

available at www.sciencedirect.com
journal homepage: www.europeanurology.com



The Evolution of Staging of Lymph Node Metastases in Clinically Localized Prostate Cancer

Georg C. Hutterer^{a,b}, Alberto Briganti^c, Felix K.-H. Chun^d, Andrea Gallina^c,
Patrizio Rigatti^c, Francesco Montorsi^c, Pierre I. Karakiewicz^{a,e,*}

^aCancer Prognostics and Health Outcomes Unit, University of Montreal Health Center, Montreal, QC, Canada

^bDepartment of Urology, Graz Medical University, Graz, Austria

^cDepartment of Urology, Vita-Salute University San Raffaele, Milan, Italy

^dDepartment of Urology, University Medical Centre Eppendorf, Hamburg, Germany

^eDepartment of Urology, University of Montreal, Montreal, QC, Canada

Article info

Keywords:

Complications
Lymph node invasion
Pelvic lymphadenectomy
Prostate cancer
Radical prostatectomy

EU * ACME
www.eu-acme.org/
[europeanurology](http://europeanurology.com)

Abstract

Objectives: We performed a systematic literature review of the staging of pelvic lymph node metastases in clinically localized prostate cancer.

Methods: The description of the evolution of the staging paradigms of lymph node invasion (LNI) in localized prostate cancer is based on a systematic review of the English language literature on this topic.

Results: A single randomized trial addressing pelvic lymph node dissection (PLND) exists and no Cochrane review covers the topic of lymph node staging in localized prostate cancer. Most publications are based on retrospective analyses, including some large multicenter validation studies. The available reports demonstrate that extended PLND improves staging and that ideally 30 lymph nodes should be removed. This represents a shift away from either no PLND or very limited PLND, in historic series. However, not all men need to be subjected to an extended PLND. At least some patients can be effectively staged with limited PLND.

Conclusions: This review illustrates the evolution of lymph node staging in prostate cancer, which changed from no staging through limited staging to extended staging. This review provides evidence-based criteria for identifying patients at risk of LNI, as well as for defining the extent of PLND, when indicated.

© 2007 European Association of Urology and European Board of Urology.
Published by Elsevier B.V. All rights reserved.

* Corresponding author. Cancer Prognostics and Health Outcomes Unit, University of Montreal Health Center (CHUM), 1058, rue St-Denis, Montréal, QC, Canada H2X 3J4. Tel. +1 514 890 8000 35336; Fax: +1 514 412 7363.
E-mail address: pierre.karakiewicz@umontreal.ca (P.I. Karakiewicz).

1. Introduction

Pelvic lymph node dissection (PLND) represents the most accurate staging procedure for presence of lymph node invasion (LNI) in clinically localized prostate cancer [1]. Unfortunately, imaging procedures such as computed tomography (CT) and standard magnetic resonance imaging (MRI) have very limited ability to predict LNI [2–4]. 2-¹⁸F-fluoro-2-deoxyglucose positron emission tomography (FDG-PET) imaging cannot improve the prediction of LNI beyond that achieved with standard clinical variables [5]. However, the use of MRI with lymphotropic superparamagnetic nanoparticles may improve the predictive value of imaging, as evidenced by 100% accuracy in a recent report [6]. Similarly, there are no sentinel lymph nodes that could determine whether a complete lymph node dissection is needed or not, as many skip areas have been reported [7].

The extent of PLND changed over time. In some historic series very limited PLNDs or no lymph node dissections were performed [8]. In more recent series the number of removed lymph nodes was as low as five from both obturator fossae [9]. The variability in PLND extent without doubt contributed to differences in LNI prevalence, which ranges from 1.1% to 26% [10–16]. Burkhard and colleagues were among the first to systematically demonstrate that the extent of PLND is closely related to the rate of LNI [17]. Several subsequent studies confirmed these findings [11,12,18,19]. Those studies showed that extended PLNDs (ePLNDs) are able to identify nodal metastases that would not otherwise be detected by more limited PLNDs (lPLND) [20]. However, opinions differ about the ideal PLND extent and investigators disagree about who should be exposed to an ePLND, as well as on the actual extent of an ePLND [10–13]. Unfortunately, only one randomized trial addressed the topic of lymph node dissection in clinically localized prostate cancer [21]. Therefore, no strict criteria can be used to determine the indications, rationale, and extent of PLND.

In this manuscript we systematically outline the evolution of the paradigms addressing the staging of LNI. Moreover, we provide a rationale for identifying patients in whom lymph node dissection should be performed. Additionally, we provide a basis for identifying those in whom an ePLND should be considered. Finally, we review the existing guidelines addressing pelvic lymph node staging.

2. Methods

The description of the evolution of the staging paradigms of LNI in localized prostate cancer was based on a systematic

review of the English language literature on this topic. All manuscripts were retrieved from PubMed and were restricted to entries with an abstract. Key words consisted of “prostate cancer” and “lymph nodes” and “metastasis,” which resulted in 675 original articles. Of these, 43 were selected for inclusion, based on content, clinical relevance, quality, level of evidence, and year of publication [1–43].

3. PLND indications

There is lack of consensus regarding the indications for PLND. Moreover, there is a clear lack of consensus regarding the extent of PLND in those patients in whom a lymph node dissection should be performed.

A number of early investigators attempted to determine the criteria for performing a lymph node dissection in patients with clinically localized prostate cancer [22–27]. Of those, Partin and colleagues pioneered a structured and validated approach to LNI prediction, which relied on readily available variables (prostate-specific antigen [PSA], clinical stage, and biopsy Gleason sum), which could be identified prior to radical prostatectomy (RP) [27]. In 2003, a nomogram was introduced to more accurately identify patients at low risk of LNI and provided a 2% increase in predictive accuracy (PA) relative to Partin tables, within the same patient population [28]. The benefit of this nomogram, relative to the Partin tables, predominantly related to the consideration of continuously coded PSA in the nomogram versus categorically coded PSA in the Partin tables. The Partin tables or the nomogram could help in discriminating between low- and high-risk LNI patients. However, neither provided a specific cut-off for performing or not performing a lymph node dissection.

Lack of strict criteria for performing a lymph node dissection, combined with low rates of LNI in several North American series, resulted in progressively fewer nodes being removed at lymph node dissection [9,27–29]. DiMarco and colleagues examined the number of removed lymph nodes in >7000 RP patients treated between 1987 and 2000 [9]. The most recent patients had on average only 5 nodes removed compared with 14 in the most historic ones.

4. Pathologic limitations of the PLND yield

PLND yield can be maximized by sensitizing the pathologist to the importance of performing the most detailed and systematic search for lymph nodes within the resected package. At most centers,

the standard identification of lymph nodes is based on tactile examination of the lymph node package and dissection of palpably identifiable nodes [30]. This technique can result in lack of identification of small or even microscopic lymph nodes. To circumvent this problem, lymph nodes may be submitted in separate packages [30]. Alternatively, the lymph node specimens may be processed and sectioned *in toto*. Finally, fat dissolution techniques may be used to dissociate the fibrofatty tissue within the specimen from lymph nodes. All of these methods can improve the nodal yield at pathologic specimen evaluation.

5. LNI versus prognosis

Interestingly, the extent of lymph node dissection failed to reflect biochemical recurrence (BCR), distant recurrence (DR), and prostate cancer-specific survival rates [9]. Similar results were reported by Masterson and colleagues. They studied >5000 patients, where the extent of PLND failed to significantly increase the rate of BCR [31]. Bhattadhar and colleagues added to the evidence that the extent of PLND does not affect the rate of BCR by demonstrating equality of BCR rates in patients with or without a PLND [32].

However, others found that the extent of PLND does affect the rate of BCR. Allaf and colleagues examined the rate of BCR in patients with up to 15% of affected lymph nodes and found that those subjected to more extensive PLND (11.6 vs. 8.9 nodes removed) had significantly lower BCR (10% vs. 43%) at 5 yr after RP [12]. Bader and colleagues further suggested that the extent of PLND may affect symptomatic progression and prostate cancer specific mortality [16]. Unfortunately, the uncontrolled nature of these reports cannot rule out that their findings are due to bias.

Although, there is consensus that the extent of PLND affects the accuracy of prostate cancer staging, there is clearly no consensus that the extent of PLND affects prognosis. To date no group of investigators has convincingly demonstrated a survival benefit related to the use of ePLND versus lPLND.

6. Complications of PLND

Of numerous studies, one addressed the effect of PLND extent on LNI rate and its complications in a randomized fashion [21]. The investigators demonstrated positive lymph nodes in 4 of 100 ePLND

samples versus 3 of 100 in lPLND samples. Complications were higher when ePLND was performed. Prostate cancer progression was not assessed. Nonetheless, the study suggested that the potential benefit related to better staging might be associated with more complications. Complications were not invariably high in all ePLND series, as evidenced by a cohort of Bader et al, where an overall complication rate of 2.1% was recorded [10]. Conversely, a substantially higher complication rate was reported by Heidenreich et al [11].

However, when the cumulative literature on PLND complications is examined, the rate of complications ranges from 2% to 51% [10-13,21,33-38]. Therefore, PLND may not be an entirely innocuous procedure, even in the hands of the most experienced surgeons. This suggests the presence of a risk-benefit ratio, where complications are weighed against better staging.

Unfortunately, the recent literature previously lacked reports in which complication rates are adjusted according to the extent of PLND, as defined by the number of removed lymph nodes. Moreover, virtually all available publications do not take into account confounding variables, such as age, stage, PSA, and grade.

The largest contemporary series ($n = 963$) addressing complications after PLND demonstrated that ePLND predisposed to significantly higher rate of lymphoceles (10.3% vs. 4.6%; $p = 0.01$) [39]. Similarly, ePLND translated into a longer hospital stay (9.9 vs. 8.2 d; $p < 0.001$). Moreover, when all prospectively recorded complications were examined as a group, ePLND patients were at a 2-fold higher risk relative to their lPLND counterparts.

Receiver operator characteristics (ROC) analyses addressing the relationship between PLND extent and the rate of overall complications, according to the number of removed lymph nodes, were performed. The ROC coordinates showed a direct relationship between the complication rate and nodal count (Fig. 1). For the first time it was demonstrated that the removal of every additional lymph node increased the complication rate in a nonnegligible fashion.

7. PLND extent and LNI rate

Bader and colleagues as well as Heidenreich and colleagues pioneered a systematic assessment of the concept of PLND extent and LNI rate. Bader et al demonstrated a false-negative rate of 5% versus 16% in the series of Heidenreich et al [10,11]. Other investigators confirmed these

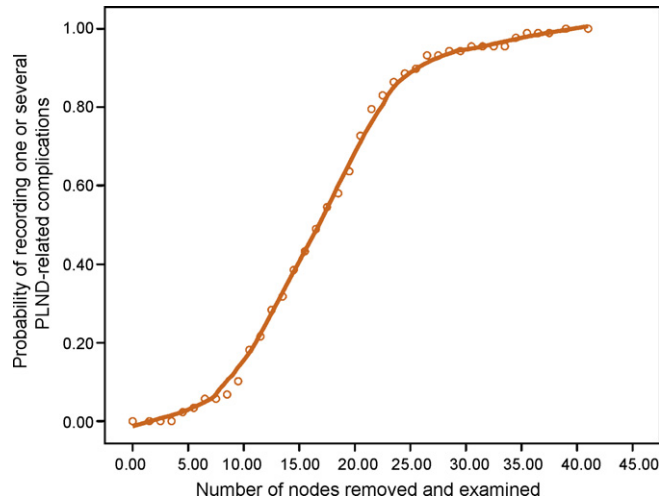


Fig. 1 – The relationship between the number of lymph nodes removed and examined (x-axis) and the probability of recording one or several PLND-related complications. PLND = pelvic lymph node dissection.

findings [37,38,40,41]. The relationship between PLND extent and the rate of LNI was recently examined by Briganti and colleagues who demonstrated that ePLND increases the ability to identify LNI in two ways. First, they reported a virtually linear increase in PA when the extent of PLND was increased (Fig. 2) [18]. Moreover, the same group of investigators demonstrated that the ability to

correctly predict the likelihood of LNI increases in a virtually exponential fashion, when the number of removed nodes is increased (Fig. 3) [19]. Interestingly, the probability of correctly predicting the rate of LNI was close to zero when <10 nodes were removed. Conversely, virtually perfect ability was reported when ≥ 30 lymph nodes were removed.

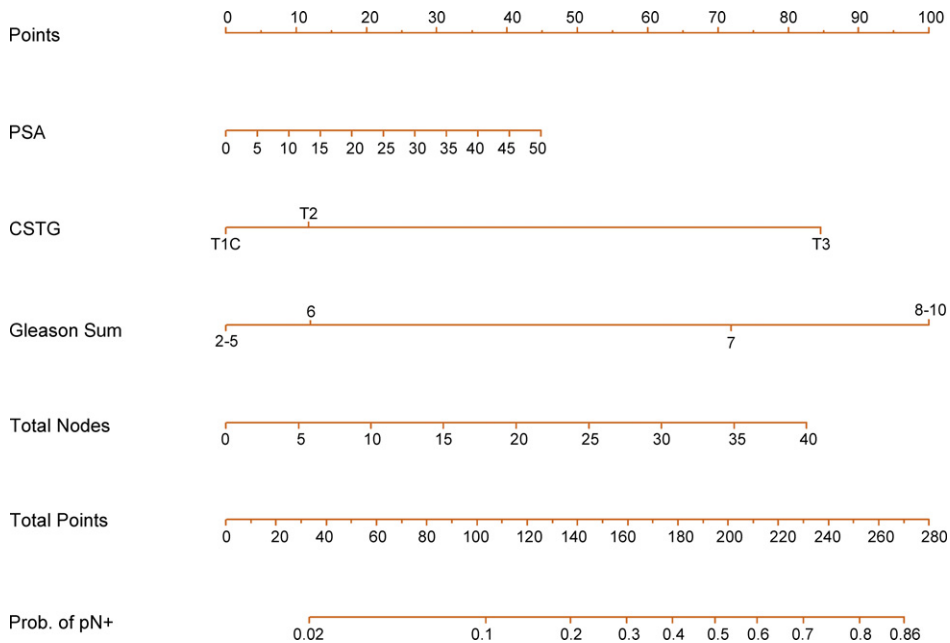


Fig. 2 – Nomogram predicting the probability of finding positive lymph nodes (pN+) at pelvic lymphadenectomy, according to pretreatment prostate-specific antigen (PSA), clinical stage (CSTG), biopsy Gleason sum (Gleason Sum), and the number of removed and examined lymph nodes (Total Nodes). It is noteworthy that the maximum effect of the number of removed and examined lymph nodes approximates the effect of clinical T3 prostate cancer, exceeds that of biopsy Gleason sum 7, and exceeds that of PSA of 50 ng/ml.

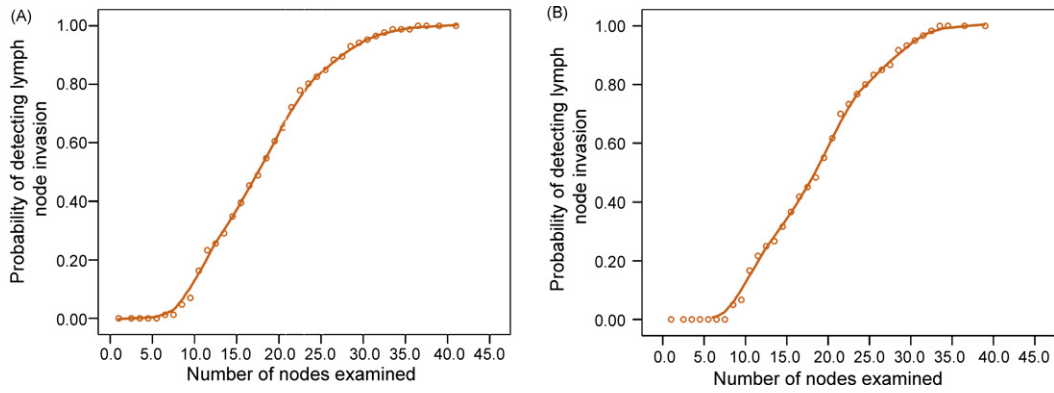


Fig. 3 – The relationship between the number of removed and examined lymph nodes and the probability of detecting lymph node invasion (LNI) in all patients (A) or in patients with biopsy Gleason sum ≥ 7 (B).

8. Contemporary tools predicting the probability of LNI

Cagiannos and colleagues as well as Partin and colleagues developed tools for prediction of LNI in patients subjected to standard or lPLND [28,29]. As reported by DiMarco and colleagues, such patients had as few as five lymph nodes removed [9]. Based on the limited extent of PLNDs performed in those series, neither the Partin tables nor the Cagiannos nomogram can be used to identify patients at risk of LNI, if an ePLND is contemplated. To circumvent this limitation, Briganti and colleagues developed a nomogram predicting the rate of LNI in patients

subjected to an ePLND (Fig. 4) [20]. Their nomogram was 76% accurate and relies on PSA, clinical stage, and biopsy Gleason sum to quantify the probability of LNI. To the best of our knowledge this nomogram represents the first tool designed for ePLND patients and awaits a prospective validation. The use of this tool could provide the most bias-free assessment of the probability of LNI, if an ePLND is considered. Conversely, an alternative nomogram can be used, if more limited PLND is planned [18]. This second nomogram (78.6% accurate) allows quantification of the effect of extending or limiting the PLND on the rate of LNI.

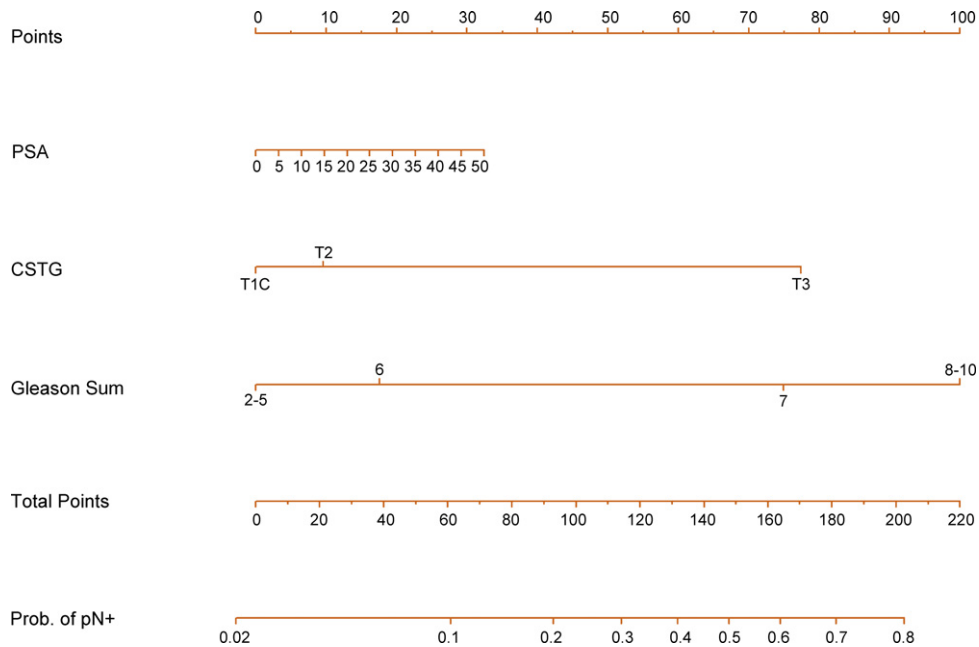


Fig. 4 – Nomogram predicting the probability of finding positive lymph nodes (pN+) at extended pelvic lymphadenectomy (minimum 10 nodes removed and examined), according to pretreatment prostate-specific antigen (PSA), clinical stage (CSTG), and biopsy Gleason sum (Gleason Sum).

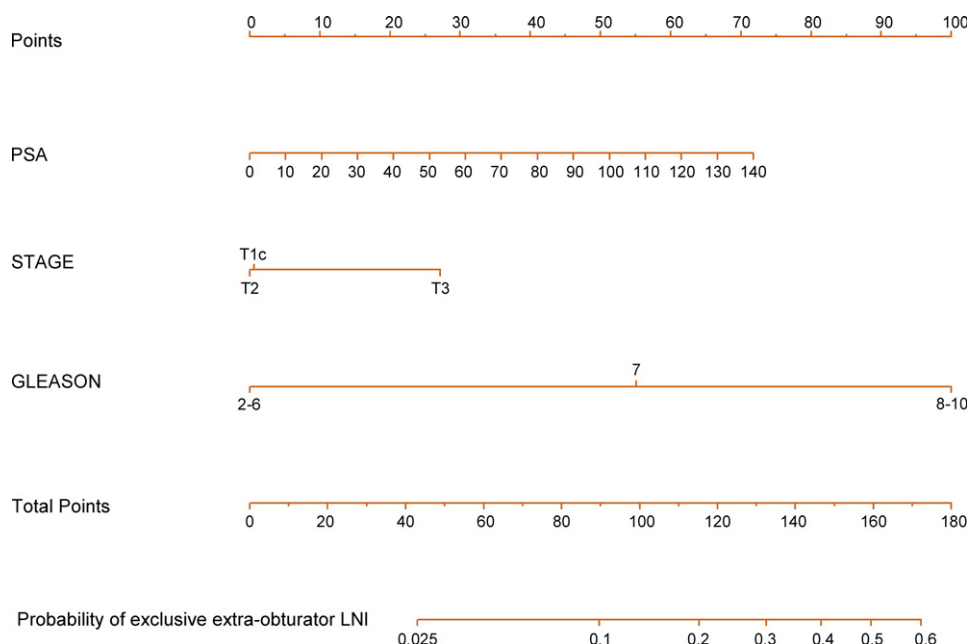


Fig. 5 – Nomogram predicting the probability of exclusive nonobturator lymph node invasion (LNI) in patients undergoing extended pelvic lymphadenectomy, according to pretreatment prostate-specific antigen (PSA), clinical stage (STAGE), and biopsy Gleason sum (GLEASON).

Briganti and colleagues also addressed the question of who should be subjected to an ePLND versus who may benefit from a more limited PLND, where only the obturator nodes are removed [42]. Within this nomogram (80.2% accurate), the authors demonstrated that an obturator PLND may indeed be safely performed in a number of patients (Fig. 5). When <10% probability of LNI outside of the obturator fossa was predicted, the nomogram had 99% negative predictive value. In Briganti's series 62% of patients fell into this category and in these men the PLND could have been safely (99%) limited to the obturator nodes. By extrapolation, such practice might result in a 50% decrease in the rate of complications.

9. Alternatives to the use of LNI predictive tools

The presence of positive lymph nodes may be predicted with nomograms. However, because these tools are based on probabilities, they may be complemented with other diagnostic aids in patients with an *a priori* low risk of LNI. For example, the Briganti et al ePLND nomogram predicts a 13% probability of LNI for individuals with PSA 7 ng/ml, biopsy Gleason sum 6/10, and clinical stage T2c [20]. Conversely, the nomogram predicts a 3% probability of LNI in patients

with PSA 2.5 ng/ml, biopsy Gleason sum 6/10, and clinical stage T1c. In such low-risk patients an alternative method to improve the PLND yield may consist of radioguided PLND. This technique was assessed by Weckermann and colleagues who demonstrated between 6.8% and 10.7% prevalence of LNI in patients with favorable clinical characteristics, such as PSA ≤ 10 ng/ml, Gleason score ≤ 6 , and clinical stage $\leq T2c$ [43]. With certainty technical improvements of this modality will continue to improve its value.

10. PLND guidelines

Several professional associations and Cancer Networks publish guidelines aimed at standardizing the management of common malignancies. In European countries, European Association of Urology (EAU) guidelines are most widely in use. In North America, the American Urological Association (AUA) and the National Comprehensive Cancer Network (NCCN) provide guidelines for the management of prostate cancer. Of these two, the NCCN guidelines have been recently updated, whereas the AUA guidelines await an update.

The EAU 2005 Prostate Cancer Guidelines confirm that accurate lymph node staging can only be achieved intraoperatively [1]. These guidelines rely

on a categorical classification of the risk of LNI, where patients with clinical stage $\leq T2$, PSA < 20 ng/ml, and Gleason score of ≤ 6 are not considered as candidates for a PLND, based on the predicted risk of $< 10\%$. By exclusion, a PLND should be considered in all other men in whom a RP is contemplated.

The most recent (1995) AUA Prostate Cancer Clinical guidelines also agree that PLND represents the gold standard for the evaluation of regional metastases (www.auanet.org/guidelines/). This benefit is contrasted with the increase in morbidity and operating room time, when a PLND is performed at RP. A 20% PLND complication rate is quoted, despite the fact that the AUA guidelines refer to PLNDs, as ePLNDs were neither performed nor discussed in this era. The AUA guidelines are less specific with regard to PLND indications. They state that the "Evidence is mounting that the majority of patients who are candidates for a radical prostatectomy or radiotherapy have a very low risk of having positive pelvic lymph nodes. When the serum PSA concentration, tumor grade and local clinical stage used together are below certain levels, a pelvic lymph node dissection may not be necessary because, as noted on page 15, the probability of positive lymph nodes is extremely low." Obviously the validity of these recommendations is somewhat undermined by their historic nature.

The NCCN Prostate Cancer Guidelines were updated in 2005 and include the 2001 update of the Partin tables, which among others predict the likelihood of LNI (www.nccn.org). The Partin predictions are used throughout the NCCN guidelines to indicate whether a PLND should be performed. In patients with clinical stage cT1–T2a, Gleason score 2–6, and PSA < 10 ng/ml prostate cancer, the PLND is optional and the Partin table-derived risk calculation is not suggested. In intermediate-risk prostate cancer patients (cT2b–T2c or Gleason score 7 or PSA 10–20 ng/ml), the PLND is indicated unless the Partin table-derived probability of LNI is $< 3\%$. In high-risk patients (cT3a or Gleason 8–10 or PSA > 20 ng/ml), PLND is recommended regardless of the Partin LNI predictions.

Either little or no detail is provided by all three guidelines on the extent of PLND. The use of a cut-off point by the EAU guidelines represents a potential limitation. The NCCN guidelines rely on a dynamic tool, which predicts the individual probability of LNI. The use of a nomogram cut-off point of 3% is clearly superior to the use of a single cut-off point because it allows a greater extent of interaction between clinical stage, biopsy Gleason, and serum PSA. Nonetheless, the use of the Partin tables for LNI risk prediction may undermine the

validity of thus obtained LNI predictions because the Partin tables were developed on patients treated with RP between 1994 and 2000, which no longer can be qualified as contemporary. Finally, the AUA guidelines LNI recommendations, which were released in 1995 and based on even more historic data, also cannot be applied to contemporary patients.

11. Conclusions

Based on the previous paragraphs a number of conclusions can be drawn. (1) Limited PLND is associated with a high rate of false-negative findings. Conversely, more extended PLND results in higher rates of LNI. (2) In patients with clinically localized prostate cancer LNI cannot be reliably predicted with imaging studies or sentinel lymph node dissection. (3) Increasing the extent of lymph node dissection results in better ability to predict the true rate of LNI and approximately 30 nodes need to be removed and examined to accurately predict whether positive lymph nodes are present. (4) The downside of more extensive PLND consists of a higher rate of complications. Specifically, the rate of lymphoceles might be higher. Moreover, patients subjected to more extended PLND have a longer hospital stay. (5) Previous tools predicting the rate of LNI no longer apply to contemporary patients, who are subjected to ePLNDs. The risk of LNI can be accurately quantified with contemporary ePLND nomograms. (6) Not all contemporary patients with clinically localized prostate cancer who require a lymph node dissection need to be subjected to an ePLND. A nomogram can accurately identify those patients in whom an obturator lymph node dissection may be safely performed. (7) Although the extent of PLND is directly proportional to the rate of LNI, there are no data indicating that the extension of PLND improves cancer control or survival. Most available data indicate that the extent of PLND is unrelated to BCR, DR, or prostate cancer-specific survival. (8) In 2007, PLND remains a purely staging procedure.

Conflicts of interest

The authors have nothing to disclose.

Acknowledgments

Pierre I. Karakiewicz is partially supported by the Fonds de la Recherche en Santé du Québec, the

CHUM Foundation, the Department of Surgery and Les Urologues Associés du CHUM.

References

- [1] Aus G, Abbou CC, Bolla M, et al. European Association of Urology. EAU guidelines on prostate cancer. *Eur Urol* 2005;48:546-51.
- [2] Wolf Jr JS, Cher M, Dall'era M, Presti Jr JC, Hricak H, Carroll PR. The use and accuracy of cross-sectional imaging and fine needle aspiration cytology for detection of pelvic lymph node metastases before radical prostatectomy. *J Urol* 1995;153:993-9.
- [3] Paik ML, Scolieri MJ, Brown SL, Spirnak JP, Resnick MI. Limitations of computerized tomography in staging invasive bladder cancer before radical cystectomy. *J Urol* 2000;163:1693-6.
- [4] Tempany CM, McNeil BJ. Advances in biomedical imaging. *JAMA* 2001;285:562-7.
- [5] Schoder H, Herrmann K, Gonen M, et al. 2-[18F]fluoro-2-deoxyglucose positron emission tomography for the detection of disease in patients with prostate-specific antigen relapse after radical prostatectomy. *Clin Cancer Res* 2005;11:4761-9.
- [6] Harisinghani MG, Barentsz J, Hahn PF, et al. Noninvasive detection of clinically occult lymph-node metastases in prostate cancer [erratum correction in *N Engl J Med* 2003;349:1010]. *N Engl J Med* 2003;348:2491-9.
- [7] Wawroschek F, Wagner T, Hamm M, et al. The influence of serial sections, immunohistochemistry, and extension of pelvic lymph node dissection on the lymph node status in clinically localized prostate cancer. *Eur Urol* 2003;43:132-7.
- [8] Porter CR, Kodama K, Gibbons RP, et al. 25-year prostate cancer control and survival outcomes: a 40-year radical prostatectomy single institution series. *J Urol* 2006;176:569-74.
- [9] DiMarco DS, Zincke H, Sebo TJ, Slezak J, Bergstralh EJ, Blute ML. The extent of lymphadenectomy for pTXNO prostate cancer does not affect prostate cancer outcome in the prostate specific antigen era. *J Urol* 2005;173:1121-5.
- [10] Bader P, Burkhard FC, Markwalder R, Studer UE. Is a limited lymph node dissection an adequate staging procedure for prostate cancer? *J Urol* 2002;168:514-8.
- [11] Heidenreich A, Varga Z, Von Knobloch R. Extended pelvic lymphadenectomy in patients undergoing radical prostatectomy: high incidence of lymph node metastasis. *J Urol* 2002;167:1681-6.
- [12] Allaf ME, Palapattu GS, Trock BJ, Carter HB, Walsh PC. Anatomical extent of lymph node dissection: impact on men with clinically localized prostate cancer. *J Urol* 2004;172:1840-4.
- [13] Stone NN, Stock RG, Unger P. Laparoscopic pelvic lymph node dissection for prostate cancer: comparison of the extended and modified techniques. *J Urol* 1997;158:1891-4.
- [14] Cheng L, Zincke H, Blute ML, Bergstralh EJ, Scherer B, Bostwick DG. Risk of prostate carcinoma death in patients with lymph node metastasis. *Cancer* 2001;91:66-73.
- [15] Palapattu GS, Allaf ME, Trock BJ, Epstein JI, Walsh PC. Prostate specific antigen progression in men with lymph node metastases following radical prostatectomy: results of long-term followup. *J Urol* 2004;172:1860-4.
- [16] 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;169:849-54.
- [17] Burkhard FC, Studer UE. The role of lymphadenectomy in prostate cancer. *Urol Oncol* 2004;22:198-202.
- [18] Briganti A, Chun FK, Salonia A, et al. Validation of a nomogram predicting the probability of lymph node invasion based on the extent of pelvic lymphadenectomy in patients with clinically localized prostate cancer. *BJU Int* 2006;98:788-93.
- [19] 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;69:147-51.
- [20] Briganti A, Chun FK, Salonia A, et al. Validation of a nomogram predicting the probability of lymph node invasion among patients undergoing radical prostatectomy and an extended pelvic lymphadenectomy. *Eur Urol* 2006;49:1019-27.
- [21] 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;169:145-7.
- [22] Bruce AW, O'Cleireachain F, Morales A, Awad SA. Carcinoma of the prostate: a critical look at staging. *J Urol* 1977;117:319-22.
- [23] Brendler CB, Cleeve LK, Anderson EE, Paulson DF. Staging pelvic lymphadenectomy for carcinoma of the prostate risk versus benefit. *J Urol* 1980;124:849-50.
- [24] Catalona WJ, Stein AJ. Accuracy of frozen section detection of lymph node metastases in prostatic carcinoma. *J Urol* 1982;127:460-1.
- [25] Livne PM, Huben RP, Wolf RM, Pontes JE. Early complications of combined pelvic lymphadenectomy and radical prostatectomy versus lymphadenectomy alone. *Prostate* 1986;8:313-8.
- [26] Rogers E, Gurpinar T, Dilliogluligil O, et al. The role of digital rectal examination, biopsy Gleason sum and prostate-specific antigen in selecting patients who require pelvic lymph node dissections for prostate cancer. *Br J Urol* 1996;78:419-25.
- [27] Partin AW, Kattan MW, Subong EN, et al. Combination of prostate-specific antigen, clinical stage, and Gleason score to predict pathological stage of localized prostate cancer. A multi-institutional update [erratum correction in *JAMA* 1997;278:118]. *JAMA* 1997;277:1445-51.
- [28] 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;170:1798-803.
- [29] Partin AW, Mangold LA, Lamm DM, Walsh PC, Epstein JI, Pearson JD. Contemporary update of prostate cancer staging nomograms (Partin tables) for the new millennium. *Urology* 2001;58:843-8.
- [30] Bochner BH, Herr HW, Reuter VE. Impact of separate versus en bloc pelvic lymph node dissection on the number of lymph nodes retrieved in cystectomy specimens. *J Urol* 2001;166:2295-6.
- [31] Masterson TA, Bianco Jr FJ, Vickers AJ, et al. The association between total and positive lymph node counts, and disease progression in clinically localized prostate cancer. *J Urol* 2006;175:1320-4.
- [32] 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;63:528-31.
- [33] Paul DB, Loening SA, Narayana AS, Culp DA. Morbidity from pelvic lymphadenectomy in staging carcinoma of the prostate. *J Urol* 1983;129:1141-4.
- [34] Augustin H, Hammerer P, Graefen M, et al. Intraoperative and perioperative morbidity of contemporary radical retropubic prostatectomy in a consecutive series of 1243 patients: results of a single center between 1999 and 2002. *Eur Urol* 2003;43:113-8.
- [35] Herrell SD, Trachtenberg J, Theodorescu D. Staging pelvic lymphadenectomy for localized carcinoma of the prostate: a comparison of 3 surgical techniques. *J Urol* 1997;157:1337-9.
- [36] Rassweiler J, Seemann O, Schulze M, Teber D, Hatzinger M, Frede T. Laparoscopic versus open radical prostatectomy: a comparative study at a single institution. *J Urol* 2003;169:1689-93.
- [37] Jeschke S, Nambirajan T, Leeb K, Ziegerhofer J, Segal W, Janetschek G. Detection of early lymph node metastases in prostate cancer by laparoscopic radioisotope guided sentinel lymph node dissection. *J Urol* 2005;173:1943-6.
- [38] McDowell II GC, Johnson JW, Tenney DM, Johnson DE. Pelvic lymphadenectomy for staging clinically localized prostate cancer. Indications, complications, and results in 217 cases. *Urology* 1990;35:476-82.
- [39] 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;50:1006-13.
- [40] Wawroschek F, Vogt H, Weckermann D, Wagner T, Harzmann R. The sentinel lymph node concept in prostate cancer—first results of gamma probe-guided sentinel lymph node identification. *Eur Urol* 1999;36:595-600.
- [41] Brenot-Rossi I, Bastide C, Garcia S, et al. Limited pelvic lymphadenectomy using the sentinel lymph node procedure in patients with localized prostate carcinoma: a pilot study. *Eur J Nucl Med Mol Imaging* 2005;32:635-40.
- [42] Briganti A, Chun FK-H, Salonia A, et al. A nomogram for staging of exclusive nonobturator lymph node metastases in men with localized prostate cancer. *Eur Urol* 2007;51:112-20.
- [43] Weckermann D, Wawroschek F, Harzmann R. Is there a need for pelvic lymph node dissection in low risk prostate cancer patients prior to definitive local therapy? *Eur Urol* 2005;47:45-51.

CME questions

Please visit www.eu-acme.org/europeanurology to answer these CME questions on-line. The CME credits will then be attributed automatically.

- An extended pelvic lymph node dissection (ePLND) increases the probability of finding lymph node invasion (LNI) from
 - 5% to >10%
 - 2% to 20%
 - 5% to <10%
 - >10% to >20%
- In patients with clinically localized prostate cancer, lymph node invasion (LNI) can be accurately predicted with
 - Computed tomography (CT)
 - Magnetic resonance imaging (MRI)
 - 2-[¹⁸F]fluoro-2-deoxyglucose positron emission tomography (FDG-PET)
 - Sentinel lymph node biopsy
 - None of the above
- Ideally, how many lymph nodes need to be removed to accurately predict the presence of lymph node invasion (LNI)?
 - 10
 - 20
 - 30
 - 40
- Extended pelvic lymph node dissection (ePLND) is associated with
 - Lower or same rate of complications as limited PLND (IPLND)
 - Longer hospital stay
 - significantly higher blood loss
 - higher rate of deep venous thrombosis (DVT)

5. Relative to a limited pelvic lymph node dissection (lPLND), an extended PLND (ePLND) is associated with
- A. Better survival rate
 - B. Lower distant progression rate
 - C. higher complication rate
 - D. lower biochemical recurrence (BCR)
6. The benefit of extended pelvic lymph node dissection (ePLND) relative to limited PLND (lPLND) has been convincingly demonstrated with regard to
- A. Cost
 - B. Staging
 - C. Technical difficulty
 - D. Disease-specific survival