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European Association of Urology

Letter to the Editor

Re: Jürgen E. Gschwend, Matthias M. Heck, Jan Lehmann, et al. Extended Versus Limited Lymph Node Dissection in Bladder Cancer Patients Undergoing Radical Cystectomy: Survival Results from a Prospective, Randomized Trial. Eur Urol 2019;75:604–11

We read with great interest the article by Gschwend et al. [1] reporting results of the first prospective randomized trial comparing different templates for lymph node dissection (LND) in bladder cancer patients treated with radical cystectomy (RC). Although the title states "limited versus extended", the study actually compared standard LND (obturator, and internal and external iliac nodes; level 1) to super-extended LND (in addition, deep obturator, common iliac, presacral, paracaval, interaortocaval, and para-aortal nodes up to the inferior mesenteric artery; level 3) according to the EAU Working Group on Muscle-invasive and Metastatic Bladder Cancer [2]. Unfortunately, the study failed to demonstrate a significant advantage of super-extended LND over standard LND for all endpoints of recurrence-free survival (RFS), cancer-specific survival (CSS), and overall survival (OS). Furthermore, Clavien grade $\geq$3 lymphoceles were more frequently observed in the super-extended LND group within 90 d after surgery.

The landmark evidence in this field so far has been based on a systematic review of 23 studies (22 retrospective and one prospective nonrandomized study) assessing the extent of LND during RC, which revealed that (super-)extended LND provided better results compared with limited or standard LND [3]. However, the present trial results are inconsistent with this finding. The authors enumerated potential reasons for their unexpected results, including the high number of lymph nodes resected in both groups, the inclusion of T1G3 tumors, and the small sample size [1]. Besides these, we speculate that their statistical analysis method could have affected the results. In Fig. 3A [1], the Kaplan-Meier curve of RFS seems peculiar: it should always be located below the curves for CSS and OS, but it is actually not. This is because the primary endpoint RFS was incorrectly applied in the present study. The authors defined RFS as "the time from RC to tumor recurrence or death from bladder cancer", but the latter part is terminologically defined as "death from any cause" [4]. Therefore, the primary endpoint in the present study should rather be described as the "recurrence-free interval" [4], and we wonder how the Kaplan-Meier curve of RFS would look if the authors had used the original definition of RFS and what the *p* value for comparison between the groups would be.

Finally, none of the previous studies showed a survival advantage of super-extended (level 3) LND compared with extended (level 2) LND [3-5]. Therefore, the super-extended LND in the present trial might be excessively invasive for patients (eg, longer operation time, higher lymphocele rate, etc.), which might result in a lower survival benefit for this group. A future clinical trial should thus compare standard (level 1) versus extended (level 2) LND to draw a more clinically relevant conclusion. In any case, results from another ongoing prospective randomized trial (SWOG S1011) are awaited.

Conflicts of interest: The authors have nothing to disclose.

References

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