



Editorial on “Development and Internal Validation of a Novel Model to Identify the Candidates for Extended Pelvic Lymph Node Dissection in Prostate Cancer”

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Most urologists who treat prostate cancer (PCa) patients are familiar with the well-known Briganti nomograms. According to the EAU guidelines on PCa (1), the indications for nodal sampling by means of extended pelvic lymph nodes (LNs) dissection (ePLND) are high-risk and intermediate-risk PCa with a risk of nodal metastases of over 5% according to the Briganti nomogram or MSKCC (2-4).

The new nomograms are based on a multivariable model taking into consideration patient characteristics collected during primary PCa diagnosis. The number of analyzed patients (n=681) is high enough to allow for reliable statistical evaluation. The “novel model” presented by the authors shows superior predictive accuracy. In the novel nomograms, the cut-off value regarding the risk of nodal disease requiring ePLND treatment is defined at 7%, which is slightly higher than in the Briganti nomograms (2). The authors point out that application of this cut-off would render approximately 70% ePLNDs unnecessary, at the cost of missing only 1.5% lymph node invasions (LNI). This finding probably has the potential to modify current PLND tactics.

Moreover, additional parameters are taken into account by the new nomograms, such as cancer involvement in the biopsy cores. Biopsy-based grading and staging as well as intraprostatic heterogeneity can contribute significantly to the nomograms' prognostic accuracy.

The manuscript is a well-written study founded on sound scientific methods. The mean number of removed LNs of 16 coincides with the median number of LNs removed in extended PLND as described by Osmonov *et al.* (5). The authors compare their findings with the previously

validated nomograms making it easy to understand which the aspects have been changed or added. The authors also emphasize the importance of an anatomically standardized ePLND template for safe detection of nodal metastases and comparability of results (1). The current template is sufficient for optimal extended LN dissection, while insufficient PLND, by contrast, may lead to a false-negative pathological report and inadequate staging. Therefore, standardization of the template and a maximized extension of PLND are crucial for adequate clinical implementation of the nomograms. In summary, this novel diagnostic tool is a further step towards preoperative prediction of LNI, thus improving the selection of patients for extended PLND.

There is one limiting aspect in this otherwise excellent study. One of the selection criteria was the exclusion of patients who received neoadjuvant hormonal therapy. The question that needs to be raised is whether the new nomograms can be safely applied to this patient group, especially as these patients are per definition at a high-risk of further disease progression and candidates for salvage surgery or cytoreductive prostatectomy. Although it was not the aim of the study, it would be interesting to know how many patients from the overall cohort developed a biochemical recurrence (BCR) during follow-up, how many of the patients with BCR experienced an isolated node relapse, and how many of them underwent salvage ePLND. It would make a lot of sense to identify the risk factors of LN relapse on the basis of these huge patients' cohorts in follow-up studies.

The other problem is associated with upstaging

after prostate specimen analysis which is often the case. Upstaging often means that there is an increased risk of LNI making adjuvant therapy necessary because LN dissection was insufficient retrospectively. According to the authors, however, LNI would be missed in only 1.5% of the patients when following the nomograms.

Relevance of this study for current scientific research

As we know, from the recent multicentral meta-analysis published by Fossati *et al.*, extended PLND, which currently represent the best available staging procedures, are associated with unsatisfactory intra and perioperative outcomes, while a direct therapeutic effect is still not proven in the current literature. The poor quality of evidence indicates the need for robust and adequately powered clinical trials (6). Further research analyzing the oncological benefit of PLND would refine knowledge and approach and it might in consequence be necessary to qualify and develop the nomograms further. But until new results are available, the current nomograms can be recommended for decision-making in PCa treatment.

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are

appropriately investigated and resolved.

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