

Impact of Histological Variants on Clinical Outcomes of Patients with Upper Urinary Tract Urothelial Carcinoma

Introduction and Objectives: To investigate the clinical and prognostic impact of variant histologies on upper tract urothelial carcinoma (UTUC) outcomes after radical nephroureterectomy (RNU).

Material and Methods: Data from 1648 UTUC patients managed by RNU without preoperative chemo- or radiotherapy were reviewed for histological differentiation and variants. We analysed the differences between pure UTUC and UTUC with variant histology, and those between the different histological variants using different stratifications.

Results: Overall, 398 (24.2%) patients had histological UTUC variants with squamous cell (9.9%) and glandular differentiation (4.4%) being the most common. Histological UTUC variants were associated with advanced tumor stage, tumor multifocality, sessile tumor architecture, tumor necrosis, lymphovascular invasion and lymph node metastasis ($p\text{-values} \leq 0.031$) compared to pure UTUC. In univariable analyses, variant UTUC histology was associated with disease recurrence ($p=0.002$) and cancer-specific mortality ($p=0.003$). In patients treated with adjuvant chemotherapy ($n=174$) there was no difference in disease recurrence and survival between variant UTUC histology and pure UTUC ($p=0.42$ and $p=0.59$, respectively). In multivariable analyses that adjusted for the effects of standard clinicopathologic characteristics, variant UTUC histology was not associated with either endpoint.

Conclusions: Almost 25% of UTUC patients treated with RNU harbor histological variants. Variant UTUC histologies are associated with features of biologically aggressive UTUC. While variant UTUC histology is associated with worse outcomes in univariable analyses, this effect did not remain significant in multivariable analyses. Systemic adjuvant chemotherapy seemed to abrogate the detrimental effect of variant histology on survival.