O3 Prognosis of primary papillary Ta-G3 bladder cancer in the non-muscle invasive spectrum

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Introduction & Objectives: Ta-G3 non-muscle invasive (NMI) bladder cancer (BC) is a relatively rare diagnosis with an ambiguous character due to the presence of an aggressive G3 component together with the lower malignant potential of the Ta component. Prognostic studies on Ta-G3 NMIBC are limited and inconclusive. Some claim that Ta-G3 tumors are as malignant as T1-G3 tumors, yet others suggest they may not be as aggressive as G3-disease invading the lamina propria. The objective of this study was to evaluate the prognostic value of Ta-G3 tumors compared to Ta-G2 and T1-G3 tumors.

Materials & Methods: Individual patient data of 5,170 primary Ta-T1 bladder tumors from 17 hospitals were analyzed. Transurethral resection of the tumor was performed between 1990 and 2018. Time to recurrence and progression were analyzed with cumulative incidence functions, log-rank tests and multivariable Cox-regression models with interaction terms stratified by institution.

Results: Ta-G3 represented 7.5% (387/5,170) of Ta-T1 tumors and 11.7% (387/3,311) of Ta tumors. Recurrence at 5 years was 48.0% (95%CI 45.3-50.7), 46.5% (95%CI 40.8-52.1) and 48.0% (95%CI 44.4-51.5) for Ta-G2, Ta-G3 and T1-G3 tumors, respectively. We found no difference in time to recurrence between Ta-G3 and Ta-G2 (P=0.94), nor between Ta-G3 and T1-G3 (P=0.40). Progression at 5 years was 2.5% (95%CI 1.7-3.3) for Ta-G2, 9.6% (95%CI 6.7-12.5) for Ta-G3 and 16.0% (95%CI 13.8-18.3) for T1-G3 tumors (figure1). Time to progression was significantly shorter for Ta-G3 than Ta-G2 (P<0.001) and longer for Ta-G3 than T1-G3 (P=0.002). However, Ta-G3 and T1-G3 patients with concurrent carcinoma in situ (CIS) and/or who received Bacillus Calmette-Guérin (BCG) induction therapy had similar times to progression. Multivariable analyses on recurrence and progression showed similar results.

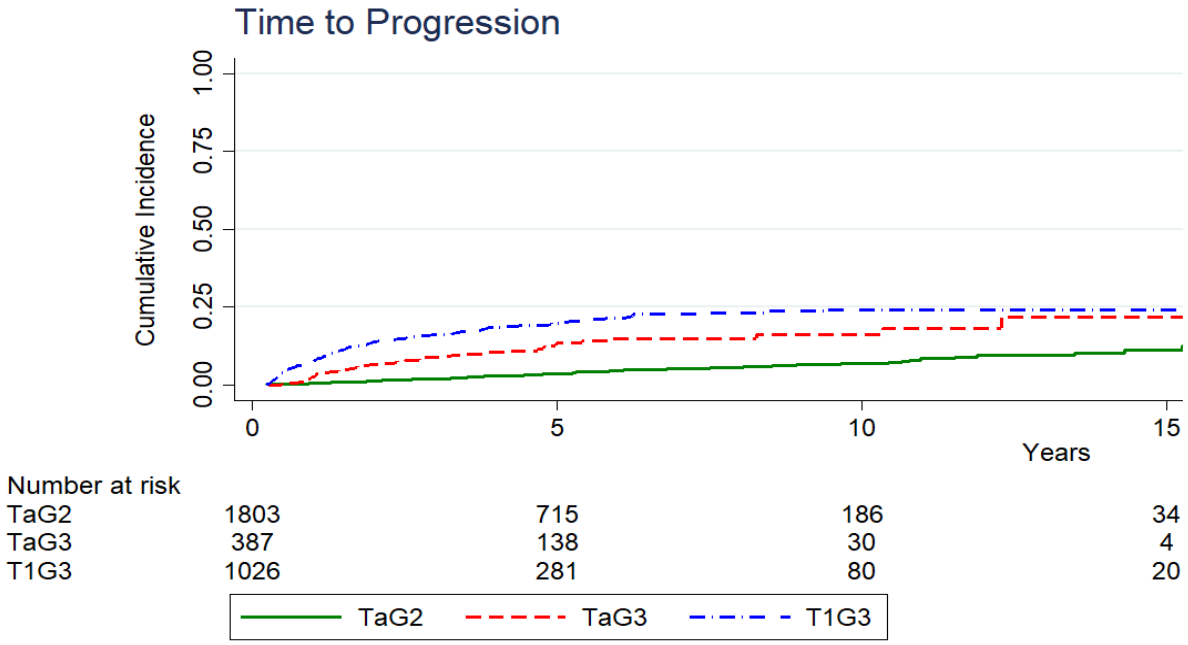

Figure 1. Cumulative incidence curves displaying the risk of progression for Ta-G2, Ta-G3 and T1-G3 carcinomas

Conclusions: Time to recurrence of Ta-G3 was comparable with both Ta-G2 and T1-G3. However, time to progression of Ta-G3 was different from both Ta-G2 and T1-G3. It appears that the prognosis of Ta-G3 tumors in terms of progression is in between Ta-G2 and T1-G3, with the exception of patients with concurrent CIS and/or who received BCG-induction therapy, since their times to progression were similar to T1-G3. Our results support the recent European Association of Urology Guideline changes for a more refined risk stratification of Ta-G3 tumors because many of these patients have a better prognosis than previously thought.