EDITORIAL

clinical

Shifting the paradigm in high-risk prostate cancer: how good is TNM alone?

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Editorial comment to "*Relative Impact of Lymph-node Metastasis and Seminal Vesical Invasion on Oncologic Outcomes Following Radical Prostatectomy" PCAN 2023.*

Locally advanced prostate cancer with pathological seminal vesicle invasion (pT3b) is a very high-risk disease associated with worse outcome and is considered difficult to cure by radical prostatectomy alone [1]. However, the ideal protocol for additional therapy (adjuvant or salvage) is still debated [2]. Therefore, studies that identify factors that can predict the prognosis of prostate cancer within the pT3b stage are applauded. In fact, such factors could be used to refine the construction of subgroup risk classification within the pT3b stage and guide better personalized cancer control.

In the current issue of Prostate Cancer and Prostatic Diseases, Pessoa et al. demonstrated no additional negative prognostic impact for the presence of a single positive pelvic lymph node in the presence of a seminal vesicle invasion [3]. On the other hand, an increased number of positive lymph node was associated with decreased cancer specific and overall survivals. The authors should be applauded for analyzing such a large cohort of patients with a median follow-up of 12 years. Long term oncologic outcomes of prostate cancer are always hard to obtain and they represent important data for the urologic community. The authors also demonstrated that patients with seminal vesicle invasion alone have similar oncologic outcome as patient with single positive pelvic lymph node involvement without seminal vesicle invasion. These findings raise some questions: how two independent risk factors yield no additional adverse outcome when merged? How can the authors be sure that a negative pelvic lymph node dissection or a single pelvic lymph node are truly the same in this historical database, with limited lymph node dissection (11 median nodes resected) and the absence of molecular imaging?

Indeed, the pN stage after pelvic lymph node dissection in the TNM classification is the gold standard for lymph node staging of prostate cancer [2]; yet this system recommends harboring all lymph nodes in the extended field of dissection to be reliable. This staging is based on the number of positive lymph nodes and do not consider their association with non-involved lymph nodes (density, ratio, log-odds ratio) and/or total number of collected nodes. Considering only the number of positive lymph nodes might unreliably predict outcome compared to new prognostic staging systems such as the ganglion quotients or lymph node ratios and natural logarithms of the lymph node odds methods [4]. Nonetheless, involvement analysis by tumor cells of the positive lymph node (microscopic vs. macroscopic/capsular effraction) can also distinguish risk subgroups with different survival rates more precisely than the condensed pN category alone [5]. Given the enormous importance of the aforementioned factors, especially in terms of prognostic and therapeutic decisions, gaining a detailed picture of the lymph node status of patients with prostate cancer is mandatory in order to correctly interpret the significance of such risk factors.

At present, patients with less than two positive pelvic lymph nodes without extra-capsular effraction and an extended pelvic lymph node dissection have more favorable oncologic outcome following radical prostatectomy that encourages observation in these patients and early salvage radiation if needed [6]. A meta-analysis of three randomized trials comparing adjuvant radiation therapy to early salvage radiation therapy demonstrated no significant difference in terms of overall survival between the two groups. However, these trials had only 19–22% of patients with pT3b stage (HR = 0.75 (0.44, 1.29) $p = 0.33$) [7]. Based on the above findings, observation alone remains an option in patients with pT3b and a single positive lymph node involvement. Even though the authors do not mention this conclusion, we think that more studies are needed so that observation could be considered a safe option for these high risk patients.

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AUTHOR CONTRIBUTIONS

FA, EH and SA conceived and designed the manuscript. FA and EH drafted the manuscript. SA provided supervision and final corrections.

COMPETING INTERESTS

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ADDITIONAL INFORMATION

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