

ASO Author Reflections: T1b Penile Cancer: An Alarm to Improve Treatment

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PAST

The management of penile cancer remains a challenging dilemma. Although advancement in the TNM staging system and treatment guidelines prompted structured risk stratification and corresponding management, supporting evidence is limited due to the low incidence and paucity of high-level evidence. The subclassification of T1 penile cancer was introduced in the 7th edition of the TNM staging system, and the T1b subgroup specifies those with lymphovascular invasion or high-grade tumor;¹ however, the prognostic significance and contemporary manage of T1b disease are unknown.

PRESENT

Our article assessed the prognostic significance of T1b disease in academic centers and a population-based database.² We also posed questions regarding how closely the

guideline recommendations for T1b disease are being followed and, if not, what are the consequences? In this article, we show that:

1. T1b disease is strongly associated with nodal metastases and adverse penile cancer-specific survival (PCSS), in both the academic center and population-based cohorts. Using T1a as a reference, PCSS was significantly poorer in T1b patients, with an adjusted hazard ratio (aHR) of 4.10 ($p = 0.03$) in the academic center cohort.
2. Although treatment guidelines have recommended surgical lymph node examination (SLNE) since 2012, only 21.7% of T1b patients followed the recommendation in the North American cancer registry. In contrast, all T1b patients from the academic center cohort underwent SLNE.
3. In clinical NOM0 patients without SLNE, compared with T1a disease, T1b was associated with an aHR of 4.40 and a subdistribution HR of 4.53 for PCSS (both $p = 0.003$). Both Cox regression and competing risk analyses confirmed the adverse survival outcomes of T1b patients without SLNE. In contrast, in the academic center cohort, patients with pN0 disease demonstrated a 3-year PCSS of 92.2%.

FUTURE

Our results provide useful baseline data for this rare disease, and also improve the evidence for supporting T1a/b stratification in both the TNM staging system and treatment guidelines. The high risk of lymph node metastases, poor survival outcome, and low rate of SLNE in T1b tumors in the North American patient population prompted reclassification of the disease to the high-risk category, rather than the intermediate-risk category, in current NCCN guidelines. Our finding regarding a fourfold

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increase in the risk of death in clinically node-negative T1b patients without SLNE emphasizes the importance of physicians' and patients' awareness of this pattern of penile cancer, similar to CIS in bladder cancer, and changing the real-world management of regional lymph nodes. As the T1b classification has been amended in the 8th edition of the TNM staging system, which included perineural invasion as another indicator,³ further improvement in risk-adapted treatment is urgently needed.

DISCLOSURES Yao Zhu, Philippe E. Spiess, and Ding-Wei Ye have no conflicts of interest to disclose.

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