# 9 Pelvic Lymphadenectomy for Localised Prostate Cancer and Robot-Assisted Radical Prostatectomy

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## 9.1 Introduction

Pelvic lymph node dissection (PLND) as a staging method in prostate cancer (PCa) is today considered the most reliable procedure for detection of lymph node invasion (LNI) [1]. The rationale for an accurate locoregional staging lymphadenectomy in PCa is to stratify patients who might benefit from adjuvant therapeutic measures. Furthermore, adequate lymphadenectomy might help to improve cancer-specific survival or progression-free survival as has been demonstrated already for various cancer types. In the last decades, the routine usage of prostate-specific antigen (PSA) screening led to a stage shift in PCa, thus, the incidence of localised and node-negative cases has increased from about 60–80 % to almost 90 %. Which patients to select for a PLND and the optimal extent of this procedure are still under debate. Several questions focus on the following issues. Not all patients suffering from prostate cancer are at the same risk of harbouring lymph node metastasis [2–21]. The risk of nodal metastasis seems to depend mainly on clinical stage, PSA level and Gleason score. PLND has also its own morbidity [24] and requires skilled surgeons since it is a challenging and time-consuming procedure [22–24]. Last but not least, the therapeutic benefit of PLND in PCa management is currently unknown because of a lack of prospective randomised trials on this subject. Therefore, many groups are questioning the need of PLND in patients with a low- risk PCa. However, the literature also shows good arguments to perform routine PLND.

This chapter aims to review the available literature concerning the lymphadenectomy in prostate cancer and its role in staging and therapy.

## 9.2 Assessment of Imaging Techniques

Currently, standard imaging procedures have only a small role in predicting LNI [25–27]. Computed tomography (CT) and magnetic resonance imaging (MRI) cannot predict LNI as accurately and reliably as can an extended PLND (ePLND). The literature mostly reports the sensitivity for the CT to predict lymph node metastases as about 35 % [25]. MRI is not doing better and even dynamic-enhanced MRI or magnetic resonance spectroscopic imaging (MRSI) showed no significant advantage over CT in predicting the presence of LNI [26, 27]. But there are some innovative techniques which might change this state in the near future [28–32]. Bellin demonstrated in a group of 30 patients with genitourinary malignancies a significantly improved sensitivity and specificity of 100 and 80 %, respectively, for accurately detecting

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pelvic lymph node metastases [29] using lymphotropic paramagnetic iron oxide nanoparticles with a size of 30–50 nm as a contrast agent at MRI (lymphotropic nanoparticle-enhanced MRI (LNMRI)). In a more recent trial in 80 men with clinically localised PCa, Harisinghani showed also an increased sensitivity for detecting lymph node metastases from 35 % when using MRI alone to 90 % with the LNMRI. Specificity also increased from 90 to 98 % [28]. In the same subject, Heesakkers demonstrated a sensitivity of magnetic resonance lymphangiography (MRL) using ferumoxtran-10 as a contrast agent as high as 82 % and a negative predictive value (NPV) of 96 % in 375 patients with intermediate- to high-risk PCa [30]. These studies, however, have some limitations which have to be addressed in the near future before LNMRI will become a routine staging method for PCa [33]. Patients enrolled in these trials underwent a limited PLND (lPLND). An ePLND was performed in a few cases only in the presence of suspicious lymph nodes outside the boundaries of lPLND. Therefore, the high reported sensitivity and NPV of LNMRI might have been falsely inflated because of the significant understaging associated with lPLND [34–41]. Moreover, the conventional LNMRI has its own limitations, namely, the difficulty to discriminate benign tissue from cancer in the presence of fibrosis or lipomatosis within the lymph node or the very high reading time required for this technique and also a high interobserver variability. On the other hand, small nodal metastases can still be missed [33].

To overcome these problems, another approach has been proposed, consisting of MRI enhanced with ultrasmall superparamagnetic particles of iron oxide (USPIO) combined with diffusion-weighted MRI (DW-MRI). This approach was much faster and nevertheless quite precise for detecting pelvic lymph node metastases in patients with PCa, even in normal-sized nodes [32]. Another promising approach described choline positron emission tomography (PET)/CT in the detection of PCa nodal metastases [31]. Schiavina showed with this technique a high accuracy in detecting LNI in intermediate- and high-risk PCa patients. The sensitivity was 60.0 %, the specificity 97.6 %, NPV was reported to be 87.2 % and the number of correctly recognised cases at PET/CT was 87.7 % [31]. All the patients in this protocol were treated with ePLND.

Sentinel lymphoscintigraphy (SLN) is another technique which has been purposed as an imaging tool for planning the necessity and the extent of PLND in patients undergoing radical prostatectomy (RP). The aim of this technique, which led to the concept of sentinel node dissection, was to decrease the rate of unnecessary ePLNDs [42–48]. This approach, however, has some significant limitations. Although the sensitivity of the radio-guided sentinel lymph node dissection for detecting patients with positive nodes is extremely high (96 %), SLN is not able to identify all metastatic lymph nodes. Second, the amount of 32 % of falsely positive nodes and the fact that technetium-containing nodes can only be found intraoperatively with the collimator if it is in direct contact with the lymph node make this method of limited value in the daily practice. Other experiments trying to localise the 99mTc-containing lymph nodes more precisely, using single-photon emission CT (SPECT) fused with CT or MRI [49], were time-consuming and depended much on the skills and endurance of the reader. Thus, the experience with this approach is limited up to now.

Therefore, despite promising new imaging techniques, pelvic lymph node dissection is still considered the most reliable procedure to accurately detect lymph node metastases in PCa [50].

## 9.3 Location of Node-Positive Disease and Extent of Pelvic Lymphadenectomy

Prostate cancer disseminates initially to regional lymph nodes (LNs) [51]. Since the lymph node staging remains the most important prognostic factor in PCa [52], precise anatomical knowledge of the lymphatic drainage is of high importance when considering the extent of PLND.Unfortunately, there is little literature

investigating the primary lymphatic landing sites in PCa. About a hundred years ago, the pathways of prostate lymphatics were already described, however, without details in primary or secondary lymphatic landing sites [53]. Several authors have since described areas in which positive lymph nodes may occur [36, 38], but there are differences in definitions of terms, for example, a lymph node may be found at the same place, but named from one group as part of the external iliac nodes, from another group as part of the internal iliac nodes or even as part of the common iliac nodes.

For the purposes of this discussion – and in accordance with the usage of most authors – three forms of lymphadenectomy in radical prostatectomy (RP) can be distinguished:

- Limited PLND: limited to the obturator fossa, between the external iliac vein, the obturator nerve and the branching off of the internal iliac artery.
- Modified PLND: obturator fossa plus the lymphatic tissue around the internal iliac artery.
- Extended PLND: includes removal of the nodes overlying the external iliac artery and vein, the nodes within the obturator fossa cranially and caudally to the obturator nerve, and the nodes medially and laterally to the internal iliac artery.

The first precise description of the prostate's primary lymphatic landing sites date from 2008 [49]. They concluded that the template of primary lymphatic landing sites is larger than previously appreciated: Nodes were found up to the inferior mesenteric artery, applying SPECT/CT/MRI after intraprostatic injection of Tc-99 m nanocolloid, which was verified with intraoperative use of a gamma probe and controlled by a systematic backup PLND. To avoid false-negative nodes, only patients without histological evidence of LN metastases were analysed. Following their meticulous analysis of the primary lymphatic landing sites in PCa, they purposed – as a compromise of operative morbidity and accuracy of staging – a template encompassing the area covered by classic extended PLND plus the nodes along the common iliac arteries up to the ureter crossing, thereby removing 75 % of all LNs.

### 9.3.1 Is There a Need for PLND in Low-Risk PCa?

Knowing the primary landing sites in PCa, important questions are still under debate: is there a need for PLND, and second, is there a place for limited PLND in low-risk PCa? A review of the recent literature shows several trials which have assessed the rate of LNI in low-risk PCa patients treated with either lPLND or ePLND [5, 54–59]. Despite a lack of uniformity in defining the low-risk PCa group, the rate of LNI in lPLND series is always low, ranging between 0.5 and 0.7 % [5, 54–56, 60]. In the largest low-risk PCa series in patients with cT1 PCa and PSA 6 ng/ml, the rate of LNI was 0.7 % [57]. These results have been confirmed by many groups [5, 56]; however, all of these studies are biased by the inclusion of patients treated with lPLND. Looking at ePLND series, the rate of LNI seems to increase in the high risk as well as in the low-risk PCa group [40, 58, 59]. Weckermann, for example, reported on a retrospective study a rate of LNI of 7.4 % in low-risk PCa (PSA < 10 ng/ml and biopsy Gleason score 6) treated with ePLND [58]. Heidenreich found a rate of LNI of 5.8 % in patients, with PSA < 10 ng/ml, T1c PCa and biopsy Gleason score 6, treated with ePLND [40]. The rate of LNI was even higher (11 %) in a study by Schumacher based on a cohort of 231 patients treated with ePLND where the PSA was <10 ng/ml [59]; however, this rate was only 3 % if only patients with T1–T2 PCa, biopsy Gleason score < 7 and PSA < 10 ng/ml were included.

Summarising the results, we can conclude that the overall LNI rate in the low-risk PCa group (PSA < 10, clinical stage T1–T2a and biopsy Gleason score 6) never exceeded 7 %, even among patients treated with ePLND [5, 35, 40, 54–59]. But we also have to acknowledge that only a few retrospective studies have assessed the impact of PLND on the outcome of low-risk PCa patients. They found no significant difference in biochemical recurrence (BCR) in a follow-up of maximum 10 years [54–56]. However, these studies enrolled only patients at very low risk of dying from progressive disease, even if left untreated, and they were all treated with lPLND, which seems, from

what we know, not to be the appropriate procedure to assess LNI in PCA [33]. Finally, the statistical power of these studies was low. Therefore, the question if a more extensive PLND might favourably affect patient survival, even in the low-risk PCa group, is still unanswered. Prospective randomised trials including patients treated with ePLND are needed to find answers to these remaining questions.

In summary, the actual available PCa guidelines do not routinely recommend a staging PLND in low-risk PCa [1, 50, 60, 61], due to the lack of prospective randomised trials proving a significant benefit in BCR or survival in low-risk PCa following PLND, and also as the risk for positive lymph nodes does not exceed 7 % [35].

### 9.3.2 Extent of PLND

The literature on PLND has shown that the rate of LNI in PCa patients increases with the extent of PLND [34–41]. As PCa nodal metastases do not follow a predefined pathway of spread, lPLND might miss affected lymph nodes, which would have been detected by ePLND [62]. As mentioned above, different ways of ePLND are described: Some authors consider ePLND to be the removal of obturator, external iliac and internal iliac nodes [6, 37, 39]. Others describe also the removal of presacral nodes as a part of ePLND [36, 38, 63, 64], otherwise a substantial likelihood of overseeing positive nodes might be the consequence [63].

Finally, there are authors describing the additional removal of common iliac nodes, at least up to the ureteral crossing, to be the appropriate way to perform ePLND [38, 49]. But even with such extensive nodal dissections, approximately 25 % of lymph nodes potentially harbouring PCa nodal metastases could possibly be left inside [49].

Nevertheless, most authors agree on the fact that an extended nodal dissection should always include removal of lymph nodes along the internal iliac artery, since up to 50 % of lymph node metastases are located in this landing site [38, 40, 49, 62, 63, 65]. General agreement has also been reached that removal of lymph nodes located in the obturator fossa alone or together with the external iliac portion might significantly underestimate the true incidence of nodal metastases in PCa [33].

Briganti et al. showed an increasing likelihood to correctly predict the LNI by increasing the number of removed nodes [34]. The probability of correctly predicting the rate of LNI was almost zero when <10 nodes were removed. Otherwise, a very low risk of false-negative nodes was reported when 30 lymph nodes were removed. These results confirm the results of an autopsy study which found that an average of 20 dissected pelvic lymph nodes can be considered a representative locoregional staging of PCa [66].

Yet, there is only one prospective randomised study assessing the rate of LNI in patients treated either with lPLND or ePLND. Interestingly it did not find a significant difference in the rate of LNI between the two surgical approaches ($N=123$; 3.2 % vs. 4 % LNI; $p=0.1$) [23]. However, the results of this study have to be interpreted with caution, since the majority of the patients included had low-risk PCa. This means a low probability of LNI, even in patients treated with ePLND. Also, there are no data showing the number of lymph nodes removed in either group, and ePLND was performed on only one side. Furthermore, the field of ePLND was not defined. In respect also of the low statistical power of the trial, the validity of this study is limited.

In summary, available data seem to support the statement that if PLND is planned in patients with PCa, an ePLND significantly increases the nodal staging accuracy by decreasing the rate of false-negative findings associated with lPLND and should therefore be recommended. It is recommended that the nodes should be sent in separate containers per region for histopathology, as this will usually be associated with a higher diagnostic gain by the uropathologist. As a compromise of operative morbidity and accuracy of staging, a template encompassing the area covered by classic extended PLND plus the nodes along the common iliac arteries up to the ureter crossing seems to be appropriate. Thirdly, the actual available PCa guidelines do not routinely recommend a staging PLND in low-risk PCa.

## 9.4 Complications of Pelvic Lymph Node Dissection

Surgeons performing PLND are often concerned about the potentially high incidence of complications in ePLND, thus making sacrifices in the extent of lymphadenectomy. An overview in PLND complication literature shows a wide range (2–51 %) of PLND-associated complications [22–24, 36, 38, 45, 67–74] (see also Table 9.1). The specific complication of ePLND is lymphocele formation. If only the rate of lymphocele formation is the subject, then most authors report less than 10 % in their series, due to meticulous surgical technique, with ligation or clipping of all lymphatic vessels, double drainage and injecting prophylactic low molecular weight heparin into the arm, not the leg [64, 75].

The largest series ($n=963$) reporting complications after PLND showed an overall rate of complications of 19.8 % in patients treated with ePLND versus 8.2 % in those treated with lPLND ($p<0.001$) [24]. If they focussed on only the rate of lymphocele formation, then it was significantly higher in patients who underwent ePLND (10.3 % vs. 4.6 %; $p=0.01$). Conversely, Heidenreich et al. found no significant difference in frequency and severity of intra- and perioperative complications in the lPLND and the ePLND group (9 % vs. 8.7 %); the reported overall complication rate was 8.8 % [36].

But complications were not invariably high in all ePLND series. Bader et al., for example, reported an overall complication rate requiring prolonged hospitalisation of only 2.1 % [38]. However, counting only lymphoceles which led to prolonged hospitalisation or re-hospitalisation may underestimate the true risk of lymphocele formation, shown in series reporting lymphoceles of any size detected by routine use of imaging modalities in all patients [76–78]. These authors reported a rate of lymphoceles of 27–61 %, irrespective of whether they were clinically apparent or required treatment.

Despite discordant results in the literature, these data seem to suggest that PLND may not be a completely harmless procedure, even in the hands of experienced surgeons. Pelvic lymphoceles can cause further complications by compression or inflammation and are associated with an increased risk of deep venous thrombosis [79].

Although it seems logical that surgical expertise may reduce PLND-associated morbidity, it remains still unproven whether any specific surgical technique – as probably performed in any larger urologic centre – reduces the risk of lymphoceles. Thus, an intense discussion whether ePLND should be performed in all patients led to the actual guidelines, where low-risk PCa patients are recommended to be spared an ePLND [1, 50, 60, 61].

## 9.5 Likelihood of Nodal Disease Based on the Use of Nomograms

Nowadays we tend to rely on nomograms to predict the likelihood of LNI or local stadium of PCa. Several nomograms and predicting tables have already been developed to predict LNI and to assess the need for lymph node dissection [2–21]. Most of these nomograms use common variables such as PSA level, clinical stage and biopsy Gleason score (Table 9.2). But we should acknowledge that most of these tools are based on retrospective trials; furthermore, the nomograms, except for two [6, 7], were developed and validated in patients treated with lPLND. Therefore, underestimation of the likelihood of LNI is possible, due to the limited nodal sampling as mentioned above. Besides, none of these trials provided the number of removed lymph nodes.

The well-known Partin tables have recently been updated by Makarov et al. [5]. This tool still uses preoperative PSA, clinical stage and biopsy Gleason score to predict pathologic stage and likelihood of LNI. The predictive accuracy was 88 %. When validated in a population-based cohort of European patients, a lower accuracy of 76 % was reported [12, 13].

Work showing the relationship between the number of nodes removed and the likelihood of detecting LNI has led to the realisation that the factor of the extent of PLND should be taken into

**Table 9.1** Available preoperative nomograms

| Study | No. of patients | Predictors | Extend of PLND | Prevalence of LNI, % | Predictive accuracy, % |
|---|---|---|---|---|---|
| Cagiannos et al. [3] | 7,014 | PSA, c-stage, biopsy gleason score | Limited | 3.7 | 76 |
| Kattan et al. [4] | 697 | PSA, c-stage, biopsy gleason score | Limited | 8 | 76.8 |
| Makarov et al. [5] | 5,730 | PSA, c-stage, biopsy gleason score | Limited | 1 | 88 |
| Briganti et al. [6] | 602 | PSA, c-stage, biopsy gleason score | *Extended* | 11 | 76 |
| Briganti et al. [7] | 278 | PSA, c-stage, biopsy gleason score, % of positive cores | *Extended* | 10.4 | 83 |
| Bluestein et al. [8] | 1,632 | PSA, c-stage, biopsy gleason score | Limited | NA | NA |
| Bishoff et al. [9] | 481 | PSA, c-stage, biopsy gleason score | Limited | 7.7 | NA |
| Narayan et al. [10] | 932 | PSA, biopsy gleason score | Limited | 11 | NA |
| Conrad et al. [14] | 344 | No. of positive biopsies, no. of biopsies containing PCa of gleason score 4 or 5 | Limited | 8.1 | NA |
| Roach et al. [15] | 212 | PSA, biopsy gleason score | Limited | 17 | NA |
| Crawford et al. [16] | 4,133 | PSA, c-stage, biopsy gleason score | Limited | NA | NA |
| Batuello et al. [17] | 6,135 | PSA, c-stage, biopsy gleason score | Limited | 4.6 | 81 |
| Han et al. [18] | 5,744 | PSA, c-stage, biopsy gleason score, age | Limited | 5 | 88 |
| Poulakis et al. [19] | 201 | PSA, c-stage, biopsy gleason score, pelvic coil MRI findings | Limited | 10 | 91 |
| Karam et al. [20] | 425 | PSA, c-stage, biopsy gleason score, preoperative plasma endoglin | Limited | 3 | 97.8 |
| Wang et al. [21] | 411 | PSA, c-stage, biopsy gleason score, pelvic coil MRI findings | Limited | 5 | 89.2 |

*PSA* prostate-specific antigen, *c-stage* clinical stage, *PCa* prostate cancer, *PLND* pelvic lymph node dissection, *LNI* lymph node invasion, *MRT* magnetic resonance tomography, *NA* not available

**Table 9.2** Reported complication rates after PLND

| Study | *N* | Rate of complications, % | Extend of PLND | Mean number of lymph nodes removed |
|---|---|---|---|---|
| Stone et al. [22] | 189 | 35.9 vs. 2 | Extended vs. limited (laparoscopic series) | 17.8 vs. 9.3 |
| Clark et al. [23] | 123 | 8.1 vs. 2.4 | Extended vs. limited | NA |
| Briganti et al. [24] | 963 | 18.9 vs. 7.3 | Extended vs. limited | 17 vs. 7 |
| Heidenrich et al. [36] | 203 | 8.7 vs. 9 | Extended vs. limited | 28 vs. 11 |
| Bader et al. [38] | 365 | 2.1 | Extended | 21 {median} |
| Jeschke et al. [43] | 71 | 7 | Extended (laparoscopic series) | NA |
| Schumacher et al. [59] | 122 | 4.8 | Extended | 22 {median} |
| Herrell et al. [67] | 68 | 20 | Limited | 9.2 |
| Keller et al. [68] | 90 | 7.8 | Extended | 19 |
| Wyler et al. [69] | 123 | 4 | Extended (laparoscopic series) | 21 |
| Pepper et al. [70] | 260 | 3.5 | Extended | NA |
| McDowell et al. [71] | 217 | 22 | Extended | NA |
| Paul et al. [72] | 150 | 51 | Extended | NA |

*N* Number of patients enrolled, *PLND* pelvic lymph node dissection

account. The first nomogram based on data of patients treated with ePLND was published by Briganti et al. [6]. An accuracy of 76 % to correctly predict local stage and LNI was reported, relying on clinical stage, PSA and biopsy Gleason score. The accuracy was even better, if data on tumour volume such as percentage of positive cores are included in multivariable models [7].

In conclusion, using nomograms we should remember one important thing: They remain probability models in any case and do not make a definite diagnostic statement about an individual patient. They always depend on the original cohorts of patients from which they were derived and validated. The accuracy of prediction is therefore limited. There is also still a debate about the cut-off of LNI probability, where a PLND could be spared. Should this be <7 % or even lower? These thoughts should be carefully discussed with the patient before radical prostatectomy. Considering the low rate of added morbidity, many urologists and patients will probably favour a higher accuracy of staging and opt for a PLND.

All of these data were recently reviewed and included in the available PCa guidelines [1, 50, 60, 61].

## 9.6 Influence of Lymphadenectomy on Outcome in RP

Besides being the most reliable staging procedure in PCa, ePLND might have a therapeutic effect on the outcome of PCa. Up to now, this question remains unanswered because of the lack of prospective randomised trials. But there are encouraging results which might support the thesis of therapeutic benefit after PLND. Already in 1987, Golimbu et al. reported a good overall survival in patients with only one involved lymph node after RP with PLND [80]. Bader et al. reported a significant correlation of the number of nodes removed during lymphadenectomy and time to progression [38]. Masterson et al. [41] also found a significant inverse association between the number of removed lymph nodes and biochemical recurrence-free (BCR-free) survival in node-negative patients ($p=0.01$). This position is supported by the Johns Hopkins group; they reported a prolonged 5-year PSA BCR-free survival in ePLND versus lPLND [37]. In another population-based study with a 10-year follow-up, patients undergoing PLND had a lower risk of prostate cancer-specific death at

10 years than did those who did not undergo lymphadenectomy [81]. The risk to die of PCa was 23 % lower after ePLND and 15 % lower after lPLND in pN0 cases after 10 years. The limitation of this trial is the lack of a standardised pathologic assessment of the removed lymph nodes, which is important for determining reliable nodal counts.

These results may be due to the removal of micrometastases, which may support the therapeutic role of PLND in this patient category. But there are also opposing results challenging this thesis. Di Marco et al., for example, found no survival benefit associated with an increasing number of removed lymph nodes in node-negative patients in a series over 13 years [82]. Bhatta-Dhar et al. retrospectively analysed the biochemical failure rate in 336 low-risk PCa patients, of whom 140 had undergone PLND and 196 had not, and found no significant difference in BCR rate after a follow-up of 60 months (14 % vs. 12 %) [54]. Berglund reported results of a retrospective CaPSURE analysis of 4,693 RP cases with and without lPLND. Stratification of patients into risk groups in this analysis showed no overall influence of lPLND versus no PLND on BCR-free survival rates in the low-risk group, but, also in the intermediate- or high-risk group, there was no benefit in BCR-free survival [56].

In summary, the question of whether PLND can have an impact on node-negative PCa still needs to be elucidated.

Considering the data above, a possible bias might complicate correct interpretation and needs to be discussed. 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 [83, 84]. The Will Rogers phenomenon is obtained when moving an element from one set to another set raises the average values of both sets. It is based on the following quote, attributed to comedian Will Rogers (1879–1935): When the Okies left Oklahoma and moved to California, they raised the average intelligence level in both states. The effect will occur when both of these conditions are met: The element being moved is below average for its current set. Removing it will, by definition, raise the average of the remaining elements. The element being moved is above the current average of the set it is entering. Adding it to the new set will, by definition, raise the average.

In the context of PLND, if the number of removed negative lymph nodes is investigated as a prognosticator, it is clear that patients treated with ePLND have a higher likelihood of being really node negative without overlooked metastases. If a patient has a positive node in an area that is covered by an extended dissection but not by a limited dissection, 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 analyses. But the same patient is included in the group with a limited dissection. This means that different groups are compared at a certain disease stage, and the benefit of the group with an extended dissection can be explained by the different disease stages. In other words, after a limited dissection, the likelihood of overlooked metastases is higher, and it is these overlooked positive nodes, instead of the removal of negative nodes, that influence the prognosis [83, 84]. 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, and 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 lPLND, 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 small nodal disease. These observations suggest that the only solution to answering the question of whether or not removal of the lymph nodes has a role beyond diagnostic purposes is to conduct a prospective randomised trial in which patients are randomised to either no PLND or ePLND [33].

Even without available evidence, proving the therapeutic role of PLND in PCa, long-term outcome of patients with LNI, undergoing RP and PLND, is not necessarily poor [85–95].

Cheng et al. reported a 79 % 10-year cancer-specific survival in a large series of 322 patients treated with RP [87]. Ninety-two percent of the patients in this trial received adjuvant androgen deprivation therapy (ADT). Boorjan et al. updated the same collective in 2007, including 505 patients treated with RP and PLND, finding a 10-year cancer-specific survival rate of 85.8 %. Again, about 90 % of those patients received ADT [88]. Bader et al. reported a 74 % 5-year cancer-specific survival rate in a cohort of 92 patients treated with RP and ePLND without adjuvant treatment [86]. Data from the same group reported by Schumacher et al. showed a 60 % cancer-specific survival rate at 10-year follow-up in 122 patients [92]. Spiess et al. found the 5- and 10-year disease-specific survival rates to be as high as 94 % and 75 %, respectively, in a series of 100 node-positive patients [93]. And even after a longer follow-up of 15 years, Briganti et al. found a cancer-specific survival rate of 78 % in 703 node-positive patients, undergoing multimodal treatment [89]. As expected, BCR-free survival rates are reported to be poorer than cancer-specific survival rates [41, 96].

Looking at the data of cancer-specific survival rate in node-positive patients, there is one interesting question to which some authors tried to find an answer: Is there a difference in cancer-specific survival (CSS) in node-positive patients depending on the amount of positive nodes? Several trials have indeed shown that patients with low volume of lymph node metastases have significantly higher CSS rates compared to patients with more extensive LNI [85–89, 92, 96, 97]. Describing the survival difference in node-positive patients, the term of lymph node density (LND) was introduced. Daneshmand et al. reported on a large retrospective study a higher risk for clinical recurrence in patients with a LND > 20 % comparing with those at a LND < 20 % (relative risk: 2.31; $p < 0.001$) [85]. Other authors confirmed these findings [87, 96]. Cheng et al., for example, showed that the 10-year cancer-specific survival rate was not significantly different from the cancer-specific survival of patients without nodal involvement. He found a cancer-specific survival rate of 94 % in patients with a single node metastasis [87]. Furthermore, even node-positive patients receiving no adjuvant treatment seem to have a better prognosis if there is only one node involved. Schumacher et al. reported significantly higher 10-year cancer-specific survival rates in patients with one or two positive nodes (78.6 %) compared with patients with >2 positive nodes (33.4 %) [92]. And Bader et al. (2003) already found BCR-free survival rates much higher in patients with one positive node compared to patients with two or more positive nodes not receiving any adjuvant therapy (39 % vs. 12 %, respectively) [86]. Briganti et al. demonstrated that patients with up to two positive nodes experienced excellent cancer-specific survival, which was significantly higher compared to patients with more than two positive nodes (84 % vs. 62 %; $p < 0.001$, at 15-year follow-up, $n = 703$). Moreover, a significant improvement in CSS prediction was reached when the number of positive nodes was considered. They proposed that their results reinforce the need for a stratification of node-positive patients according to the number of positive nodes and that patient classification according to number of positive nodes should be considered a key variable for CSS predictions of node-positive patients [89].

Summarising all these data, we can conclude that the impact of PLND as a curative treatment remains an unanswered question. Only prospective randomised trials comparing the effect of PLND versus no PLND in high-risk patients would show the role of PLND on survival rates in PCa patients. Nevertheless, there is some indirect evidence that ePLND may have a therapeutic benefit on PCa patients, particularly in those patients with low LNI. Thus, such studies are unlikely to pass an ethical committee.

## 9.7 Pelvic Lymphadenectomy in Robot-Assisted Radical Prostatectomy

Robot-assisted laparoscopic radical prostatectomy is becoming a popular procedure worldwide. A rapidly increasing number of publications

reporting various refinements of technique as well as functional outcomes and early oncologic results show the increasing importance of this approach [98–100]. The first report from PLND in robot-assisted laparoscopic prostatectomy (RALP) dates from 2001 [101]. Guilloneau showed the feasibility of a PLND even in RALP. However, since then, the PLND undertaken with laparoscopic or robot-assisted RP has usually been performed as a limited lymphadenectomy. This is in contrast to the ongoing debate concerning the extent of and the indication for a lymph node dissection in patients undergoing RP for PCa. However, increasing evidence supports an extended lymph node dissection in patients with prostate cancer once the prostate-specific antigen (PSA) level is >10 ng/ml or the Gleason score totals ≥7. Feicke et al. recently reported their experience and technique of extended PLND in RALP and confirmed the feasibility of this approach; furthermore, the lymph node yield as well as the complication rate was reported to be in the range of open series [102].

## 9.8 Technique of PLND in Robot-Assisted RP

As with any other procedure, the robot-assisted laparoscopic extended pelvic lymph node dissection (RALEPLND) has to be standardised. The intraoperative orientation is facilitated by proceeding from one landmark to the next.

Most authors propose a template for PLND according to Bader et al. and their recent modification by Mattei et al., proposing to include the common iliac region up to the ureteral crossing [38, 40, 49, 69, 103].

Of high importance is the identification of several important landmarks: the median and medial umbilical folds and the external iliac artery usually recognised with its pulsation. Frequently, the vas deferens and the ureter are already visible beneath the peritoneum, after mobilising the right ascending and left descending as well as sigmoid colon.

After identification of these landmarks, the incision of the peritoneum starts laterally to the medial umbilical fold longitudinally along the external iliac vessels. Distally, the incision and dissection is carried out until the pubic bone is clearly identified. Proximally, the peritoneal incision proceeds up to the crossing of the ureter over the common iliac artery. The vas deferens is cauterised and divided. After these steps, the cranial and caudal boundaries of the lymph node dissection are defined.

We start the ePLND within the obturator fossa. The technique does not differ from the operative surgical technique employed at open RP. The most important step in this region is the identification of the obturator nerve, which has to be preserved. The dissection is initiated at the angle between the external iliac vein and the ramus ossis pubis. Only after clear identification of the obturator nerve is the distal end of the packet secured with Weck Hem-o-lok® clips and divided. The packet is dissected beneath the external iliac vein and mobilised to the pelvic side wall, which is the lateral boundary of this area. The proximal attachments of the packet are dissected using a combination of sharp and blunt dissection, if possible without cauterisation, always paying attention to avoid any injury to the nerve. In most cases the packet can be evacuated through the 12-mm laparoscopic port. If not, the use of a specimen bag can be considered in order to avoid spilling of tumour cells.

The next step is the dissection of the external iliac packet. It starts distally with the division of the adventitia overlying the external iliac vein. The distal end of the packet is divided and secured with Hem-o-lok® clips. Care must be taken not to disturb the tissues overlying and surrounding the external iliac artery as these contain the lymphatic vessels that drain the leg. Disruption of these lymphatic vessels carries the risk of lymphocele formation and lymphedema of the lower extremities. The lymphatic packet is grasped and retracted in a cranio-medial direction, which allows for blunt and sharp dissection of the packet from the underlying vein. The dissection proceeds until the ureter crossing is reached.

The internal iliac artery is usually identified after the initial peritoneal incision. Normally, the bifurcation of the common iliac artery is visible

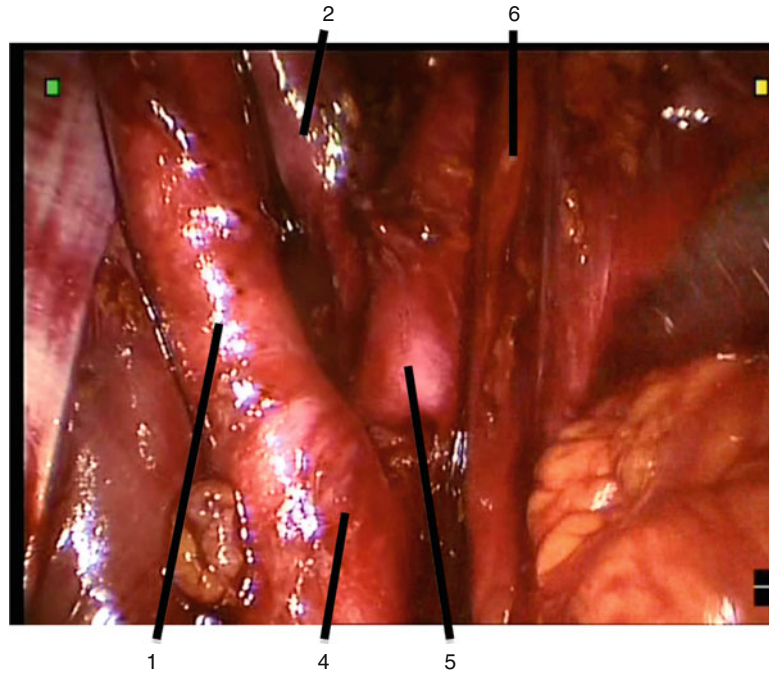


**Fig. 9.1** Proximal situs after ePLND. *1* – external iliac artery. *2* – external iliac vein. *4* – common iliac artery. *5* – internal iliac artery. *6* – ureter

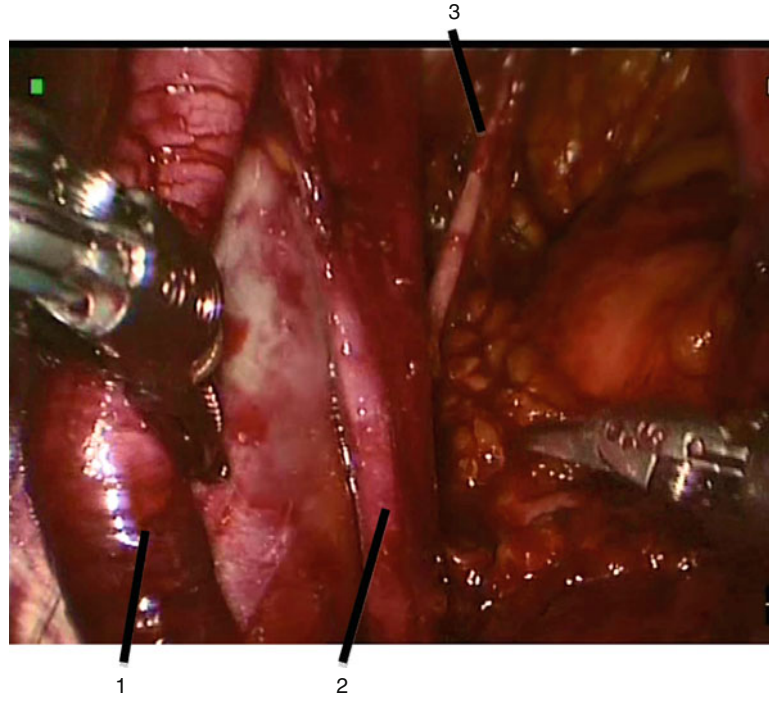


**Fig. 9.2** Separation of the external iliac artery and vein distal to the bifurcation of the common iliac artery, in order to assure that all lymphatic tissue has been cleared out of this region. *1* – external iliac artery. *2* – external iliac vein. *3* – obturator nerve

after the completion of the dissection of the external packet (Fig. 9.1). Alternatively, following the medial umbilical ligament down to the pelvic floor will lead to the internal iliac artery. The lymphatic tissue overlying the internal iliac artery and its obturator and especially the medial vesical branches is completely removed. Special attention is paid to the careful dissection of the tissues medial to the internal iliac artery, since there are often minor bleeding spots.

At the end of the lymphadenectomy, we separate the external iliac artery and vein just distal to the bifurcation of the common iliac artery, in order to control the obturator nerve in its proximal course and to assure that all lymphatic tissue has been cleared out of this region (Fig. 9.2).

The lymph node packets from each region are removed and sent to the pathologist separately.

Complications of robotic ePLND are bleeding, lymphocele formation and vascular or neural injury. Clipping of lymphatic vessels is of great importance to prevent lymphocele formation. The transperitoneal approach better precludes a lymphocele formation. Bleeding can normally be controlled by clipping or gentle coagulation, and nerve injury should not occur with proper technique, avoiding sharp dissection or clipping before identification of the obturator nerve.

## Conclusion

From this review we can conclude the following: PLND is still considered the most accurate procedure to detect local lymph node metastasis, allowing a reliable staging in PCa. Up to now, current imaging techniques cannot give equivalent information comparing to an ePLND. Second, lPLND is not able to detect all positive lymph nodes in every case. The actual literature associates lPLND with a high rate of false-negative findings. Increasing the extent of PLND leads to a more reliable assessment of LNI. On the other hand, the more extensive the PLND is performed, the higher the rate of complications is reported. The extent of lymph node involvement, however, is one of the strongest prognostic factors of cancer-specific survival. However, outcome of node-positive patients undergoing ePLND is not invariably poor; patients with a low nodal burden show often a good long-term survival.

Thirdly, most authors agree that a staging ePLND might be spared in low-risk PCa, since up to now, no prospective randomised studies could find a better cancer control or improved survival after ePLND in these patients. But it seems important to keep in mind that there is still a substantial risk of preoperative understaging and undergrading which must be taken into account on an individual basis when deciding to perform PLND or not. Furthermore, the assumption that low-risk PCa patients are of low risk harbouring lymph node metastasis is based on nomograms derived from series of lPLND, which explains their limited value. The risk of leaving metastases inside by sparing PLND must therefore be discussed with the patient. In this case, a rising PSA soon after RP will probably bring the diagnosis some months later. Fourthly, the feasibility of lPLND as well as ePLND in robot-assisted prostatectomy is well reported and therefore should not be spared if indicated. And as a last conclusion, actual guidelines and most authors agree that if PLND is planned at the time of RP, it should be extended.

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