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Utilization of neoadjuvant chemotherapy (NAC) and pathologic outcomes in upper tract urothelial carcinoma (UTUC).

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Background: UTUC is a rare malignancy with a poorer prognosis compared to bladder urothelial carcinoma. Radical nephroureterectomy (RNU) remains the standard treatment for high-risk UTUC. Considering the decline in renal function with RNU and promising pathologic complete response rates from the phase II trial ECOG-ACRIN 8141, NAC has emerged as a favored perioperative treatment regimen for chemo-eligible patients with high-risk UTUC. However, RCTs exploring NAC's efficacy are absent, and large-scale studies examining NAC's role and predictors for its use are scarce. Methods: This study aimed to assess trends in NAC utilization, determinants for receiving NAC, and pathologic outcomes. The National Cancer Database was queried for patients with high-grade cMo UTUC treated with RNU from 2004-2019. Outcomes included pathologic response (pR) and pathologic complete response (pCR), defined as \leq pT1pNo/X and pT0pNo/X, respectively. Multivariate regressions were adjusted for relevant patient and tumor characteristics. Results: Of 6,436 patients treated with RNU alone and 209 with RNU and NAC, older age, greater home distance from the treatment facility, and higher comorbidity scores decreased the likelihood of receiving NAC. In contrast, higher cT stage (OR 1.72, p=0.028) and cN+ status (OR 7.40, p<0.001) predicted NAC treatment. NAC was more commonly used in academic centers (OR 2.02, p < 0.001). Use of NAC peaked in 2016 at 10%, but dropped to ~2% by 2019. There was minimal nodal response to NAC (23.4% cN+ vs 22.0% pN+). NAC was associated with 34.0% pR and 5.3% pCR rates, increasing the likelihood of pCR (OR 57.5, p<0.001). In cT2-4 UTUC, 19.3% and 7.1% of patients had pR and pCR with NAC, and NAC improved odds of pR (OR 1.78, p=0.024). Conclusions: Our study demonstrated variable NAC use for UTUC, illustrating the evolving landscape of perioperative systemic therapies. We report significant response rates even in cT2-4 UTUC. Our observed poor nodal response to NAC emphasizes the crucial role of retroperitoneal lymph node dissection in staging, regardless of NAC status. We note poor NAC utilization in non-academic settings and among patients living farther from care facilities, underscoring the need for improved care quality in the context of regionalization and multi-disciplinary approaches in UTUC management. Research Sponsor: None.

	RNU Alone	RNU & NAC	p-value
Median Age	73	67	<0.001
Facility Type			<0.001
Non-Academic	4147.64.4%	97. 46.4%	
Academic	2289, 35,6%	112. 53.6%	
Comorbidity Index	,	,	<0.001
0	4192.65.1%	165. 78.9%	
1	1437, 22,3%	32, 15,3%	
≥2	807, 12,5%	12. 5.7%	
Tumor Size		,	<0.001
<2 cm	984, 15,3%	49.23.4%	
≥2 cm	5452, 84,7%	160.76.6%	
cT		,	<0.001
<ct2< td=""><td>2592, 40,2%</td><td>69.33.0%</td><td></td></ct2<>	2592, 40,2%	69.33.0%	
≥cT2	3844, 39,8%	140.67.0%	
pT		,	<0.001
<pre>cnT2</pre>	2509 39 0%	74 35 4%	
>nT2	3927 61 0%	135 64 6%	
cN	0521,011010	100, 0 11010	<0.001
cN0	6219 96 6%	160 76 6%	
cN+	217 3 4%	49 23 4%	
pN	211,0110	15, 20110	<0.001
pN0	2644 41 1%	117 56 0%	20.001
nN+	370 5 7%	46 22 0%	
pNx	3422, 53.2%	46, 22.0%	