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Prospective evaluation of pre-operative neutrophil / lymphocyte ratio (NLR) as a prognosticator in upper tract urothelial carcinoma (UTUC) patients treated conservatively

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Objectives

To prospectively evaluate the prognostic value of neutrophil / lymphocyte ratio (NLR) in conservatively treated UTUC patients.

Materials and Methods

- Since 2016, NLR was prospectively collected and evaluated in 30 consecutive UTUC patients (Group 1).
- It was compared to a retrospective post-hoc dataset from 130 consecutive UTUC patients (2005-2015) (Group 2).
- All patients underwent uretero-rensoscopy and RIRS (retrograde intra renal surgery) for UTUC.
- EAU guidelines follow-up scheme was applied: panendoscopy+cytology every 3 months for 1st year, then 6 monthly for 2 years, then annually + yearly UroCT.
- At 1st patient encounter, white blood cells (WBC), platelet (PLT), neutrophil (N), and lymphocyte (L) counts, were collected and recorded.
- NLR was derived by dividing N by L.
- These data were compared with tumor characteristics: stage (Ta vs. \geq T1), grade (G1 vs. \geq G2), focality (uni vs. multi), site (ureter vs. kidney vs. ureter+kidney), and size (\leq 1 cm vs. $>$ 1 cm).
- The endpoints were: recurrence at the first follow-up, multiple recurrences during follow-up, and progression (Grade+/-Stage).
- They were stratified by the NLR cut-off point, according to the receiver operating characteristic analysis.
- T-test and chi-square test were used to evaluate parametric and non parametric variables.
- Statistical significance was considered at $p < 0.05$.

Results

- The mean NLR value was 2.90 \pm 1.05 in Group 1 and 3.48 \pm 1.92 in Group 2 ($p=0.79$).
- Significantly higher NLR values were observed in Group 1 and Group 2 patients with \geq pT1 ($p=0.03$ and $p=0.0001$), \geq G2 ($p=0.03$ and $p=0.0009$), multifocal ($p=0.01$ and $p=0.028$), $>$ 1 cm tumor ($p=0.04$ and $p=0.0001$), respectively.
- The optimal NLR cut-off value was 3 for all the endpoints.
- Patients with **NLR $>$ 3** exhibited significantly higher risk of recurrence at first follow-up (**$p=0.04$, OR 5.33 in Group 1 and $p=0.007$, OR 2.94 in Group 2**), significantly higher risk of multiple recurrences (**$p=0.02$, OR 7.33 in Group 1 and $p=0.006$, OR 1.54 in Group 2**).
- No disease progression has so far been observed in Group 1 due to the short follow-up of this prospective cohort to date, while patients in Group 2 with NLR $>$ 3 exhibited 5 fold disease progression risk (**$p=0.04$, OR 5.00**).

Conclusions

- The pre-operative evaluation of NLR may provide valuable prognostic information for the clinical management of UTUC patients treated conservatively.
- NLR $>$ 3 was associated with higher recurrence and progression rates.
- It may identify those needing more frequent endoscopic follow-up, and lower thresholds to conversion to more aggressive surgical strategies.
- Prospective multicenter multinational studies are needed to validate the role of NLR as a prognosticator of recurrence and progression in these patients.

Tumor characteristics	NLR		P value
	Group 1	Group 2	
Ta	2.37 (0.79)	3.25 (1.72)	0.11
\geq T1	3.68 (0.31)	4.52 (2.39)	0.03
P value	0.03	0.0001	
Single	2.36 (0.78)	3.35 (1.60)	0.02
Multifocal	2.86 (0.70)	3.69 (2.33)	0.10
P value	0.49	0.028	
Low grade	2.06 (0.47)	3.04 (1.68)	0.01
High grade	3.26 (0.85)	4.27 (2.07)	0.20
P value	0.001	0.0009	
$<$ 1 cm	2.35 (0.68)	2.87 (1.67)	0.17
$>$ 1 cm	2.52 (0.91)	3.96 (1.98)	0.02
P value	0.04	0.0001	
Ureter	3.13 (0.99)	3.35 (1.64)	0.31
Kidney	3.10 (0.97)	3.76 (2.07)	0.06
Kidney+ureter	3.28 (1.52)	3.85 (2.16)	0.72
P value	0.59	0.57	

NLR cut-off $>$ 3

	Group 1		Group 2	
	p value	OR	p value	OR
Recurrence at 1 st follow up	0.04	5.33	0.007	2.94
Multiple recurrences in follow up	0.02	7.33	0.006	1.54
Radical surgery in 1 st instance	0.17	4.80	0.01	3.06