Predictive Model for Systemic Recurrence Following Cisplatin-Based Neoadjuvant Chemotherapy and Radical Nephroureterectomy for Upper Tract Urothelial Carcinoma

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Introduction & Objective

- Based on the established benefit of neoadjuvant chemotherapy (NAC) in urothelial cancer of the bladder, NAC is increasingly used prior to radical nephroureterectomy (RNU) for upper tract urothelial carcinoma (UTUC).
- Systemic recurrence (SR) following RNU carries a dismal prognosis.

STUDY GOAL

To determine factors that predict higher risk of systemic recurrence following NAC and RNU.

Materials & Methods

- Retrospective evaluation of multi-center database
  - Study period: 2004-2018
- UTUC patients who had NAC followed by RNU
  - NAC strictly cisplatin-based
- Final pathology dichotomized: pT < 2 vs pT ≥ 2
- SR defined as any recurrence outside the urinary tract.
- Univariate (UV) and multivariate (MV) Cox regression analysis performed
- Factors identified on UV analysis as significant were grouped into 3 groups (0, 1-2, and 3 risk factors)
- Recurrence-free survival evaluated using the Kaplan-Meier analysis and log-rank test.

Results

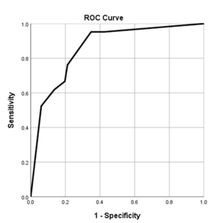
Table 1. Patient Baseline Characteristics

		Number of Patients (%)	
Age [IQR]; years		67.0	[61.0-73.3]
Gender	*Male*	80	(72.7)
	Female	30	(17.3)
Race	*White*	93	(84.5)
	Non-white	13	(11.8)
ECOG PS	*0-1*	68	(61.8)
	2-3	6	(5.5)
Hydronephrosis	*None or mild*	62	(56.4)
	Moderate to severe	38	(34.5)
NAC Agent	*MVAC*	59	(53.6)
	GC	51	(46.4)
Tumor Stage	*pT0*	15	(13.6)
	pTa-Tis-T1	44	(40)
	pT2	14	(12.7)
	pT3	30	(27.3)
	pT4	7	(6.4)
Tumor Grade	*Low*	3	(2.7)
	High	95	(86.4)
Tumor Location	*Renal pelvis/calyces*	48	(43.6)
	Ureter	27	(24.5)
	Both	16	(14.5)
Tumor Focality	*Unifocal*	59	(53.6)
	Multifocal	27	(24.5)
pLVI	*Yes*	30	(17.3)
	No	64	(58.2)
pN stage	*pN0*	71	(64.5)
	pN1-3	31	(28.2)
Surgical Margins	*Positive*	8	(7.3)
	Negative	101	(91.8)
Surgical Approach	*Open*	40	(36.4)
	Minimally Invasive	63	(57.3)
	Combined	7	(6.4)
History of Bladder Cancer	*No*	68	(61.8)
	Yes- Synchronous	7	(6.4)
	Yes- Prior	33	(30)

- N= 110 patients
- Final pT stage: pT < 2 in 59 patients; pT ≥ 2 in 51 patients.
- SR in 23.6% (26/110); 24 of those within 19 months.

Table 2. Univariate and Multivariate Cox Regression Analysis for Predictors of Systemic Recurrence

		Univariate Analysis			Multivariate Analysis		
		OR	[95% CI]	p-value	OR	[95% CI]	p-value
pT	Less than pT2						
	pT2 or more	10.4	3.28-33.2	**<0.001**	5.30	1.24-22.7	**0.024**
pLVI	*No*						
	Yes	11.0	3.66-33.4	**<0.001**	3.56	0.95-14.0	0.059
pN	*pN0*						
	pN1-3	9.56	3.44-26.5	**<0.001**	3.59	0.93-13.8	0.064
Surgical Margins	*Negative*						
	Positive	3.59	0.83-15.5	0.087	0.77	0.09-6.53	0.81



- UVA:
  - pT ≥ 2, LVI, pN, and tumor size were all associated with higher recurrence.
- MVA:
  - Only pT ≥ 2 significant; p = 0.024
  - ROC curve AUC 0.86; p < 0.001
- Stratifying according to number of risk factors, the 2-year recurrence-free survival was 97.4%, 72.7%, and 26.7% for 0, 1-2, and 3 risk factors respectively (log-rank <0.001)

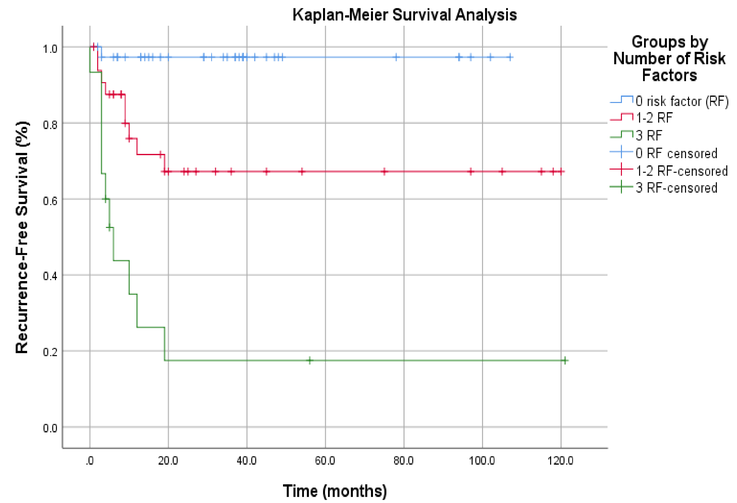


Figure 1. Kaplan-Meier curves for recurrence-free survival in groups stratified according to risk factors for systemic recurrence

Conclusions

- We created a predictive model for SR following NAC and RNU for UTUC to direct decision-making after surgery.
- A pathology of muscle invasive UTUC, when combined with LVI, nodal involvement, and positive surgical margins, can predict the risk of SR with high accuracy.