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Pelvic Lymph Node Dissection in Prostate Cancer: Is It Really Necessary? A Multicentric Longitudinal Study Assessing Oncological Outcomes in Patients With Prostate Cancer Undergoing Pelvic Lymph Node Dissection vs Radical Prostatectomy Only

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Study Need and Importance: Previous clinical practice guidelines have recommended pelvic lymph node dissection (PLND) as an integral part of radical prostatectomy (RP) in intermediate-risk and high-risk prostate cancer (PCa) to facilitate reliable staging and guide treatment after prostatectomy. With the availability of prostate-specific membrane antigen positron emission tomography scans, it is controversial whether PLND at the time of RP is still the most reliable and accurate staging modality for lymph node assessment. Furthermore, the oncological benefit of PLND remains unclear.

What We Found: In this longitudinal multicenter cohort study, we reviewed data of 2346 consecutive patients with PCa (of whom 70% underwent a PLND at the time of RP) and found out that extended lymph node dissection was significantly associated with a lower risk of a metastatic event in patients with National Comprehensive Cancer Network/D'Amico intermediate-risk (HR, 0.48, 95% CI, 0.25-0.90, $P = .023$) and high-risk (HR, 0.57, 95% CI, 0.36-0.91, $P = .02$) PCa and should therefore be considered in men undergoing RP. Our multivariable Cox proportional hazards regression demonstrated that PSA, International Society of Urological Pathology grade group, and pathological T-stage are further significant prognostic variables for metastasis-free survival. However, there was no difference in recurrence-free survival between men who had a PLND and those who did not (HR, 1.07, 95% CI, 0.87-1.32, $P = .52$).

Limitations: Limitations of this study include lack of randomization, its retrospective design, potential for unmeasured confounding, and low number of patients not having undergone PLND, especially in high-risk cases.

Interpretation for Patient Care: Our study suggests that there is a therapeutic benefit to be gained by performing an extended PLND at the time of RP in patients with National Comprehensive Cancer Network/D'Amico intermediate-risk and high-risk PCa. This is important for patient counseling when deciding whether a PLND should be performed at the time of RP. However, further research with more uniform standardization to PLND and long-term oncological data derived from randomized controlled trials are required to substantiate these findings.

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Pelvic Lymph Node Dissection in Prostate Cancer: Is It Really Necessary? A Multicentric Longitudinal Study Assessing Oncological Outcomes in Patients With Prostate Cancer Undergoing Pelvic Lymph Node Dissection vs Radical Prostatectomy Only

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Purpose: With the availability of prostate-specific membrane antigen positron emission tomography scans, it is controversial whether pelvic lymph node dissection (PLND) at the time of radical prostatectomy (RP) is still the most reliable and accurate staging modality for lymph node assessment. Furthermore, the oncological benefit of PLND remains unclear. The aim of this study was to assess whether omitting PLND in patients undergoing RP for prostate cancer (PCa) is associated with the risk of tumor recurrence and progression to metastasis.

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Data analysis and interpretation: Furrer, Sathianathen, Papa, Corcoran.
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Materials and Methods: In this longitudinal multicenter cohort study, we reviewed data of 2346 consecutive patients with PCa who underwent RP with (n = 1650) and without (n = 696) extended PLND between January 1996 and December 2021. Recurrence-free survival and metastasis-free survival (MFS) were analyzed as a time-to-event outcome using Kaplan-Meier analyses with log-rank tests. To assess the effect of PLND, we created multivariable Cox proportional hazards models adjusting for relevant clinical and demographic characteristics.

Results: Median follow-up was 44 months. There was no difference in recurrence-free survival between men who had a PLND and those who did not (HR, 1.07, 95% CI, 0.87-1.32, $P = .52$). Patients with D'Amico high-risk disease (PSA >20 μg/L and/or International Society of Urological Pathology grade group ≥4) demonstrated a significantly prolonged MFS if they underwent PLND (HR, 0.57, 95% CI, 0.36-0.91, $P = .02$). PLND also improved MFS in patients with intermediate-risk disease (HR, 0.48, 95% CI, 0.25-0.90, $P = .023$). Further significant prognostic variables for MFS on multivariable Cox proportional hazards regression were PSA, International Society of Urological Pathology grade group, and pathological T-stage.

Conclusions: PLND improves MFS in patients with D'Amico intermediate-risk and high-risk PCa and may therefore be considered in men undergoing RP.

Key Words: pelvic lymph node dissection, radical prostatectomy, metastatic-free survival, recurrence-free survival, oncological outcomes, staging modalities

Previous clinical practice guidelines have recommended pelvic lymph node dissection (PLND) as an integral part of radical prostatectomy (RP) in intermediate-risk and high-risk prostate cancer (PCa) to facilitate reliable staging and guide treatment after prostatectomy. This may also improve cancer control by eradicating micrometastases.[1] Several studies have recently shown a decrease in the use of PLND at the time of RP,[2] raising uncertainties regarding the extent of current surgical treatment of PCa. According to the National Cancer Database, the reported rate of PLND (of any extent) in patients undergoing RP for intermediate-risk/high-risk PCa was approximately 70%, with only 25% undergoing an extended PLND.[3] A certain degree of reluctance among surgeons in adopting extended PLND seems to be supported by the findings of a randomized controlled trial conducted in the United States revealing only a marginal difference in nodal yields between limited PLND and extended PLND, with counts of 12 and 14, respectively.[4]

To underline this observation and despite clear recommendations of current guidelines to perform extended PLND in intermediate-risk and high-risk patients, the practice of any PLND during RP and the extent of dissection even in high-risk patients are largely dependent on individual surgeon preference. A recent study of patients with high-risk localized PCa undergoing RP reported that extended and limited PLND were performed in 36% and 28%, respectively, whereas PLND was even omitted in 33%.[5]

With improvement in staging ability, for example, using prostate-specific membrane antigen (PSMA) positron emission tomography (PET)/CT, it is currently unclear whether PLND at the time of RP is still the most reliable and accurate staging modality for lymph node (LN) assessment and whether it should be routinely recommended in men undergoing RP.[3,6] To date, some guidelines still recommend performing a PLND depending on the patient's risk of LN metastasis at the time of RP; however, this is not consistent. For example, the European Association of Urology[7] advocates for anatomically extended PLND for intermediate-risk PCa if the estimated risk of positive LNs exceeds 5%, as well as for high-risk cases, whereas the National Comprehensive Cancer Network clinical guidelines recommend PLND only in patients with a nomogram-calculated LN involvement risk ≥ 2%.[8]

Although recent studies have concluded that there was no significant difference in oncologic outcomes in patients with D'Amico high-risk or intermediate-risk PCa in whom PLND was or was not performed at RP, others indicate a possible therapeutic benefit of LN removal in node-negative patients with more extensive PLND at RP being associated with lower cancer-specific mortality in patients with D'Amico intermediate-risk and high-risk PCa without evidence of LN invasion.[9] As such, the therapeutic value of PLND remains controversial. Furthermore, there is considerable debate over extent of PLND. This is because the impact of the extent of the lymph node dissection on the pattern of nodal recurrence is not known.[10] However, advocates of PLND claim that extended dissection improves the diagnostic yield and prognostic utility after surgery.[11]

The aim of this study was therefore to assess whether omitting PLND (any extent) in patients undergoing RP for PCa has an impact on tumor recurrence and progression to metastasis.

MATERIALS AND METHODS

Patient Population

In this longitudinal multicenter cohort study, we reviewed data of 2346 consecutive patients with PCa who underwent open (n = 1264) and robotic (n = 956) RP with (n =

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1650) and without (n = 696) extended PLND at a total of 5 institutions, including the University Hospital of Bern, The Royal Melbourne Hospital, Epworth Health Care, Peter MacCallum Cancer Centre, and St Vincent's Hospital between January 1996 and December 2021. We excluded patients who received adjuvant therapy (n = 21 who received adjuvant radiotherapy [RT]) to maintain a uniform cohort and be able to assess the impact of PLND on outcomes. Baseline clinical and pathological data are presented in Table 1.

The study was conducted in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement and approved by the Ethics Committee of Canton Bern, Switzerland (KEKBE 2016-00156), and Melbourne Health (QA2020180).

Template of Lymph Node Dissection

Every patient received an extended PLND once the indication for RP was given. In the period from 1996 to 2008, the template included LNs located along the external iliac vein up to the common iliac bifurcation as well as those in the obturator fossa and along the internal iliac artery. Later than that, the template additionally included LNs located up to the midcommon iliac region where the ureter crosses the iliac vessels, as well as those located dorsolateral to the external iliac vessels and bifurcation of the common iliac vessels, in the fossa of Marcille and on the medial aspect of the internal iliac vessels.

Risk Group Stratification

Patients were classified into low-risk, intermediate-risk, and high-risk groups using pretreatment PSA level, biopsy Gleason score, and pathological (pT) rather than clinical tumor (cT) stage. As such, our inclusion criteria are not completely in agreement with the preoperative clinical assessment according to the D'Amico risk group classification criteria. However, this was on purpose given clinical staging (and preoperative risk assessment) using D'Amico criteria may underestimate potentially aggressive PCa in up to 37.5% of patients.[12] Consequently, caution is recommended when D'Amico criteria are solely used for preoperative decision-making. Therefore, to, firstly, more accurately reflect and, secondly, not underestimate the oncological risk of the underlying PCa, we decided to use the identical pathological rather than clinical parameters to categorize patients.

Table 1. *Demographics and Clinical Characteristics*

	No PLND	PLND	*P* value
No.	696	1650	
Age, median (IQR), y	64 (59-68)	64 (59-69)	.093
PSA, median (IQR), ng/mL	6 (5-9)	9 (6-15)	< .001
ISUP grade, No. (%)			< .001
1	34 (4.9)	529 (32)	
2	366 (53)	513 (31)	
3	183 (26)	276 (17)	
4	35 (5.0)	156 (9.5)	
5	77 (11)	170 (10)	
pT 3-4, No. (%)	68 (9.8)	303 (19)	< .001
Tumor volume, median (IQR), cc	3 (2-7)	10 (5-20)	< .001
PSM, No. (%)	185 (27)	568 (35)	< .001
No. of LNs removed, median (IQR)	NA	23 (15-32)	
pN+, No. (%)	NA	298 (22)	

Abbreviations: ISUP, International Society of Urological Pathology; LN, lymph node; NA, not applicable; PLND, pelvic lymph node dissection; PSM, positive surgical margins.

Oncological Outcomes

PSM was defined as malignant cells at the inked margin of the prostatectomy specimen. Biochemical recurrence (BCR) was defined as PSA $\geq$ 0.2 ng/mL in 2 consecutive measurements.[13] Local recurrence was defined as tumor recurrence in the prostatic bed including the areas adjacent to the vesicourethral anastomosis, rectovesical space, and within seminal vesicle remnants or seminal vesicle bed.

We used a broad definition of metastasis to include recurrence in pelvic regional LNs in addition to LN metastases outside of the pelvis as well as bony and visceral metastases. In this study, metastases were identified by conventional imaging after prostatectomy.

Surgical Procedure

In essence, a standardized surgical technique was performed by using either an open retropubic or robot-assisted laparoscopic approach. The decision regarding the preoperative administration of the anticoagulant agents was made on an individual patient basis.[14] All patients in whom PLND was performed underwent extended template removal of nodal tissue (from the external iliac, hypogastric, and obturator areas).[15] Limited or superextended PLND has not been performed in any of the centers.

Statistical Analysis

Continuous variables are reported as medians if not normally distributed and compared with Wilcoxon rank sum tests. Continuous variables that were normally distributed were reported as means and compared using *t* tests. Categorical variables were reported as counts and percentages and compared using a χ^2 test. Recurrence-free survival (RFS) and metastasis-free survival (MFS) were analyzed as a time-to-event outcomes. Start time was the time of RP, and patients without the event were censored at the last time they were known to be free from recurrence or metastasis. To assess the effect of PLND, we created multivariable Cox proportional hazards models adjusting for relevant clinical and demographic characteristics, including age, PSA, Gleason grade group, local tumor stage, tumor volume, and the presence of a positive surgical margin. We also performed subgroup analyses for all outcomes based on D'Amico/National Comprehensive Cancer Network (NCCN) risk groups. Statistical significance was set at $P < .05$, and all tests were 2-sided. Data analysis was performed in R. For detailed description of the methods, see Supplementary File 1 (https://www.jurology.com).

RESULTS

A total of 2346 patients were included in this multicenter analysis of whom 1650 (70%) underwent a PLND. The clinical and pathological characteristics of the cohort are outlined in Table 1. There were significant baseline differences between the 2 groups, with those who underwent a PLND having higher risk disease. This group also had larger tumor volumes and a higher incidence of extraprostatic disease. Of those who had a PLND,

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the median number of LNs removed was 23 (IQR, 15-32), and 22% (n = 298) had pathologically positive nodes. The median follow-up was 44 months (IQR, 16-91).

Disease recurrence was seen in 844 of the cohort. There was no statistically significant difference in RFS between men who had a PLND and those who did not (HR, 1.07, 95% CI, 0.87-1.32, $P = .52$). PSA, International Society of Urological Pathology (ISUP) grade, pathological T-stage, and positive surgical margin status were all significant variables in affecting RFS. We did not observe that PLND was associated with lower risk of tumor recurrence in any of the D'Amico subgroups (Table 2).

The incidence of metastases was 341. Undergoing a PLND had no statistically significant association with MFS in the overall cohort (HR, 0.72, 95% CI, 0.50-1.06, $P = .09$). The only significant prognostic variables for MFS on multivariable Cox proportional hazard regression were PSA, ISUP grade group, and pathological T-stage. However, patients with D'Amico high-risk disease (PSA >20 and/or ISUP GG ≥4) demonstrated a statistically significantly lower risk of a metastatic event if they underwent a PLND (HR, 0.57, 95% CI, 0.36-0.91, $P = .02$). Patients with intermediate-risk disease also had a lower risk of a metastatic event when undergoing a PLND (HR, 0.48, 95% CI, 0.25-0.90, $P = .023$). Subgroup analysis was not possible for patients with low-risk disease because of the low incidence of metastatic events in this subcohort (n = 6). The full multivariable model results are provided in Supplementary Appendix Table 1 (https://www.jurology.com).

DISCUSSION

Our study suggests that there is a therapeutic benefit to be gained by performing a PLND at the time of RP because we found a significantly prolonged MFS in patients with NCCN/D'Amico intermediate-risk and high-risk PCa who underwent PLND. This is one of the largest studies in the literature to demonstrate a long-term oncological benefit with PLND. However, we did not observe a difference in RFS between men who had a PLND and those who did not. As expected, PSA, ISUP grade, and pathological T-stage were significant prognostic variables for MFS and RFS on multivariable Cox proportional hazards regression. Furthermore, PSM was a significant prognostic variable for RFS but not MFS.

In line with our findings, several authors published data indicating improved oncological outcomes in patients with limited LN metastasis who underwent PLND at the time of RP. These recent studies reported beneficial association with improvement of the prognosis of long-term oncological outcomes by reducing occurrence of metastasis.[16,17] Furthermore, Heidenreich reported that extended PLND could significantly reduce the cancer-specific mortality of PCa, with a 15% reduction in node-negative and 23% reduction in node-positive disease.[18] Preisser et al[9] showed that more extensive PLND at the time of RP is associated with lower cancer-specific mortality in D'Amico intermediate-risk and high-risk patients without evidence of LN disease. These findings may be explained by removal of nodal micrometastasis at the time of RP.[19]

The literature is inconsistent regarding whether PLND improves outcomes. A recent phase 3 randomized controlled trial by Lestingi et al comparing extended vs limited PLND during RP for intermediate-risk and high-risk PCa showed that extended PLND provides better pathological staging, but differences in early oncological outcomes were not demonstrated. Furthermore, a subgroup analysis suggested a potential benefit in BCR-free survival in patients with ISUP grade group 3 to 5 PCa. The authors concluded that further RCTs with larger cohorts and longer follow-up are necessary to better define the role of extended PLND during RP.[20] Conversely, other published studies did not show any benefit of extended PLND.[21] Preisser et al[21] showed that omitting PLND was not associated with higher risk of occurrence of distant metastasis and cancer-specific mortality in a multi-institutional cohort of 9742 patients with D'Amico high-risk or intermediate-risk disease and concluded that the therapeutic value of PLND in these patients remains unclear. However, the LN count in this study was lower than ours (median 14 LNs) and may suggest that an extended lymph node dissection is required for an oncological benefit. Furthermore, only 7% of the cohort in the study by Preisser et al did not undergo PLND, and therefore, there may not be sufficient power to detect a difference. Other recent studies concluded that PLND can be avoided in some of those patients with an unneglectable risk of nodal disease.[22] However, one of the issues when interpreting these studies is that there are significant variations with

Table 2. *Multivariable Cox Proportional Hazard Ratios for Pelvic Lymph Node Dissection*

	HR	95% CI	*P* value
Recurrence-free survival			
All patients	1.07	0.87-1.32	.52
High-risk	0.82	0.61-1.10	.18
Intermediate-risk	0.90	0.67-1.22	.51
Metastasis-free survival			
All patients	0.72	0.50-1.06	.09
High-risk	0.57	0.36-0.91	.02
Intermediate-risk	0.48	0.25-0.90	.023

For the results of the full multivariable model, see Supplementary Appendix Table 1 (https://www.jurology.com). Recurrence-free and metastasis-free survival in patients with high-risk and intermediate-risk prostate cancer undergoing radical prostatectomy with or without pelvic lymph node dissection—full multivariable model results.

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regard to the extent and technique of PLND. Owing to this shortcoming and the presence of discrepant results of retrospective studies, the evidence for the benefit of PLND is uncertain.

Surgeons omitting PLND even in high-risk PCa argue that patients can be treated with postoperative radiation (whole-pelvis RT) if needed. Tilki et al[23] described the possibility of a significant reduction in all-cause mortality risk in patients with nodal-positive disease or pathological Gleason score 8 to 10 and pT3/4 undergoing adjuvant radiation therapy after RP. Furthermore, those surgeons doubt oncological significance in patients at high risk of node-positive disease as they postulate that high-risk disease is a systemic disease, and therefore, the benefit of PLND remains uncertain while adjuvant and salvage treatment may still be offered in patients with LN metastases. Therefore, in their view, PLND should not be used in the surgical management of PCa as its risks (including lymphocele, lymphorrhea, lower limb lymphedema, and thromboembolism) outweigh any potential staging benefit.[24]

The role of PLND for staging was well established compared with conventional imaging but is now being questioned again in the era of novel imaging. Clinicians have been reliant on conventional staging modalities with CT and bone scan to assess for disease spread, but PSMA-PET/CT has been shown to be significantly more sensitive than the aforementioned tests.[25] As evident in the literature, PSMA-PET/CT is more sensitive for nodal staging compared with other modalities; however, small LN metastases, under the spatial resolution of PET (~5 mm), may still be missed. As such, LN missing nodal disease may lead to suboptimal treatment decisions. A prospective phase 3 multicenter imaging trial involving patients with intermediate-risk and high-risk PCa undergoing RP and PLND showed a sensitivity and specificity of 68Ga-PSMA-11-PET of 0.40 and 0.95, respectively.[26]

Although there has been level 1 evidence demonstrating that adjuvant RT is not superior to early salvage therapy; these trials had only a small proportion of node-positive patients and more recent data suggest that pN+ patients do benefit with adjuvant RT.[23] In addition, STAMPEDE demonstrated improved oncological outcomes with systemic treatment in patients with high-risk, nonmetastatic disease, including those that were node positive.[27] Thus, contrary to the line of thought that accurate nodal staging would not change management and that postoperative PSA would guide decision-making, there is new evidence suggesting otherwise and emphasizes the need for accurate nodal staging.

Interestingly, the effect of PLND on BCR and consequently RFS remains unclear. The wider literature is variable with studies that show no effect of PLND on BCR,[21] whereas others found lower BCR rates in patients undergoing PLND.[28] We did not find a statistically significant difference in RFS with vs without PLND. This is somewhat surprising because it would be assumed that the "debulking effect" of the removal of the pelvic LNs would reduce the occurrence of micrometastases in LNs and hence decrease BCR. BCR is driven by multiple factors, such as positive surgical margin, which is more common in intermediate-risk and high-risk disease, and therefore PLND may not be associated with this outcome as much as disease dissemination (metastasis). A study of PSMA-PET/CT in the secondary staging setting after RP demonstrated PSMA uptake in the prostatic vascular pedicle and vesicourethral anastomosis, and these sites of local recurrence may be more important in RFS.[29] It is possible that at least in some patients metastasis occurs by hierarchical spread, so disruption of lymphatic channels as they exit in the pelvis may limit wider dissemination, without affecting recurrence in the pelvic regions not included in an extended template. This, however, is purely speculative, although ongoing lineage tracing studies of LN and bony metastasis may offer some insights. It is pertinent to note, however, that BCR per se has been found to be a poor surrogate for long-term oncological outcomes after primary treatment.[30]

This study did have some limitations. First, there was no randomization and this was a retrospective analysis of prospectively collected data. The number of patients not having undergone PLND, especially in high-risk cases, was lower, and there may be confounding factors that could have a negative influence on our findings. PLND templates of the various institutions involved in this study may vary to a certain degree. Furthermore, nodal retrieval rates are associated with several factors including handling of specimens and pathological processing. Certain surgeons may still have been in the RP learning curve, which could have resulted in a lower number of LNs removed in less experienced surgeons. We also included all surgical modalities (robotic and open). In addition, given that the majority of the patients underwent surgery before the PSMA-PET/CT era, we cannot comment on its consequences on accuracy in preoperative and postoperative N and M-staging. This is because PSMA-PET with 18F-PSMA has only been authorized in Switzerland in October 2019, and only since the start of 2021, a [68Ga] Ga-PSMA-11 radiolabeling kit has been approved for clinical use by the Australian Therapeutic Goods Administration. In both countries, it has not been routinely used in preoperative staging but only in a small number of patients.

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However, although PSMA-PET/CT is more accurate for staging than CT and bone scan for high-risk disease, no outcome data exist to date to inform subsequent management. As such, the most recent EAU guidelines recommend that treatment should not be changed based on PSMA-PET/CT findings in any risk group staging, in view of current available data.

To the best of our knowledge, other than the work of Preisser et al,[21] this is the only multicenter study assessing the association of PLND on metastasis-free survival outcomes after RP and challenges their findings. The data provided are not only useful for surgeons decision-making and indication but also patient counseling and management. However, long-term data obtained from randomized controlled trials[20] are needed.

CONCLUSIONS

PLND is significantly associated with a lower risk of a metastatic event in patients with NCCN/D'Amico intermediate-risk and high-risk PCa and should therefore be considered in men undergoing RP. However, more uniform standardization to PLND and long-term oncological data derived from RCTs are required to substantiate these findings.

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EDITORIAL COMMENTS

Extended pelvic lymph node dissection (ePLND) during radical prostatectomy has been endorsed by both the AUA and the National Comprehensive Cancer Network, particularly for patients with unfavorable intermediate-risk and high-risk prostate cancer.[1,2] This recommendation primarily stems from its utility as a staging tool, offering valuable prognostic information. However, ePLND has not consistently demonstrated improvements in metastasis-free survival, cancer-specific survival, or overall survival. Yet, there are incontrovertible data that a well-done ePLND is better at nodal staging than imaging including prostate-specific membrane antigen positron emission tomography scans, and a low-volume pN1 can be cured with surgery alone. In addition, data exist suggesting molecular involvement of nodes especially in high-grade disease that is negative in traditional histopathology (pN0).

In this multicenter cohort study, the authors assessed the role of pelvic lymph node dissection (PLND) at the time of radical prostatectomy in patients with prostate cancer.[3] In comparison with no PLND, they found that ePLND was significantly associated with a lower risk of metastatic progression in both intermediate-risk and high-risk groups, as defined by National Comprehensive Cancer Network/D'Amico criteria, with hazard ratios of 0.48 and 0.57, respectively. However, no significant difference was observed in biochemical recurrence between those who underwent PLND and those who did not.

These findings contribute to the growing body of evidence, complementing a recently reported randomized trial by Touijer et al[4] comparing limited vs ePLND, and suggest a potential role for ePLND in reducing metastatic progression. However, interpretation of these findings must be cautious. The absence of biochemical recurrence differences between groups raises concerns about selection bias in imaging decision. Furthermore, the lack of data on subsequent management strategies for patients with pN1 introduces potential confounding factors. In the absence of robust prospective data, the decision to perform PLND should be individualized, balancing potential oncologic benefit with procedural risks.

We commend the authors for their thoughtful and informative study, which perhaps strengthens our understanding of the value of ePLND and supports clinicians in guiding patients through complex treatment decisions with greater confidence and clarity.

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Furrer et al[1] report a multi-institutional analysis investigating the potential benefits of performing lymphadenectomy at the time of radical prostatectomy. They find that the performance of lymphadenectomy did not affect recurrence-free survival rates but did seem to improve metastasis-free survival in intermediate-risk and high-risk patients. The authors are to be commended for their contribution to the literature on this long-standing and controversial topic.

However, a key factor not addressed in the manuscript is the potential impact of adjuvant or salvage therapies administered postoperatively. It is plausible that a greater proportion of patients in the lymphadenectomy group received such therapies, either because lymph nodes were positive or because they were higher-risk patients more likely to have advanced stage disease, positive margins, etc. If this is the case, the improved metastasis-free survival observed in the lymphadenectomy group may be attributable to the adjuvant or salvage therapies, rather than to lymphadenectomy itself. Clarifying the use and timing of adjuvant or salvage therapies would strengthen the interpretation of these findings and help delineate the independent impact of lymphadenectomy in this setting.

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