTUC = upper tract urothelial carcinoma

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and pN+ demonstrated 2-year OS of 80%, 86% and 42% (p <0.001) and 2-year RFS of 53%, 61% and 35% (p <0.001), respectively. KMAs comparing pNx, pN0 ≥10 nodes and pN0 <10 nodes showed no significant difference in 2-year OS (82% vs 85% vs 84%, p=0.6) but elicited significantly higher 2-year RFS in the pN0 ≥10 group (60% vs 74% vs 54%, p=0.043).

Conclusions: LND during nephroureterectomy in patients with positive lymph nodes provides prognostic data, but is not associated with improved OS. LND yields ≥10 in patients with clinical node negative disease were associated with improved RFS. In high-grade and large tumors, lymphadenectomy should be considered.

Key Words: lymph node excision, nephrectomy, nephroureterectomy

Upper tract urothelial carcinoma (UTUC) is a rare malignancy, representing only 5%−10% of urothelial carcinomas (UCs).[1] Despite low incidence, UTUC is typically diagnosed at high stage and carries a poorer prognosis than UC of the bladder.[2] Thirty percent of patients with UTUC present with lymph node (LN) metastasis, an independent risk factor for poor oncologic outcomes.[3,4]

Benefits of LN dissection (LND) in UC of the bladder on oncologic outcomes are well-established.[5,6] Although bladder UC and UTUC share similar characteristics, it is unclear whether oncologic benefits are present for LND in UTUC.[7,8] Nephroureterectomy with bladder cuff excision is the standard treatment for UTUC, but studies assessing value of LND in nephroureterectomy on oncologic outcomes have been more controversial.[1,8,9] Recent European Association of Urology guidelines recommend LND for optimal tumor staging in clinical circumstances suspicious for LN positivity, but impact of LND in circumstances of clinical node negativity are unclear.[10,11] We sought to evaluate impact of LND on prognosis, survival and oncologic outcomes in a contemporary cohort of patients with UTUC.

METHODS

Patient Populations/Study Design

We performed a multicenter retrospective analysis utilizing the ROBUUST registry (for RObotic surgery for Upper Tract Urothelial Cancer Study) of UTUC patients undergoing nephroureterectomy from 2006−2019. Our evaluation and operative protocols have been recently described.[12] Institutional Review Board approval was obtained at all centers (IRB No. 161197). Patients presenting with signs and symptoms for UTUC underwent radiological staging and tissue confirmation via ureteroscopic or percutaneous biopsy. Decision to proceed with LND was based on presence of clinical lymphadenopathy or risk for LN metastasis. Anatomical template of LND was at the treating surgeon's discretion. We excluded patients who presented with metastatic disease and variant histologies.

Data Collected

This is a retrospectively collected data set by data set managers at participating institutions. Demographic, clinical and disease features were recorded. Demographics included patient age, gender and body mass index (BMI, kg/m^2). Clinical disease features included tumor size (cm), grade and node status at time of diagnosis, and receipt of neoadjuvant or adjuvant chemotherapy. Perioperative parameters included estimated blood loss (EBL, ml), and intraoperative and 30-day complications (Clavien).[13] Pathological data included tumor size and stage,[14] focality, grade, presence of lymphovascular invasion, LNs removed and margin status. Survival outcome data included recurrence, overall survival (OS) and cancer-specific survival (CSS).

Statistical Analysis

The cohort was divided into patients who did not undergo LND (pNx), patients who underwent LND with negative LNs (pN0) and patients who underwent LND with positive nodes (pN+). Primary outcome was OS. Secondary outcomes were CSS and recurrence-free survival (RFS). Descriptive analyses were conducted utilizing Kruskall Wallis Test (nonparametric 1-way ANOVA) and Mann Whitney U tests (see supplementary Table, https://www.jurology.com) for categorical variables and ANOVA for continuous variables. Multivariable analyses (MVAs) using Cox regression was conducted for OS, CSS and RFS utilizing clinically significant variables and known risk factors found on descriptive analyses. Logistic regression MVAs were conducted for predictors of pathological node positivity. Kaplan-Meier analyses (KMAs) evaluated survival outcomes based on nodal status. SPSS® v.27 (IBM®, Armonk, New York) were utilized for statistical analyses, with p <0.05 considered significant.

RESULTS

A total of 877 patients were analyzed (mean followup 13.4 months). LND was performed in 358 (40.8%), with pN+ in 73 (8.3%). Mean number of nodes removed for pN0 and pN+ was 9.8 and 10.2, respectively. Table 1 presents demographics and disease characteristics comparing pNx, pN0 and pN+ patients. Compared to pN0/pNx patients, pN+ patients had larger mean clinical tumor size (pN+ 4.1 vs pN0 3.6 vs pNx 3.3 cm, p=0.01), greater proportion presenting with clinical lymphadenopathy (pN+ 23.3% vs pN0 4.2% vs pNx 4.3%, p <0.001) and high-stage (Tis/III/IV) tumors (pN+ 98.6% vs pN0 82.8% vs pNx 80.2%, p <0.001). Patients with pN+ had greater EBL compared to both pN0/pNx patients (pN+ 241 vs pN0 155 vs pNx 143 ml, p <0.001). Patients had no differences in

Table 1. *Demographics and clinical disease characteristics*

Variable	LNx	LN0	LN+	p Value
No. pts	519	285	73	
Mean mos followup (SD)	13.7 (16.7)	15.6 (18)	10.9 (13.6)	
Mean yrs age (SD)	71.3 (10.1)	69.1 (9.6)	71.1 (9.8)	0.01
No. sex (%):				0.007
Female	232 (65.4)	95 (33.3)	28 (38.4)	
Male	287 (55.3)	190 (66.7)	45 (61.6)	
Mean kg/m^2 BMI (SD)	27.3 (5.1)	27.7 (5.8)	26.5 (4.3)	0.2
Mean cm clinical tumor size (SD)	3.3 (1.9)	3.6 (1.9)	4.1 (2.1)	0.01
No. multifocal (%)	159 (30.6)	53 (18.6)	14 (19.2)	<0.001
No. lymphadenopathy (%)	22 (4.3)	12 (4.2)	17 (23.3)	<0.001
Mean ml EBL (SD)	143 (166)	155 (134)	241 (333)	<0.001
No. complications (%):				
Intraop	17 (3.3)	7 (2.5)	5 (6.8)	0.2
Postop	125 (24.1)	59 (20.8)	22 (30.1)	0.5
No. chemotherapy (%):				
Neoadjuvant	34 (6.6)	30 (10.5)	13 (17.8)	0.003
Adjuvant	40 (7.7)	23 (8.2)	26 (36.6)	<0.001
No. pos margin (%)	25 (4.8)	9 (3.2)	11 (15.3)	<0.001
Mean No. nodes removed (SD)	0 (0.0)	9.8 (9.5)	10.2 (9.5)	<0.001
No. tumor grade (%):				<0.001
Low (I, II)	103 (19.8)	49 (17.2)	1 (1.4)	
High (Ca *in situ*, III, IV)	416 (80.2)	236 (82.8)	72 (98.6)	
No. pathological stage (%):				<0.001
Low (I, II)	370 (71.3)	213 (74.7)	16 (21.9)	
High (Tis, III, IV)	149 (28.7)	72 (25.3)	57 (78.1)	
No. lymphovascular invasion (%)	100 (19.3)	35 (12.3)	53 (72.6)	<0.001

*p Value generated using Kruskall-Wallis Test.

intraoperative (p=0.2) and postoperative complications (p=0.5). Compared to pN0 and pNx patients, pN+ patients had a greater proportion of positive surgical margins (pN+ 15.3% vs pN0 3.2% vs pNx 4.8%, p <0.001), high-grade tumors (pN+ 78.1% vs pN0 25.3% vs pNx 28.7%, p <0.001) and lymphovascular invasion (pN+ 72.6% vs pN0 12.3% vs pNx 19.3%, p <0.001). Patients with pN+ were more likely to receive neoadjuvant therapy (p=0.003).

Table 2 demonstrates MVAs for outcomes and LN positivity. Cox regression for all-cause mortality noted increasing age (HR 1.06, p <0.001), pN+ (HR 2.77, p <0.001) and pathological stage pTis/3/4 (HR 3.89, p <0.001) as risk factors associated with worsened all-cause mortality. Cox regression for cancer-specific mortality noted male sex (HR 2.38, p=0.008), pN+ (HR 2.74, p=0.006) and pathological stage pTis/3/4 (HR 4.18, p=0.003) as predictive for cancer-specific mortality. Cox regression for recurrence found multifocality (HR 1.59, p=0.002), pN+ (HR 1.8, p=0.005) and lymphovascular invasion (HR 1.23, p=0.033) to be associated with increased risk for recurrence. Logistic regression evaluating predictors for pN+ disease found high clinical tumor grade (OR 11.74, p=0.015) and increasing tumor size (OR 1.14, p=0.001) to be associated with LN positivity (Table 2).

Figure 1, *A*demonstrates KMA of OS stratified by nodal status. The 2-year OS for pNx, pN0 and pN+ groups was noted to be 80%, 86% and 42% respectively, with pN+ patients demonstrating significantly worse 2-year survival (p <0.001). KMA of CSS is shown in Figure 1, B. The 2-year CSS for pNx, pN0 and pN+ groups was noted to be 90%, 91% and 45%, respectively, with pN+ patients demonstrating significantly worse 2-year CSS (p <0.001). Figure 1, C demonstrates KMA of RFS. The 2-year RFS for pNx, pN0 and pN+ groups was noted to be 53%, 61% and 35%, respectively, with pN+ patients demonstrating significantly increased 2-year recurrence (p <0.001). Figure 2 demonstrates KMA of comparison of OS, CSS and RFS based on nodal count obtained in the nonmetastatic group, comparing pNx (0 LN), pN0 (≥10 nodes) and pN0 (<10 nodes). We noted no significant differences between groups with respect to 2-year OS (pNx 82% vs pN0 ≥10 nodes 85% and pN0 <10 nodes 84% [p=0.6], Figure 2, A) and 2-year CSS (pNx 89% vs pN0 ≥10 nodes 90% and pN0 <10 nodes 93% [p=0.9], Figure 2, B). However, we noted significantly higher

Table 2. *Multivariable analyses*

Variable	HR (95% CI)	p Value
Factors associated with all-cause mortality		
Increasing age (continuous)	1.06 (1.03–1.09)	<0.001
Sex (male vs female)	1.13 (0.73–1.76)	0.6
Increasing BMI (continuous)	1.03 (0.99–1.07)	0.18
Multifocal vs unifocal	1.33 (0.72–2.44)	0.4
High grade vs low grade	1.44 (0.61–3.39)	0.4
LN status (LNx referent):		
LN0	1.60 (0.93–2.76)	0.09
LN1	2.77 (1.59–4.84)	<0.001
Stage (Tis, III, IV vs 0, I, II)	3.89 (2.29–6.63)	<0.001
Lymphovascular invasion (yes vs no)	1.34 (0.95–1.90)	0.09
Increasing tumor size (continuous)	0.94 (0.85–1.05)	0.3
Factors associated with cancer-specific mortality		
Increasing age (continuous)	1.01 (0.98–1.05)	0.4
Sex (male vs female)	2.38 (1.26–4.51)	0.008
Multifocal vs unifocal	1.67 (0.72–3.85)	0.2
High grade vs low grade	1.66 (0.21–13.29)	0.6
LN status (LNx referent):		
LN0	1.58 (0.75–3.33)	0.2
LN1	2.74 (1.34–5.61)	0.006
Stage (Tis, III, IV vs 0, I, II)	4.18 (1.61–10.85)	0.003
Increasing tumor size (continuous)	1.04 (0.83–1.23)	0.9
Factors associated with recurrence		
Increasing age (continuous)	1.01 (0.99–1.03)	0.08
Sex (male vs female)	1.08 (0.82–1.40)	0.6
Increasing BMI (continuous)	1.02 (0.99–1.04)	0.2
Multifocal vs unifocal	1.59 (1.19–2.13)	0.002
High grade vs low grade	1.03 (0.71–1.48)	0.9
LN status (LNx referent):		
LN0	1.01 (0.75–1.35)	0.9
LN1	1.80 (1.20–2.71)	0.005
Stage (Tis, III, IV vs 0, I, II)	1.07 (0.80–1.45)	0.6
Increasing tumor size (continuous)	0.99 (0.93–1.05)	0.6
Lymphovascular invasion (yes vs no)	1.23 (1.02–1.78)	0.033
Factors associated with LN positivity		
Increasing age (continuous)	1.02 (0.99–1.04)	0.3
Sex (male vs female)	1.16 (0.70–1.93)	0.6
Increasing BMI (continuous)	0.98 (0.93–1.04)	0.5
Multifocal vs unifocal	0.83 (0.44–1.57)	0.6
High grade vs low grade	11.74 (1.62–85.11)	0.015
Increasing tumor size (continuous)	1.14 (1.05–1.24)	0.001

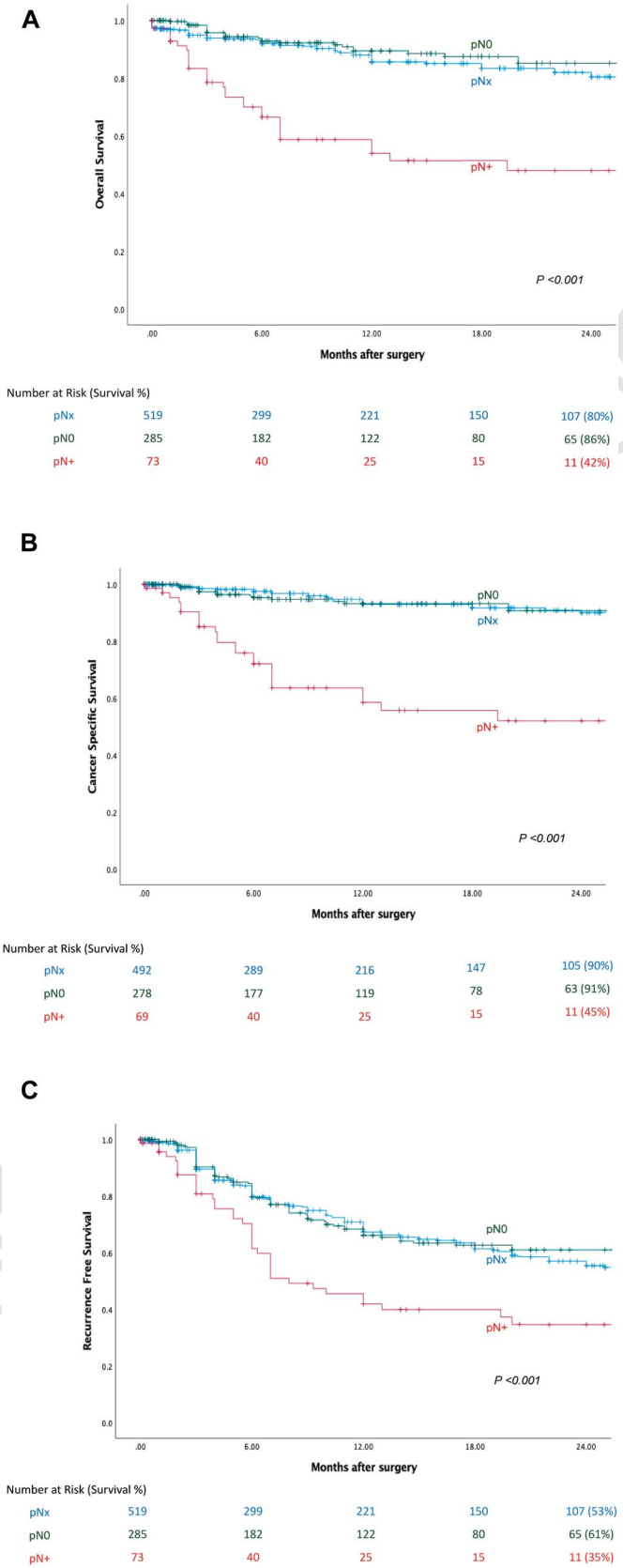

Figure 1. KMAs comparing pNx, pN0 and pN+ groups for survival outcomes. *A*, OS. *B*, CSS. *C*, RFS.

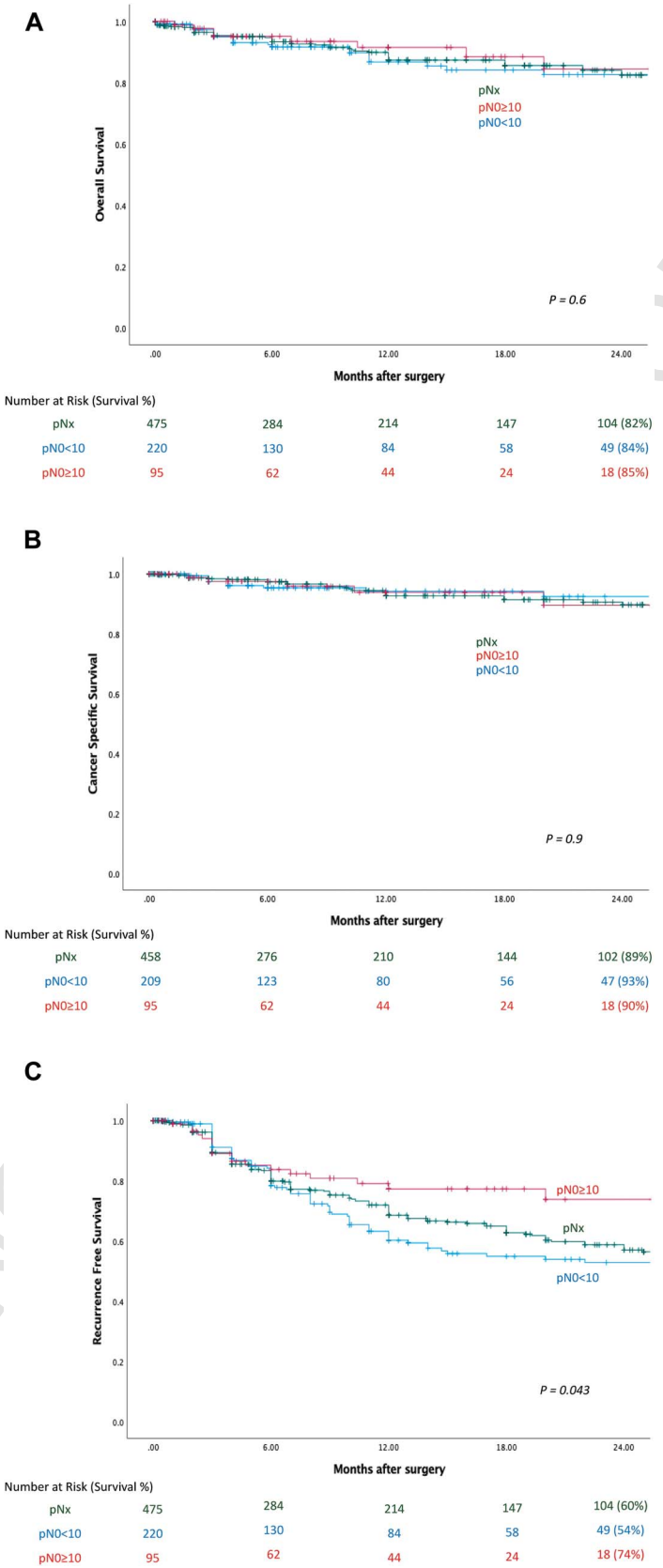

Figure 2. KMAs comparing pNx, pN0 >10, pN0 ≤10 for survival outcomes. *A*, OS. *B*, CSS. *C*, RFS.

2-year RFS in pN0 ≥10 nodes compared to pN0 <10 nodes and pNx (noted to be 74%, 54% and 60%, respectively, p=0.043; Figure 2, C).

DISCUSSION

We report findings of a large multicenter retrospective cohort study examining impact of LND in the setting of robotic nephroureterectomy. Our findings suggest that while LND is not associated with cancer-specific and OS benefit in the setting of pathological LN negative disease, it may provide important prognostic information, and when 10 or more LNs are obtained, improved RFS can be observed. Furthermore, patients at higher risk for LN-positive disease, namely high tumor grade and large tumor size of ≥4.5 cm, should be considered for LND. While our latter finding is novel and requires confirmatory investigation, it calls for promulgation of selection criteria and technical guidelines for LND in the setting of localized UTUC to refine staging, prognostication and oncologic outcomes.

The prognostic benefits of LND during radical nephroureterectomy are well established. Secin et al retrospectively analyzed 252 cN0/cN+ patients undergoing radical nephroureterectomy and demonstrated a 11% pN+ rate with significantly decreased 5-year CSS of pN+ patients compared to pN0 and pNx patients (pN+ 0% vs pN0 56% vs pNx 73%, p <0.0005), though no difference between pNx and pN0 patients (p=0.40).[15] Importantly, 60% of patients with pN+ disease had suspicious clinically positive imaging prior to surgery, as well as 23% of the total cohort. Similar results emphasizing survival advantage in pN0/pNx patients relative to pN+ patients have been reproduced by other multicenter national database studies of cN0/cN+ cohorts.[16–20] Similarly, our findings noted that when compared to pN+, patients with pN0/pNx experienced better OS (pN+ 42% vs pN0 86%, pNx 80%, p <0.001) and RFS (pN+ 35% vs pN0 61%, pNx 53%, p <0.001).

Therapeutic benefits of LND are more controversial. In a multicenter retrospective analysis of 1,130 patients undergoing nephroureterectomy (36.5% pN0, 12.4% pN+ and 51.1% pNx; median followup 45 months), Roscigno et al reported improved 5-year CSS in pN0 disease compared to pNx (77% vs 69%, p=0.024).[17] In contrast, Ikeda et al analyzed 404 patients (40 [10%] pN+, number of nodes removed 8; 182 [46%] pN0, number of nodes removed 6; and 177 [44%] pNx, with median followup 43 months) and found that patients with ≤pT2 disease received no benefit, but those with pT3 or more advanced staging had improved OS (HR=2.07, p=0.002) and CSS (HR=2.66, p=0.001) with LND.[20] Lughezzani et al analyzed 2,824 cN0 (median number of nodes not reported)/cN+ patients undergoing nephroureterectomy and found no significant difference in 5-year CSS between pNx vs pN0 (78 vs 81 months, p=0.09).[18] In our analysis of pN0 (median number nodes removed 9.8) and pN+ (median number nodes removed 10.2) patients, we found no benefits in OS, CSS and RFS for patients with pN0 compared to pNx at 2-year followup (OS, pN0 86% vs pNx 80%, p=0.09; CSS, pN0 91% vs pNx 90%, p=0.55; RFS pN0 61% vs pNx 53%, p=0.06). Taken together, these findings suggest that primary benefit in this group is likely prognostic, not therapeutic, and thus LND may be reserved in patients for whom such information is meaningful.

Nonetheless we noted improved RFS in patients who underwent LND and whose nodal count was ≥10 compared to pN0 patients with <10 nodes dissected and pNx patients (74% vs 54% vs 60%, p=0.043). Currently there is no consensus on the optimal standard template for LND in UTUC. Rather, the number of LNs removed can be used as a surrogate to determine the extent and quality of the LND procedure. A meta-analysis conducted by Choo et al identified improved ACM in pN0 UTUC patients with a higher number of nodes removed (HR 0.86, p <0.01).[21] Roscigno et al retrospectively analyzed 552 patients with UTUC who underwent nephroureterectomy with LAN, demonstrating that patients with LN yield ≥8 showed improved RFS (HR 0.49, p <0.01) and CSS (HR 0.42, p <0.01).[22] Our findings, while not showing improvement in OS and CSS for pN0 patients with ≥10 LNs, showed significantly improved RFS. Taken together, these data call for further investigation into impact of LN yield and standardization of LND templates to optimize outcomes in cN0 UTUC.

A potential concern for performance of LND at time of nephroureterectomy is increased risk of surgical complications. A meta-analysis of 18,584 patients by Chan et al noted that LND did not increase the risk of postoperative complications (RR 1.06, p=0.07).[23] Pearce et al analyzed 16,619 patients who underwent nephroureterectomy (11,682 open/2,638 laparoscopic/2,286 robotic) between 2009 to 2012 and noted that while LND increases the risk of intraoperative complications (OR 1.3, p=0.049), performance of robotic nephroureterectomy was associated with decreased risk of overall complications compared to open approach (OR 0.55, p=0.001).[24] In our cohort, LND was not associated with significant differences in intraoperative (p=0.2) or postoperative (p=0.5) complications, suggesting that lymphadenectomy in the setting of a robotic approach did not increase risk of adverse events and may be considered an important portion of the procedure that provides clear prognostic benefit in select patients.

Selection criteria for performance of lymphadenectomy at time of nephroureterectomy beyond clinical principle (lymphadenopathy on preoperative images or intraoperative examination) and in setting of clinically negative LNs are unclear, and little has been reported with respect to predictors of LN positivity. In our series, we identified high tumor grade (OR=11.74, p=0.015) as well as increasing tumor size (OR=1.14, p=0.001) as independent predictors of pN+ disease. Inokuchi et al performed a multicenter analysis of 2,037 patients with UTUC in which LND was performed 1,046 (51.4%), of whom 223 patients (10.9%) were pN+. In a MVA for predictors of pN+, advanced age (>70 years, OR=1.68, p=0.007), clinical T3+ disease (OR=2.34, p <0.001) and clinically positive LNs (OR=12.6, p <0.001) on imaging were predictive for pathological LN invasion.[25] Their regression model did not include clinical tumor size or grade, but age, hydronephrosis and tumor location were not noted to be predictive for LN positivity. Our findings build on those of Inokuchi et al and suggest that in patients with high-grade disease and large tumors LND may be considered for risk stratification to detect pN+ disease. Furthermore, we observed only 1 case of low-grade pN+ disease, in a patient with tumor size of 6 cm, similar to Secin et al, who identified no instances of low-grade node-positive disease in a series of 252 patients.[15] Taken together, these findings suggest that LND may be safely omitted in patients with small and low-grade tumors.

Obtaining prognostic information regarding LN status has assumed increasing importance due to emerging data supporting utilization of adjuvant and neoadjuvant therapy. Utilizing the National Cancer Database, Pelcovits et al analyzed 794 patients with pN+ UTUC and found that adjuvant therapy had significant improvement in OS (p <0.001).[26] Recent publication by Birtle et al of the POUT clinical trial supports investigation of LN disease status at time of nephroureterectomy.[27] POUT randomized 261 patients with advanced localized or LN-invasive nonmetastatic UTUC to adjuvant chemotherapy or surveillance, and found improved disease-free survival (HR=0.45, p <0.001) and metastasis-free survival (HR=0.48, p=0.0007) with adjuvant therapy at 30-month followup.[27] In a meta-analysis conducted by Leow et al, neoadjuvant therapy had a significant improvement in OS (HR=0.44, p <0.001) and CSS (HR=0.38, p <0.001) compared to nephroureterectomy alone.[28] As a paradigm shift towards utilization of adjuvant and neoadjuvant therapy occurs, identification of LN metastasis is critical. While requiring confirmation, our findings suggest optimization of selection for lymphadenectomy.

There are important limitations to note. The retrospective study design is subject to inherent biases. Our series lacks a standardized dissection template and lack of central pathology review which may limit accuracy of LN yield. Nonetheless, surgeries were performed by experienced urological surgeons at centers of excellence according to previously reported protocols.[12] Patients with high tumor stage or grade were more likely to receive LND, which may bias our results. Additionally, a small number of patients were ultimately pN+ which can impart selection bias. Despite these limitations, our study is unique in its delineation of selection criteria for lymphadenectomy and demonstration of potential survival benefit in patients with LN yields ≥10. While findings may be hypothesis-generating and further investigation is requisite, their applicability is bolstered by the large, international cohort of diverse patients.

CONCLUSIONS

Lymphadenectomy in patients undergoing robotic nephroureterectomy is not associated with increased complications, can provide important prognostic information, and should be considered in patients with high-grade disease and large tumors even in the setting of clinical node-negative disease. Furthermore, LN yields ≥10 in cN0 patients may be associated with improved RFS. Our data point to refinement of selection criteria and outcomes for lymphadenectomy in nephroureterectomy patients.

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