

## **Time to Disease Recurrence is a Predictor of Cancer-Specific Mortality After Radical Nephroureterectomy**

**Introduction and Objective:** While the natural history of upper tract urothelial carcinoma (UTUC) from radical nephroureterectomy (RNU) to disease recurrence has been intensively investigated, clinical outcomes and risk factors after disease recurrence remain poorly understood. To describe the natural history and identify predictors of cancer-specific survival in patients who experience disease recurrence after RNU for UTUC.

**Material and Methods:** There were 597 patients with disease recurrence from a retrospective multi-institutional cohort of 2,494 UTUC patients treated with RNU who comprised the study cohort. Multivariable Cox regression model addressed time to cancer-specific mortality after disease recurrence.

**Results:** The median time from RNU to disease recurrence was 12 months (IQR 5-22). There were 491 of 597 (82%) patients who died from UTUC and 8 patients (1.3%) died from other causes. The median time from disease recurrence to death of UTUC was 10 months. Actuarial cancer-specific survival estimate at 12 months after disease recurrence was 35%. On multivariable analysis that adjusted for the effects of standard clinico-pathologic characteristics, higher tumor stages (HR pT3 vs. pT0-T1: 1.66,  $p=0.001$ ; HR pT4 vs. pT0-T1: 1.90,  $p=0.002$ ), absence of lymph node dissection (HR 1.28,  $p=0.041$ ), ureteral tumor location (HR 1.44,  $p<0.0005$ ) and a shorter interval from surgery to disease recurrence ( $p<0.0005$ ) were significantly associated with cancer-specific mortality. The adjusted 6, 12 and 24 months post-recurrence cancer-specific mortality was 73%, 60% and 57%, respectively.

**Conclusion:** Approximately 80% of patients who experience disease recurrence after RNU die within the first 2 years post-recurrence. Patients with non-organ-confined stage, absence of lymph node dissection, ureteral tumor location and/or shorter time to disease recurrence died of their tumor faster than their counterparts. These factors should be considered in patient counseling and risk-stratification for salvage treatment decision-making.