Lymphadenectomy in Prostate Cancer: Technique and Outcomes

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1 Introduction

Prostate cancer (PCa) is currently the most common non-cutaneous malignancy and the second leading cause of cancer death in men in Western countries. With the advent of prostate-specific antigen (PSA) and screening programs, although cases of confined organ tumors are currently more frequent, about 10–20% of patients have locally advanced disease or lymph node metastases at the time of diagnosis [1].

The PCa can spread both via the hematogenous route, the axial skeleton being the preferred site of metastases, and via the lymphatic way, represented mainly by the drainage of the pelvic lymph nodes [2]. Despite recent advances in imaging techniques, there are still difficulties in assessing lymph node involvement. The sensitivity of Computed Tomography and Magnetic Resonance in detecting lymph node metastases is close to 35% insufficient [3, 4]. The Positron Emission Tomography (PET) [68Ga] prostate-specific membrane antigen (PSMA) in the setting of primary staging also is controversial, given the paucity of data [5].

Lymphadenectomy, or lymph node dissection (LND), has become part of radical prostatectomy (RP) since the operation became popular in the 1980s by Walsh [6]. The goal of any anatomical lymphadenectomy in patients with high-risk human cancers of any type is to identify microscopic lymph node metastases to improve locoregional staging and facilitate discussions regarding the need for adjuvant systemic therapy and improve long-term oncological outcomes [7].

The actual therapeutic role of LND during RP for the management of PCa remains controversial in terms of oncological impact. Reports suggest that LND improves pathological staging and that extending the pelvic LND (PLND) template may increase its staging accuracy [8]. Nevertheless, the oncological benefit of the procedure is still unclear. Recently, two Randomized Controlled Trials (RCT) comparing extended vs. limited PLND in intermediate- and high-risk PCa patients demonstrated no Biochemical Recurrence differences in a short follow-up [9, 10]. A recent systematic review revealed that performing PLND during RP failed to improve oncological outcomes, including survival [11]. Although, it is generally accepted that extended PLND provides essential information for staging and prognosis.

Furthermore, complications are a significant concern related to the procedure. PLND may be associated with an increased risk of adverse events, morbidity, length of stay, and healthcare costs, mainly related to significant lymphoceles [11]. However, the assertion that more extensive PLND leads to higher complication rates has not always been confirmed [12, 13].

This chapter will review indications, techniques, and results of extended pelvic lymphadenectomy (ePLND) in the surgical treatment of PCa patients.

1.1 Current Guideline Recommendations for Extended PLND in Prostate Cancer

The American Urological Association (AUA) / American Society for Radiation Oncology (ASTRO) / Society of Urologic Oncology (SUO) guidelines reserve the LND for patients with PCa at higher risk for LNI, high-risk or unfavorable intermediate-risk. Still, they do not indicate the extent of the dissection. They also emphasize the importance

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of guiding patients about LND complications, including lymphocele and its treatment [14].

The European Association of Urology (EAU), European Association of Nuclear Medicine (EANM), European Society for Radiotherapy and Oncology (ESTRO), European Society of Urogenital Radiology (ESUR), and International Society of Geriatric Oncology (SIOG) recommendations indicate the LND for PCa patients with locally advanced, high-risk, and intermediate-risk disease whose LNI estimate is greater than 5% in the preoperative nomograms. In patients where LND is indicated, it should be extended. The recommended extended template dissects the regions bilaterally: obturator, external iliac, and internal iliac. Although, if updated versions of preoperative nomograms are used, including multiparametric Magnetic Resonance Image findings and Target Biopsy results, more patients may spare from an unnecessary PLND (using a threshold of 7%) [15].

The National Comprehensive Cancer Network (NCCN) suggests that an extended PLND is preferred when PLND is performed and recommended for patients whose predicated probability of nodal metastases by nomograms is ≥2%. According to NCCN recommendation, an extended PLND includes removing all node-bearing tissue from an area bound by the external iliac vein anteriorly, the pelvic sidewall laterally, the bladder wall medially, the floor of the pelvis posteriorly, Cooper's ligament distally, and the internal iliac artery proximally. Besides that, PLND can be performed using an open, laparoscopic, or robotic technique [16].

The individual risk of finding positive LNs can be estimated using externally validated preoperative nomograms. Tools currently for identifying ePLND candidates are based on clinical parameters and showed excellent predictive accuracy on internal and external validation [17–20]. The variables included in models predicting lymph node invasion, guidelines, indications, and recommendations to perform PLND are summarized in Table 1.

Table 1 Guidelines, indications, and recommendations to perform pelvic lymph node dissection in prostate cancer

Guideline	Indications to perform PLND	Clinical variables considered	Recommended PLND
AUA / ASTRO / SUO	High-risk	PSA	Do not specify the template
	Unfavorable intermediate-risk	Clinical stage	
		ISUP grade group	
EAU / EANM / ESTRO / ESUR / SIOG	Intermediate-risk according to nomograms	PSA	Extended
	Probability of LNM > 5% (2012 Briganti nomogram)	Clinical stage (mpMRI[a])	
	Probability of LNM > 7% (2018 Gandaglia nomogram)[a]	Primary Gleason grade	
		Secondary Gleason grade	
	High-risk	Positive cores %	
		Maximum lesion diameter at mpMRI[a]	
	Locally advanced	Biopsy Gleason grade group at MRI-targeted biopsy[a]	
		Percentage of cores with clinically significant PCa at systematic biopsy[a]	
NCCN	Probability of nodal metastases by nomogram is ≥2%	Preoperative PSA	Extended
	MSKCC nomogram	Primary biopsy Gleason grade	
		Secondary biopsy Gleason grade	
		Clinical tumor stage	
		Negative biopsy cores	
		Positive biopsy cores	

ASTRO American Society for Radiation Oncology, *AUA* American urological association, *EAU* European Association of Urology, *EANM* European Association of Nuclear Medicine (EANM), *ESTRO* European Society for Radiotherapy and Oncology, *ESUR* European Society of Urogenital Radiology, *LNM* Lymph node metastases, *mpMRI* Multiparametric magnetic resonance imaging, *MSKCC* Memorial Sloan cancer Kettering center, *NCCN* National Comprehensive Cancer Network, *PCa* Prostate cancer, *PLND* Pelvic lymph node dissection, *PSA* Prostate specific antigen, *SIOG* International Society of Geriatric Oncology, *SUO* Society of Urologic Oncology

[a]Exclusive variables

2 Lymphadenectomy and Staging of Prostate Cancer: Templates and Patterns of Lymph Node Involvement

There was a lot of misunderstanding about nomenclature and LND templates. To standardize the extent of this dissection, the reference expert panel from the EAU Prostate Cancer Guideline Panel the following types of LND as follows (Fig. 1):

- ***Limited lymphadenectomy***: obturator lymph nodes.
- ***Standard lymphadenectomy***: obturator and external iliac lymph nodes.

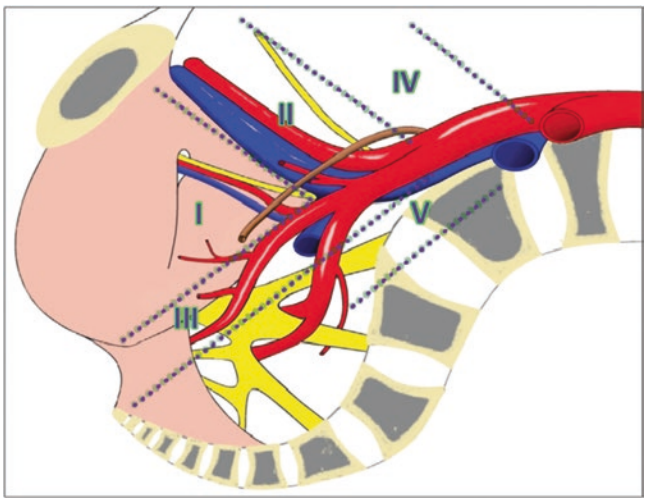

Fig. 1 Anatomical areas for the definition of the extent of dissection. I = obturator nodes; II = external iliac nodes; III = internal iliac nodes; IV = common iliac notes; V = presacral nodes

- ***Extended lymphadenectomy***: obturator lymph nodes, external iliac, and internal iliac.
- ***Super-extended lymphadenectomy***: obturator lymph nodes, external iliac, internal iliac, common iliac, and presacral [11, 21].

The dissection limits of the ePLND template include:

- ***Cranial***: crossing of the ureter over the common iliac vessels.
- ***Caudal***: deep circumflex vein and femoral canal.
- ***Lateral***: genital femoral nerve.
- ***Medial***: perivesical fat [11, 21].

The PCa does not follow a predetermined and constant pattern of nodal dissemination, and about 50% of these lymph node metastases are located along the internal iliac artery [3]. Retrospective series showed that the rate of pelvic lymph nodes invaded in patients with PCA is directly proportional to the extent of LND. The more lymph nodes dissected, the greater the number of affected lymph nodes, denoting the importance of performing ePLND [12, 22–25].

However, studies have indicated that resection of at least 20 lymph nodes is necessary for the PCa staging to be adequate, similar to that demonstrated in the Bladder Cancer LND [26]. Figure 2 illustrates the distribution of positive node patients by dissection area for extended PLND cases with at least one positive lymph node in a recently published trial [9]. Interestingly, almost two-thirds of patients with positive nodes had metastases at the internal iliac area.

A mapping study published by Briganti and colleagues included 19 patients with high-risk PCa (sharing at least two

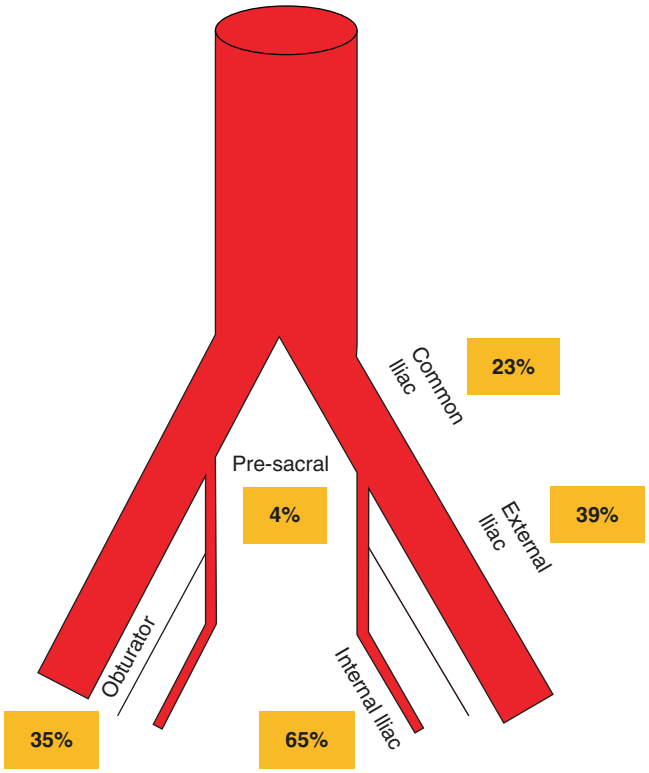

Fig. 2 Distribution of node-positive patients (N1) undergoing extended pelvic lymph node dissection per region [9]

out of the three following parameters: PSA >20 ng/ml, cT3, biopsy Gleason score ≥ 8). All patients were treated with RP and removal of the obturator, hypogastric, external iliac, presacral, common iliac, para-aortal/para-caval, and inter-aortocaval lymph nodes. Only patients with positive common iliac lymph nodes had positive retroperitoneal lymph nodes, demonstrating an ascending pathway for metastatic PCa cells [27].

Another mapping study by Joniau et al. with 74 localized PCa patients and a lymph node involvement risk of ≥10% but ≤35% (Partin tables) or a cT3 tumor provided fundamental insight into the pattern of lymphatic spread. After intraprostatic technetium-99 m nano colloid injection, surgery was performed with a sentinel node procedure and a super-extended LND followed by RP. The predominant site for lymphatic metastases was the internal iliac region. Extended PLND correctly staged the majority of positive lymph nodes patients, but 13% of the positive lymph nodes would have been missed [28].

Extended PLND significantly increases the yield of both total lymph nodes and lymph node metastases independent of the risk classification of PCa. Lymph node metastases will be detected in about 5–6%, 20–25%, and 30–40% of low-, intermediate-, and high-risk PCa, respectively [23].

In high-volume referral centers, the open, laparoscopic, or robotic LND techniques are feasible and have similar

oncological outcomes [29]. However, even in the presence of extensive nodal dissections, approximately 15% of the lymph nodes potentially bearing PCa metastases will not be removed because they are in regions not covered by the pelvic LND [21], as mesorectum, inguinal, or retroperitoneal [30].

2.1 Preoperative Prediction of Positive Nodes Using 68Ga-PSMA PET

One of the newest and most promising techniques for the staging of PCa, the Positron Emission Tomography (PET) [68Ga] prostate-specific membrane antigen (PSMA), has a high specificity for detecting pelvic lymph node metastases in primary PCa and a remarkably high positive predictive value in detecting lymph node metastases in patients with biochemical recurrence (BCR). This overview of the current literature with nine retrospective and two prospective studies described the sensitivity and specificity of 68Ga-PSMA PET for detecting pelvic lymph node metastases before initial treatment, which ranged from 33.3% to 100% and 80% to 100%, respectively [17].

Another recent review and meta-analysis included 37 articles and 4790 patients. The results highlighted the excellent sensitivity and specificity of 68Ga-PSMA PET in advanced prostate cancer. Specifically, on a per-patient analysis, the sensitivity and specificity of 68Ga-PSMA PET were 77% and 97%, respectively, following pelvic lymph node dissection at the time of RP. Sensitivity and specificity were 75% and 99% on a per-lesion analysis, respectively [5].

The US Food and Drug Administration (FDA) has recently approved Gallium 68 PSMA-11 as the first drug for PET imaging of PSMA positive lesions in men with PCa. However, one prospective multicenter single-arm open-label phase 3 imaging trial that supported the FDA decision showed a sensitivity of 0.4, also a low sensitivity in evaluating lymph node involvement. From December 2015 to August 2019, 633 intermediate to high-risk PCa patients underwent one 68Ga-PSMA-11 PET for primary staging, and 277/633 (44%) subsequently underwent RP and PLND. The median initial PSA was 11.1 [0.04–147]. Seventy five/two hundred and seventy-seven patients (27%) had N1 disease per histopathology. Sensitivity, specificity, positive predictive value and negative predictive value for N1 detection was 0.40 [0.34, 0.46], 0.95 [0.92, 0.97], 0.75 [0.70, 0.80], 0.81 [0.76, 0.85], respectively. Higher PSAs and larger node sizes correlated with increased sensitivity [18].

Therefore, PET [68Ga] PSMA cannot replace pelvic LND to exclude lymph node metastases: LND is still the gold standard for lymph node staging [5, 17].

3 Surgical Technique

This surgical technique can be used with both currently used robotic platforms (Intuitive *Da Vinci Xi* or *Si*©) and can be performed before or after RP according to the surgeon's preference.

The fourth robotic arm is used to pull the structures medially with the Prograsp Forceps. Incision of the adventitial fascia is made above the external iliac vessels from the top downwards. The incision line stretches from the bifurcation of the common iliac vessels to contact the pubic bone (Cooper's ligament). Parts of the perivascular adventitia are bluntly separated from the vessel's walls and the lateral pelvic wall to the lateral limit of the genitofemoral nerve (Fig. 3).

Slight shifting of the dissected conglomerate to cranial helps to identify the obturator nerve. Furthermore, preparation is strictly along and above the obturator nerve up to the meeting point with the internal iliac artery. The packet is ligated to occlude lymphatic leakage and prevent lymphocele (Fig. 4).

The dissection proceeds caudally to the femoral canal and the deep circumflex vein; the end next to Cooper's ligament is clipped. Sequentially, the tissue along the internal iliac vessels is dissected to skeletonize the obturator nerve (Fig. 5); the back next to the common iliac vessels is clipped.

The ureter, which ascends with the peritoneum, is identified and hitched. The crossing of the ureter at the bifurcation of the common iliac artery marks the caudal end of the dissection (Fig. 6). The bilateral tissue has been released from the extended template and can be extracted safely as a whole using an endo bag.

The Marcille's triangle or fossa is a pelvic anatomical region limited by the fifth lumbar vertebra medially, from the inner edge of the large muscle psoas laterally, from the upper edge of the wing, and the sacrum below. Lymph nodes of this anatomical region are related to the prostate lymphatic system, and some authors discuss Marcille's lymphadenectomy when planning an ePLND in high-risk PCa. Porcaro et al. analyzed 221 patients who underwent ePLND and robotic-assisted RP: Marcille's lymph node involvement was found in 5 (2.3%) patients. However, this involvement was associated with multiple lymph node metastases in other template locations in high-risk PCa patients [19].

The pelvic plexus and the erectile nerves are at risk in standard dissection during the medial dissection in the area of the internal iliac artery and towards the bladder wall. During ePLND, the nerves are also at risk at their origin in the presacral area and medial to the common iliac vessels. Decreased erectile function in patients with a more extended yield of lymph nodes relative to patients with a lower yield or

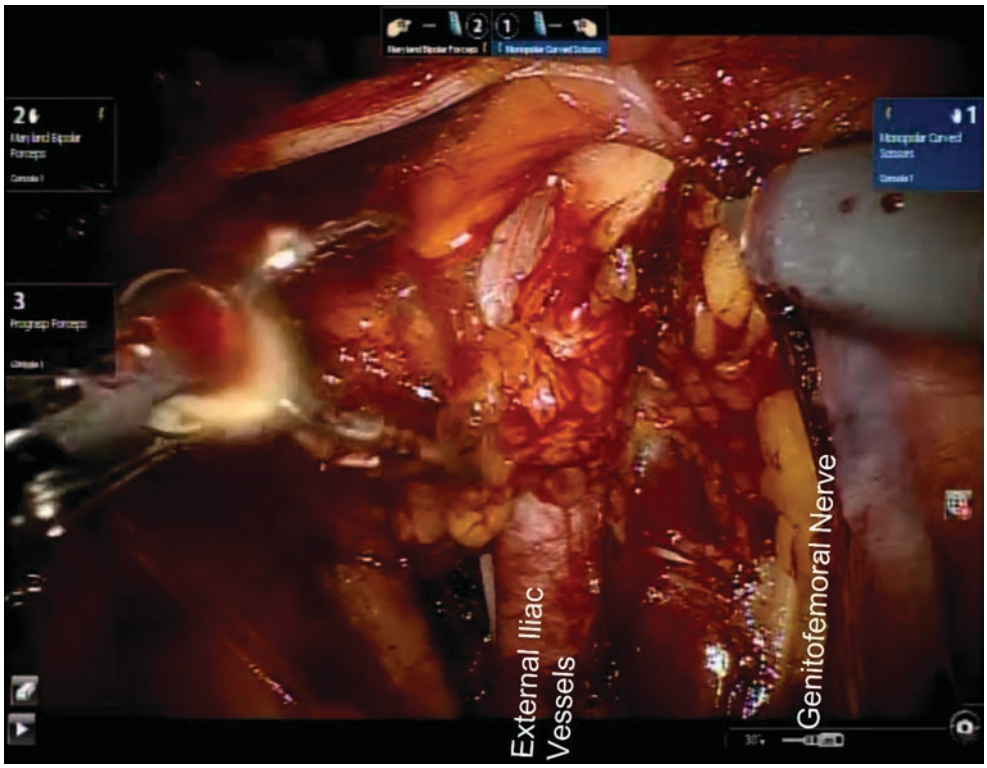

Fig. 3 Extended pelvic lymph node dissection surgical step (right side). Blunt lymphatic dissection anteriorly to the external iliac artery, from common iliac cranially to Cooper's ligament caudally

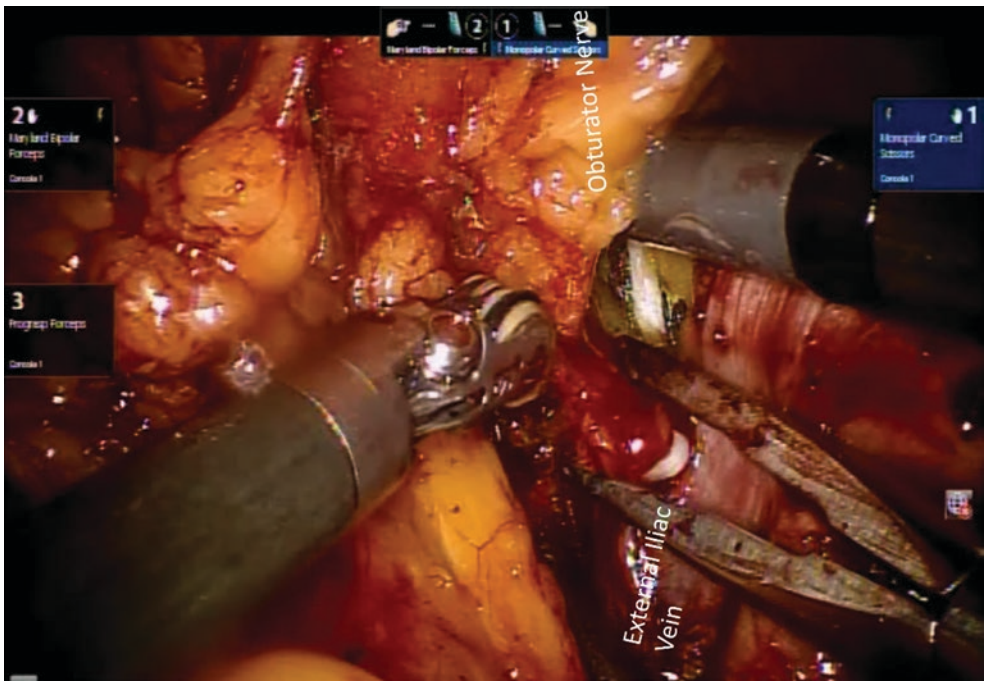

Fig. 4 Extended pelvic lymph node dissection surgical step (right side). Ligation of lymph nodal tissue cranially to the obturator nerve

no lymph node dissection has been demonstrated [20, 31]. Others could not find any influence from the extent of PLND on erectile function [32]. Nevertheless, from an anatomic point of view, ePLND occurs near or inside the pelvic plexus and thus can lead to injury of erectile nerves [33].

Lymphocele is the most common complication after PLND. Over the years, various techniques have been introduced to prevent lymphocele, but no conclusion can be drawn regarding the superiority of one technique over another. In this prospective study, 220 patients undergoing

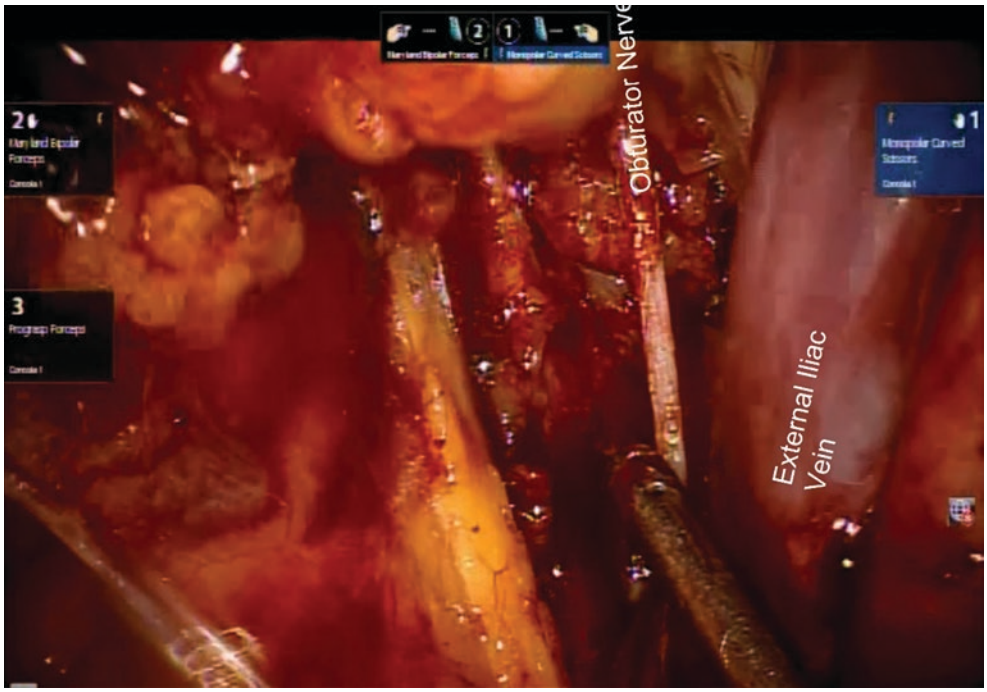

Fig. 5 Extended pelvic lymph node dissection surgical step (right side). Skeletonization of the obturator nerve

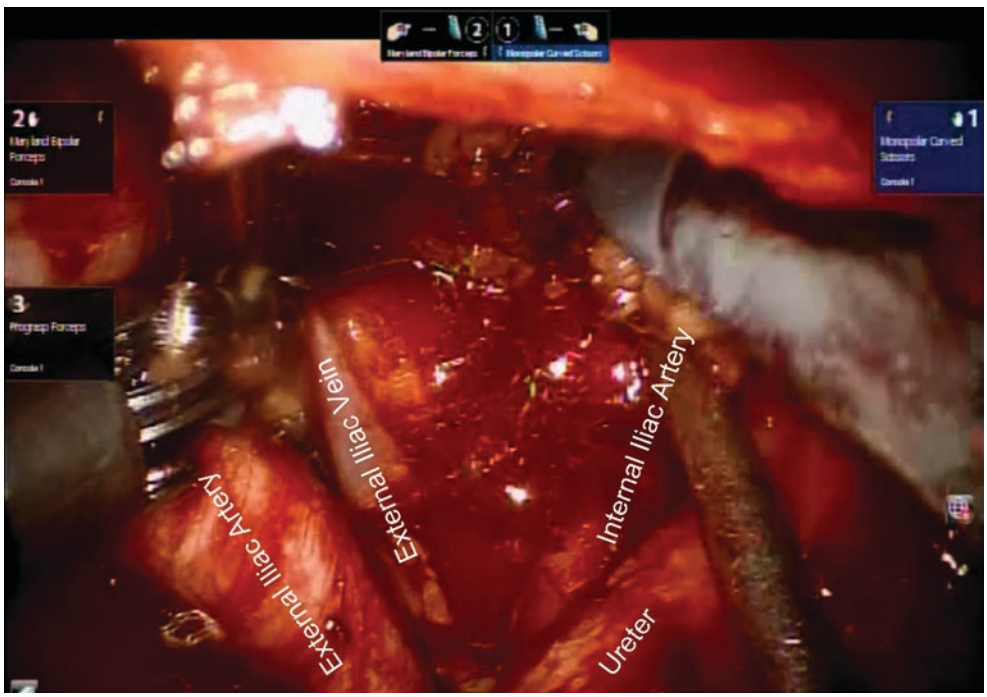

Fig. 6 Extended pelvic lymph node dissection surgical step (left side). The cranial limit of the template is the crossing of the ureter at the bifurcation of the common iliac artery

robot-assisted RP between 2012 and 2015 were randomized to receive titanium clips (group A, $n = 110$) or bipolar coagulation (group B, $n = 110$) to seal lymphatic vessels during ePLND. There were no statistically significant differences between groups A and B regarding overall lymphocele incidence (47% vs. 48%; difference − 0.91%, 95% confidence interval [CI] -2.6 to 0.7; $p = 0.9$) and the rate of clinically significant lymphocele [5% vs. 4%; difference 0.75%, 95% CI, 0.1–3.2; $p = 0.7$]. The two groups were comparable regarding mean (±SD) lymphocele volume (30 ± 32 vs. 35 ± 39 ml; $p = 0.6$), lymphocele location (unilateral, 37% vs. 35%, $p = 0.7$; bilateral, 13% vs. 14%, $p = 0.9$), and time to lymphocele diagnosis (95% vs. 98% on a postoperative day 10; $p = 0.5$) [34].

4 Perioperative Outcomes and Complications

There is much discussion in the literature about what the LND extension model should be. Such doubts are due to the uncertain benefit of LND in therapeutic terms and the potential increase in complications as the dissection limit increases.

The pelvic lymph node dissection is a challenging procedure that is time-consuming and carries a greater risk of surgical complications, with rates ranging from 2 to 51% [8]. One of the most extensive series with 963 patients that compared adverse events of the types of LND showed 19.8% of complications in the extended LND vs. 8.2% in the limited one ($p < 0.001$); when analyzed individually, only the lymphocele was significantly higher in patients undergoing extensive dissection (10.3% vs. 4.6%, respectively; $p = 0.02$) [13]. On the other hand, Bader et al. found only 2.1% of complications needed to prolong the length of hospital stay in patients undergoing ePLND [22].

Similarly, Fossati et al. compared LND vs. no-LND (20 retrospective studies) and compared the extended dissection vs. limited (3 prospective and 15 retrospective studies). LND and extended dissection were associated with significantly worse intra- and postoperative non-oncological outcomes, such as bleeding, lymphocele, and increased surgical time. The retrospective nature of most studies and the lack of standardized definitions for the extension of the LND are the main limitations of its conclusions [11].

The baseline characteristics of the principal comparative studies evaluating non-oncological outcomes are summarized in Table 2 [11, 12, 35]. Overall, 18 studies compared no PLND vs. any form of PLND, while 14 studies compared lPLND/sPLND vs. ePLND/sePLND. The non-oncological results are summarized in Table 3 [11, 12, 35].

4.1 Intraoperative and Perioperative Outcomes

Data were obtained from 16 retrospective studies regarding operative time, blood loss, and postoperative complications [36–51]. In the main, PLND was associated with a significantly higher risk of lymphocele in most studies that addressed the outcome.

In an RCT, 123 patients were randomized to ePLND on the right hemipelvis vs. lPLND on the left hemipelvis. Complications including lymphocele (3% vs. 1%) and lower extremity edema (3% vs. 2%) occurred more commonly on the side subjected to ePLND compared to lPLND [52]. When considering data from nine retrospective studies, conflicting results were observed. Three studies showed significantly higher intraoperative and postoperative complications in the ePLND group than lPLND/sPLND [53–55], while four studies did not find significant differences [56–59]. Similarly, the lymphocele rate was significantly higher in the ePLND group in four studies [53, 54, 60, 61], while no significant differences were observed in three others [56–58].

In another RCT, the rates of grade 2 and grade 3 complications were comparable between the limited (7.3%) and extended PLND groups (6.4%) [10].

4.2 Functional Outcomes

Three retrospective studies did not find any significant differences between PLND and no PLND regarding erectile function recovery [OR 0.95, 95% CI 0.63–1.43, $p = 0.8$ [32]; and HR 0.9; $p = 0.8$ [62]; $p = 0.48$ [59]].

One retrospective comparative study did not find any significant differences regarding urinary continence (HR 1.07, 95% CI 0.87–1.31; $p = 0.5$) and erectile function recovery (HR 1.11, 95% CI 0.75–1.63; $p = 0.6$) between ePLND and lPLND [63].

There were no differences in the International Index of Erectile Function scores in an RCT between ePLND and lPLND [10].

Extending the LND template beyond the ePLND template may cause at least a significant delay in recovery of urinary continence, maybe due to bladder denervation. Seikkula et al. demonstrated in a cohort of 172 PCa patients who underwent RP and PLND that patients undergoing super-extended PLND have a lower chance of regaining urinary continence [hazard ratio (HR) 0.59, 95% CI 0.39–0.90, $p = 0.026$]. Age at the surgery also had a significant influence on continence [64].

Nevertheless, some academic studies have suggested robot-assisted RP superiority over pure laparoscopic or open RP in operative and functional outcomes. Several reviews and meta-analyses of the literature recently highlighted the potential benefit of robot-assisted RP regarding the functional outcomes without hindering oncologic control. Few controlled trials with small cohorts have compared pure laparoscopic radical prostatectomy and robot-assisted RP, suggesting better early functional outcomes using robotic assistance. However, the level of evidence remains weak given the lack of randomized controlled trials and the number of factors (surgeon experience, disease staging, nerve-sparing techniques) that need to be considered [65].

Table 2 Baseline characteristics for studies addressing non-oncological outcomes

Study	Surgical	Treatment	*N*	Follow-up (mo)	Age (year)	PSA (ng/ml)	Biopsy Gleason score	Clinical T stage	Pathologic T stage	Pathologic Gleason score	Surgical margin	Number of lymph nodes dissected	Number of positive lymph nodes	Outcomes
No PLND versus any PLND														
Ostby-Deglum 2015	Robotic: 100%	No PLND	609	3.0	63	NR	NR	NR	NR	NR	NR	NR	NR	Insufficient
				[0.5–6.1]	[42–78]									Erection
Violette 2015	Robotic: 100%	No PLND	392	NR	60 (7)	6.9 (3)	6: 58.9% (n = 231)	NR	NR	NR	NR	NR	NR	OT
							7: 41.1% (n = 161)							
Tyritzis 2015	Open: 24%	No PLND	2997	NR	63.5	6.6 [0.1–20.0]	≤6: 58.1% (n = 1732)	T1: 65.5% (n = 1914)	T2: 77.2% (n = 2266)	≤7: 96.2% (n = 2846)	NR	NR	NR	DVT
	Robotic: 76%				[37.2–75.0]		3 + 4: 33.9% (n = 1011)	T2: 33.2% (n = 969)	T3: 22.6% (n = 662)	≥8: 3.8% (n = 113)				
							4 + 3: 6.1% (n = 182)	T3: 1.3% (n = 38)	T4: 0.2% (n = 6)					
							≥8: 1.8% (n = 54)							
		PLND	547		64.8	9.4 [0.7–20.0]	≤6: 13% (n = 71)	T1: 35.1% (n = 187)	T2: 48% (n = 258)	≤7: 78.8% (n = 423)				
					[42.3–75.0]		3 + 4: 31.3% (n = 171)	T2: 52.2% (n = 278)	T3: 50.5% (n = 271)	≥8: 21.2% (n = 114)				
							4 + 3: 28.9% (n = 158)	T3: 12.8% (n = 68)	T4: 1.5% (n = 8)					
							≥8: 26.7% (n = 146)							
Boehm 2015	Open: 95%	No PLND	4884	NR	64 (59–67)	NR	≤6: 29.2% (n = 3412)	NR	pT2: 70% (n = 8172)	NR	NR	NR	NR	Blood
	Robotic: 5%	PLND	6810				3 + 4: 53.8% (n = 6303)		pT3a: 20% (n = 2327)					Transfusion
							4 + 3: 13.0% (n = 1529)		≥pT3b: 10% (n = 1223)					
							≥8: 3.8 (n = 443)							

Liss 2013	Robotic: 100%	No PLND	207	NR	61 (6.9)	4.9 (4.0–6.5)	≤6: 93.5% (*n* = 188)	T1: 78.3% (*n* = 162)	T1: 92.3% (*n* = 191)	NR	NR	NA	NA	OT, eBL,
							7: 4.5% (*n* = 9)	T2: 21.7% (*n* = 45)	T2: 6.8% (*n* = 14)					Transfusion
							≥8: 2% (*n* = 4)	T3: 0% (*n* = 0)	T3: 1% (*n* = 2)					Rate, LoS,
														Complication rate,
														Lymphocele rate
		sPLND	231		63 (6.8)	6.1 (4.4–9.2)	≤6: 58.9% (*n* = 136)	T1: 58.9% (*n* = 136)	T1: 72.7% (*n* = 168)			18 [12–25]	0.3% (*n* = 13)	
							7: 39.4% (*n* = 91)	T2: 39.4% (*n* = 91)	T2: 26.4% (*n* = 61)					
							≥8: 1.7% (*n* = 4)	T3: 1.7% (*n* = 4)	T3: 0.9% (*n* = 2)					
		ePLND	54		61 (7.2)	8.5 (5.5–13.5)	≤6: 27.8% (*n* = 15)	T1: 27.8% (*n* = 15)	T1: 42.6% (*n* = 23)			20 (16–28)	2% (*n* = 24)	
							7: 68.5% (*n* = 37)	T2: 68.5% (*n* = 37)	T2: 55.6% (*n* = 30)					
							≥8: 3.7% (*n* = 2)	T3: 3.7% (*n* = 2)	T3: 1.9% (*n* = 1)					
van der Poel 2012	Robotic: 100%	No PLND	464	NR	60.7 (6.2)	NR	< 7: 90.5% (*n* = 420)	T1: 36.4% (*n* = 169)	T0: 1.5% (*n* = 7)	<7: 65.7% (*n* = 305)	NR	0	NA	Lymphocele, DVT,
							7: 8.6% (*n* = 40)	T2: 61.4% (*n* = 285)	T2: 84.5% (*n* = 392)	7: 29.1% (*n* = 135)				Clavien grade,
							>7: 0.7% (*n* = 4)	T3: 2.2% (*n* = 10)	T3: 11.0% (*n* = 51)	>7: 5.2% (*n* = 24)				Hematoma, ileus,
									T4: 3.0% (*n* = 14)					Anastomosis dehiscence
		sPLND	440		62.5 (5.8)	47.9 (23.2)	<7: 25.9% (*n* = 114)	T1: 34.1% (*n* = 150)	T0: 0.2% (*n* = 1)	<7: 65.7% (*n* = 305)		14 [11–19]	8.4% (*n* = 37)	
							7: 54.1% (*n* = 238)	T2: 59.3% (*n* = 261)	T2: 59.8% (*n* = 263)	7: 29.1% (*n* = 135)				
							>7: 20% (*n* = 88)	T3: 20.7 (*n* = 91)	T3: 34.3% (*n* = 151)	>7: 5.2% (*n* = 24)				

(continued)

Table 2 (continued)

Study	Surgical	Treatment	*N*	Follow-up (mo)	Age (year)	PSA (ng/ml)	Biopsy Gleason score	Clinical T stage	Pathologic T stage	Pathologic Gleason score	Surgical margin	Number of lymph nodes dissected	Number of positive lymph nodes	Outcomes
									T4: 5.7% (*n* = 25)					
Schmitges 2012	Open: 93%	No PLND	36,699	NR	61.7 (7.2)	NR	NR	NR	NR	NR	NR	NR	Nx: 56.8% (*n* = 20,862)	DVT
	Minimally												N0–1: 43.2% (*n* = 15,837)	
	Invasive: 7%													
Schmitges 2012	Open: 93%	No PLND	20,862	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	LoS, hospital charges,
	Minimally													Rectal lacteration rate
	Invasive: 7%													
Gandaglia	Open: 100%	No PLND	161	33.2	62.6	5.43	5: 14.9% (*n* = 24)	T1c: 75.9% (*n* = 122)	T2: 96.3% (*n* = 155)	2–6: 59% (*n* = 95)	NR	0	NR	Erectile function
					(47.8–77.8)	(IQR: 0.25–10)	6: 85.1% (*n* = 137)	T2a: 24.1% (*n* = 39)	T3a: 3.7% (*n* = 6)	7: 41% (*n* = 66)				Recovery rate
									T3b: 0% (*n* = 0)	8–10: 0% (*n* = 0)				
		ePLND	235		62.3	6	5: 23% (*n* = 54)	T1c: 62% (*n* = 147)	T2: 79.1% (*n* = 186)	2–6: 46% (*n* = 108)		20 [1–40]		
					(40.5–78.9)	(IQR: 0.57–10)	6: 77% (*n* = 181)	T2a: 38% (*n* = 88)	T3a: 15.3% (*n* = 36)	7: 48.9% (*n* = 115)				
									T3b: 5.5% (*n* = 13)	8–10: 5.1% (*n* = 12)				
Schmitges 2012	Open: 100%	No PLND	580	NR	64	6.3 (R: 0.5–93)	6: 44.2% (*n* = 637)	T1: 85.4% (*n* = 1230)	T2: 70.2% (*n* = 1011)	6: 28.9% (*n* = 417)	NR	NR	Nx: 40.2% (*n* = 579)	RBC, transfusion,
					(R: 37–77)		7: 35.6% (*n* = 513)	T2: 14.1% (*n* = 203)	T3: 29.8% (*n* = 430)	7: 66.7% (*n* = 961)			N0: 54.7% (*n* = 788)	Prolonged drainage,
							≥8: 8.8% (*n* = 127)	T3: 0.6% (*n* = 8)		8: 4.4% (*n* = 63)			N1–2: 5.1% (*n* = 74)	Lymphocele
Touijer 2011	Lap: 100%	lPND	174	NR	NR	7 [5–11]	<7: 14%	T1: 61%	NR	NR	NR	9 [6–13]	4.5%	OT,
							7: 71%	T2a: 14%						Postoperative

							8–10: 15%	>T2b: 24%						Complications
		sPLND	595			6 [5–9]	<7: 11%	T1: 57%				13 [9–18]	14.3%	
							7: 72%	T2a: 18%						
							8–10: 14%	>T2b: 24%						
		No PLND	202			NR	NR	NR				NA	NA	
Yong 2011	Robotic: 100%	No PLND	182	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	OT
Eifler 2011	Lap: 100%	No PLND	302	>3	57.7 (6.7)	4.8 (NR)	7: 15.6% (*n* = 47)	NR	NR	NR	NR	0	0	OT, VTE
Khoder 2011	Retro: 89.8%	No PLND	8	NR										Lymphocele
	EERPE: 6.5%													
	Perineal: 3.8%													
Lin 2011	Lap: 100%	No PLND	120	33.9	NR	NR	NR	NR	NR	NR	NR	NR	NR	Inguinal hernia
Hruza 2010	Lap: 100%	No PLND	761	50	63.8 (6.15)	7.6 [IQR: 5.3–11.5]	NR	<T3a: 70.2% (*n* = 1486)	T2: 57.4% (*n* = 1261)	4–5: 10.8% (*n* = 229)	R0: 76.6%	NR	NA	Complication rate
				[IQR: 26–72]					T3a: 26.5% (*n* = 588)	6: 31.8% (*n* = 676)	(*n* = 1683)			
									T3b: 11.8% (*n* = 260)	7: 48.1% (*n* = 1020)				
									T4: 4% (*n* = 89)	8–10: 9.3% (*n* = 197)				
		PLND	1438										1.9% (*n* = 41)	
Zorn 2009	Robotic: 100%	No PLND	859	NR	59.2	5.5	6: 81% (*n* = 696)	cT1c: 71% (*n* = 618)	NR	6: 69.3% (*n* = 595)	NR	NA	NA	OT, eBL, blood
					(R: 40–77)	(R: 0.06–32)	7: 19% (*n* = 163)	cT2a–cT2b: 29% (*n* = 241)		7: 28.8% (*n* = 247)				Transfusions, LoS,
										8–10: 1.9% (*n* = 17)				Postoperative

(continued)

Table 2 (continued)

Study	Surgical	Treatment	*N*	Follow-up (mo)	Age (year)	PSA (ng/ml)	Biopsy Gleason score	Clinical T stage	Pathologic T stage	Pathologic Gleason score	Surgical margin	Number of lymph nodes dissected	Number of positive lymph nodes	Outcomes
														Complications,
														Symptomatic
														Lymphocele
		PLND	296		61.0	9.0 (R: 0–89-52)	6: 17% (*n* = 52)	cT1c: 61% (*n* = 180)		6: 16.2% (*n* = 48)		12.5 (IQR: 7–16)	7.8% (*n* = 23)	
					(R: 44–85)		7: 62% (*n* = 182)	cT2a–cT2b: 38% (*n* = 112)		7: 67.9% (*n* = 201)				
							8–10: 21% (*n* = 62)	cT3: 1% (*n* = 4)		8–10: 15.9% (*n* = 47)				
Stolzenburg 2005	EERPE: 100%	No PLND	700	17.3	63.4	10.7	NR	NR	T2a: 12.7 (*n* = 89)	4: 11% (*n* = 77)	R1: 19.7%	NR	NR	OT
				(R: 3–39)	(R: 42–77)	(R: 1.4–82)			T2b: 7.7% (*n* = 54)	5: 19.3% (*n* = 135)	(*n* = 138)			
									T2c: 35% (*n* = 245)	6: 23% (*n* = 161)				
									T3a: 32.7 (*n* = 229)	7: 35.4% (*n* = 248)				
									T3b: 11.2 (*n* = 79)	8: 8.3% (*n* = 58)				
									T4: 0.6 (*n* = 4)	9: 2.4% (*n* = 17)				
										10: 0.6% (*n* = 4)				
Limited/standard PLND versus (super) extended PLND														
Hatzichristodoulou 2015	Open: 100%	ePLND	262	48	64.9 (7.5)	8.3 (6.3)	6: 0% (*n* = 0)	≤T1c: 57.3% (*n* = 150)	pT2: 76.3% (*n* = 200)	6: 40.1% (*n* = 105)	NR	20.4 (9.7)	NR	Continence recovery rate
				[R: 24–84]			7: 88.6% (*n* = 232)	>T1c: 42.7% (*n* = 112)	pT3a: 13% (*n* = 34)	7: 47.7% (*n* = 125)				(12 mo), spontaneous EF
							8: 8.0% (*n* = 21)		pT3b: 9.9% (*n* = 26)	8–10: 12.2% (*n* = 32)				Recovery (12 mo),
							9: 3.4% (*n* = 9)		pT4: 0.8% (*n* = 2)					Trifecta rates (2-year)

		lPLND	198		64.6 (7.8)	9.9 (7.8)	6: 100% (n = 198)	≤T1c: 74.7% (n = 148)	pT2: 80.8% (n = 160)	6: 44.9% (n = 89)		4.7 (4)		
							7: 0% (n = 0)	>T1c: 25.3% (n = 50)	pT3a: 13.6% (n = 27)	7: 50.6% (n = 100)				
							8: 0% (n = 0)		pT3b: 5.6% (n = 11)	8–10: 4.5% (n = 9)				
							9: 0% (n = 0)		pT4: 0% (n = 0)					
Kim 2013	Robotic: 100%	sPLND	294	36	65	8.4	≤6: 33.4% (n = 98)	T1: 66.3% (n = 195)	T2: 62.2% (n = 183)	NR	NR	12 [R: 9–16]	3.4% (n = 10)	Complication rate,
					[R: 60–69]	[R: 5.3–37.7]	7: 48.3% (n = 142)	T2: 21.4% (n = 63)	T3a: 28.6% (n = 84)					Lymphocele, lymphedema,
							≥8: 18.3% (n = 54)	T3: 12.3% (n = 36)	T3b: 9.2% (n = 27)					Neuropraxia
		ePLND	170		66	10.4	≤6: 17.7% (n = 30)	T1: 45.9% (n = 78)	T2: 56.5% (n = 96)			21 [R: 16–25]	13.5% (n = 23)	
					[R: 62–70]	[R: 6.6–16.1]	7: 39.4% (n = 67)	T2: 41.2% (n = 70)	T3a: 28.8% (n = 49)					
							≥8: 42.9% (n = 73)	T3: 12.9% (n = 22)	T3b: 14.7% (n = 25)					
Hoshi 2015	Open: 100%	sPLND	599	40 [R: 1–261]	NR	NR	NR	NR	NR	NR	NR	NR	High risk: 7.1% (n = 13)	eBL, lymphocele,
													Int risk: 0.6% (n = 1)	Intra- and postoperative
													Low risk: 0% (n = 0)	Complications
		Semi-ePLND	131										High risk: 20% (n = 12)	
													Int risk: 3.3% (n = 1)	
													Low risk: 0% (n = 0)	

(continued)

Table 2 (continued)

Study	Surgical	Treatment	*N*	Follow-up (mo)	Age (year)	PSA (ng/ml)	Biopsy Gleason score	Clinical T stage	Pathologic T stage	Pathologic Gleason score	Surgical margin	Number of lymph nodes dissected	Number of positive lymph nodes	Outcomes
Jung 2012	Robotic: 100%	sPLND	155	24	66	8.7	<7: 32.3% (*n* = 50)	≤T2: 43.9% (*n* = 68)	T2: 51.6% (*n* = 80)	<7: 23.9% (*n* = 37)	R1: 37.4%	15	5.2%	OT, PLND time,
				[IQR: 15–34]	[IQR: 61–70]	[IQR: 5.8–14.3]	7: 33.5% (*n* = 52)	T3: 56.1% (*n* = 87)	T3a: 38.1% (*n* = 59)	7: 50.9% (*n* = 79)	(*n* = 58)	[IQR: 11–19]	(*n* = 8)	eBL, LoS, PLND related
							>7: 34.2% (*n* = 53)		T3b: 9.0% (*n* = 14)	>7: 25.2% (*n* = 39)				Complications
									T4: 1.3% (*n* = 2)					
		ePLND	45	13	67	15.5	<7: 11.1% (*n* = 5)	≤T2: 28.9% (*n* = 13)	T2: 35.6% (*n* = 16)	<7: 6.7% (*n* = 3)	R1: 55.6%	24	22.2%	
				[IQR: 10–17]	[IQR: 63–72]	[IQR: 7.6–24.6]	7: 28.9% (*n* = 13)	T3: 71.1% (*n* = 32)	T3a: 53.3% (*n* = 24)	7: 42.2% (*n* = 19)	(*n* = 25)	[IQR: 18–28]	(*n* = 10)	
							>7: 60% (*n* = 27)		T3b: 8.9% (*n* = 4)	>7: 51.1% (*n* = 23)				
									T4: 2.2%% (*n* = 1)					
Yuh 2013	Robotic: 100%	lPLND	204	NR	64	5.9	6: 6.4% (*n* = 13)	T1: 72.1% (*n* = 147)	T2a/b: 7.4% (*n* = 15)	NR	NR	7 (IQR 5–9)	3.9% (*n* = 8)	eBL, OT, DVT
					[IQR: 58–70]	[IQR: 4.4–9.1]	3 + 4: 54.9% (*n* = 112)	T2:27.4% (*n* = 56)	T2c: 57.8% (*n* = 118)					Complication rate,
							4 + 3: 22.1% (*n* = 45)	T3: 0.5% (*n* = 1)	T3a: 23.5% (*n* = 48)					Lymphocele,
							8: 12.2% (*n* = 25)		T3b: 11.3% (*n* = 923)					Discharge at day 1
							9: 4.4% (*n* = 9)							
		ePLND	202		64	5.5	6: 5.9% (*n* = 12)	T1: 68.8% (*n* = 139)	T2a/b: 12.4% (*n* = 25)			21.5 (IQR: 17–27)	11.9% (*n* = 24)	

					[IQR: 58–69]	[IQR: 4.2–8.3]	3 + 4: 59.9% (*n* = 112)	T2:30.2% (*n* = 61)	T2c: 60.7% (*n* = 122)					
							4 + 3: 19.8% (*n* = 40)	T3: 1% (*n* = 2)	T3a: 16.8% (*n* = 34)					
							8: 11.4% (*n* = 23)		T3b: 10.4% (*n* = 21)					
							9: 3.0% (*n* = 6)							
Eden 2010	Lap: 100%	sPLND	311	NR	63	11	7 [4–10]	T1: 32.8% (*n* = 102)	NR	NR	NR	6.1 [2–8]	NR	Transfusion rate, eBL,
					[43–76]	[2–20]		T2: 63% (*n* = 196)						OT, LoS, complication
								T3: 4.2% (*n* = 13)						Rate
		ePLND	121		63	8	7 [6–10]	T1: 33.1% (*n* = 40)				17.5 [2–23]		
					[43–74]	[1–15]		T2: 57% (*n* = 174)						
								T3: 9.9% (*n* = 12)						
Naselli 2010	NR	lPLND	98	≥6 mo	NR	6.43	NR	NR	<T3: 74.5% (*n* = 73)	≤6: 46.9% (*n* = 46)	NR	6 [R: 2–14]	N1: 1% (*n* = 2)	Lymphocele,
						[R: 1.95–65]			T3a: 22.4% (*n* = 22)	7: 46.9% (*n* = 46)				Reintervention
									T3b: 8.2% (*n* = 8)	8–10: 6.1% (*n* = 6)				
		ePLND	249			7.22			<T3: 67.5% (*n* = 168)	≤6: 36.9% (*n* = 92)		16 [R: 10–67]	N1: 11.7% (*n* = 29)	
						[R: 2.2–98]			T3a: 30.1% (*n* = 75)	7: 50.6% (*n* = 126)				
									T3b: 15.7% (*n* = 39)	8–10: 12.5% (*n* = 31)				

(continued)

Table 2 (continued)

Study	Surgical	Treatment	*N*	Follow-up (mo)	Age (year)	PSA (ng/ml)	Biopsy Gleason score	Clinical T stage	Pathologic T stage	Pathologic Gleason score	Surgical margin	Number of lymph nodes dissected	Number of positive lymph nodes	Outcomes
Lindberg 2009	NR	lPLND	64	NR	64 (NR)	NR	NR	NR	NR	NR	NR	7 [R: 3–18]	N1: 6% (*n* = 4)	eBL, OT, lymphocele,
														DVT, PE, hematoma,
														Wound infections, sepsis,
														Complication rate
		ePLND	108		64 (NR)							17 [R: 5–40]	N1: 20% (*n* = 22)	
Musch 2008	Open: 100%	lPLND	867	NR	65 (6)	4.1–10: 8% (*n* = 111)	2–6: 65.7% (*n* = 907)	T1: 41.9% (*n* = 578)	T2: 48.3% (*n* = 666)	2–6: 51.8% (*n* = 715)	R: 31.5%	NR	N +: n = 148	Lymphocele,
						10.1–20: 25.4% (*n* = 350)	7: 12.4% (*n* = 171)	T2: 50% (*n* = 690)	T3a: 28.3% (*n* = 391)	7: 26.1% (*n* = 360)	(*n* = 435)			Reintervention
						>20: 13.1% (*n* = 181)	8–10: 17.4% (*n* = 240)	T3: 6.9% (*n* = 95)	T3b: 15.7% (*n* = 217)	8–10: 20.6% (*n* = 284)				
									T4: 5.9% (*n* = 82)					
		ePLND	434											
Klevecka 2007	Open: 100%	lPLND	740	NR	65 (6)	<2.6: 4.9% (*n* = 49)	2–4: 21.8% (*n* = 218)	T1a/b: 3.4% (*n* = 34)	T2a: 7.8% (*n* = 78)	NR	R1: 32.7% (*n* = 327)	NR	10.9% (*n* = 109)	Lymphocele,
						2.6–4.0: 3.6% (*n* = 36)	5–6: 42.2% (*n* = 422)	T1c: 32.7% (*n* = 327)	T2b: 20.5% (*n* = 205)					DVT, PE,
						4.1–10.0: 49.5% (*n* = 495)	7–10: 21.0% (*n* = 210)	T2: 56.8% (*n* = 568)	T2c: 18.9 (*n* = 189)					Reintervention,
						10.1–20.0: 26.6% (*n* = 266)		cT3: 7.1% (*n* = 71)	T3a: 28.8 (*n* = 288)					Postoperative bleeding,
						≥20.1: 15.4% (*n* = 154)			T3b: 17.5% (*n* = 175)					Secondary
									T4: 6.5% (*n* = 65)					Wound healing

		ePLND	236											
Clark 2003	Open: 100%	lPLND	123	NR	61	<10: 84.6% (*n* = 104)	≤6: 67.5% (*n* = 83)	T1c: 72% (*n* = 88)	NR	NR	NR	NR	2.4% (*n* = 3)	Lymphocele, leg edema,
					(R: 45–75)		7: 20.3% (*n* = 25)	T2a: 21% (*n* = 26)						DVT, pelvic abscess,
							8–10: 12.2% (*n* = 15)	T2b: 5.7% (*n* = 7)						Ureteral injury, overall
								T3: 1.3% (*n* = 2)						Unilateral complication
		ePLND	123											
Heidenreich 2002	Open: 100%	sPLND	100	NR	63.5	14.9	5.2 (2.6)	T1c: 10% (*n* = 10)	3.5 (R: 1–4)	NR	NR	11 (R: 6–19)	12% (*n* = 12)	eBL, OT, rectal lesions,
					(R: 49–72)	(R: 1.6–109)		T2: 65% (*n* = 65)						Lymphocele, DVT, PE,
								T3: 25% (*n* = 25)						Obturator nerve lesion
		ePLND	103	NR	61.8	15.9	4.6 (2.3)	T1c: 8.7% (*n* = 9)	3.6 (R: 1–4)	NR	NR	28 (R: 21–42)	26.2% (*n* = 27)	
					(R: 51–71)	(R: 1.2–129)		T2: 59% (*n* = 61)						
								T3: 32% (*n* = 33)						
Mistretta 2017	Robotic: 100%	sPLND	109	32	66.3	12.1	6: 15.6% (*n* = 17)	T1: 45.9% (*n* = 50)	T2a-b: 15.7% (*n* = 17)	6: 15% (*n* = 16)	R1: 21.1%	11	12.8%	eBL, OT, LoS,
				(R: 6–72)	(IQR: 63–71)	(IQR: 4.9–12.9)	3 + 4: 37.6% (*n* = 41)	T2: 50.5% (*n* = 55)	T2c: 50% (*n* = 55)	3 + 4: 41.1% (*n* = 44)	(*n* = 109)	[IQR: 7–17]	(*n* = 14)	Intraoperative complications,
				(*n* = 184)			4 + 3: 22.9% (*n* = 25)	T3: 3.7% (*n* = 4)	T3a: 21.3% (*n* = 23)	4 + 3: 24.3% (*n* = 28)				Postoperative complications,
							8: 15.6% (*n* = 17)		T3b: 13% (*n* = 14)	8: 8.4% (*n* = 9)				Postoperative sexual function
							9: 8.3% (*n* = 9)			9: 11.2% (*n* = 12)				
	Robotic: 100%	ePLND	75		66	13.2	6: 20% (*n* = 15)	T1:37.3% (*n* = 28)	T2a-b: 4% (*n* = 3)	6: 8.2% (*n* = 6)	R1: 33.3%	21	29.3%	

(continued)

Table 2 (continued)

Study	Surgical	Treatment	*N*	Follow-up (mo)	Age (year)	PSA (ng/ml)	Biopsy Gleason score	Clinical T stage	Pathologic T stage	Pathologic Gleason score	Surgical margin	Number of lymph nodes dissected	Number of positive lymph nodes	Outcomes
					(IQR: 59–70)	(IQR: 6.2–17.4)	3 + 4: 32% (*n* = 24)	T2: 50.7% (*n* = 38)	T2c: 48% (*n* = 36)	3 + 4: 47.9% (*n* = 35)	(*n* = 75)	[IQR: 16–29]	(*n* = 22)	
							4 + 3: 18.7% (*n* = 14)	T3: 12% (*n* = 9)	T3a: 26.7% (*n* = 20)	4 + 3: 13.7% (*n* = 12)				
							8: 21.3% (*n* = 16)		T3b: 21.3% (*n* = 16)	8: 11% (*n* = 8)				
							9: 8% (*n* = 6)			9: 19.2% (*n* = 14)				
Touijer 2021	Open	lPLND	700	37.2	62	5.9	6: 10% (*n* = 72)	T1c: 61% (*n* = 400)	T3a: 54% (*n* = 375)	6: 5.9% (*n* = 40)	NR	12 (IQR: 8–17)	11.6% (*n* = 81)	Postoperative complications,
RCT	Lap			(IQR: 18–60)	(IQR: 57–67)	(IQR: 4.3–8.6)	3 + 4: 52% (*n* = 362)	T2a,b,c: 29.4% (*n* = 206)	T3b: 12% (*n* = 85)	3 + 4: 58% (*n* = 399)				Erectile function recovery
	Robotic						4 + 3: 19% (*n* = 135)	T3a,b: 7% (*n* = 49)		4 + 3: 23% (*n* = 160)				
							≥8: 18% (*n* = 129)			≥8: 12% (*n* = 84)				
		ePLND	740		63	5.7	6: 9.4% (*n* = 69)	T1c: 61% (*n* = 418)	T3a: 49% (*n* = 364)	6: 7.3% (*n* = 53)		14 (IQR: 10–20)	13.5% (*n* = 100)	
					(IQR: 57–67)	(IQR: 4.2–8.2)	3 + 4: 52% (*n* = 383)	T2a,b,c: 31.5% (*n* = 233)	T3b: 12% (*n* = 89)	3 + 4: 53% (*n* = 385)				
							4 + 3: 17% (*n* = 125)	T3a,b: 5.3% (*n* = 39)		4 + 3: 24% (*n* = 173)				
							≥8: 22% (*n* = 160)			≥8: 16% (*n* = 118)				

DVT deep venous thromboembolism, *eBL* estimated blood loss, *EERPE* endoscopic extraperitoneal radical prostatectomy, *ePLND* extended PLND, *IQR* interquartile range, *lap* laparoscopic, *LoS* length of hospital stay, *lPLND* limited PLND, *NA* not available, *NR* not reported, *OT* operating time, *PE* pulmonary embolism, *PLND* pelvic lymph node dissection, *RCT* randomized controlled trial, *R* range, *sPLND* standard PLND, *VTE* venous thromboembolism. Data for categorical variables are reported as frequency (proportion). Data for continuous variables are reported as either median [range or IQR] or mean (range or IQR)

Table 3 Results from studies addressing non-oncologic outcomes

Study	Subpopulation	Intervention	Comparator		Outcomes measured	*N at baseline*			*Outcome results*			Reported	Notes
	(if applicable)	(Int)	(Com)			Int	Com		Int		Com	*p* values	
No PLND vs any PLND													
Ostby-Deglum 2015	NA	PLND		No PLND	Insuficient erection	169	440		Univariate analysis: OR 0.95			0.82	
									[95% CI: 0.63–1.43]				
Violette 2015	NA	PLND		No PLND	OT	392			Univariate analysis: OR 1.94			Uni: 0.03	
									[95% CI: 1.09–3.47]			Multi: 0.13	
									MVA: OR 1.65 [95% CI: 0.86–3.17]				
Boehm 2015	NA	PLND		No PLND	Blood transfusion rate	6810	4884		11.4%		9.7%	0.0036	
									RR: 1.18 (95% CI: 1.05–1.32)			NR	
Tyritzis 2015	NA	PLND		No PLND	DVT	547	2997		2.9% ($n = 15$)		0.3% ($n = 10$)	NR	
									Age-adjusted RR: 7.80				
									(95%CI: 3.51–17.30)				
					PE				1.3% ($n = 7$)		0.2% ($n = 6$)		
									Age-adjusted RR: 6.29				
									(95%CI: 2.11–18.73)				
Liss 2013	NA	ePLND	sPLND	No PLND	OT (min)	54	231	207	186	182	176	0.211	
					Blood loss (ml)				150 [100–200]	100 [100–200]	100 [100–200]	0.322	
					Blood transfusion rate				1.9% ($n = 1$)	0.9% ($n = 2$)	2.4% ($n = 5$)	0.436	
					LoS (d)				1.1	1.3	1.6	NR	
					Complication rate				16.7% ($n = 9$)	18.2% ($n = 42$)	13.5% ($n = 28$)	0.412	
					Lymphocele rate (no surgery)				5.6% ($n = 3$)	2.2% ($n = 5$)	0% ($n = 0$)	0.011	
					Lymphocele rate (surgery)				0% ($n = 0$)	3% ($n = 7$)	0% ($n = 0$)	0.018	
van der Poel 2012	NA	sPLND		No PLND	Lymphocele rate	440	464		1.5% ($n = 7$)		0% ($n = 0$)	NR	
					DVT				1.5% ($n = 7$)		0% ($n = 0$)	NR	

(continued)

Table 3 (continued)

Study	Subpopulation	Intervention	Comparator		Outcomes measured	*N at baseline*			*Outcome results*			Reported	Notes
	(if applicable)	(Int)	(Com)			Int	Com		Int		Com	*p* values	
					Clavien grading				1: 6.1% (*n* = 27)		1: 5.0% (*n* = 23)	0.147	
									2: 5.7% (*n* = 25)		2: 4.3% (*n* = 20)		
									3: 2.0% (*n* = 9)		3: 1.7% (*n* = 8)		
									4: 0.2% (*n* = 1)		4: 0% (*n* = 0)		
					Hematoma				3.5% (*n* = 15)		2.1% (*n* = 10)	NR	
					Ileus				0.3% (*n* = 1)		0.2% (*n* = 1)	NR	
					Anastomosis dehiscence				1.1% (*n* = 4)		0.2% (*n* = 1)	NR	
Schmitges 2012	NA	PLND		No PLND	DVT	36,699			MVA: OR: 1.07 (95% CI: 0.67–1.69)		0.78		
									(corrected for: ASC, year of				
									Surgery, age, race, CCI, PLND,				
									Surgical approach)				
Schmitges 2012	NA	PLND		No PLND	LoS >3 d	15,837	20,862		OR 1.50 (95% CI: 1.26–1.78)			ADJ: <0.001	
					Hospital charges >37,621 dollars				OR 0.84 (95% CI: 0.59–1.19)			ADJ: 0.31	
					Rectal lacerations				0.7% (*n* = 105)		0.8% (*n* = 159)	UnADJ: 0.27 ADJ: 0.1	
Gandaglia 2012	NA	ePLND		No PLND E	Erectile function recovery rate	235	161		43.8% (*n* = 103) (1-year)		39.4% (*n* = 63) (1-year)	NR	
									49.7% (*n* = 117) (2-year)		46.6% (*n* = 75) (2-year)		
									Unadjusted HR: 0.8			0.3	
									Adjusted HR: 0.9			0.8	
Schmitges 2012	NA	ePLND	lPLND	No PLND	Transfusion rate (ref = no PLND)	69	792	580	Limited: OR: 1.33 (95% CI: 0.79–2.34)			0.29	
									Extended: OR: 2.04 (95% CI: 0.76–5.51)			0.16	
					Prolonged drainage (ref = no PLND)				Limited: OR: 2.81 (95% CI: 1.32–5.95)			0.007	

									Extended: OR: 3.38 (95% CI: 1.09–10.45)			0.035	
					Pelvic lymphocele (ref = no PLND)				Limited: OR: 12.60 (95% CI: 5.00–31.98)			<0.001	
									Extended: OR: 17.24 (95% CI: 5.37–55.39)			<0.001	
Touijer 2011	NA	ePLND	Lplnd	No PLND	OT (min)	595	174	202	240 [205–270]	210 [180–240]	180 [170–219]	<0.001	
					DVT				1.7% ($n = 10$)	1.1% ($n = 2$)	1.0% ($n = 2$)	1	
					PE				1.3% ($n = 8$)	0.6% ($n = 1$)	0.5% ($n = 1$)	0.5	
					Ureteral injury				0.3% ($n = 2$)	0% ($n = 0$)	0.5% ($n = 1$)	0.7	
					Clavien grading				1: 8.2% ($n = 49$)	1: 4.6% ($n = 8$)	1: 0% ($n = 0$)	0.3	
									2: 3% ($n = 18$)	2: 1.7% ($n = 3$)	2: 1.5% ($n = 3$)		
									3: 4.5% ($n = 27$)	3: 4% ($n = 7$)	3: 0.5% ($n = 1$)		
									4: 0% ($n = 0$)	4: 0% ($n = 0$)	4: 0% ($n = 0$)		
									5: 0% ($n = 0$)	5: 0% ($n = 0$)	5: 0% ($n = 0$)		
									None: 84% ($n = 501$)	None: 90% ($n = 156$)	None: 90% ($n = 156$)		
					Lymphocele rate				5.9% ($n = 35$)	5.2% ($n = 9$)	0% ($n = 0$)	0.9	
					Drainage (ml)				320 [195–540]	235 [140–400]	165 [110–250]	<0.001	
Yong 2011	NA	PLND		No PLND	OT	341	182		OR: 0.66 (95% CI: 0.37–1.18)			0.159	
Eifler 2011	NA	PLND		No PLND	OT (min)	468	302		195		207	0.0008	
					DVT				1.5% ($n = 7$)		0% ($n = 0$)	0.047	
Khoder 2011	NA	PLND		No PLND	Lymphocele rate	1078	85		MVA: OR: 2.6 (95% CI: 1.3–4.9)			0.004	
Lin 2011, retrospective	NA	PLND		No PLND	Inguinal hernia incidence	170	120		HR: 1.02 (95% CI: 0.38–2.75)			0.851	

(continued)

Table 3 (continued)

Study	Subpopulation	Intervention	Comparator		Outcomes measured	*N at baseline*		*Outcome results*			Reported	Notes
	(if applicable)	(Int)	(Com)			Int	Com	Int		Com	*p* values	
Hruza 2010	NA	PLND		No PLND	Complication rate	1438	761	MVA: OR: 1.077 (95% CI: 0.834–1.390)			0.570	
Zorn 2009	NA	PLND		No PLND	OT (min)	296	859	224 (R: 160–320)		216 (R: 120–330)	0.09	
					Blood loss (ml)			206 (R: 50–750)		229 (R: 50–700)	0.14	
					Blood transfusion rate			3% ($n = 9$)		1.7% ($n = 15$)	0.4	
					LoS (d)			1.32 (R: 1–5)		1.24 (R: 1–4)	0.4	
					Postoperative complications			9% ($n = 27$)		7% ($n = 63$)	0.8	
					Pelvic lymphocele			2% ($n = 6$)		0% ($n = 0$)	0.9	
					FFS (low)			82%		81%	0.83	
					FFS (intermediate)			63%		71%	0.21	
					FFS (high)			48%		42%	0.45	
Stolzenburg 2005	NA	PLND		No PLND	OT (min)	700		170		115	NR	
Limited/standard PLND vs (super)-extended PLND												
Hatzichristodoulou 2015	NA	ePLND		lPLND	Continence recovery rate (12 mo)	262	198	89.7%		93.4%	0.204	
								MVA: 1.07 [0.87–1.31]			0.508	
								(corrected for age at surgery, preoperative				
								IIEF-5 score, iPSA, pGS, pT, prostate volume)				
					Spontaneous EF recovery (12 mo)			40.4%		47.5%	0.534	
								MVA: 1.11 [0.75–1.63]			0.600	
								(corrected for age at surgery, preoperative				
								IIEF-5 score, iPSA, pGS, pT, prostate volume)				
					Trifecta rates (2-year)			44.1%		47.5%	0.451	
Hoshi 2015	NA	Semi-ePLND		sPLND	Blood loss (ml)	131	599	NR		NR	NS	
					Lymphoceles			0% ($n = 0$)		0% ($n = 0$)	NS	

					Intra- and postoperative complications				0% ($n = 0$)		0% ($n = 0$)	NS	
Kim 2013	NA	ePLND		sPLND	Complication rate	170	294		11.8% ($n = 20$)		2.4% ($n = 7$)	<0.001	
					Lymphocele				2.4% ($n = 4$)		0.3% ($n = 4$)	0.043	
					Lymphedema				8.8% ($n = 15$)		1.4% ($n = 4$)	<0.001	
					Neuropraxia				0.6% ($n = 1$)		0.7% ($n = 2$)	0.905	
Yuh 2013	NA	ePLND		lPLND	Blood loss (ml)	202	204		200 [IQR 150–250]		200 [IQR 150–250]	0.7	
					OT				3 [IQR 2.9–3.3]		2.8 [IQR 2.7–3.2]	<0.001	
					Complication rate				22.8% ($n = 46$)		21.6% ($n = 44$)	0.8	
					Lymphocele				2.5% ($n = 5$)		2.9% ($n = 6$)	NR	
					DVT 1%				($n = 2$) 2.9%		($n = 6$)	NR	
					Major complications				MVA OR: 0.60 (95% CI: 0.25–1.46)			0.3	
					Discharge at day 1				74.8% ($n = 151$)		85.3% ($n = 174$)	0.004	
					Lymphocele plus DVT				NR			0.3	
Jung 2012	NA	ePLND		sPLND	OT (min)	45	155		190 [IQR: 165–211]		196 [IQR: 180–224]	0.027	
					PLND time (min)				26 [IQR: 20–35]		47 [IQR: 36–58]	<0.001	
					Blood loss (ml)				250 [IQR: 150–400]		200 [IQR: 100–300]	0.088	
					LoS (d)				4 [IQR: 3–7]		4 [IQR: 3–7]	0.998	
					PLND-related complications				3.2% ($n = 5$)		2.2% ($n = 1$)	1	
Eden 2010	NA	ePLND		sPLND	Transfusion rate	121	311		2.5% ($n = 3$)		0.8% ($n = 2$)	0.27	
					Blood loss (ml)				200 [10–800]		200 [10–1300]	0.13	
					OT (min)				206.5 [99–331]		180 [117–537]	<0.001	

(continued)

Table 3 (continued)

Study	Subpopulation	Intervention	Comparator		Outcomes measured	*N at baseline*		*Outcome results*		Reported	Notes
	(if applicable)	(Int)	(Com)			Int	Com	Int	Com	*p* values	
					LoS (d)			3 [2–4]	3 [2–5]	0.77	
					Complication rate			8.3% ($n = 10$)	3.6% ($n = 9$)	0.10	
Naselli 2010	NA	ePLND		lPLND	Symptomatic lymphocele	249	98	9.6% ($n = 24$)	2% ($n = 2$)	0.028	
								RR: 4.723			
					DVT 1.6%			($n = 4$) 0%	($n = 0$)	NR	
Lindberg 2009	NA	ePLND		lPLND	Blood loss (ml)	108	64	700 [NR]	1100 [NR]	NR	
					OT difference			421 min (ePLND vs lPLND)			
					Lymphocele 1			7.6% ($n = 19$)	9.4% ($n = 6$)		
					DVT			0.9% ($n = 1$)	1.5% ($n = 1$)		
					PE			4.6% ($n = 5$)	1.5% ($n = 1$)		
					Hematoma			1.9% ($n = 2$)	0% ($n = 0$)		
					Wound infections			3.7% ($n = 4$)	0% ($n = 0$)		
					Sepsis			1.9% ($n = 2$)	0% ($n = 0$)		
					Complication rate			30.6% ($n = 33$)	12.5% ($n = 8$)	0.007	
Musch 2008	NA	ePLND		lPLND	Lymphocele	434	867	HR: 2.88 [95% CI: 1.735–4.773]		<0.0001	MVA corrected
											For age, BMI, ASA
					Reintervention			HR: 2.37 [95% CI: 1.494–3.750]		<0.0001	
Klevecka 2007	NA	ePLND		lPLND	Lymphocele	236	740	8.1% ($n = 19$)	2.8% ($n = 21$)	<0.001	Univariate
											Analysis only
					DVT			1.3% ($n = 3$)	1.4% ($n = 10$)	0.93	
					PE			0.9% ($n = 2$)	0.8% ($n = 6$)	0.96	
					Reintervention			10.2% ($n = 24$)	3.1% ($n = 23$)	<0.0001	
					Postoperative bleeding			3.4% ($n = 8$)	1.6% ($n = 12$)	0.10	
					Secondary wound healing			2.1% ($n = 5$)	2.2% ($n = 16$)	0.97	

Clark 2003	NA	ePLND		lPLND	Lymphocele	123	123		3.3% ($n = 4$) (3/4 at side of extended)			NR	Pts randomized
													To one side limited,
													One side extended
					Leg edema				4.1% ($n = 5$) (3/5 at side of extended)				
					DVT				1.6% ($n = 2$) (2/2 at side of extended)				
					Pelvic abscess				0.8% ($n = 1$) (1/1 at side of extended)				
					Ureteral injury				0.8% ($n = 1$) (1/1 at side of extended)				
					Overall unilateral complication rate				75% of total complications on			0.08	
									Side of extended dissection				
Heidenreich 2002	NA	ePLND		sPLND	Blood loss (mL)	103	100		650 (R: 200–1950)		590 (R: 150–2100)	NR	
					OT (min)				179 (R: 140–235)		125 (R: 85–150)	<0.03	
					Rectal lesions				1.1% ($n = 1$)		1% ($n = 1$)	NR	
					Lymphocele				10.6% ($n = 9$)		6% ($n = 6$)	NR	
					DVT				4.2% ($n = 4$)		6% ($n = 6$)	NR	
					PE				2.1% ($n = 2$)		2% ($n = 2$)	NR	
					Obturator nerve lesion				1.1% ($n = 1$)		2% ($n = 2$)	NR	
Mistretta 2017	NA	ePLND		sPLND	OT (min)	75	109		240.4 (IQR: 210–300)		270 (IQR: 215–300)	0.27	
					Blood loss (mL)				150 (IQR: 150–400)		300 (IQR: 150–500)	0.11	
					Intraoperative complications				3.5% ($n = 8$)		8.2% ($n = 12$)	0.2	
					LoS				4 (IQR: 3–6)		3 (IQR: 2–5)	0.07	
					Perioperative complications				30.6% ($n = 34$)		25.3% ($n = 19$)	0.51	
					Anastomotic leak				15.6% ($n = 17$)		12% ($n = 9$)	NR	
					Blood transfusion				1.8% ($n = 2$)		0	NR	

(continued)

Table 3 (continued)

Study	Subpopulation	Intervention	Comparator		Outcomes measured	*N at baseline*		*Outcome results*			Reported	Notes
	(if applicable)	(Int)	(Com)			Int	Com	Int		Com	*p* values	
					Lymphocele			6.4% ($n = 7$)		9,3% ($n = 7$)	NR	
					Hematomas			7.3% ($n = 8$)		4% ($n = 3$)	NR	
					Erectile dysfunction			88.3% ($n = 66$)		83% ($n = 90$)	0.48	
Touijer 2021	NA	ePLND		lPLND	Post-operative complication rate	740	400	The rates of grade 2 and grade 3 complications were comparable			NR	
RCT								Between the limited (7.3%) and extended PLND groups (6.4%)				
					Erectile function recovery			In all analyses, the 95% CI excluded a > 1 point reduction in international index of			NR	
								Erectile function scores for the extended template group			NR	

DVT deep venous thromboembolism, *ePLND* extended PLND, *HR* hazard ratio, *EIIF* international index of erectile function, *lPLND* limited PLND, *LRP* laparoscopic surgery, *LoS* length of hospital stay, *MVA* multivariate analysis, *NA* not applicable, *NR* not reported, *OT* operating time, *OR* odds ratio, *PE* pulmonary embolism, *pGS* pathologic Gleason score, *PLND* pelvic lymph node dissection, *PRIAS* prostate cancer research international active surveillance, *PSA* prostate-specific antigen, *RARP* robot-assisted radical prostatectomy, *RCT* randomized clinical trial, *RR* relative risk, *sPLND* standard PLND

5 Oncological Outcomes

The oncological benefit of ePLND is controversial due to the existence of disparate results in the literature.

Furthermore, it should be acknowledged that the positive association between PLND extent and cancer outcome in node-negative patients might be based on a misinterpretation of these data caused by the Will Rogers phenomenon that limits all retrospective studies [66]. Suppose the number of removed negative lymph nodes is investigated as a prognosticator. In that case, patients treated with ePLND have a higher likelihood of being node-negative without overlooked metastases. Suppose a patient has a positive node in an area covered by an extended dissection but not by a limited dissection. In that case, this patient is excluded from the analyses in the group of ePLND patients (as he is node-positive, and only node-negative patients are left in the calculations) but is included in the group with a limited dissection. This means that different groups are compared at a particular disease stage, and the other disease stages can explain the benefit of the group with an extended dissection. In other words, after a limited dissection, the likelihood of overlooked metastases is higher. These missed positive nodes, instead of the removal of negative nodes, influence the prognosis. Similar results can be achieved when considering only patients with positive nodes. Indeed, in patients in whom many nodes are removed, the incidence of finding positive nodes would be high. The outcome of these patients would be relatively good because many patients would have only small-volume metastatic disease. At the same time, when comparing node-positive patients between a series with ePLND or limited PLND, the patients with positive nodes would again have a much better outcome in the series with ePLND because they would contain the patients who had a small nodal disease [8].

It is believed that the advantage, even in negative cases, is due to the resection of micro-metastases. Pagliarulo et al. reexamined 3914 negative lymph nodes in 274 pT3 patients and found that 13.3% of the 180 patients initially defined as pN0 harbored hidden metastases at immunohistochemistry. These patients had worse survival rates than those genuinely negative lymph nodes and had results comparable to patients who had initially been diagnosed as positive lymph nodes [67].

The baseline characteristics of the principal comparative studies evaluating oncological outcomes are summarized in Table 4 [11, 68]. Overall, 16 studies compared no pelvic lymph node dissection (PLND) vs. any form of PLND, whereas 14 studies compared limited PLND (lPLND) or standard PLND (sPLND) vs. extended PLND (ePLND) or super-extended PLND (sePLND). The oncological results are summarized in Table 5 [11, 68] and will be described in more detail below according to biochemical recurrence, distant metastases, cancer-specific survival, overall survival, and RCT.

5.1 Impact of Extended PLND on Biochemical Recurrence

Biochemical recurrence was evaluated in 21 studies, of which five involved lPLND, three sPLND, nine ePLND, and seven undefined PLND [9, 10, 38, 39, 53, 56, 63, 69–81]. Of these, 16 did not find any statistically significant difference between the two groups [9, 10, 53, 56, 59, 63, 70–78, 80]. This negative finding was also applied to the various subgroups of patients (e.g., low-risk disease [72]; also pT2, pT3, or pT2 R0 disease [73]. Therefore, there were no differences in BCR when comparing types of PLND with each other.

Counterintuitive findings were observed in two different retrospective studies regarding the impact of PLND compared to no PLND on BCR [38, 39]. Specifically, Boehm et al. evaluated a cohort of 11,127 patients, including 6810 pN0 patients and 4884 pNx patients treated with radical prostatectomy between 1992 and 2011 [38]. Through multivariable Cox regression analysis, pNx was associated with a lower risk of BCR compared to pN0 (HR 0.81; 95% confidence interval (CI) 0.72–0.9; $p < 0.05$). Despite multivariable analysis, the significant baseline differences between the two groups may explain the higher risk of recurrence among pN0 patients. Furthermore, the extent of PLND was not reported. Conversely, Liss et al. analyzed a cohort of 492 patients treated with robotic-assisted radical prostatectomy between 2007 and 2011 [39]; 54 received ePLND, 231 received sPLND, and 207 did not receive any PLND. At a median follow-up of approximately 1 year, BCR was significantly different among the three groups: 30% vs. 15% vs. 3.4%, respectively ($p < 0.001$). However, when ePLND was compared to sPLND in high-risk patients only, no significant differences were observed ($p = 0.294$). Therefore these two studies showing negative BCR results in the ePLND groups must be due to biases.

EPLND did not provide a better biochemical outcome in two comparative retrospective studies [53, 56]. Allaf et al. showed a statistically significant benefit of ePLND over limited/standard PLND, but only in specific subgroups of patients: pN1 patients with <15% of retrieved nodes affected (43% vs. 10%; $p = 0.01$) [81]. However, counterintuitive findings were observed in a retrospective study in which ePLND was associated with a higher risk of 7-year BCR than lPLND in pT2 patients only (5% vs. 0%; $p = 0.01$) [63]. This result may reflect the selection bias of the study because surgeons tended to perform more extensive nodal dissection in higher risk patients.

Table 4 Baseline characteristics for studies addressing oncological outcomes

Study	Surgical	Treatment	*N*	Follow-up (mo)	Age (year)	PSA (ng/ml)	Biopsy Gleason score	Clinical T stage	Pathologic T stage	Pathologic Gleason score	Surgical margin	Number of lymph nodes dissected	Number of positive lymph nodes	Outcomes
No PLND versus any PLND														
Karl 2015	Open: 87%	No PLND	608	48 [NR]	64.9	<4: 8% (n = 43)	NR	NR	pT3a: 100%	≤6: 14% (n = 77)	R1: 100%	NR	NR	BRFS
	Lap: 8%				[R: 42–78)	4–9.9: 53% (n = 282)				3 + 4: 56% (n = 301)				
	Robotic: 2%					10–19.9: 27% (n = 142)				4 + 3: 21% (n = 112)				
	Perineal: 3%					≥20: 12% (n = 64)				8: 9% (n = 46)				
Gandaglia 2015	NR	No PLND	1710	40 (32.2)	64	5.4	NR	T1c: 91.2% (n = 1560)	NR	NR	NR	NR	NR	BCR
					[IQR: 59–68]	[IQR: 4.2–6.8]		T2: 8.8% (n = 150)						
Koo 2015	Open: 29%	No PLND	327	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	BRFS
	Robotic: 71%	PLND	403											
Boehm 2015	Open: 95%	No PLND	4884	NR	64 (59–67)	NR	≤6: 29.2% (n = 3412)	NR	pT2: 70% (n = 8172)	NR	NR	NR	NR	BFFS
	Robotic: 5%	PLND	6810				3 + 4: 53.8% (n = 6303)		pT3a: 20% (n = 2327)					MFS
							4 + 3: 13.0% (n = 1529)		≥pT3b: 10% (n = 1223)					CSS
							≥8: 3.8 (n = 443)							
Liss 2013	Robotic: 100%	No PLND	207	NR	61 (6.9)	4.9 (4.0–6.5)	≤6: 93.5% (n = 188)	T1: 78.3% (n = 162)	T1: 92.3% (n = 191)	NR	NR	NA	NA	BFFS
							7: 4.5% (n = 9)	T2: 21.7% (n = 45)	T2: 6.8% (n = 14)					
							≥8: 2% (n = 4)	T3: 0% (n = 0)	T3: 1% (n = 2)					
		sPLND	231		63 (6.8)	6.1 (4.4–9.2)	≤6: 58.9% (n = 136)	T1: 58.9% (n = 136)	T1: 72.7% (n = 168)			18 [12–25]	0.3% (n = 13)	
							7: 39.4% (n = 91)	T2: 39.4% (n = 91)	T2: 26.4% (n = 61)					
							≥8: 1.7% (n = 4)	T3: 1.7% (n = 4)	T3: 0.9% (n = 2)					

		ePLND	54		61 (7.2)	8.5 (5.5–13.5)	≤6: 27.8% (*n* = 15)	T1: 27.8% (*n* = 15)	T1: 42.6% (*n* = 23)			20 (16–28)	2% (*n* = 24)	
							7: 68.5% (*n* = 37)	T2: 68.5% (*n* = 37)	T2: 55.6% (*n* = 30)					
							≥8: 3.7% (*n* = 2)	T3: 3.7% (*n* = 2)	T3: 1.9% (*n* = 1)					
Mitsuzuka 2013	Open: 100%	No PLND	75	NR	63 [NR]	5.9 (NR)	≤6: 45.3% (*n* = 34)	T1c: 90.7% (*n* = 68)		NR	NR	NR	NA	BFFS
							7: 48% (*n* = 36)	T2a: 9.3% (*n* = 9)						MFS
							≥8: 6.7% (*n* = 5)							CSS, OS
		PLND	147		67 [NR}	6.4 (NR)	≤6: 28.6% (*n* = 42)	T1c: 70.1% (*n* = 103)					0.7% (*n* = 1)	
							7: 61.2% (*n* = 90)	T2a: 29.9% (*n* = 44)						
							≥8: 10.2% (*n* = 15)							
Masuda 2013	Single-port	No PLND	379	49.8 (NR)	65.8 (NR)	8.4 (NR)	NR	NR	T3a: 32.5% (*n* = 123)	NR	R1: 25.3% (*n* = 96)	NR	NR	BFFS
	Surgery: 100%								T3b: 4.0% (*n* = 15)					
	(MIES-RP)													
Daimon 2012	Lap: 100%	No PLND	54	69.4 [NR]	65.2 (NR)	6.37 (NR)	NR	NR	NR	NR	NR	NR	NR	BFFS
		Limited	85		54.8 (NR)	6.48 (NR)	NR							
Ost 2012	NR	No PLND	46	60 [6–136]	NR	NR	NR	NR	NR	NR	NR	0	NR	BFFS
		ePLND	179											LFFS
Ku 2011	Open: 88%	No PLND	88	37	66.9 (6.0)	15.8 (15.9)	<7: 11.4% (*n* = 10)	<T2c = 86.4% (*n* = 76)	NR	<7: 9.1% (*n* = 8)	R0: 54.5%	NR	NR	BF
	Lap: 2.5%						7: 13.6% (*n* = 12)	T2c: 13.6% (*n* = 12)		7: 54.4% (*n* = 48)	(*n* = 48)			
	Robotic: 9.5%						8: 48.9% (*n* = 43)			8: 12.5% (*n* = 11)	R +: 45%			
							9: 23.9% (*n* = 21)			9: 22.7% (*n* = 20)	(*n* = 40)			
							10: 2.3% (*n* = 2)			10: 1.1% (*n* = 1)				

(continued)

Table 4 (continued)

Study	Surgical	Treatment	*N*	Follow-up (mo)	Age (year)	PSA (ng/ml)	Biopsy Gleason score	Clinical T stage	Pathologic T stage	Pathologic Gleason score	Surgical margin	Number of lymph nodes dissected	Number of positive lymph nodes	Outcomes
		PLND	111		65.3 (6.9)	21.5 (35.9)	<7: 11.7% (*n* = 13)	<T2c: 89.2% (*n* = 99)		<7: 2.7% (*n* = 3)	R0: 54.1%			
							7: 19.8% (*n* = 22)	T2c: 10.8% (*n* = 12)		7: 66.7% (*n* = 74)	(*n* = 60)			
							8: 42.3% (*n* = 47)			8: 10.8% (*n* = 12)	R +: 45.9%			
							9: 24.3% (*n* = 27)			9: 19.8% (*n* = 22)	(*n* = 51)			
							10: 1.8% (*n* = 2)			10: 0% (*n* = 0)				
Porter 2010	Open: 43%	No PLND	410	139	NR	NR	NR	NR	NR	NR	NR	NR	NR	PCSM
	Perineal: 57%	PLND	342											
Weight 2008	Open: 100%	No PLND	196	88 [NR]	>65: 74%	4: 15% (*n* = 30)	NR	NR	T3a: 45% (*n* = 23)	≤6: 60% (*n* = 117)	NR	NA	NA	BFFS
					(*n* = 146)	4–10: 85% (*n* = 166)			T3b: 2% (*n* = 1)	7: 40% (*n* = 79)				
		PLND	140	94.5 [NR]	>65: 76%	4: 19% (*n* = 19)			T3a: 48% (*n* = 34)	≤6: 54% (*n* = 76)		9 [IQR: 5–13]	NR	
					(*n* = 107)	4–10: 86% (*n* = 121)			T3b: 5% (*n* = 4)	7: 46% (*n* = 64)				
Berglund 2007	NR	No PLND	732	31.9 (40.5)	<65: 74%	<4: 22% (*n* = 155)	2–4: 4% (*n* = 29)	T1: 60% (*n* = 416)	NR	NR	NR	NA	NA	FFS: Free
					(n = 540)	4.1–10: 68% (*n* = 472)	5–6: 81% (*n* = 583)	T2: 39% (*n* = 268)						From BF or
						10.1–20: 7% (*n* = 48)	7: 14% (*n* = 100)	T3: 1% (*n* = 7)						Free from
						>20: 2% (*n* = 16)	8–10: 1% (*n* = 4)	T4: 0% (*n* = 0)						2nd treatment
		lPLND	3961	49.5 (30.4)	< 65: 67%	<4: 14% (*n* = 514)	Gl2–4: 7% (*n* = 278)	T1: 42% (*n* = 1612)				5.8 (5.4)	NR	
					(*n* = 2659)	4.1–10: 64% (*n* = 2372)	Gl5–6: 62% (*n* = 2347)	T2: 56% (*n* = 2123)						
						10.1–20: 16% (*n* = 599)	Gl7: 24% (*n* = 916)	T3: 2% (*n* = 82)						

						>20: 6% (*n* = 217)	Gl8–10: 7% (*n* = 254)	T4: 0% (*n* = 2)						
Bhatta-Dhar 2004	NR	No PLND	196	NR	<65: 74%	≤4: 15% (*n* = 30)	NR	T1–T2a: 95% (*n* = 186)	T3a: 23% (*n* = 45)	≤6: 60% (*n* = 117)	NR	NA	NA	BFFS
					(*n* = 146)	4–10: 85% (*n* = 166)		T2b–T2c: 5% (*n* = 10)	T3b: 1% (*n* = 2)	≥7: 40% (*n* = 79)				
		PLND	140		<65: 76%	≤4: 14% (*n* = 19)		T1–T2a: 95% (*n* = 133)	T3a: 34% (*n* = 48)	≤6: 54% (*n* = 76)		NR	NR	
					(*n* = 107)	4–10: 86% (*n* = 121)		T2b–T2c: 5% (*n* = 7)	T3b: 4% (*n* = 5)	≥7: 46% (*n* = 64)				
Fergany 2000	Open: 100%	No PLND	203	38	≤65: 74%	≤4: 15% (*n* = 31)	≤6: 100% (*n* = 203)	≤cT1–T2a: 95%	pT3a: 23% (*n* = 47)	≤6: 61% (*n* = 123)	NR	NR	NA	BFFS
				(R: 1–141)	(n = 150)			(*n* = 193)	pT3b: 1% (*n* = 2)					
		PLND	372		≤65: 72%	≤4: 24% (*n* = 88)	≤6: 100% (*n* = 372)	≤cT1–T2a: 88%	pT3a: 41% (*n* = 153)	≤6: 60% (*n* = 223)			2% (*n* = 6)	
					(n = 267)			(*n* = 327)	pT3b: 4% (*n* = 14)					
Preisser 2020	Open	No PLND	707	60.7	63.6	7.5 (5.5–10.3)	6: 53.6% (*n* = 379)	cT1: 42.1% (*n* = 298)	pT2: 64.9% (*n* = 459)	NR	R1: 29.8%			BFFS
	Lap				(59.1–68.2)		7: 40.9% (*n* = 289)	cT2: 52.5% (*n* = 371)	pT3a: 22.9% (*n* = 162)		(*n* = 211)			MFS
	Robotic						≥8: 5.5% (*n* = 39)	cT3: 5.4% (*n* = 38)	≥pT3b: 12.2% (*n* = 86)					CSS
		PLND	9035	30.5	65.5	8.7 (5.8–14.0)	6: 6.1% (*n* = 551)	cT1: 53.7% (*n* = 4854)	pT2: 43.7% (*n* = 3951)	NR	R1: 27.8%	14 (IQR: 8–21)	19% (*n* = 1714)	
					60.2–69.8)		7: 58.8% (*n* = 5317)	cT2: 41.4% (*n* = 3736)	pT3a: 30.2% (*n* = 2727)		(n = 2512)			
							≥8: 35.1% (*n* = 3167)	cT3: 4.9% (*n* = 445)	≥pT3b: 26.1% (*n* = 2357)					

(continued)

Table 4 (continued)

Study	Surgical	Treatment	*N*	Follow-up (mo)	Age (year)	PSA (ng/ml)	Biopsy Gleason score	Clinical T stage	Pathologic T stage	Pathologic Gleason score	Surgical margin	Number of lymph nodes dissected	Number of positive lymph nodes	Outcomes
Limited/standard PLND versus (super) extended PLND														
Hatzichristodoulou 2015	Open: 100%	ePLND	262	48	64.9 (7.5)	8.3 (6.3)	6: 0% ($n = 0$)	≤T1c: 57.3% ($n = 150$)	pT2: 76.3% ($n = 200$)	6: 40.1% ($n = 105$)	NR	20.4 (9.7)	NR	BFFS
				[R: 24–84]			7: 88.6% ($n = 232$)	>T1c: 42.7% ($n = 112$)	pT3a: 13% ($n = 34$)	7: 47.7% ($n = 125$)				
							8: 8.0% (n = 21)		pT3b: 9.9% ($n = 26$)	8–10: 12.2% ($n = 32$)				
							9: 3.4% ($n = 9$)		pT4: 0.8% ($n = 2$)					
		lPLND	198		64.6 (7.8)	9.9 (7.8)	6: 100% ($n = 198$)	≤T1c: 74.7% ($n = 148$)	pT2: 80.8% ($n = 160$)	6: 44.9% ($n = 89$)		4.7 (4)		
							7: 0% ($n = 0$)	>T1c: 25.3% ($n = 50$)	pT3a: 13.6% ($n = 27$)	7: 50.6% ($n = 100$)				
							8: 0% ($n = 0$)		pT3b: 5.6% ($n = 11$)	8–10: 4.5% ($n = 9$)				
							9: 0% ($n = 0$)		pT4: 0% ($n = 0$)					
Kim 2013	Robotic: 100%	sPLND	294	36	65	8.4	≤6: 33.4% ($n = 98$)	T1: 66.3% ($n = 195$)	T2: 62.2% ($n = 183$)	NR	NR	12 [R: 9–16]	3.4% ($n = 10$)	BFFS
					[R: 60–69]	[R: 5.3–37.7]	7: 48.3% ($n = 142$)	T2: 21.4% ($n = 63$)	T3a: 28.6% ($n = 84$)					
							≥8: 18.3% ($n = 54$)	T3: 12.3% ($n = 36$)	T3b: 9.2% ($n = 27$)					
		ePLND	170		66	10.4	≤6: 17.7% ($n = 30$)	T1: 45.9% ($n = 78$)	T2: 56.5% ($n = 96$)			21 [R: 16–25]	13.5% ($n = 23$)	
					[R: 62–70]	[R: 6.6–16.1]	7: 39.4% ($n = 67$)	T2: 41.2% ($n = 70$)	T3a: 28.8% ($n = 49$)					
							≥8: 42.9% ($n = 73$)	T3: 12.9% ($n = 22$)	T3b: 14.7% ($n = 25$)					
Jung 2012	Robotic: 100%	sPLND	155	24	66	8.7	<7: 32.3% ($n = 50$)	≤T2: 43.9% ($n = 68$)	T2: 51.6% ($n = 80$)	<7: 23.9% ($n = 37$)	R1: 37.4%	15	5.2%	BFFS
				[IQR: 15–34]	[IQR: 61–70]	[IQR: 5.8–14.3]	7: 33.5% ($n = 52$)	T3: 56.1% ($n = 87$)	T3a: 38.1% ($n = 59$)	7: 50.9% ($n = 79$)	($n = 58$)	[IQR: 11–19]	($n = 8$)	

							>7: 34.2% (*n* = 53)		T3b: 9.0% (*n* = 14)	>7: 25.2% (*n* = 39)				
									T4: 1.3% (*n* = 2)					
		ePLND	45	13	67	15.5	<7: 11.1% (*n* = 5)	≤T2: 28.9% (*n* = 13)	T2: 35.6% (*n* = 16)	<7: 6.7% (*n* = 3)	R1: 55.6%	24	22.2%	
				[IQR: 10–17]	[IQR: 63–72]	[IQR: 7.6–24.6]	7: 28.9% (*n* = 13)	T3: 71.1% (*n* = 32)	T3a: 53.3% (*n* = 24)	7: 42.2% (*n* = 19)	(*n* = 25)	[IQR: 18–28]	(*n* = 10)	
							>7: 60% (*n* = 27)		T3b: 8.9% (*n* = 4)	>7: 51.1% (*n* = 23)				
									T4: 2.2%% (*n* = 1)					
Allaf 2004	Open: 100%	lPLND	1865	93.6 (NR)	57.9	7.2 (NR)	NR	NR	≥T3a: 32% (*n* = 597)	≤6: 64.2% (*n* = 1198)	R1: 9.2%	8.9 (NR)	1.2% (*n* = 22)	BFFS
					(R: 35–74)					7: 30.8% (*n* = 575)	(*n* = 172)			
										8–10: 4.8% (*n* = 90)				
		ePLND	2135	94.8 (NR)	56.7	7.1 (NR)			≥T3a: 32.2% (*n* = 688)	≤6: 67% (*n* = 1431)	R1: 8.4%	11.6 (NR)	3.3% (*n* = 71)	
					(R: 33–74)					7: 28.6% (*n* = 610)	(*n* = 179)			
										8–10: 3.8% (*n* = 82)				
Mistretta 2017	Robotic: 100%	sPLND	109	32	66.3	12.1	6: 15.6% (*n* = 17)	T1: 45.9% (*n* = 50)	T2a-b: 15.7% (*n* = 17)	6: 15% (*n* = 16)	R1: 21.1%	11	12.8%	BCR
				(R: 6–72)	(IQR: 63–71)	(IQR: 4.9–12.9)	3 + 4: 37.6% (*n* = 41)	T2: 50.5% (*n* = 55)	T2c: 50% (*n* = 55)	3 + 4: 41.1% (*n* = 44)	(*n* = 109)	[IQR: 7–17]	(*n* = 14)	Adjuvant
				(*n* = 184)			4 + 3: 22.9% (*n* = 25)	T3: 3.7% (*n* = 4)	T3a: 21.3% (*n* = 23)	4 + 3: 24.3% (*n* = 28)				Therapy
							8: 15.6% (*n* = 17)		T3b: 13% (*n* = 14)	8: 8.4% (*n* = 9)				

(continued)

Table 4 (continued)

Study	Surgical	Treatment	*N*	Follow-up (mo)	Age (year)	PSA (ng/ml)	Biopsy Gleason score	Clinical T stage	Pathologic T stage	Pathologic Gleason score	Surgical margin	Number of lymph nodes dissected	Number of positive lymph nodes	Outcomes
							9: 8.3% (*n* = 9)			9: 11.2% (*n* = 12)				
	Robotic: 100%	ePLND	75		66	13.2	6: 20% (*n* = 15)	T1:37.3% (*n* = 28)	T2a-b: 4% (*n* = 3)	6: 8.2% (*n* = 6)	R1: 33.3%	21	29.3%	
					(IQR: 59–70)	(IQR: 6.2–17.4)	3 + 4: 32% (*n* = 24)	T2: 50.7% (*n* = 38)	T2c: 48% (*n* = 36)	3 + 4: 47.9% (*n* = 35)	(*n* = 75)	[IQR: 16–29]	(*n* = 22)	
							4 + 3: 18.7% (*n* = 14)	T3: 12% (*n* = 9)	T3a: 26.7% (*n* = 20)	4 + 3: 13.7% (*n* = 12)				
							8: 21.3% (*n* = 16)		T3b: 21.3% (*n* = 16)	8: 11% (*n* = 8)				
							9: 8% (*n* = 6)			9: 19.2% (*n* = 14)				
Lestingi 2020	Open: 100%	ePLND	150	55	63.4	10.5	6: 37% (*n* = 55)	T1: 57% (*n* = 82)	T0: 0	6: 2.7% (*n* = 4)	44% (*n* = 65)	17 (IQR: 13–24)	17% (*n* = 25)	BFFS
RCT				(IQR: 35.9–64.3)	(59.1–67)	(IQR: 6.5–17)	3 + 4: 42% (*n* = 63)	T2: 21% (*n* = 31)	T2: 41% (*n* = 61)	3 + 4: 55% (*n* = 83)				MFS
							4 + 3: 12% (*n* = 18)	T3: 22% (*n* = 32)	T3a: 45% (*n* = 67)	4 + 3: 30% (*n* = 45)				CSS
							4 + 4: 5.4% (*n* = 8)		T3b: 14% (*n* = 21)	8: 1.3% (*n* = 2)				
							4 + 5: 3.4% (*n* = 5)		T4: 0.7% (*n* = 1)	9, 10: 11% (*n* = 16)				
		lPLND	150	54.1	63	10.4	6: 36% (*n* = 54)	T1: 52% (*n* = 76)	T0: 0.7% (*n* = 1)	6: 4% (*n* = 6)	37% (n = 55)	3 (IQR: 2–5)	3.4% (*n* = 5)	
				(IQR: 37–61.5)	(58.8–67.3)	(IQR: 6.9–13.9)	3 + 4: 38% (*n* = 57)	T2: 23% (*n* = 33)	T2: 38% (*n* = 57)	3 + 4: 49% (*n* = 73)				
							4 + 3: 13% (*n* = 19)	T3: 25% (*n* = 37)	T3a: 43% (*n* = 64)	4 + 3: 31% (*n* = 46)				
							4 + 4: 8.7% (*n* = 13)		T3b: 18% (*n* = 27)	8: 0.7% (*n* = 1)				
							4 + 5: 4% (*n* = 6)		T4: 0.7% (*n* = 1)	9, 10: 15% (*n* = 23)				

Touijer 2021	Open	lPLND	700	37.2	62	5.9	6: 10% (n = 72)	T1c: 61% (n = 400)	T3a: 54% (n = 375)	6: 5.9% (n = 40)	NR	12 (IQR: 8–17)	11.6% (n = 81)	BFFS
RCT	Lap			(IQR: 18–60)	(IQR: 57–67)	(IQR: 4.3–8.6)	3 + 4: 52% (n = 362)	T2a,b,c: 29.4% (n = 206)	T3b: 12% (n = 85)	3 + 4: 58% (n = 399)				
	Robotic						4 + 3: 19% (n = 135)	T3a,b: 7% (n = 49)		4 + 3: 23% (n = 160)				
							≥8: 18% (n = 129)			≥8: 12% (n = 84)				
		ePLND	740		63	5.7	6: 9.4% (n = 69)	T1c: 61% (n = 418)	T3a: 49% (n = 364)	6: 7.3% (n = 53)		14 (IQR: 10–20)	13.5% (n = 100)	
					(IQR: 57–67)	(IQR: 4.2–8.2)	3 + 4: 52% (n = 383)	T2a,b,c: 31.5% (n = 233)	T3b: 12% (n = 89)	3 + 4: 53% (n = 385)				
							4 + 3: 17% (n = 125)	T3a,b: 5.3% (n = 39)		4 + 3: 24% (n = 173)				
							≥8: 22% (n = 160)			≥8: 16% (n = 118)				

BCR biochemical recurrence, *BF* biochemical failure, *BFFS* BF-free survival, *CSS* cancer-specific survival, *ePLND* extended PLND, *IQR* interquartile range, *lap* laparoscopic, *LFFS* local failure-free survival, *lPLND* limited PLND, *MFS* metastases-free survival, *MIESRP* minimum incision endoscopic radical prostatectomy, *NA* not available, *NR* not reported, *OS* overall survival, *PCSM* prostate cancer–specific mortality, *PSA* prostate-specific antigen, *PLND* pelvic lymph node dissection, *R* range, *RCT* randomized clinical trial, *sPLND* standard PLND
Data for categorical variables are reported as frequency (proportion). Data for continuous variables are reported as either median [range or IQR] or mean (range)

Table 5 Results from studies addressing oncologic outcomes

Study	Subgroup if applicable	Intervention (Int)	Comparator (Comp)		Outcome(s)	Int (n)	Comp (n)		Intervention: Outcome	Comparator: Outcome		*p* value	Comment
No PLND versus any PLND													
Karl 2015	NA	PLND		No PLND	BFFS	357	179		Univariate analysis: HR: 1.69 [1.25–2.29] MVA: HR: 1.29 [0.94–1.78]			Univariate analysis: 0.001 MVA: 0.12	–
Gandaglia 2015	Patients eligible for active surveillance according to PRIAS	PLND		No PLND	BCR	381	1329		MVA: HR: 0.72 [95% CI: 0.37–1.38]			0.3	MVA corrected for: Age, iPSA, PSM, pT, pGS, pN status
Koo 2015	PSM + and undetectable PSA <6 wk	PLND		No PLND	BFFS	403	327		Univariate analysis: 1.099 [95% CI: 0.564–2.141]			0.08	–
Boehm 2015	NA	PLND		No PLND	BFFS	6810	4884		HR: 0.81 (95% CI: 0.72–0.9)			<0.05	pNx versus pN0 (pN + excluded)
					MFS				HR: 0.62 (95% CI: 0.41–0.92)			<0.05	
					OS				HR: 0.92 (95% CI: 0.74–1.14)			0.46	
Liss 2013	NA	ePLND	sPLND	No PLND	BFFS	54	231	207	29.6% (*n* = 16)	14.7% (*n* = 34)	3.4% (*n* = 7)	<0.001	–
Mitsuzuka 2013	Low risk disease	PLND		No PLND	MFS	147	75		100%		100%	NR	Median follow- up PLND: 60 mo no PLND: 26 mo
					CSS				100%		100%	NR	
					OS				98.6% (*n* = 145)		98.7% (*n* = 74)	NR	
					BFFS		NR		NR			0.65	
Masuda 2013	pT2–3 N0/x	PLND		No PLND	BFFS	187	202		MVA total cohort: HR: 1.26 (95% CI: 0.70–2.30)			0.45	Excluded N1
									pT2 disease: HR: 1.00 (95% CI: 0.43–2.26)			1.0	
									pT3 disease: HR: 1.86 (95% CI: 0.75–5.28)			0.19	
									pT2 R0 disease: HR: 0.50 (95% CI: 0.18–1.35)			0.17	

Daimon 2012	NA	lPLND		No PLND	BFFS (5-year)	85	54		90.1% ($n = 77$)		82.4% ($n = 44$)	0.28	
					BFFS (7-year)				88.3% ($n = 75$)		82.4% ($n = 44$)	0.28	
Ost	NA	ePLND		No PLND	BFFS (7-year)	179	46		84%		83%	NR	
									HR: 0.8 [95% CI: 0.2–2.6]			UnADJ: 0.96 ADJ: 0.69	
					LFFS (7-year)			87%		88%		NR	
									HR: 0.09 [95% CI: 0.01–0.6]			UnADJ: 0.35	
												ADJ: 0.009	
Ku 2011	NA	PLND	No PLND		BF	111	88	33.3% ($n = 37$)		35.2% ($n = 31$)		0.36	
Porter 2010	NA	PLND	No PLND		PCSM	342	410	RR: 0.7 (95% CI: 0.2–2.4)				0.6	
Weight 2008	NA	PLND	No PLND		BFFS	140	196	84% (10-year)		88% (10-year)		0.33	
Berglund 2007	NA	lPLND	No PLND		FFS (overall)	3961	732	74%		70%		0.11	
					FFS (low)			82%		81%		0.83	
					FFS(intermediate)			63%		71%		0.21	
					FFS (high)			48%		42%		0.45	
Bhatta-Dhar 2004	NA	PLND	No PLND		BFFS	140	196	86% (6-year)		88% (6-year)		0.28	
Fergany 2000	NA	PLND	No PLND		BFFS	372	203	91% (4-year)		97% (4-year)		0.16	
								MVA: “Not significant”				0.24	
Preisser 2020	NA	PLND	No PLND		BFFS	707	9035		60.4%	65.6%		0.07	2:1 propensity score matching, balanced for PSA, pathologic tumor stage, primary pathologic Gleason and surgical margin status
					MFS				87%	90%		0.06	
					PCSM				95.2%	96.4%		0.2	
Limited/standard PLND versus (super) extended PLND													
Hatzichristodoulou 2015	NA	ePLND	lPLND		BFFS (7-year)	262	198	pT2 94.8% pT3 81.2%		pT2 100% pT3 94.7%		pT2: 0.011 pT3: 0.3	–
Kim 2013	NA	sPLND	ePLND		BFFS (3-year)	170	294	72.7%		79.8%		0.05	(BFFS: Propensity score–matched cohort: $p = 0.497$)
Jung 2012	NA	sPLND	ePLND		BFFS	155	45	77.9%		64.4%		NS	
Allaf 2004	pN+	ePLND	lPLND		BFFS (5-year)	2135	1865	34.4%		16.5%		0.04	
	pN+ (<15% of							42.9%		10%		0.01	
	Retrieved nodes												
	Affected)												

(continued)

Table 5 (continued)

Study	Subgroup if applicable	Intervention (Int)	Comparator (Comp)	Outcome(s)	Int (n)	Comp (n)	Intervention: Outcome	Comparator: Outcome	*p* value	Comment
Mistretta 2017	NA	ePLND	sPLND	BCR	75	109	9.3%	16%	0.32	
Lestingi 2020	ISUP GG 3–5	ePLND	lPLND	BFFS (5-year)	150	150	HR: 0.91 (95% CI 0.63–1.32)		0.6	
RCT										
Touijer 2021	NA	ePLND	lPLND	BFFS	740	700	HR: 1.04 (95% CI 0.93–1.15)		0.5	
RCT										

BCR biochemical recurrence, *BF* biochemical failure, *BFFS* biochemical failure-free survival, *bGS* biopsy Gleason score, *CSS* cancer-specific survival, *eBL* estimated blood loss, *ePLND* extended PLND, *FFS* failure-free survival, *GS* Gleason score, *HR* hazard ratio, *iPSA* initial PSA, *ISUP* international society urological pathology Gleason grade; *lPLND* limited PLND, *IPTW* inverse probability-of-treatment weighting, *LFFS* local failure-free survival, *MFS* metastases-free survival, *MVA* multivariate analysis, *NA* not applicable, *NR* not reported, *OS* overall survival, *PCSM* prostate cancer-specific mortality, *PE* pulmonary embolism, *pGS* pathologic Gleason score, *PLND* pelvic lymph node dissection, *pN+* lymph node positive, *PSM* positive surgical margin, *RCT* randomized clinical trial, *sPLND* standard PLND

5.2 Extended PLND and the Risk of Distant Metastases

Distant metastasis following RP was evaluated in two retrospective studies that reported conflicting results [38, 72]. Mitsuzuka et al. analyzed a series of 222 low-risk patients. They found metastasis-free survival (MFS) of 100% in both sPLND and no-PLND groups at a median follow-up of 60 and 26 mo, respectively [72]. Conversely, the already mentioned study by Boehm et al. found that no PLND was associated with a lower risk of distant metastasis on multivariable analysis (HR 0.62; 95% CI 0.41–0.92; $p < 0.05$) [38]. Baseline differences among pNx and pN0 patients and selection bias may explain these MFS findings.

5.3 Extended PLND and Cancer-Specific and Overall Mortality

Cancer-specific and overall mortality were analyzed in four studies. Of these, PLND was standard in one study [72], while its extent was not reported in the other three studies [38, 80, 82]. Mean follow-up ranged from 30.5 mo [80] to 11 year [82]. None of these studies demonstrated statistically significant differences in cancer-specific mortality [72, 80, 82] or overall mortality [38, 72] between PLND and no PLND.

In a multi-institutional database of 9742 patients (whose probability of lymph node invasion according to the Briganti nomogram was greater than 5%) submitted to RP from 2000 to 2017 with or without PLND, a median of 14 lymph nodes (IQR 8–21) were removed in the PLND cohort and 1714 of these cases (19.0%) harbored lymph node metastasis. After propensity score matching the biochemical recurrence-free, metastasis-free, and cancer-specific mortality-free survival rates were 60.4% vs. 65.6% ($p = 0.07$), 87.0% vs. 90.0% ($p = 0.06$) and 95.2% vs. 96.4% ($p = 0.2$) for pelvic lymph node dissection vs. no pelvic lymph node dissection 120 months after radical prostatectomy. Multivariable Cox regression models adjusted for postoperative and preoperative tumor characteristics revealed that PLND performed at RP was no independent predictor of biochemical recurrence, metastasis, or cancer-specific mortality (all $p \geq 0.1$) [80].

5.4 Randomized Controlled Trials (RCTs)

As already commented, patients undergoing an ePLND are more likely to be correctly staged as pN0 or pN1, making retrospective observational comparisons of oncological results between limited vs. extended dissection problematic (Will Rogers phenomenon) [66].

To fill this knowledge gap, the first phase III randomized controlled trial (RCT) to investigate the therapeutic role of ePLND compared to lPLND in patients with intermediate- and high-risk localized PCa undergoing RP was recently published. Three hundred patients were randomized and treated at a single institution (Instituto do Cancer do Estado de Sao Paulo, Hospital das Clinicas, Faculdade de Medicina da Universidade de Sao Paulo, ICESP-HCFMUSP, Brazil) between May 2012 and December 2016 (1:1; 150 lPLND [obturator nodes bilaterally]; and 150 ePLND [obturator, external iliac, internal iliac, common iliac, and presacral nodes bilaterally]). By showing five times more lymph node metastases in extended dissection, this trial confirmed that ePLND provides better pathological staging, while differences in early oncological outcomes were not demonstrated. The median BRFS was 61.4 mo in the lPLND group and not reached in the ePLND group (hazard ratio [HR] 0.91, 95% CI 0.63–1.32; $p = 0.6$) (Fig. 7a). Median MFS was not

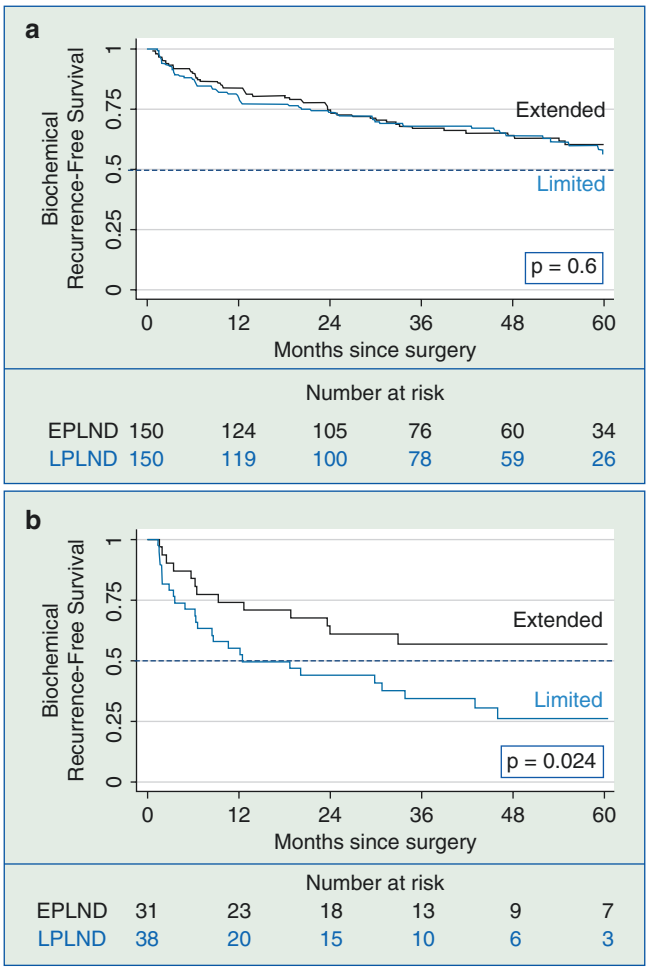

Fig. 7 Kaplan-Meier estimates of biochemical recurrence-free (BRF) survival in the intention-to-treat analysis according to limited (LPLND) or extended pelvic lymph node dissection (EPLND) in (**a**) the overall cohort and (**b**) the subgroup with preoperative biopsy International Society of Urological Pathology grades 3–5 [9]

reached in either group (HR 0.57, 95% CI 0.17–1.8; $p = 0.3$). CSS data were not available because no patient died from PCa before the cut-off date. In an exploratory subgroup analysis, patients with preoperative biopsy International Society of Urological Pathology (ISUP) grade groups 3–5 who were allocated to ePLND had better BRFS (HR 0.33, 95% CI 0.14–0.74, interaction $p = 0.007$) (Fig. 7b) [23]. Therefore, this RCT confirmed that ePLND provides better pathological staging, while differences in early oncological outcomes were not demonstrated. Subgroup analysis suggests a potential BCRFS benefit in patients diagnosed with ISUP grade groups 3–5; however, these findings should be considered hypothesis-generating. Further RCTs with larger cohorts and longer follow-up are necessary to better define the role of ePLND during RP [9].

The oncological results of this RCT were similar to those of the most significant systematic review on the topic (66 studies, 275,269 patients). Fossati et al. demonstrated that the overall quality of the evidence was low due to bias. Comparing 21 retrospective studies without LND vs. any LND, no significant difference was reached in favor of LND for BRFS, distant metastases, overall survival (OS), or cancer-specific survival (CSS). Comparing lPLND vs. ePLND in BRFS, only two out of 13 studies showed a benefit of ePLND in specific subgroups: intermediate risk and pN1 with less than 15% of lymph node invasion (LNI). Both previous studies with benefits in these subgroups were larger cohorts (585 and 4000 patients, respectively) and operated by only two surgeons in each study [11]. The caveat in these studies is that if ePLND leads to identifying men with a low LNI rate than lPLND, patients could spend a good deal of time free of disease, but there would be no final impact on survival [11].

Another single-center RCT was recently reported. Surgeons were randomized to perform limited (external iliac nodes) or extended (external iliac, obturator fossa, and hypogastric nodes) PLND for 3-mo periods between October 2011 and March 2017. Of 1440 patients included in the final analysis, 700 were randomized to limited PLND and 740 to extended PLND. The median number of nodes retrieved was 12 (interquartile range [IQR] 8–17) for limited PLND and 14 (IQR 10–20) extended PLND; the corresponding rate of positive nodes was 12% and 14% (difference − 1.9%, 95% CI -5.4% to 1.5%; $p = 0.3$). With a median follow-up of 3.1 year, there was no significant difference in biochemical recurrence rate between the groups (HR 1.04, 95% CI 0.93–1.15; $p = 0.5$). Rates for grade 2 and 3 complications were similar at 7.3% for limited vs. 6.4% for extended PLND; there were no grade 4 or 5 complications [10]. As the differences between the groups are minimal, a bias has likely occurred by the surgeon. Therefore, extended PLND did not improve freedom from biochemical recurrence over limited PLND for clinically localized prostate cancer men. However, there were smaller than expected differences in the nodal count and the rate of positive nodes between the two templates. Moreover, in the trial by Touijer et al., the number of removed lymph nodes was similar for the limited and extended PLND templates (median 12 vs. 14). Thus, it is not possible to conclude that BCR-free survival is similar in the "limited" vs. "extended" PLND arms because it seems both groups were extended.

A randomized trial comparing PLND to no node dissection is warranted. An RCT has recently started recruiting in Switzerland (NCT03921996) comparing ePLND vs. no PLND during RP for intermediate- and high-risk PCa. Results from clinical trials such as the German SEAL trial (AP 77/13) are also awaited, randomizing a total of 950 patients with intermediate- or high-risk PCa to improve 10-year survival from 83% with lPLND to 88% with ePLND.

5.5 Potential Benefits of Extended PLND in Prostate Cancer

It is also worth mentioning that not all patients with positive lymph nodes have the same risk of progression and death. In a multicenter series of 703 patients with multimodal treatment, those with two or fewer positive lymph nodes had a significantly better result on 15 year-CSS compared to patients with more than two positive lymph nodes (84% vs. 62%, $p < 0.001$). After accounting for all the other predictors, patients with more than two positive nodes had a 1.9-fold higher risk of dying for prostate cancer than patients with two or fewer positive nodes [83].

Another consecutive series of 122 node-positive patients with negative preoperative staging examinations, no neoadjuvant hormonal or Radiotherapy, and who underwent extended PLND (≥10 lymph nodes in the surgical specimen) followed by RP without immediate androgen deprivation therapy (ADT) had similar results. In patients with ≤ two or ≥ three positive nodes removed, median cancer-specific survival at 10 year was 78.6% and 33.4%, respectively ($p < 0.001$). Therefore, there is a direct benefit of PLND for patients with up to two positive lymph nodes, whose oncological evolution is similar to patients with pN0 [84].

Preisser et al. within the Surveillance, Epidemiology and End Results (SEER) database (2004–2014), identified 28,147 patients with D'Amico intermediate- (67.3%) or high-risk (32.7%) characteristics who underwent RP with PLND, without evidence of LNI. Continuously coded removed lymph node count achieved independent predictor status (HR: 0.955, $P = 0.01$), where each additional removed lymph node reduced CSM risk by 4.5% [85].

Recently, Sood et al. analyzed 311,061 PCa patients undergoing RP between 2004 and 2015 on the National Cancer Database (NCDB), and 49,470 (15.9%) patients underwent an ePLND. The median number of lymph nodes removed in patients undergoing none/limited PLND vs. ePLND were 2 and 14, respectively ($P < 0.001$). With a 54-mo median follow-up, they also demonstrated an independent direct benefit of PLND in OS if the risk of LNI is greater than 20% [86].

Another benefit of LND, this time indirect, is to select the patient for adjuvant treatments better. Messing et al. demonstrated that early androgen deprivation therapy (ADT) benefited patients with nodal metastases submitted to RP and LND, compared to those who received treatment later [87].

Abdollah et al. showed benefited from adjuvant Radiotherapy in two groups of patients: (1) patients with positive lymph node (PLN) count ≤2, Gleason score 7 to 10, pT3b/pT4 stage, or positive surgical margins (HR: 0.30; $P = 0.002$); and (2) patients with PLN count of 3 to 4 (HR: 0.21; $P = 0.02$), regardless of other tumor characteristics [88].

Abdollah et al. also examined data of 315 pN1 PCa patients treated with RP and ePLND between 2000 and 2012 at one tertiary care center. All patients received adjuvant hormonal therapy with or without adjuvant Radiotherapy. The number of removed lymph nodes (RLN) independently predicted lower Cancer-Specific Mortality (CSM) rate (HR: 0.93; $p = 0.02$). The most informative cut-off for the number of RLNs was 14. At 10 year, the CSM-free survival rates were significantly higher for patients with ≥14 RLNs compared to their counterparts with <14 RLNs ($p = 0.04$) [89].

Fossati et al. also performed a multi-institutional review of men with a rising PSA after RP treated with salvage radiation therapy (sRT). On multivariable analysis, the risk of BCR after sRT was inversely associated with the number of nodes resected at RP (hazards ratio [HR]: 0.98; 95% CI: 0.96–0.99; $p = 0.049$). The increased extent of dissection was also independently associated with a decreased risk of clinical recurrence after sRT (HR: 0.97; 95%CI: 0.94–0.99; $p = 0.042$). These data support the importance of an extensive LND at surgery and may be used in prognosis assessment when sRT is considered [90].

More recently, Touijer et al., in a retrospective and multicenter cohort of 1338 patients with positive lymph nodes (27% with more than ten years of follow-up), demonstrated that those submitted to Radiotherapy and ADT had better OS and CSS when compared to patients with observation or isolated ADT [91]. Nevertheless, LND is the best option available to determine lymph node metastases and, therefore, the best option to select patients for adjuvant treatments.

6 Salvage Lymphadenectomy

The aims of metastasis-directed therapy in patients with node-only recurrence would optimize locoregional control, limit the risk of distant progression, avoid immediate ADT, and potentially improve cancer-specific survival. In addition, recent developments in PCa recurrence PET/CT imaging have improved the detection of clinical recurrence even at a low PSA level. They could guide node-directed salvage therapy at an early stage of biochemical recurrence [92].

Salvage lymphadenectomy (SLND) is a treatment option offered in high-volume centers by experienced surgeons for patients with BCR post RP. The series of SLND with better oncological outcomes occurs in patients with restricted criteria: PSA < 4 ng/mL, Gleason ≤7 (ISUP 1–3), exclusively low-lymph node disease volume limited to the pelvis proven by PET PSMA. Good disease-free survival could also be anticipated by considering the number of positive nodes during SLND, PSA decrease after surgery, and absence of confirmed extrapelvic positive nodes at the final pathology. Thus, patients with pure pelvic involvement and favorable pathology features may be the ideal candidates for node-directed salvage strategies without a systematic adjuvant approach [92]. These manuscripts showed 9–22% (mean 15%) of patients free of BCR in five years [93, 94]. This benefit may be due to removing lymph nodes guided by imaging tests in patients with positive nodes better selected in the preoperative period.

However, pathological data from SLND studies suggested that only a tiny proportion of patients have lymph node metastases limited to the positive spots. Therefore, any nodal salvage treatment should not be directed only to the suspicious lymph nodes at imaging but also to contiguous nodal areas [95].

The available data suggest that SLND can delay clinical progression and postpone hormonal therapy in almost one-third of the patients, although most will have BCR. An accurate and attentive preoperative patient selection may help improve these outcomes. The most frequent complication after SLND was lymphorrhea (15.3%), followed by fever (14.5%) and ileus (11.2%). It is noteworthy that all examined cohorts originated from retrospective single-institution series, with limited sample size and short follow-up. Consequently, the current findings cannot be generalized and warrant further investigation in future prospective trials [94].

In a recent systematic review and meta-analysis with 27 SLND series, prostate-specific membrane antigen or choline positron emission tomography/computed tomography was the reference detection technique. SLND was performed by open or laparoscopic approach with <10% of grade 3 or more complication rate. Mean follow-up was 29.4 mo. Complete biochemical response after SLND was achieved in

13–79.5% of cases (mean 44.3%). The 2- and 5-year biochemical progression-free survival rates ranged from 23% to 64% and from 6% to 31%, respectively. Five-year overall survival was approximately 84%. The main drawbacks limiting the interpretation of the effectiveness of SLND were the retrospective design of single-center series, heterogeneity between series in terms of adjuvant treatment, endpoints, definitions of progression and study population, and the absence of long-term follow-up. The selection bias is of significant concern in this setting, especially since a control group (standard of care) lacks all except one series. Accumulated data suggest that SLND is a safe metastasis-directed therapy option in nodal recurrence after primary treatment. However, a high level of evidence is still missing to draw any clinically meaningful conclusion about the oncological impact of SLND on long-term endpoints [92].

Similarly, Bravi et al. recently demonstrated in a study that included 189 patients who experienced PSA rise and nodal-only recurrence after RP and underwent SLND at 11 tertiary referral centers between 2002 and 2011. Lymph node recurrence was documented by positron emission tomography/computed tomography (PET/CT) scan using either 11C-choline or 68Ga prostate-specific membrane antigen ligand. A third of men treated with SLND for PET-detected nodal recurrence of PCa died long term, with PCa being the leading cause of death. Salvage LND alone was associated with durable long-term outcomes in a minority of men who significantly benefited from additional treatments after surgery. Taken together, all these data argue against the use of metastasis-directed therapy alone for patients with node-only recurrent PCa. These men should instead be considered at high risk of systemic dissemination already at the time of sLND. Therefore, in general, SLND only helps postpone the introduction of ADT and should be used only as an integral part of multimodal treatment [96].

7 Conclusions

Limited lymphadenectomy significantly underestimates the actual incidence of lymph node metastasis and should no longer be performed for staging.

Extended lymphadenectomy is currently the gold standard in lymph node staging. It should be reserved for patients at higher risk of lymph node invasion:

1. Intermediate-risk patients with a chance of lymph node invasion greater than 5% (Briganti's nomogram) or greater than 7% (if MRI and target biopsy information are used).
2. High-risk.
3. Locally advanced.
4. ISUP Gleason Grade 3–5 in the biopsy.

The oncological role of extended lymphadenectomy is not defined. It can help patients directly (up to two positive lymph nodes), indirectly (select for adjuvant treatments), or may be beneficial in patients with ISUP in biopsy 3–5.

Extended lymph node dissection is also associated with significantly worse intra- and postoperative non-oncological outcomes, such as bleeding, lymphocele, and increased surgical time.

The oncological role of salvage lymphadenectomy also is not clear.

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