REVIEW

Current status of pelvic lymph node dissection in prostate cancer: the New York PLND nomogram

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Introduction: *Controversy persists concerning the role of pelvic lymph node dissection (PLND) in patients with clinically localized prostate cancer undergoing radical prostatectomy. The aim of this review is to critically evaluate the current status on PLND in prostate cancer.*
Methods: *A review of the literature was performed concerning radical prostatectomy and PLND with respect to oncological outcome, associated complications, nodal yield, indications and minimal number of nodes required.*
Results: *PLND is still the modality of choice for detecting lymph node metastasis in prostate cancer. Current imaging techniques are not accurate enough for detecting nodal metastases. Extended PLND has complications that increase with extent of dissection. Nodal yield at PLND is directly related to the lymph node invasion (LNI) rate and greater nodal yield is associated with superior staging accuracy. Based on MSKCC nomogram and in conjunction with prospective confirmation studies a novel nomogram (the New York nomogram) was designed.*
Conclusion: *Removing at least 10 lymph nodes is recommended to detect LNI. For patients with high and intermediate risk disease, extended PLND at least for external iliac, obturator and hypogastric lymph nodes should be performed during radical prostatectomy. However, for patients with low risk disease, PLND is not necessary and is not recommended, because the chance of metastasis is low.*

Key Words: lymph node metastasis, localized prostate cancer, pelvic lymph node dissection, radical prostatectomy, frozen section

Introduction

Pelvic lymph node dissection (PLND) has been performed as a part of radical prostatectomy since more than 30 years ago. It represents accurate staging procedure for presence of lymph node invasion (LNI) in clinically localized prostate cancer.[1] But the role of PLND in prostate cancer remains controversial. Although it is generally accepted that PLND provides important information regarding pathological tumor staging and prognosis, the extent of PLND (limited versus extended) and the candidates most suitable for this procedure are still a matter of debate. The prevalence of LNI ranges from 1.1% to 26% and is related to PLND extent.[2-4] Indeed, extended PLNDs identify metastases that would not otherwise be detected by a limited PLND.[5] No consensus has yet been reached about the extent of PLND or, more specifically, the number of lymph nodes that should be removed to achieve optimal cancer staging.[2-4]

Some authors based their decision on preoperative nomograms considering preoperative prostate-specific antigen (PSA) serum levels, clinical stage, number of positive biopsies, and Gleason score of prostate biopsies for risk calculations[6-8] and others prefer performing PLND in all patients. Two nomograms based on the data of extended PLND have been published.[9,10] In these nomograms the calculations have been based on PLNDs with a mean of < 10 lymph nodes removed.

Methods

A review of the literature was performed concerning radical prostatectomy and PLND with respect to oncological outcome, associated complications, nodal

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yield, indications and minimal number of nodes required.

Prostate gland lymphatic system and types of PLND

Prostate gland lymphatic system includes periprostatic subcapsular network and three groups of ducts: the ascending duct from the cranial gland running to the external iliac nodes, the lateral duct running to the hypogastric nodes, and the posterior duct running to the lateral and subaortic sacral nodes of the promontory.

There are multiple variations of PLND: limited PLND (lPLND) can be considered for the removal of the lymphatic tissue inferior to the bifurcation of the common iliac artery, bound inferiorly by the femoral canal, laterally by the pelvic sidewall, and medially and inferiorly by obturator nerve, collectively (external iliac nodes), standard PLND (sPLND) consists of a lPLND and all lymphatic tissue in the obturator fossa, deep and proximal to the obturator nerve (the obturator nodes) and extended PLND (ePLND) should include both of the above along with all fibrofatty tissue surrounding the hypogastric vessels posteriorly (the hypogastric nodes), Figure 1.[11-15]

In a study by Bader et al[2] on metastatic cancer deposits from a cohort of 88 relatively high risk men with node positive disease after radical prostatectomy and extended pelvic lymphadenectomy, the most common site for metastasis (60%) was the obturator fossa, however, 58% had deposits in the internal iliac (hypogastric) and 36% in the external iliac nodal areas, while 19% had positive nodes in the hypogastric distribution alone. Allaf et al[16] found a significant difference in lymph nodes yield between a standard PLND/extended PLND and limited PLND in open radical prostatectomy. Mattei et al[17] have used a multimodality technique to precise mapping of the primary prostatic lymphatic metastases landing site. They have suggested that PLND for prostate cancer should include not only the external and obturator region as well as the portions medial and lateral to the internal iliac vessels, but also the common iliac lymph nodes at least up to the ureteric crossing, thus removing approximately 75% of all nodes potentially harboring metastasis.

Number of nodes

Heidenreich et al[18] found that the number of dissected lymph nodes is directly associated with an increase in the detection of positive lymph nodes. Weingartner et al[19] in a cadaveric study compared nodal counts in cadavers without prostate cancer subjected to sPLND with actual counts resected during radical prostatectomy and sPLND. They found that a mean of 20 dissected pelvic lymph nodes can be considered a representative sampling that enables exact staging of prostate cancer. Estimates of lymph node counts

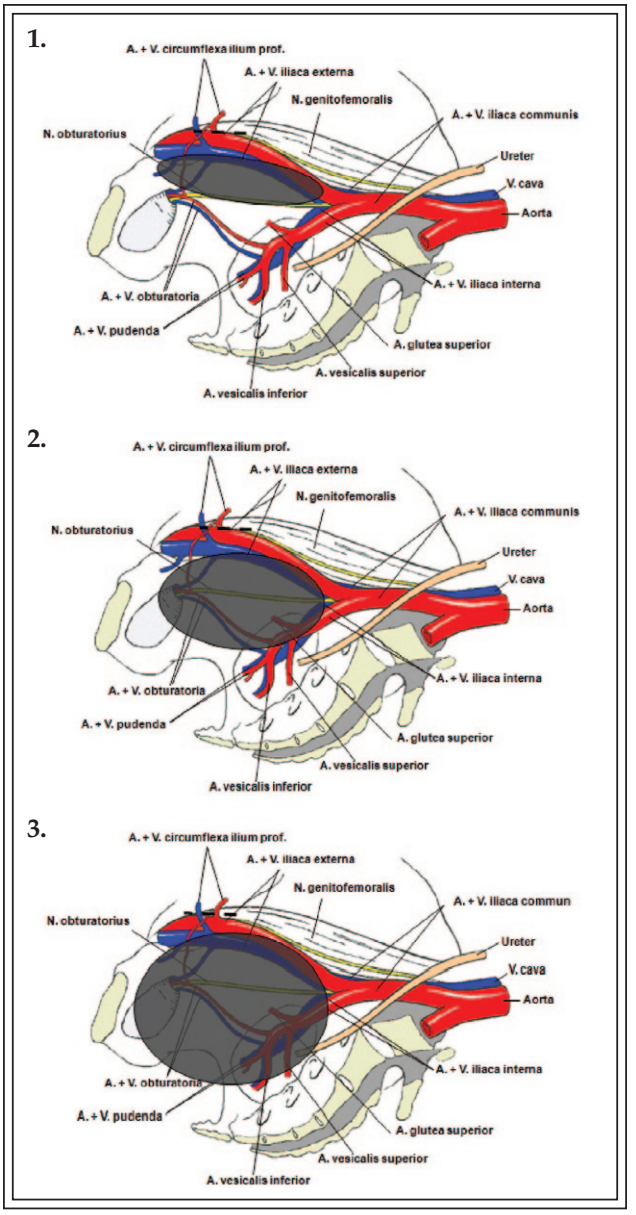

Figure 1. Pelvic lymph node dissection regions. **1. Limited dissection region:** External iliac vein lymph nodes group **2. Standard dissection region:** External iliac vein lymph nodes group + Obturator fossa lymph nodes **3. Extended dissection region:** External iliac vein lymph nodes group + Obturator fossa lymph nodes + Internal iliac (hypogastric) lymph nodes

necessary for optimal staging accuracy have ranged from 20 to 28.[19]

In a study by Briganti et al[20] 858 patients aged 45 to 85 years which predominantly had been treated with ePLND before radical retropubic prostatectomy participated. The pretreatment PSA level was 0.24 ng/mL to 49.9 ng/mL, lesions were stage T1c or T2 with a biopsy Gleason score of ≤ 6 or 7. 2 to 40 nodes were removed. They concluded that the LNI rate increased with the number of removed nodes, Figure 2, and removing of 10 nodes or less yields < 10% ability to detect LNI, however, 28 nodes yields 90% ability to detect LNI.[20]

In a comparison between limited and extended laparoscopic PLNDs by Stone et al[21] have been demonstrated a 2-fold increase in the number of removed lymph nodes (9 versus 18) and a 3-fold increase in the frequency of lymph node metastases (7% versus 23%).

Heidenreich et al have reported that a mean of 28 and 11 lymph nodes is removed by the extended and the limited technique, respectively; the number of positive lymph nodes increased from 12% to 26%.[13,14] These data have been supported by Wawroschek et al[22] and Briganti et al.[9,10] They reported positive lymph nodes in 32% and 20% of their patients, respectively. In another study by Schumacher et al[23] have been demonstrated that the incidence of positive nodes in patients with clinically localized prostate cancer, a serum PSA < 10 ng/mL and a Gleason score ≥ 7 in the prostatectomy specimen was 25% after extended PLND. They evaluated 231 patients with a median serum PSA of 6.7 ng/mL and a median age of 62 years. They removed median of 20 (range 10-72) nodes. Positive nodes were found in 26 of 231 patients (11%), the majority of them (81%) had a Gleason score ≥ 7 in the surgical specimen. Of the patients with a Gleason score ≥ 7 in the prostatectomy specimen 25% had positive nodes, whereas only 3% with a Gleason score ≤6 were node positive.[23] In summary on the basis of previous studies, it is recommended to remove at least 10 lymph nodes to detect LNI in prostate cancer.

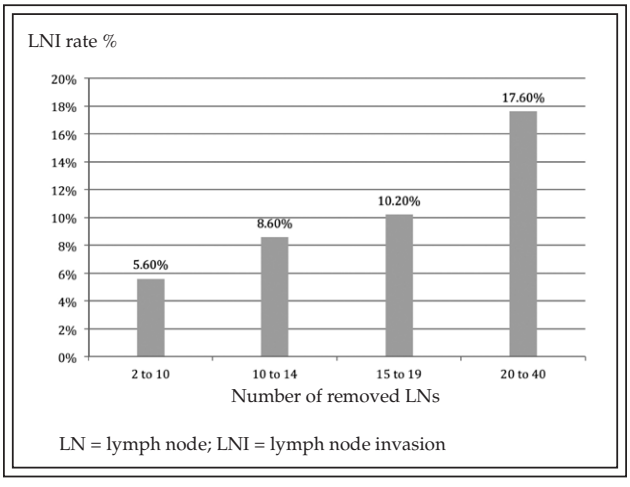

Figure 2. Lymph node invasion rate increased with the number of removed nodes.

Patient selection for PLND

Conventional computed tomography (CT) and magnetic resonance imaging (MRI) as imaging techniques are unreliable for the detection of small metastatic deposits (< 1 cm-1.5 cm) or for detecting pathologic enlargement or predicting pathologic lymph node status[19] and therefore pelvic lymphadenectomy remains the gold standard for detecting LNI in prostate cancer.

Updated Partin tables,[24] preoperative nomograms[6,7] and Memorial Sloan-Kettering nomograms[25] do not recommend performing PLND in patients with a preoperative PSA serum level < 10 ng/mL, a biopsy Gleason score < 7, and a clinical stage ≤ 2a because the incidence of positive lymph nodes is said to be approximately only 1%-5%,[6-8] Figure 3. In a study by Schumacher et al,[23] the incidence of positive nodes in patients with clinically localized prostate cancer, a serum PSA < 10 ng/mL and a Gleason score ≥ 7 in the prostatectomy specimen was 25% after extended PLND. Crawford et al[6] identified biopsy Gleason score ≤ 6, a preoperative PSA serum level ≤ 10.6 ng/mL, and stage cT1c as predictors for low risk lymph node metastases.

In a recent study by Yu et al[26] the Partin tables have been validated. They examined the predictive ability of the tables in 11,185 men selected from the National Cancer Institute Surveillance, Epidemiology and End Results database from 2004 to 2005 who

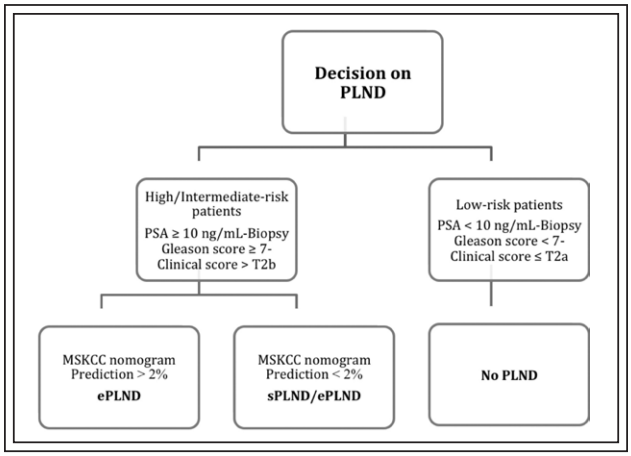

Figure 3. The New York PLND nomogram.

underwent radical prostatectomy.[26] Cagiannos et al[25] developed a predictive nomogram that was based on sPLND and data from multiple institutions. Their nomogram had predictive accuracy of 0.78 based on 5510 patients and a 3.7% rate of LNI. Conrad et al[27] published a diagnostic algorithm based on a variety of preoperative parameters of 600 patients undergoing radical prostatectomy. On the basis of number of biopsy cores in prostate cancer with Gleason score ≥ 7, three risk groups were identified. Risk for lymph node metastases was 45%, 19%, or 2% if 4-6, 1-3, or no biopsy was involved with Gleason score 8-10 prostate cancer respectively.

Allaf et al[16] reported a significant diagnostic benefit of ePLND in a group of 2135 men with low risk prostate cancer compared with a group of 1835 men undergoing radical prostatectomy and limited PLND. Extended PLND removed more lymph nodes (11.6 versus 8.9, $p < 0.0001$) and detected more lymph node metastases (3.2% versus 1.1%, $p < 0.0001$) than limited PLND. Briganti et al[20] have created a multivariable nomogram based on ePLND in patients with low risk and intermediate/high risk prostate cancer and have argued that the probability of correctly identifying those with LNI is, in part, dependent on the number of nodes sampled. The nomogram for low risk prostate cancer was developed in 781 patients and internally validated in 200 patients; multivariate analysis identified clinical stage, biopsy Gleason sum, and number of lymph nodes removed as significant predictors for occult lymphonodular metastases, and resulted in an accuracy of 78.6%.[20]

In summary and on the basis of preoperative nomograms we recommend performing extended PLND in patients with high and intermediate risk disease, at least for external iliac, obturator and hypogastric lymph nodes, because the risk of positive lymph node in these patients is ≥ 2%. However, for patients with low risk disease, we recommend performing no PLND at all, because the chance of metastasis by most nomograms appears to range between 0% and 4% in these patients, Figure 3.

Impact of PLND on survival

The possibility of therapeutic benefit for pelvic lymphadenectomy has been suggested by some studies, but the results have been inconsistent.[2,12,13,28]

Briganti et al[29] demonstrated that patients with two or fewer positive lymph nodes on the final stage of disease had significantly better outcomes at 15 years compared with those with more than two positive lymph nodes. Palapattu et al[30] found that 52% of men with a positive node density of less than 15%, a Gleason score ≤ 7, and negative seminal vesicle invasion remained free of biochemical failure (BCF) at 5 years. Allaf et al[4] reported the therapeutic benefit of ePLND in patients with limited lymph node disease. Among men with lymph node metastases involving less than 15% of extracted nodes, the 5 year PSA progression-free survival was 43% versus 10% for the lPLND ($p = 0.01$). In another study, Daneshmand et al[31] found that a positive node density of less than 20% improved disease progression rates and survival, Table 1.

TABLE 1. **Biochemical recurrence rate and cancer-specific survival after pelvic lymph node dissection**

Study	No. of patients (yr)	Median follow up	CSS %		BCR %	
			5 yr	10 yr	5 yr	10 yr
Masterson et al[47]	175	4.4	-	-	23	19
Bader et al[12]	92	3.75	74	62	25	10
Schumacher et al[23]	122	5.6	84.50	60.10	13.90	2.90
Messing[48]	98	11.9	70	50	-	-
Palapattu et al[30]	143	6	-	-	26.50	10.90
Han et al[49]	135	6.3	-	-	26	10
Cadeddu et al[50]*	19	5.5	93	56	-	-
Gjertson et al[51]*	24	6.1	-	-	15	-
Daneshmand et al[31]*	235	11.4	-	-	54	39
Zwergel et al[52]*	147	3.5	86.50	73.70	77.40	53
Briganti et al[29]*	703	9.4	90	82	71	58

CSS = cancer-specific survival; BCR = biochemical recurrence rate
*with adjuvant therapy

Joslyn and Konety[32] demonstrated that patients undergoing excision of at least four lymph nodes (node-positive and node-negative patients) or more than 10 nodes (only node-negative patients) had a lower risk of prostate cancer-specific death at 10 years than did those who did not undergo lymphadenectomy. They concluded that performing ePLND in patients undergoing radical prostatectomy could improve the accuracy of staging and reduce the risk of prostate cancer-specific death in the long term.

However, some studies suggest that the prevalence of node-positive disease may be routinely underestimated. Ross et al[33] reported six of the 26 patients previously classified as N0 after radical prostatectomy and PLND to be positive for nodal involvement by superparamagnetic nanoparticle MRI. In another study Pagliarulo et al[34] re-examined 3914 'negative' nodes by immunohistochemistry in 274 pT3patients. They found that 13.3% of 180 patients who were originally defined as being N0 actually had lymph node metastasis. Survival rates in these patients were significantly poorer than patients who were truly lymph node negative.[34] With regard to biochemical recurrence rates of patients undergoing radical prostatectomy for low risk prostate cancer, some studies have suggested that lymph node dissection is apparently unnecessary.[35,36]

Bhatta-dhar et al[35] reviewed the records of 336 patients with favorable tumor characteristics (prostate-specific antigen 10 ng/mL or less, biopsy Gleason score 6 or less, and clinical stage T1 or T2) not receiving adjuvant or neoadjuvant therapy with (n = 140) and without (n = 196) PLND. They demonstrated that 6 year biochemical relapse-free rate for the PLND versus no-PLND group was 86% and 88%, respectively (p = 0.28) and concluded that omission of PLND in patients with favorable tumor characteristics does not adversely affect biochemical relapse rates. In a similar study Fergany et al[36] compared biochemical relapse rates of 372 and 203 patients with low risk prostate cancer undergoing radical prostatectomy with and without PLND, respectively. The 4 year progression free survival rates were 91% and 97% following radical prostatectomy with or without PLND, respectively.

Impact of frozen section in PLND

Pelvic lymph nodes excised at the time of PLND are often assessed intraoperatively using frozen section (FS) analysis and presence of lymph node metastasis is associated with poor prognosis in prostate cancer. Radical prostatectomy may be aborted if a nodal metastasis is found on FS, under the assumption that patients with metastatic cancer do not benefit from radical surgery.[37] The routine FS during PLND is common but not uniformly used, and has been questioned by several studies.[38,39] In addition, the role of FS in identifying small lymph node metastases is in question.[40]

In a large cohort, Song et al[40] evaluated the accuracy of frozen section for detection of pelvic lymph node metastases in 349 men undergoing bilateral PLND. The number of lymph nodes sampled during surgery ranged from one (in 65% of patients) to three or more (11%). Twenty-eight cases of metastatic carcinoma were detected that 11 of which were identified during FS analysis, but FS failed to detect the other 17 cases. All of 17 false negatives, contained metastases smaller than 5 mm. The sensitivity of FS analysis was 36%, with a false-negative rate of 64% in their study. They concluded that frozen section is highly sensitive for detection of large metastases, but poorly sensitive for detection of metastases smaller than 5 mm. Song and coworkers recommended that a two-step approach applied to routine FS: an initial gross examination, followed by confirmatory frozen section analysis only for grossly suspicious pelvic lymph nodes.[40]

In summary FS analysis is not accurate enough for detection of pelvic lymph node metastasis in prostate cancer.

Complications

Pelvic lymph node dissection is a challenging surgery technically and may be associated with intraoperative and postoperative complications to range from 25 to 50%.[14,41-43] Commonly described complications are the subsequent formation of lymphocele (the most common), obturator nerve injury, vascular injury, venous thrombo-embolism, pulmonary emboli, and increased operating room time.[44,45]

Clark et al[41] compared complication rates by randomly assigning patients to have an ePLND on one side of the pelvis and an lPLND on the other in 123 patients undergoing open radical prostatectomy. They reported a nonsignificant but likely clinically relevant difference, in which the side with the ePLND had more complications. In another study by Briganti et al[43] the complication rates between 767 ePLND patients and 196 lPLND patients have been compared. They found that in patients subjected to ePLND, the overall rate of complications was 19.8% versus 8.2% in those treated with lPLND ($p < 0.001$). However, in individual analyses of specific complications, lymphocele formation (drain output in excess of 50 mL/day for more than 7 days after catheter removal) rate was significantly higher after ePLND (10.3% versus 4.6%; p = 0.01).

Heidenreich et al[3] reported 9% of his ePLND cohort (average: 28 nodes) had at least one complication, which did not differ from a comparison group (8.7%), in which more-limited PLND was performed. In their study operating room time was significantly longer in patients subjected to more-extensive PLND (179 min versus 125 min; $p < 0.03$). With regard to laparoscopic PLND, Stone et al[21] demonstrated higher complication rate of laparoscopic ePLND compared with laparoscopic lPLND (35.9% versus 2%; $p < 0.001$).

Sentinel lymph node dissection - an alternative to ePLND

Despite the obvious advantage, ePLND has certain morbidity and is a time consuming procedure. To decrease the morbidity of ePLND the concept of radioisotope-guided sentinel lymph node (SLN) dissection in prostate cancer was introduced and Wawroscheck et al[22] validated it. They reported that sensitivity of the SLN staging was comparable to that of ePLND with a significant reduction in the dissection extend. SLN dissection method is a combination of imaging, surgery and histology techniques. There is no lower threshold of size in this method and SLN dissection can detect micro metastases smaller than 2 mm. Jeschke et al[46] performed laparoscopic SLN dissection in 140 patients with clinically localized prostate cancer, preceding radical prostatectomy. Mean PSA level was 8.26 ng/mL and clinical stage was T1C in 84.4% and T2 in 14.8% of the patients. They reported SLN metastases in 13.5% of patients and similar sensitivity as extended PLND with limitations in prostate cancer staging. In summary, SLN dissection has lower morbidity than ePLND with similar sensitivity, however, should be the subject of more studies.

Conclusion

There is controversy about the role of PLND for prostate cancer. Novel mapping and imaging techniques such as MR lymphography with superparamagnetic nanoparticles, suggest that even with an ePLND, up to one third of metastases will be missed. For all patients with high and intermediate risk disease, extended PLND at least for external iliac, obturator and hypogastric lymph nodes should be performed during radical prostatectomy, because the risk of positive lymph node in these patients is ≥ 2%. However, for patients with low risk disease, we recommend performing no PLND at all, because the chance of metastasis by most nomograms appears to range between 0% and 4% in these patients, Figure 3. Also, in high risk patients the extent of PLND is controversial and should be the subject of more trials to determine long term therapeutic benefit. □

References

1. Aus G, Abbou CC, Bolla M et al. EAU guidelines on prostate cancer. *Eur Urol* 2005;48(4):546-551.
2. Bader P, Burkhard FC, Markwalder R, Studer UE. Is a limited lymph node dissection an adequate staging procedure for prostate cancer? *J Urol* 2002;168(2):514-518.
3. Heidenreich A, Richter S, Thuer D, Pfister D. Prognostic parameters, complications, and oncologic and functional outcome of salvage radical prostatectomy for locally recurrent prostate cancer after 21st century radiotherapy. *Eur Urol* 2010;57(3):437-443.
4. Allaf ME, Partin AW, Carter HB. The importance of pelvic lymph node dissection in men with clinically localized prostate cancer. *Rev Urol* 2006;8(3):112-119.
5. McLaughlin AP, Saltzstein SL, McCullough DL, Gittes RF. Prostatic carcinoma: incidence and location of unsuspected lymphatic metastases. *J Urol* 1976;115(1):89-94.
6. Crawford ED, Batuello JT, Snow P et al. The use of artificial intelligence technology to predict lymph node spread in men with clinically localized prostate carcinoma. *Cancer* 2000;88(9):2105-2109.
7. Batuello JT, Gamito EJ, Crawford ED et al. Artificial neural network model for the assessment of lymph node spread in patients with clinically localized prostate cancer. *Urology* 2001;57(3):481-485.
8. Partin AW, Kattan MW, Subing ENP et al. Combination of prostate-specific antigen, clinical stage, and Gleason sum to predict pathological stage of localized prostate cancer: a multi-institutional update. *JAMA* 1997;277(18):1445-1451.
9. Briganti A, Chun FK, Salonia A et al. Validation of a nomogrampredicting the probability of lymph node invasion based on the extent of pelvic lymphadenectomy in patients with clinically localized prostate cancer. *BJU Int* 2006;98(4):788-793.
10. Briganti A, Chun FK, Salonia A et al. Validation of a nomogrampredicting the probability of lymph node invasion among patients undergoing radical prostatectomy and an extended pelvic lymphadenectomy. *Eur Urol* 2006;49(6):1019-1027.
11. Algari M, Colton MD, Seidmon EJ, Greenberg RE, Hanno PM. The staging pelvic lymphadenectomy: implication as an adjunctive procedure for clinically localized prostate cancer. *J Urol* 1997;80(2):243-246.
12. Bader P, Burkhard FC, Markwalder R, Studer UE. Disease progression and survival of patients with positive lymph nodes after radical prostatectomy. Is there a chance of cure? *J Urol* 2003;169(3):849-854.
13. Heidenreich A, von Knobloch R, Varga Z. Extended pelvic lymphadenectomy in patients undergoing radical prostatectomy: high incidence of lymph node metastases. *J Urol* 2002;167(4):1681-1686.
14. Heidenreich A, von Knobloch R, Varga Z, Hofmann R. Extended pelvic lymphadenectomy in men undergoing radical retropubic prostatectomy—data on >300 cases. *Proc ASCO* 2005;22:409s (abst. 4612).
15. Hyndman ME, Mullins JK, Pavlovich CP. Pelvic node dissection in prostate cancer: extended, limited, or not at all? *Curr Opin Urol* 2010;20(3):211-217.
16. Allaf ME, Palapattu GS, Trock BJ et al. Anatomical extent of lymph node dissection: impact on men with clinically localized prostate cancer. *J Urol* 2004;172(5 Pt 1):1840-1844.

17. Mattei A, Fuechel FG, Bhatta Dhar N et al. The template of the primary lymphatic landing sites of the prostate should be revisited: Results of a multimodality mapping study. *Eur Urol* 2008;53(1):118-125
18. Heidenreich A, Ohlmann CH, Polyakov S. Anatomical extent of pelvic lymphadenectomy in patients undergoing radical prostatectomy. *Eur Urol* 2007;52(1):29-37.
19. Weingartner K, Ramaswamy A, Bittinger A, Gerharz EW, Voge D, Riedmiller H. Anatomical basis for pelvic lymphadenectomy in prostate cancer: results of an autopsy study and implications for the clinic. *J Urol* 1996; 156(6):1969-1971.
20. Briganti A, Chun FK, Salonia A et al. Critical assessment of ideal nodal yield at pelvic lymphadenectomy to accurately diagnose prostate cancer nodal metastasis in patients undergoing radical retropubic prostatectomy. *Urology* 2007;69(1):147-151.
21. Stone NN, Stock RG, Unger P. Laparoscopic pelvic lymph node dissection for prostate cancer: comparison of the extended and modified technique. *J Urol* 1997;158(5):1891-1894.
22. Wawroschek F, Vogt H, Wengenmair H et al. Prostate lymphoscintigraphy and radio-guided surgery for sentinel lymph node identification in prostate cancer. *Urol Int* 2003;70(4):303-310.
23. Schumacher MC, Burkhard FC, Thalmann GN, Fleischmann A, Studer UE. Is pelvic lymph node dissection necessary in patients with a serum PSA < 10 ng/ml undergoing radical prostatectomy for prostate cancer? *Eur Urol* 2006;50(2):272-279.
24. Makarov DV, Trock BJ, Humphreys EB et al. Updated nomogram to predict pathologic stage of prostate cancer given prostate-specific antigen level, clinical stage, and biopsy Gleason score (Partin tables) based on cases from 2000 to 2005. *Urology* 2007;69(6):1095-1101.
25. Cagiannos I, Karakiewicz P, Eastham JA et al. A preoperative nomogram identifying decreased risk of positive pelvic lymph nodes in patients with prostate cancer. *J Urol* 2003;170(5):1798-1803.
26. Yu JB, Makarov DV, Sharma R et al. Validation of the partin nomogram for prostate cancer in a national sample. *J Urol* 2010;183(1):105-111.
27. Conrad S, Graefen M, Pichlmaer U et al. Prospective validation of an algoithm with systematic sextant biopsy to predict lymph node metastasis in patients with clinically localized prostatic carcinoma. *J Urol* 2002;167(2 Pt1):521-525.
28. DiMarco DS, Zincke H, Sebo TJ et al. The extent of lymphadenectomy for pTXN0 prostate cancer does not affect prostate cancer outcome in the prostate specific antigen era. *J Urol* 2005;173(4):1121-1125.
29. Briganti A, Karnes JR, Da Pozzo LF et al. Two positive nodes represent a significant cut-off value for cancer specific survival in patients with node positive prostate cancer. A new proposal based on a two-institution experience on 703 consecutive Nþ patients treated with radical prostatectomy, extended pelvic lymph node dissection and adjuvant therapy. *Eur Urol* 2009;55(2):261-270.
30. Palapattu GS, Allaf ME, Trock BJ et al. Prostate specific antigen progression in men with lymph node metastases following radical prostatectomy: results of long-term follow up. *J Urol* 2004;172(5 Pt 1):1860-1864.
31. Daneshmand S, Quek ML, Stein JP et al. Prognosis of patients with lymph node positive prostate cancer following radical prostatectomy: long-term results. *J Urol* 2004;172(6 Pt 1):2252-2255.
32. Joslyn SA, Konety BR. Impact of extent of lymphadenectomy on survival after radical prostatectomy for prostate cancer. *Urology* 2006;68(1):121-125.
33. Ross RW, Zietman AL, Xie W et al. Lymphotropic nanoparticle-enhanced magnetic resonance imaging (LNMRI) identifies occult lymph node metastases in prostate cancer patients prior to salvage radiation therapy. *Clin Imaging* 2009;33(4):301-305.
34. Pagliarulo V, Hawes D, Brands FH et al. Detection of occult lymph node metastases in locally advanced node-negative prostate cancer. *J Clin Oncol* 2006;24(18):2735-2742.
35. Bhatta-Dhar N, Reuther AM, Zippe C, Klein EA. No difference in six-year biochemical failure rates with or without pelvic lymph node dissection during radical prostatectomy in low-risk patients with localized prostate cancer. *Urology* 2004;63(3):528-531.
36. Fergany A, Kupelian PA, Levin HS, Zippe CD, Reddy C, Klein EA. No difference in biochemical failure rates with or without pelvic lymph node dissection during radical prostatectomy in low-risk patients. *Urology* 2000;56(1):92-95.
37. Peneau M, Villers A, Molinie V, Theis D, Soulie M. Indications for pelvic lymphadenectomy in clinically localized prostate cancer. *Prog Urol* 2004;14(3):287-294.
38. Young MP, Kirby RS, O'Donoghue EP, Parkinson MC. Accuracy and cost of intraoperative lymph node frozen sections at radical prostatectomy. *J Clin Pathol* 1999;52(12):925-927.
39. Kakehi Y, Kamoto T, Okuno H, Terai A, Terachi T, Ogawa O. Per-operative frozen section examination of pelvic nodes is unnecessary for the majority of clinically localized prostate cancers in the prostatespecific antigen era. *Int J Urol* 2000;7(8):281-286.
40. Song J, Li M, Zagaja GP, Taxy JB, Shalhav AL, Al-Ahmadie HA. Intraoperative frozen section assessment of pelvic lymph nodes during radical prostatectomy is of limited value. *BJU Int* 2010;106(10):1463-1467.
41. Clark T, Parekh DJ, Cookson MS et al. Randomized prospective evaluation of extended versus limited lymph node dissection in patients with clinically localized prostate cancer. *J Urol* 2003;169(1):145-147.
42. Paul DB, Loening SA, Narayana AS, Culp DA. Morbidity from pelvic lymphadenectomy in staging carcinoma of the prostate. *J Urol* 1983;129(6):1141-1144.
43. Briganti A, Chun FK, Salonia A et al. Complications and other surgical outcomes associated with extended pelvic lymphadenectomy in men with localized prostate cancer. *Eur Urol* 2006; 50(5):1006-1013.
44. Eifler JB. Jr LAW, Walsh PC, Pavlovich CP. Pelvic lymph node dissection is associated with venous thrombo-embolism risk during laparoscopic radical prostatectomy [abstract]. 67th Annual Mid-Atlantic AUA Meeting 2009.
45. Secin FP, Jiborn T, Bjartell AS et al. Multiinstitutional study of symptomatic deep venous thrombosis and pulmonary embolism in prostate cancer patients undergoing laparoscopic or robot-assisted laparoscopic radical prostatectomy. *Eur Urol* 2008;53(1):134-145.
46. Jeschke S, Beri A, Grüll M, Ziegerhofer J et al. Laparoscopic radioisotope-guided sentinel lymph node dissection in staging of prostate cancer. *Eur Urol* 2008;53(1):126-132.
47. Masterson TA, Bianco FJ Jr, Vickers AJ et al. The association between total and positive lymph node counts, and disease progression in clinically localized prostate cancer. *J Urol* 2006;175(4):1320-1324;discussion 1324-1325.
48. Messing EM. Disease progression and survival of patients with positive lymph nodes after radical prostatectomy. Is there a chance of cure? *J Urol* 2003;170(5):1955;author reply 1955-1956.
49. Han M, Piantadosi S, Zahurak ML et al. Serum acid phosphatase level and biochemical recurrence following radical prostatectomy for men with clinically localized prostate cancer. *Urology* 2001;57(4):707-711.
50. Cadeddu JA, Elashry OM, Snyder O et al. Effect of laparoscopic pelvic lymph node dissection on the natural history of D1 (T1-3, N1-3, M0) prostate cancer. *Urology* 1997;50(3):391-394.
51. Gjertson CK, Asher KP, Sclar JD et al. Local control and long-term disease-free survival for stage D1 (T2-T4N1-N2M0) prostate cancer after radical prostatectomy in the PSA era. *Urology* 2007;70(4):723-727.
52. Zwergel U, Lehmann J, Wullich B et al. Lymph node positive prostate cancer: long-term survival data after radical prostatectomy. *J Urol* 2004;171(3):1128-1131.