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Lymphadenectomy in Bladder, Kidney and Prostate Cancers*

Learning Objective: At the conclusion of this continuing medical education activity, the participant will be able to describe the lymphatic drainage of the bladder, kidney and prostate, and cite the data supportive of the role of lymphadenectomy in the surgical management of bladder, kidney and prostate cancers.

Bernard H. Bochner, MD
Disclosures: Olympus: Consultant/Advisor
Attending Surgeon, Professor

Jonathan A. Coleman, MD
Disclosures: Steba: Scientific Study/Trial
Attending Surgeon, Professor

and

Karim A. Touijer, MD, MPH
Disclosures: Elucida Oncology: Patent Co-inventor
Attending Surgeon, Professor

Urology Service Department of Surgery
Memorial Sloan Kettering Cancer Center
Department of Urology
Weill Cornell Medical College
New York, New York

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PROSTATE CANCER

The wide utilization of prostate specific antigen as a screening tool in the early 1990s has led to a downward stage migration in prostate cancer.[1] Subsequently a large proportion of newly diagnosed prostate cancer cases showed negative lymph nodes at radical prostatectomy. The decreasing prevalence of nodal metastasis at the time led some investigators to propose a limited version of the original pelvic lymph node dissection or omit the lymphadenectomy altogether.[1–3]

In recent years the SPCG4, PIVOT and PROTECT trials have demonstrated comparable survival outcomes between active monitoring and treatment in men with low risk prostate cancer.[4–6] Active surveillance acceptance grew to become the preferred management strategy for low risk prostate cancer.[7] **Consequently the focus of surgical indications shifted toward high risk and locally advanced prostate cancer.[8] As such, the prevalence of lymph node metastasis at radical prostatectomy increased.** These changes have renewed the debate about the value of lymphadenectomy in prostate cancer and brought forth a lack of consensus with regard to the indications and anatomical limits of pelvic lymph node dissection at the time of radical prostatectomy.[9, 10]

Detection and prediction of lymph node metastasis. Pelvic lymph node dissection is to date the most accurate staging procedure in prostate cancer. The diagnostic accuracy of cross-sectional imaging is limited (see table). A meta-analysis of the performance of computerized tomography and magnetic resonance imaging in detecting pelvic nodal metastasis in prostate cancer showed a sensitivity range from 5% to 94% for CT and from 6% to 83% for MRI.[11] Specificity ranged from 59% to 99% for CT and from 65% to 99% for MRI. Pooled sensitivity and specificity for CT were 0.42 (95% CI 0.26–0.56) and 0.82 (95% CI 0.80–0.83), respectively. For MRI the pooled sensitivity and specificity were 0.39 (95% CI 0.22–0.56) and 0.82 (95% CI 0.79–0.83). Cross-sectional imaging tests often rely on morphological information such as size criteria to determine the diagnosis of a metastatic node (1 cm short axis in an ovoid node and 0.8 cm in a round node). However, a detailed analysis of pathological characteristics of metastatic nodes in contemporary experience showed a median diameter of the largest metastatic LN of 9 mm (IQR 5–16) and a median maximum diameter of the metastatic focus within the node of 3 mm (IQR 2–6).[12] Morphologically these micrometastases are challenging to detect. Hence, there is an inherent need for more sensitive lymph node staging.

Table. Performance of imaging for lymph node involvement of prostate, bladder and kidney cancer

	Ca Type		
	Prostate	Bladder	Kidney
CT:			
% Sensitivity	5–94	24–47	75–77
% Specificity	59–99	92–97	75–82
MRI:			
% Sensitivity	6–83	55–87	100
% Specificity	65–99	94–100	92–96
PET:*			
% Sensitivity	59–81	33–100	
% Specificity	87–99	58–100	

*FDG-PET was used in patients with bladder and kidney cancer, and PSMA-PET was used in patients with intermediate and high risk prostate cancer.

Molecular imaging targeting prostate specific membrane antigen expression on the surface of prostate cancer cells holds the promise of improving the detection of metastatic nodes. In a meta-analysis of radiolabeled PSMA-PET/CT Kim et al reported a pooled sensitivity of 0.71 (95% CI 0.59–0.81) and a pooled specificity of 0.95 (95% CI 0.87–0.99).[13] This report was based on 298 patients from 6 studies. In a series of 130 patients with high risk prostate cancer undergoing primary PLND Maurer et al reported a sensitivity of 65.9% and a specificity of 98.9% for ^{68}Ga-PSMA-PET.[14] Based on a smaller experience (30 high risk patients), van Leeuwen et al reported comparable sensitivity and specificity.[15] However, the sensitivity is lowest in smaller nodes; 91% of the missed metastatic nodes in this study were less than 5 mm. PSMA-PET imaging is a step toward better preoperative staging of nodal disease. However, the results are preliminary and the tracer is not widely available at this time.

Several algorithms and nomograms have been created to predict lymph node status before radical prostatectomy. Partin et al combined pre-treatment PSA, biopsy Gleason sum and clinical stage to predict pathological stage and lymph node invasion with an overall accuracy measured by the area under the receiver operator characteristics curve of 0.74.[16] Cagiannos et al reported a preoperative nomogram that takes into consideration PSA, clinical stage, biopsy Gleason sum and the institutional specific prevalence of positive lymph nodes with an AUC of 0.76.[17] Given the difference in staging accuracy between the limited and extended PLND anatomical template, Godoy et al updated the Memorial Sloan Kettering nomogram by including only patients who underwent an extended PLND.[18] This nomogram, which included patients treated with open, laparoscopic and robotic techniques, had a good calibration and high discriminative accuracy (AUC 0.862). Briganti et al published a nomogram based on an extended PLND experience and included PSA, Gleason score, clinical stage and the percentage of positive cores as covariates.[19] This nomogram demonstrated good predictive accuracy (AUC 0.87). Both the nomograms by Godoy[18] and Briganti[19] et al provided a decision curve analysis to help clinicians choose a safe cutoff for the indication of PLND. According to the nomogram by Briganti et al, choosing a cutoff of 5% or less would avoid a

ABBREVIATIONS: AUA (American Urological Association), CT (computerized tomography), FDG (fluorodeoxyglucose), LN (lymph node), LND (lymph node dissection), LNI (lymph node involvement), MRI (magnetic resonance imaging), PET (positron emission tomography), PLND (pelvic lymph node dissection), PSA (prostate specific antigen), PSMA (prostate specific membrane antigen), RCC (renal cell carcinoma)

PLND in 65.5% of the patients at the risk of missing lymph node metastasis in 6 (1.5%).[19] **The National Comprehensive Cancer Network guidelines recommend a nomogram prediction of 2% or greater to perform PLND during the surgical treatment of prostate cancer.[20]** Based on the Memorial Sloan Kettering nomogram, patients with a risk of lymph node invasion below 2% are essentially low risk (PSA less than 10, cT1c–cT2a disease, International Society of Urological Pathology grade group 1/Gleason 6), and therefore mostly active surveillance candidates.

Anatomical extent of pelvic lymph node dissection. For clarity a PLND including only the nodal packet located between the posterior aspect of the external iliac vein and the obturator nerve (zone 1: external iliac packet) is considered limited (fig. 1). A dissection encompassing the external iliac, obturator fossa and the hypogastric nodal packets is considered an extended PLND (see videos).

The prevalence of lymph node metastasis in contemporary radical prostatectomy series varies widely (1.1% to 26%).[17,19,21–23] This range is likely due to differences in both disease risk distribution and extent of lymphadenectomy. Several reports have shown an almost linear relationship between the number of nodes removed and the number of metastatic nodes detected,[24, 25] supporting the superior staging accuracy of the extended PLND. Touijer et al compared limited vs extended PLND and reported up to a threefold increase in detection of metastatic nodes.[22] Bader et al published a mapping study of the nodal metastasis distribution in the pelvis and showed that 58% of the patients harbor positive nodes in the hypogastric packet, with 19% having positive nodes found exclusively in the region of the hypogastric artery and its branches.[10] Excluding the hypogastric nodal packet as in the limited PLND can significantly hinder the staging quality of lymphadenectomy. Heidenreich et al reported on a superextended template that included the nodal tissue over the common iliac artery and presacral area, and reported nodal metastasis in the common iliac and presacral region in only 3.1% of the patients.[21] Heidenreich et al concluded that routinely adding the presacral and common iliac nodal packets is not necessary.

Several retrospective studies have failed to show a biochemical recurrence-free survival benefit of extended PLND over limited PLND.[23, 26] A large randomized clinical trial comparing biochemical recurrence rate between limited and extended PLND has reached its accrual target of 1600 patients at Memorial Sloan Kettering Cancer Center. Other ongoing trials (NCT01812902 and NCT0155508) are being conducted in Brazil and Germany. **These 3 trials will provide level I evidence to address the ongoing debate about the therapeutic benefit of extended PLND over the limited one.**

Although PLND is relatively well tolerated, complications such as symptomatic lymphoceles and ureteral, vascular and nerve injury have been reported. In a series of 971 consecutive laparoscopic radical prostatectomies Touijer et al compared morbidity between 3 groups: no PLND, limited PLND and extended PLND.[27] In this study lymphadenectomy was associated with higher morbidity when compared to no lymphadenectomy (symptomatic lymphoceles: 0% in no PLND, 5.2% in limited PLND and 5.9% in extended PLND, and venous

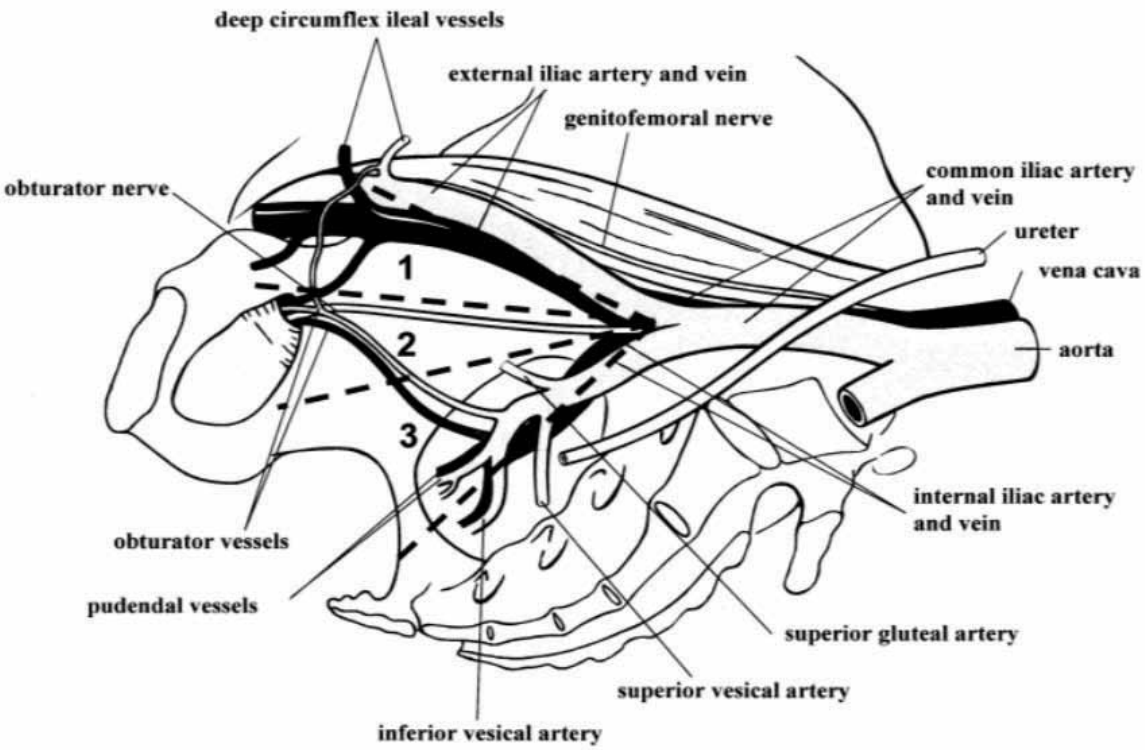

Figure 1. Anatomical template of limited (zone 1 external iliac node packet) and extended LN dissection for prostate cancer (zones 1, 2 and 3—external iliac, obturator fossa and hypogastric nodal packets, respectively). Reprinted with permission from *The Journal of Urology®*.

thromboembolic events: 1% vs 1.1% vs 2.1%). However, there was no evidence that the incidence of complications would be reduced by a limited PLND. The risk/benefit of extended vs limited PLND was estimated to be 1 additional grade 3 complication per 20 additional patients with nodal metastases detected. Other contemporary series reported lymphoceles rates ranging from 3.3% to 9% for the limited PLND vs 9.4% to 10.6% after extended PLND.[21,28]

The guidelines of both the European Association of Urology and the National Comprehensive Cancer Network recommend the xtended PLND.[29,30] However, the AUA guidelines did not elect one PLND template over the other, and balanced the risks and benefits of each approach.[31] The statement from the AUA recognized PLND as the most effective way to detect nodal metastasis but stressed the lack of evidence supporting its therapeutic benefit.

Management of node positive prostate cancer. The presence of lymph node metastasis is a major determinant of prostate cancer mortality. However, lymph node metastasis does not necessarily equate to systemic dissemination of cancer. **Long-term follow-up data on men with positive nodes treated with radical prostatectomy only have shown up to 28% (95% CI 21–36) freedom from biochemical recurrence at 10 years.[32]** In addition, a multimodality approach including radical prostatectomy with adjuvant androgen deprivation therapy and radiation therapy was associated with improvement in overall and cancer specific survival compared to either radical prostatectomy alone or radical prostatectomy and adjuvant androgen deprivation therapy. Patients with the highest risk disease seemed to derive the greatest survival benefit.[33,34]

These data highlight the importance of a multimodal approach aimed at maximizing local control and argue against the former strategies of withholding surgery in patients with clinically node positive disease (cN+) or aborting the radical prostatectomy if the nodes were positive on intraoperative fresh frozen section. In fact, more than 30% of men with cN+ prostate cancer are eventually found to have pathologically negative lymph nodes.[35] Frozen section can miss a significant number of micrometastatic disease in the lymph nodes,[36,37] and radical prostatectomy can reduce the risk of local failure.[38]

BLADDER CANCER

Lymphatic drainage of the bladder. The lymphatic drainage of the bladder has been well documented in both anatomical dissections of the bladder and clinical mapping studies of patients with bladder cancer undergoing lymphadenectomy. The primary lymphatic drainage of the bladder consists of a partial ring of lymph nodes within the anatomical true pelvis. **Several different primary drainage regions have been identified. These include the external iliac LNs overlying the external iliac artery and vein including a lateral extension, which lie within the groove between the external iliac artery and the psoas muscle, as well as the obturator LNs and the hypogastric LNs**. A primary drainage pathway has also been identified to the presacral LNs. The primary zones drain into the common iliac LNs and then into the retroperitoneal zones.[39] Mapping studies in patients with bladder cancer undergoing radical cystectomy and PLND for treatment have also documented the locations and frequency of involvement of the regional LNs.[40] The obturator region is the most common primary drainage site of involvement with positive LNs (approximately 25%). Least frequently involved are the presacral LNs, in which up to 8% of patients may demonstrate involvement. **Purely unilateral tumors (those involving only the left or right lateral bladder walls) that metastasize to the regional LNs will have contralateral LN involvement in nearly 25% of patients.** The most common progression of spread appears to involve the primary drainage sites first (external, hypogastric and obturator) and then move to the secondary drainage regions. However, up to 6% to 7% of patients may show skip lesions, in which only the secondary sites are involved, bypassing the primary node basins.

Accuracy of imaging to detect lymph nodes. Anatomical imaging, whether CT or MRI, is most commonly used to image the pelvic and retroperitoneal lymph nodes as part of disease staging prior to, during or after therapy for bladder cancer. For either modality the following features are evaluated to determine whether a LN is considered involved with disease: size, round shape, irregular margin, absence of fatty hilum, intense enhancement (MRI and CT) and radiotracer uptake (PET/CT, see table). Studies have found 40% to 85% accuracy using CT to detect malignant LNs.[41] Contemporary MRI imaging using diffusion weighted imaging and T2-weighted sequences has a reported sensitivity of 55% to 87%, specificity of 94% to 100%, and accuracy of 88% to 96% for malignant node detection on a per-pelvic side basis.[42] A prospective study of 122 patients with bladder cancer found a 41% sensitivity, 92% specificity and 80% accuracy for the detection of positive nodal disease using MRI.[43] Studies have demonstrated the utility of ultrasmall superparamagnetic iron oxide particles used as a contrast enhancing agent with MRI to identify involved LNs.[44] Overall performance with iron oxide nanoparticles appears improved over standard MRI with sensitivities of 60% to 100% and a specificity of 91% to 96%.[45]

The performance properties for ^{18}FDG-PET/CT for lymph node staging at radical cystectomy have been extensively studied. **A recent meta-analysis of 20 studies found a sensitivity of 56% (range 33% to 100%) and a specificity of 92% (58% to 100%).[46]** Others have demonstrated a better ability of ^{18}FDG-PET/CT to detect LN involvement with a positive predictive value of 78%, a negative predictive value of 91%, sensitivity of 70% and specificity of 94%;[47] however, differences in patient population may explain variations in reported performance characteristics. For example ^{18}FDG-PET/CT appears to perform better in the advanced stage setting, with a specificity of 94% and sensitivity of 81% using a maximum standard unit value above 4 to determine a positive scan.[48] In general, guidelines have not recommended the routine use of PET for staging patients with non-metastatic disease by CT or MRI. However, in the setting of clinically suspicious lymph nodes that are not amenable to biopsy, PET may be of benefit in treatment selection.

Frequency and outcome of patients with LN positive bladder cancer following radical cystectomy. **The frequency with which the pelvic LNs are involved in patients with invasive bladder cancer primarily varies based on extent of invasion (T stage).** The original association between depth of invasion of a primary tumor and risk of lymph node involvement dates back to autopsy studies by Jewett and Strong.[49] Since then, clinical series have reported the frequency of lymph node involvement based on pathological stage: early stage disease, approximately

20%; extravesicle involvement, up to 40%; locally advanced tumors that invade adjacent organs, up to 70%.[50] Most regionally involved LNs identified at radical cystectomy contain small volume disease, with typically 1 to 2 positive LNs. The cell type of the primary tumor may also affect the frequency of regional LN involvement. In particular, micropapillary bladder tumors have a very high frequency of lymphovascular involvement and regional LN spread.[51]

Therapeutic role of the PLND for bladder cancer. The therapeutic role of the pelvic lymphadenectomy at the time of radical cystectomy has been documented over the last 80+ years. Pelvic recurrence rates have been noted to be significantly higher in patients who do not undergo a pelvic lymphadenectomy. Early series recognized the utility of the PLND as a means to improve local pelvic control.[20] Contemporary surgical series observed that node positive patients as a group have a 30% to 40% 5-year disease-free survival following radical cystectomy and PLND.[50, 52, 53] This suggests that a subset of patients will develop limited regional metastatic disease alone and can be rendered disease-free by removing those little deposits with the bladder. Much discussion has been centered around extent of the node dissection necessary to optimize both staging and therapeutic benefit. **Based on anatomical mapping studies that have reported the number of LNs removed in various anatomical zones, it has been suggested to optimize surgical staging that a minimum of 12 LNs be pathologically evaluated from the bilateral external, internal and hypogastric LNs.[54]**

Historically control of the regional pelvic LNs was not included in the surgical management of invasive bladder cancer.[20] Initial surgical series that eliminated a PLND documented a significant rate of pelvic failure, including many with suspected LN recurrences. As PLND was incorporated with radical cystectomy, the outcomes of patients with pelvic LN involvement became available and demonstrated that few if any LN positive patients survived beyond a few years after surgery.[55] This led many clinicians to question the role of the PLND for patients with bladder cancer. However, more contemporary series have demonstrated that up to a third of current day LN positive patients are rendered disease-free with surgery alone. As additional clinical data became available suggesting an improvement in cancer specific outcomes in patients who did undergo a PLND, more surgeons began incorporating it routinely into practice. Recent U.S. national data demonstrate that PLND is increasingly being used at radical cystectomy and that more LNs are being removed when a PLND is completed compared to historically managed patients.[56, 57]

Optimal extent of the PLND at radical cystectomy. The extent of the lymph node dissection required to optimize therapeutic benefit remains controversial. Initial studies demonstrating improvements in overall survival in those patients who underwent a more extensive lymph node dissection may have been a result of surgical bias within the comparison groups.[53, 58] Older, more heavily comorbid patients are less likely to undergo a PLND at radical cystectomy, and if they do undergo a PLND, it tends to retrieve fewer LNs. Therefore, number of LNs retrieved will correlate with overall survival but this is likely comparing overall survival of older, sicker patients to younger healthier patients.[59] Stage migration also clouds the association between outcome and number of LNs retrieved. Patients with fewer LNs removed are less accurately staged at the node level. As an example, a patient who has 4 LNs removed may, in fact, be more likely to harbor unidentified LN involvement compared to a patient with 40 LNs removed and examined. The patient with a greater number of LNs reviewed is more likely to have been accurately staged as LN negative or positive. Groups of LN "negative" patients with lesser numbers of nodes therefore represent a combined group of true LN negative and patients with occult positive nodes missed on the less extensive dissection.

A randomized study comparing limited vs more extensive LN dissections would provide high level evidence of a potential benefit (fig. 2). Design of a study comparing a standard LN dissection up to the bifurcation of the common iliac vessels to an extended dissection up to the base of the inferior mesenteric

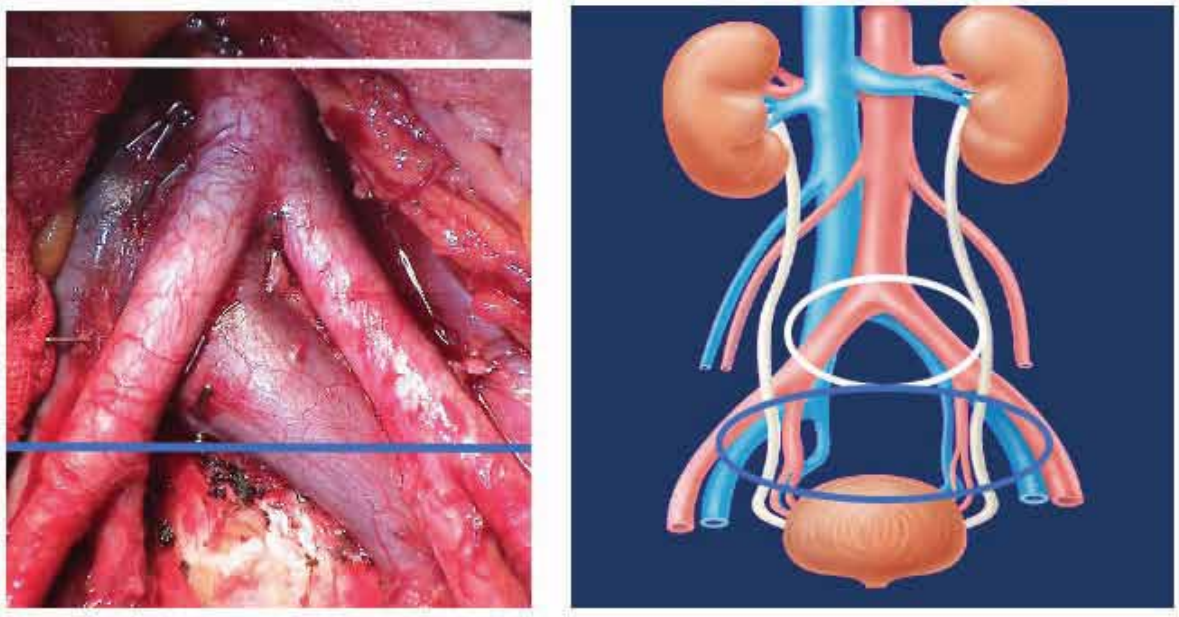

Figure 2. Intraoperative photo (*left*) and diagram (*right*) depict anatomical limits of dissection of standard (blue line and circle) and extended (white line and circle) pelvic lymph node dissections.

artery would require knowledge of the percentage of patients who would potentially benefit from removal of these more proximal LNs (those with common iliac LN or lower retroperitoneal LN involvement) and the expected recurrence-free survival in those patients with common iliac LN or lower retroperitoneal LN involvement who underwent surgical removal of those positive LNs (extended LN dissection). For example if all patients with common iliac/lower retroperitoneal LNs were observed to recur despite resection, then it would be reasonable to assume no benefit from removal of these more proximal involved LNs. Observational studies have provided data on both questions.[60,61] **In an unselected group of patients with ≥pT2 disease approximately 15% of patients will have N3 disease (involvement of the common iliac LNs). Of these patients 25% to 37% are free of disease at 5 years.** This information would support a potential recurrence-free survival benefit of approximately 5% (one-third of 15% of patients rendered disease-free from routine use of extended LN dissection in a group of patients with T2 or greater disease).

Randomized trial data are available comparing a more limited to a more extensive PLND at the time of radical cystectomy in patients with bladder cancer. Gschwend et al completed a phase 3 randomized trial comparing removal of the bilateral external, obturator (above obturator nerve) and hypogastric to an extended dissection that also included the deeper obturator, common iliac, presacral, para-aortic and paracaval LNs up to the base of the inferior mesenteric artery.[62] The study was powered to identify a 15% difference in recurrence-free survival, a rather large anticipated improvement. The study included 401 patients with bladder cancer, including those with early stage T1 disease. Overall, 8% of patients had LN positive disease, including only 1 patient with N3 disease. The 5-year recurrence-free survival estimate showed an advantage in the extended LND group reaching 64.6% compared to 59.2% in the limited LND group, but this difference (5.45%, 95% CI 6.43–17.33) did not reach statistical significance. Similar differences in favor of the extended dissection were observed in 5-year cancer specific survival (65% vs 59%) and 5-year overall survival (59% vs 50%); however, the study was not powered to statistically confirm these smaller differences (p=0.10 and p=0.12, respectively).

Another randomized trial (SWOG S1011) is also designed to study limited vs extended PLND for patients with bladder cancer. It is designed to identify a 25% reduction in the hazard ratio of recurrence (HR 0.75). Patients with clinical evidence of LN involvement above the common iliac bifurcation, however, are not eligible for randomization in this trial, and therefore it will be evaluating whether removal of clinically normal LNs above the common iliac bifurcation improves cancer outcomes. Outcomes are anticipated in the coming years.

Clinical circumstances that limit use of the PLND. Clinical situations may require judicious use of a lesser extent of PLND in selected patients. In patients with severe vascular disease great care is needed to avoid injury during the PLND. Aneurysms or severely atherosclerotic vessels may be associated with a perivascular fibrosis, are more vulnerable to injury during dissection and may be prone to subsequent aneurysm/false aneurysm formation. In the absence of gross disease it is reasonable clinical judgement to avoid manipulation of regions that appear at risk. In addition, following pelvic radiation therapy a dense pelvic fibrotic reaction may be encountered. The lymphatic tissues overlying the pelvic and lower retroperitoneal vessels may be encased in scarring, making the dissection very difficult. The dense adherence of the LNs to the vasculature will increase the risk of vascular injury (particularly venous) during the PLND and may require limiting or avoiding dissection of these regions. In the patient with prior pelvic radiation therapy to the sidewalls, performance of an extended PLND is associated with a higher risk of severe lower extremity lymphedema and should be avoided in the absence of gross disease above the common iliac bifurcation. Following prior pelvic surgery there may also be a variable degree of scarring along the pelvic sidewall vessels. Factors such as the extent of prior LN dissection and postoperative complications (i.e. infection, bleeding) will affect whether a PLND can be completed.

LYMPHADENECTOMY AND KIDNEY CANCER SURGERY

At present, the role of regional lymphadenectomy for kidney cancer is regarded as a staging procedure with the key purpose to provide information on tumor extent to allow accurate patient risk stratification. **The presence of lymph node involvement is a strong independent risk factor for poor cancer specific and overall survival,[63] and therefore accurately identifying and characterizing nodal disease at the time of therapeutic surgical treatment is critical to clinical decisions in postoperative patient management, including eligibility for early adjunctive therapies and clinical trials that have the potential for additional oncologic benefit.**

Despite these factors, lymph node dissection is infrequently utilized, performed in 20% to 30% of high risk, suitable cases due in part to the fact that direct therapeutic benefits from LND in RCC have not been established.[64, 65] **Level I evidence from EORTC 30881 failed to demonstrate improvement in overall survival, time to progression and progression-free survival with LND, albeit in a low risk patient population staged using the 1978 Union for International Cancer Control TNM system.[66]** In this trial 772 radical nephrectomy patients were randomly assigned to surgery with or without node dissection with the intent to detect a 10% improvement in 5-year survival, assuming a baseline rate of 70%. In the LND arm LNI was found in 14 patients (4%) despite utilizing an extended node template from the diaphragmatic crus to the bifurcation of the iliac vessels, indicating a low risk population insufficient to address the primary outcome. Noted in the study was a 20% node positivity rate among 51 LND patients with palpably abnormal nodes discovered at the time of surgery. At odds with the primary outcomes of this study are several retrospective series demonstrating long-term disease-free survival in roughly 15% of patients with LNI following nephrectomy and LND, suggesting that a proportion of patients with LNI may derive clinical benefit, although favorable outcomes in LNI cases were also associated with less aggressive tumor features, such as grade, stage and histological subtype.[67] Without randomization, however, the impact of surgical intervention and systemic response is difficult to ascertain in these series.

The presence of isolated LNI is rare, and detection is highly dependent on the extent of LND as well as pathological assessment to identify micrometastatic disease.[63, 68, 69] Patient selection features have been shown to play a role with increased risk of LNI seen in patients with tumors larger than 10 cm, T3 or T4 disease, Fuhrman grade 3 or 4 disease, sarcomatoid differentiation or tumor necrosis.[70] Preoperative cross-sectional imaging

features of enlarged nodes (1 cm or greater) and perinephric or renal sinus fat invasion are associated with LNI in 20% to 30% of patients, which may help to identify higher risk patient cohorts, although LNI may also be found in roughly 4% to 5% of patients with clinically normal appearing nodes (see table).[71,72]

Pathways of nodal metastases and LND templates are less well established in RCC, where lymphatic channels can be variable although generally follow anatomically described right-to-left retroperitoneal lymphatic flow as well as retro crural routes of egress. Key concerns in performing LND at the time of nephrectomy include the issues of increased surgical time and patient exposure to greater risks of adverse events. Surgical complications of LND, such as thromboembolism, bleeding, lymphatic leak, bowel injury and infection, do not appear worse with standard LND procedures in RCC.[66, 68] Proposed templates of dissection are varied and may include superextended approaches in isolated cases, although more typically the approach to remove renal hilar nodes surrounding the renal pedicle and ipsilateral great vessel to remove visibly abnormal, safely reachable nodes is generally advocated. AUA guidelines recommend node dissection be performed in the setting of clinically suspicious nodes.[73]

DID YOU KNOW?

- Lymph node dissection for bladder cancer plays an important role in staging and cancer control. For staging the primary LN drainage regions on both sides should be removed to ensure adequate LN sampling. The optimal extent of dissection for therapeutic purposes remains controversial, but increasing data support a more extended dissection in high risk patients.
- In the treatment of clinically localized prostate cancer the extended pelvic lymph node dissection, including the external iliac, obturator fossa and hypogastric nodal chains, remains the most accurate staging procedure. However, the therapeutic benefit conferred by extended pelvic lymph node dissection remains unproven.
- Accurately determining the presence of lymph node involvement with lymphadenectomy for kidney cancer, especially in patients with high risk features, has clinical value in determining eligibility for use of adjunctive therapy in patients with renal carcinoma. Phase 3 trial data do not identify increased morbidity associated with lymphadenectomy performed during nephrectomy.
- To date, regional lymph node dissection for patients with low risk kidney cancer has not demonstrated a therapeutic advantage. Guidelines do recommend lymph node dissection in the presence of suspicious regional lymph nodes.

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Study Questions Volume 39 Lesson 37

1. A major risk factor for increased lower extremity lymphedema following an extended pelvic lymph node dissection at the time of radical cystectomy for bladder cancer is
   a. advanced age
   b. prior pelvic infection
   c. prior pelvic radiation
   d. prior systemic chemotherapy

2. In prostate cancer staging of the pelvic lymph nodes is best performed by
   a. PSMA-PET/CT
   b. multiparametric MRI
   c. using modern nomograms
   d. extended pelvic lymph node dissection

3. A patient with a 9 cm right renal mass and 2 enlarged paracaval lymph nodes seen on CT is being consented for nephrectomy, and lymph node dissection is discussed. Performing a node dissection is most likely to
   a. increase risk of bleeding and thrombosis complications
   b. increase cancer specific survival
   c. provide the best means to determine if the nodes are positive
   d. reduce tumor burden and ultimately improve efficacy of postoperative immunotherapy

4. A 67-year-old healthy man is undergoing a robotic radical prostatectomy and a lymph node dissection for a Gleason 4+3 tumor, cT2b and a PSA of 20 ng/ml. The MRI showed a 2 cm anterior lesion with invasion of the fibromuscular stroma (PI-RADS™ version 2: 5). During surgery a round left obturator node that measures 1.2 cm is found. The next step is
   a. complete the node dissection bilaterally and do not proceed with prostatectomy
   b. complete the node dissection bilaterally, send nodes for frozen section and proceed with prostatectomy if the nodes are negative
   c. complete the node dissection bilaterally and proceed with prostatectomy
   d. abort the entire procedure

5. A 72-year-old woman has a 1.5 cm sessile completely unilateral tumor on the left lateral wall that is muscle invasive at transurethral resection of bladder tumor. Pathology reveals a micropapillary muscle invasive tumor. Imaging does not reveal any obvious nodal disease. She is scheduled for a radical cystectomy. The lymph node dissection should include the following nodes:
   a. bilateral external iliac
   b. left external and internal iliac and hypogastric
   c. bilateral external and internal iliac and hypogastric
   d. bilateral external and internal iliac, hypogastric, deep obturator, common iliac, presacral, para-aortic and paracaval

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