Platinum Priority – Editorial

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Pelvic Lymphadenectomy in Clinically Localised Prostate Cancer: Counting Lymph Nodes or Dissecting Primary Landing Zones of the Prostate?

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The role of extended pelvic lymph node dissection (ePLND) in the management of men with clinically organ-confined prostate cancer (PCa) is controversial because its therapeutic benefit has never been proven in prospective clinical trials [1]. However, ePLND clearly results in more dissected lymph nodes (LNs), thus increasing the detection rate of metastatic LNs, which improves locoregional staging and might enable a risk-adapted approach with regard to adjuvant therapy [2,3].

The diagnostic accuracy of such an anatomic LN dissection relies on a meticulous surgical technique with a complete dissection of all LNs located in the primary landing zones of the prostate that includes the obturator fossa, and the external, internal, and common iliac artery up to the ureteral crossing [4]. According to data obtained from the ePLND of cadavers, a mean number of 22.7 LNs with a range from 8 to 56 will be located in the primary landing zone [5]. Due to the striking interindividual differences in LN counts, however, it is always difficult to assess the completeness of the surgical dissection even in experienced centres.

In this issue of European Urology, Kluth et al. presented a multi-institutional retrospective analysis of 7135 and 4209 patients with clinically organ-confined PCa composed of a development and a validation cohort, respectively [6]. They attempted to develop a novel pathologic (postoperative) nodal staging score (pNSS) that calculates the probability that a patient with histologically negative pelvic LNs is staged correctly. According to their data, the number of examined nodes, pT stage, radical prostatectomy (RP) Gleason score, status of surgical margins, and serum prostate-specific antigen concentration indicate the accuracy of correct nodal staging. The probability of missing nodal disease decreases with an increasing number of LNs examined, which is not a surprising or new finding. But a novel finding is the suggestion that the highest diagnostic accuracy seems to depend on the number of examined LNs, pT stage, and the RP Gleason score as demonstrated in their tables and figures. In the discussion section, the authors claim they can estimate the true nodal stage of PCa patients based on the new calculation model and that this tool can help in the decision-making process concerning the most optimal adjuvant treatment.

Although the authors are to be congratulated for the potentially useful approach towards standardisation of ePLND, some words of caution need to be considered before the tool is used clinically.

The tool is based on the assumption that the type of PLND performed by the authors represents an adequately performed anatomic LN dissection covering the primary landing zones of the prostate. However, the described technique does not reflect the standards of ePLND. Neither the area of the external iliac artery nor the area of the common iliac artery up to the ureteral crossing was dissected. In this approach, about 20% of LN metastases might potentially be missed, information we have gleaned from anatomic and functional imaging studies [2,7,8].

Although the mean number of LNs examined was higher in the validation group compared with the development group (16 vs 6 LNs), it is still considerably lower than in the
cadaveric study and in clinical series with a mean number of 22.7 and 28 LNs, respectively [2,5]. Therefore, the probabilities calculated still might be too low and not completely accurate.

Despite the complete clearance of the primary lymphatic drainage sites of the prostate, LN counts underlie some huge interindividual differences. As demonstrated by Weingärtner et al. [5], the range of LN counts varies between 8 and 56. Therefore, it will be extremely challenging to apply the proposed tool in a patient in whom the iliac vessels and the obturator fossa have been completely skeletonised and in whom only 10–12 LNs have been identified on pathohistologic analysis. It is difficult to discern whether the low number of LNs is due to improper surgical technique, inadequate pathohistologic analysis, or interindividual variations. Therefore, it might be more important to meticulously dissect the described primary landing zones of the prostate instead of counting LNs and to stratify the need for adjuvant therapy based on the completeness of dissection.

About 6% of all patients with low-risk PCa harbour LN metastases at the time of RP when an ePLND is performed properly [9]. The data of the authors suggest that the examination of one single LN is sufficient to obtain a 90% pathologic pNSS. But from where should this single LN be taken, and is this type of calculation adequate and realistic? The mathematical conclusion derived from the formula used in the statistical analysis might reflect the bias involved in the calculation model, and certainly even patients with low-risk PCa who harbour a high risk for the presence of LN metastases need to undergo a complete ePLND, an approach that has also been described [10].

The number of LNs obtained depends not only on the surgeon but also on the pathologist. The number of LNs varies significantly with the number of specimens sent for pathohistologic analysis, and it also depends on the technique used to process the specimens [11]. Based on the retrospective nature of the study, we do not have any information concerning the processing of LN samples in the development cohort that might have resulted in a significant bias. The awareness of the necessity of a thorough pathohistologic work-up of the dissected LNs was much more pronounced in the reference centre of the validation cohort than in the development cohort, a fact that certainly had an impact on the results.

In the discussion section, the authors develop clinical scenarios of adjuvant treatment options based on the pNSS that have not been proven in prospective clinical trials and are based on evidence-based medicine level 3 recommendations only. In fact, the role of adjuvant androgen-deprivation therapy for LN-positive disease was questioned with no benefit of survival [12]. None of the few prospective randomised trials performed so far has demonstrated a benefit from the irradiation of pelvic LNs [1]. Only the retrospective study of DaPozzo et al. reported on some benefits of the combined treatment approach [13]. Even the updated results of the European Organisation for Research and Treatment of Cancer and AUO/ARO trial on adjuvant radiation therapy in patients with locally advanced disease have not demonstrated a survival benefit [14,15]. Currently, the only benefit of adjuvant treatment options is an improvement of biochemical progression-free survival.

In summary, the authors have presented a new way to interpret the results of PLND in PCa concerning its diagnostic accuracy. However, due to the retrospective nature of the study, the new tool has to be validated in a present series of patients who undergo RP with a limited and an extended PLND to proof the calculations. The authors also have pinpointed the ongoing problem of ePLND in PCa, the standardisation of the dissection fields, and the processing of the specimens. For these reasons, the study represents another important step in the improvement of surgical PCa therapy.

Conflicts of interest: The authors have nothing to disclose.

References
