BJUI
BJU INTERNATIONAL

Percentage of positive biopsies predicts lymph node involvement in men with low-risk prostate cancer undergoing radical prostatectomy and extended pelvic lymphadenectomy

Axel Heidenreich, David Pfister, David Thüer and Bernhard Brehmer

Department of Urology, RWTH University Aachen, Aachen, Germany

Accepted for publication 10 March 2010

Study Type – Diagnostic (exploratory cohort)
Level of Evidence 2b

What's known on the subject? and What does the study add?
The current retrospective study evaluates predictive clinical parameters associated with lymph node metastasis in a homogeneous cohort of 499 men with low-risk prostate cancer who underwent radical prostatectomy. Low-risk profile and <50% of biopsies involved with cancer are strong predictors of metastasis-free lymph nodes so that patients do not have to undergo extended pelvic lymphadenectomy.

OBJECTIVE

To evaluate preoperative predictive risk factors associated with lymph node metastases (LNM) in a cohort of low-risk prostate cancer (PCA) patients.

PATIENTS AND METHODS

The charts of 499 patients were retrospectively reviewed to identify prognostic risk factors for the presence of LNM. Pathohistological data and Gleason score of the radical prostatectomy (RP) specimen, number of removed nodes, number of positive lymph nodes, and anatomical distribution of LNM were tabulated and evaluated. A correlation between clinical stage, preoperative serum prostate-specific antigen (PSA), biopsy Gleason score, number of biopsies taken, percentage of positive biopsies and the presence of LNM were calculated. All 499 men underwent retropubic RP and extended pelvic lymphadenectomy (EPLND).

RESULTS

LNM were identified in 29 (5.8%) patients. A prediction model based on clinical stage, PSA, and biopsy Gleason score had a predictive accuracy of 79.2%. The addition of number of positive biopsies and % positive cores improved its predictive accuracy to 81.5% and 87.8%, respectively. The predicted frequency of LNM by the original nomogram was 7.4% and differed by less than 3% with the actual observation of LNM. The predictive accuracy of the nomogram was 81.5% as compared with 87.8% of the prediction model of this study.

CONCLUSIONS

The percentage of positive cores involved with PCA is the most reliable predictor of LNM and indicates the need for EPLND. The Briganti nomogram has been validated and a general applicability for predicting the presence of LNM was proven.

KEYWORDS

Prostate cancer, pelvic lymphadenectomy, lymph node metastases, D1 disease, nomogram, prediction, staging lymphadenectomy

INTRODUCTION

The role and the anatomical extent of pelvic lymphadenectomy in men undergoing radical prostatectomy (RP) for localized prostate cancer (PCA) remains a matter of intense and controversial debate [1–4]. Currently, pelvic lymphadenectomy remains the most accurate staging procedure for the detection of occult microscopic lymph node metastasis (LNM) even in the presence of innovative imaging modalities such as ^{11}choline-PET scan and high-resolution MRI using lymphotropic superparamagnetic nanoparticles [5–7]. The rationale for performing pelvic lymphadenectomy in PCA lies in the accurate diagnosis of occult microscopic LNM in order to stratify patients who might benefit from adjuvant therapeutic measures [5,8].

Recent data suggest that an anatomically adequate, extended pelvic lymphadectomy (EPLND) might be necessary to detect occult lymph node involvement in men undergoing RP [1–3]. Also, the possibility of a positive impact on disease progression by EPLND has been suggested, however, these data have been inconsistent in the literature [9–13].

The advent of PSA has resulted in a significant migration towards an earlier PCA stage in newly diagnosed cases, with an apparently lower risk of LNM; the risk decreasing from rates of 21% to 40% in the 1980s to only 6% in 2010 [14]. Furthermore, the ability to better predict a low likelihood of lymph node involvement also seems to have been improved by the use of retrospectively

TABLE 1 Preoperative predictors of lymph node invasion – descriptive statistics

Variable	All patients	Patients with pN0 disease	Patients with pN+ disease	*P* value
Number of patients	499	470	29	
Age	63.2 (50–75)	63.6 (52–75)	62.9 (50–74)	n.s.
Clinical stage				
cT1c	384 (77%)	371 (78.9%)	22 (75.9%)	n.s.
cT2a	115 (23%)	99 (21.1%)	7 (24.1%)	n.s.
PSA	7.01 (2.5–10.0)	7.10 (2.5–10.0)	6.94 (2.6–9.5)	n.s.
Biopsy Gleason sum				
≤4	64	62/64 (96.9%)	2/64 (3.1%)	<0.001
5 & 6	435	408/435 (93.8%)	27/435 (6.2%)	<0.001
Number of biopsies taken				
6	286 (57.3%)	258 (54.9%)	14 (48.3%)	n.s.
8–10	83 (16.7%)	80 (17%)	6 (20.7%)	n.s.
≥12	129 (25.8%)	132 (28.1%)	9 (31%)	n.s.
Number of total cores	8.0 (6–12)	8.5 (6–12)	8.4 (6–12)	n.s.
Number of positive cores	2.41 (1–10)	2.23 (1–6)	4.57 (1–10)	<0.001
Percentage of positive cores	31.8 (8–68)	30.7 (8–68)	42.9 (17–88)	<0.001

PSA, prostate-specific antigen; n.s., not significant.

developed nomograms attempting to identify patients at low risk and at high risk at time of RP [15–20]. However, none of the recently published series strictly focussed on a homogeneous cohort of low-risk PCA patients to evaluate predictive factors of lymph node involvement. It was, therefore, the aim of this retrospective study to identify preoperative risk factors associated with LNM.

PATIENTS AND METHODS

Between January 2002 and August 2009, 499 consecutive patients underwent retropubic RP and EPLND for clinically localized PCA. The patients represented 76% of the total number of patients operated during the same time period for PCA (499/656). All patients demonstrated a preoperative low-risk profile according to the D'Amico criteria defined by a PSA serum level <10 ng/mL, clinical stage cT1c – 2a and biopsy Gleason score ≤6 [14]. None of the patients included in this retrospective study had received neoadjuvant androgen deprivation therapy. Transrectal, ultrasound guided biopsies were performed by the referring urologists in private practice or by our institution. 70% of all biopsy specimens were evaluated by the same pathologist. A sextant biopsy was performed in 286 (57.4%) patients and 83 (16.6%) and 129 (25.9%) patients underwent octant biopsy or a set of ≥12 biopsies. Baseline demographics and clinicopathological preoperative parameters are shown in Table 1.

In all patients, pathohistological data and Gleason score of the radical prostatectomy specimen, number of removed nodes per patient, number of positive lymph nodes, and anatomical distribution of lymph node metastases were tabulated and evaluated. A correlation between preoperative serum PSA, number of biopsies, number of positive biopsies, percentage of positive biopsies, biopsy Gleason score and the presence of LNM was calculated.

Radical prostatectomy was performed as described recently [21]. EPLND was performed via a short lower midline incision before RP, as described previously [1,22]. In brief, the cranial border of lymph node dissection was defined by the ureteric crossing of the common iliac artery, laterally all lymphatic tissue overlying the external iliac artery, but not the pelvic side wall, was removed. Inferiorly, the femoral canal represents the caudal margin of dissection and posteromedially all lymphatic tissue surrounding the obturator nerve, obturator vessels and the internal iliac artery was removed completely. Lymphatic vessels were either clipped or ligated, but no electrocautery was used in order to achieve complete occlusion of the lymphatics and to prevent lymphoceles. The dissected lymph nodes were sent for pathohistological analysis in separate packages, fixed in neutral buffered 4% formaldehyde for 24 h and placed in acetone for lipolysis. All lymph nodes were cut in 3-mm sections, embedded in paraffine and stained with haematoxylin and eosin. All specimens were histologically analysed, irrespective of size and macroscopic morphology.

Data were stratified for statistical analysis according to preoperative PSA, clinical stage, primary and secondary biopsy Gleason score, number of biopsies taken, percentage of positive biopsies. Associations between potential predictive markers and the presence of LNM were analysed by univariate analysis using the Student's *t*-test for continuous variables and the Fisher exact test for categorical variables. The association between each predictive factor and the presence of lymph node metastases was assessed by univariate and multivariate logistic regression analysis). Significant factors on univariate analysis were entered into multivariate analysis (Cox proportional hazards regression analysis) with $P < 0.05$ considered significant. All tests were done with StatView™ (SAS Institute Inc., Cary, NC, USA).

Validation data were obtained from the 499 consecutive patients. Table 2 lists the clinical and biopsy characteristics of the validation series and the original patients used to develop the nomogram. Each patient's data were entered into a logistic model formula derived from the original publication of Briganti *et al.* [20] and each individual probability of lymph node invasion was calculated. Calibration of the nomogram was assessed by comparing its predicted probability of LNM with actual presence of LNM. All statistical tests performed were two sided.

RESULTS

The mean number of removed lymph nodes per patient was 21 (10–42). The mean surgical time was 126 (90–155) min; the mean surgical time for EPLND only was 32 (25–43) min. The mean blood loss was 320 (150–800) mL with a transfusion rate of 0.5% (2/499). Peri- and postoperative complications are listed in Table 3; in total, 9.5% of the patients developed one or two complications.

Lymph node metastases were identified in 29 (5.8%) patients, whereas no lymph node involvement was identified in 470 (94.2%) of

TABLE 2 Descriptive statistics of preoperative variables for the cohorts

Variable	Current series	Briganti *et al.* [20]
Number of patients	499	278
Age	63.2 (50–75)	66.2 (47–83)
Clinical stage		
cT1c	384 (77%)	165 (59.4%)
cT2a	115 (23%)	105 (37.8%, cT2a-2c)
cT2b-c	0	8 (2.9%)
cT3	0	
PSA	7.01 (2.5–10.0)	9.9 (1.1–49.9)
Biopsy Gleason sum		
≤4	64 (12.8%)	12 (4.3%)
5 & 6	435 (87.2%)	171 (61.5%)
7	0	75 (27%)
8–10	0	20 (7.2%)
Number of biopsies taken		
6	286 (57.3%)	
8–10	83 (16.7%)	
≥12	129 (25.8%)	
Number of total cores	8.0 (6–16)	12 (3–23)
Number of positive cores	2.41 (1–10)	5.1 (1–19)
Percentage of positive cores	31.8 (8–68)	44.7 (7.1–100)

PSA, prostate-specific antigen.

TABLE 3 Peri- and postoperative complications

Complication	*n* (%)
Transfusion rate	3 (0.6%)
Rectal injury	1 (0.2%)
Ureteric injury	1 (0.2%)
Lesion of the obturator nerve	1 (0.2%)
Deep venous thrombosis	19 (3.8%)
Pulmonary embolus	2 (0.4%)
Myocardial infarction	1 (0.2%)
Pneumonia	2 (0.4%)
Lymphocele, total*	41 (8.2%)
Lymphocele, intervention	8 (1.6%)

**All patients underwent routine ultrasonography at day 1, 3, 5 and 42 after radical prostatectomy for the detection of lymphoceles irrespective of symptoms.*

TABLE 4 Uni- and multivariate logistic regression analysis for the prediction of lymph node metastases with the predictive accuracy for the entire cohort

	Univariate logistic¥ regression analysis		Multivariate logistic regression analysis			
			Base model*	Base model plus number of positive cores	Base model plus % positive cores	Base model plus # and % positive cores
Predictor	OR, *P* value	Predictive accuracy	OR; *P* value	OR, *P* value	OR; *P* value	OR; *P* value
PSA	0.98; ns	52.3%	1.0; 0.35	1.02; 0.35	0.99; 0.29	0.98; 0.45
Clinical stage cT2a vs cT1c	0.95; ns	56.3%	0.90; 0.5	0.92; 0.6	0.95; 0.3	0.96; 0.35
Biopsy Gleason sum 5/6 vs 2–4	2.5; <0.001	65.4%	2.3; 0.09	2.4; 0.08	2.5; 0.1	2.3; 0.09
Number of positive cores	1.6; <0.001	72.4%	–	1.5; 0.01	–	1.7; 0.002
Percentage of positive cores	1.9; <0.001	82.3%	–	–	2.0; 0.001	1.9; 0.003
Multivariate predictive accuracy	–	–	79.2%	81.5%	87.8%	87.3%

**Base model: prostate-specific antigen (PSA), clinical stage and biopsy Gleason sum.*

men undergoing RP and EPLND. Twelve out of 29 patients (42.8%) exhibited only 1 positive lymph node, whereas 10 (34.3%) and 7 (22.8%) patients demonstrated 2 and ≥2 positive lymph nodes, respectively. Sixteen (55.1%) lymph node metastases were anatomically located in the obturator fossa and around the external iliac artery; 9 (31.4%) and 4 (14.3%) metastases were located in the area of the internal iliac artery and the common iliac artery, respectively.

Radical prostatectomy and EPLND was performed in 64 patients with a biopsy Gleason score of ≤4 (12.9%) and in 435 patients with a biopsy Gleason score of 5 and 6 (87.1%). In patients with Gleason score 4, RP and not active surveillance or low-dose brachytherapy was performed at the wish of the patient. Whereas only 2/64 (3.1%) patients with biopsy Gleason score 4 exhibited LNM, positive lymph nodes were identified in 27/435 (6.2%) patients with a biopsy Gleason score 5 and 6 ($P < 0.03$).

Table 1 shows the descriptive statistics of the entire cohort according to the presence or absence of LNM. In the cohort of low-risk PCA patients, only the number of positive cores and the percentage of positive cores differed significantly between patients with or without LNM ($P < 0.001$). The preoperative variables serum PSA, clinical stage, number of biopsies taken, and biopsy Gleason score did not differ statistically significant between lymph node positive and negative patients.

Table 4 shows the univariate and multivariate analysis in which the association between predictors and the presence of LNM is assessed. In univariate predictive accuracy

analysis, percentage of positive biopsies was the most accurate predictor of LNM (82.3%) followed by the number of positive cores (72.4%), whereas the other variables demonstrated no significant differences between the groups. Also, in multivariate analysis both variables remained statistically significant predictors for the presence of LNM with the percentage of positive cores being the predictive parameter with the highest accuracy. Of the men with lymph node involvement 91.4% (26/29) demonstrated ≥50% of the cores being involved with cancer, whereas only 17.6% of men without nodal disease showed more than 50% of the biopsy cores being positive for PCA. Sensitivity and specificity to predict lymph node involvement are 91.4% and 82.1%, respectively; positive and negative values are 24% and 99.3%, respectively. These parameters were used to develop and validate patterns to predict the probability of LNM. The parameters were subjected to 10 000 bootstrap resamples for internal validation. After 10 000 bootstrap resamples the predictive accuracy of the model including the percentage of positive biopsies was 87.8%.

With regard to the prediction of LNM, 22/27 (81.5%) patients with LNM would have been identified correctly. The diagnostic benefit of EPLND, therefore, was reduced to 1.4% (7/499 patients) of the entire cohort. Based on these data, a total of 492 EPLNDs could have been omitted without a negative impact on oncological outcome.

Table 2 lists the preoperative serum PSA levels, clinical stages and biopsy Gleason scores from our patients and the original patients used to develop the nomogram. Differences exist with regard to the pre-treatment PSA level which was lower in the original patients ($P < 0.03$). Also, locally advanced prostate cancer and biopsy Gleason score 8–10 PCA were identified more frequently in the original data set ($P < 0.001$). However, if the hypothesis is correct that the nomogram will accurately predict LNM across a range of patients, these differences should be of no consequence.

Using the Briganti nomogram [20], the predictive accuracy of the nomogram including the percentage of positive biopsy cores was 81.5% as compared with a predictive accuracy of 87.5% for the prediction model developed in our study.

DISCUSSION

It is well accepted that EPLND at time of RP is the only reliable diagnostic procedure to achieve individual and adequate staging information with regard to lymph node involvement [5]. However, the extent of pelvic lymphadenectomy (PLND) (none/limited vs extended) and the candidates most suitable for this procedure are still a matter of intense debate [1–4].

It remains unclear if any additional information and any therapeutic benefit can be retrieved from EPLND in men with low-risk PCA. Recent studies have demonstrated that a limited PLND has no positive impact on biochemical disease-free survival in men undergoing RP for low- risk PCA [11,12]. Masterson *et al.* [13] have shown that EPLND correlates significantly with freedom from biochemical relapse in men without nodal involvement.

In this study comprising 499 men with low-risk PCA we explored the ability of the key variables preoperative serum PSA, clinical stage and percentage of positive biopsies to predict the presence of LNM. Positive lymph nodes were identified in 5.8% of the entire cohort and 3.1% and 6.2% of men with a biopsy Gleason score ≤4 and 5 to 6 harboured positive lymph nodes.

The frequency of LNM in our study is in accordance with previous reports focussing on low-risk PCA [2,3,8]. Allaf *et al.* [9] reported positive lymph nodes in 3.2% and 1.1% in a cohort of 4000 men undergoing extended and limited lymphadenectomy, respectively. The lower incidence of occult pelvic LNM as compared with our series might be attributable to the lower total number of dissected lymph nodes in their EPLND group (11 vs 21). The low number of dissected lymph nodes is in accordance with recent results from CaPSURE [23] which demonstrate that the proportion of men undergoing PLND in conjunction with RP decreased from 94% to 80% from 1992 to 2004. A mean of only 5.7 lymph nodes were removed which is far too few for adequate locoregional staging and for any therapeutic benefit. The frequency of positive lymph nodes in our series is comparable with the recently published data by Weckermann *et al.* [3] and Schumacher *et al.* [2]. Weckermann *et al.* [3] reported on a frequency of 5.4% and 11.3% in men with low-risk PCA and cT2a/b and cT2c disease, respectively. They identified positive lymph nodes in 5.4% of patients with low-risk PCA and positive biopsies in only one lobe; if the biopsy Gleason score was ≤6 only 2.8% of the patients were found to have positive lymph nodes.

Schumacher *et al.* [2] describe positive lymph nodes in 11% of 231 patients with a preoperative serum PSA <10 ng/mL irrespective of clinical stage and biopsy Gleason score. The frequency of positive lymph nodes, however, in men with organ-confined disease and a prostatectomy specimen Gleason score ≤6 was only 3.4%, whereas the incidence increased significantly with increasing pT-stage and Gleason score. Despite the low frequency of positive lymph nodes it would still be helpful to identify predictive variables for the presence of LNM as established nodal disease will change the clinical management of PCA [24].

Since the decision-making process to perform EPLND is made preoperatively and has to be based on reliable clinical variables, we assessed all available preoperative parameters to accurately predict the presence of LNM. To our knowledge, no previous study has addressed the clinical utility of these variables for predicting LNM in a homogenous cohort of low-risk PCA patients subjected to RP. Our data demonstrate that the combination of PSA, clinical stage and the presence of ≥50% positive cores can accurately predict the presence of LNM with a true positivity of 87%. In multivariate analysis, the percentage of positive cores was the most significant predictor ($P < 0.001$) and surpassed all other variables. The mean number of positive cores was inferior to the percentage of positive biopsies and cannot be used as a reliable prognosticator for predicting LNM. Stratifying patients with ≤ and ≥50% of biopsies being involved with PCA we were able to correctly identify 23/35 (65.7%) patients with LNM. Combining the predictors of low-risk PCA (PSA <10 ng/mL, biopsy Gleason sum ≤6 and clinical stage cT1c/cT2a) with a high number of positive biopsies would have spared EPLND in 492 patients with a false-negative rate of only 1.4%. Therefore, our current strategy is only to perform EPLND in low-risk PCA with more than 50% of the biopsy cores being involved with cancer.

Others have tested the use of systematic biopsies to improve the preoperative prediction of pelvic LNM in patients with

clinically organ confined disease [15–20]. Conrad *et al.* [15] found that the number of cores containing any Gleason grade 4 or 5 pattern were the prognostic parameters with the highest accuracy in predicting LNM. The total number of positive cores alone was not able to predict the lymph node status with sufficient accuracy. The developed predictive algorithm was retrospectively validated by another 443 patients and the authors demonstrated a negative predictive value of 97.5% for the low-risk group (no biopsy with Gleason grade 4/5) and a specificity of 94.1% [16]. However, the limitations of these investigations are the correlation of biopsy findings with a limited pelvic lymph node dissection only. In another retrospective analysis, Freedland *et al.* [18] identified the percentage of tissue with cancer and the percentage of positive biopsies as significant risk factors for predicting adverse pathohistological findings of RP such as positive surgical margins, seminal vesicle invasion, LNM and time to PSA recurrence. The study, however, has severe limitations with regard to the predictability of LNM since only 6% of the entire cohort harboured LNM and a limited PLND was performed. Quinn *et al.* [19] evaluated the importance of percentage of positive biopsies and the presence or peri-neural invasion in a cohort of 696 men with localized PCA treated with RP. The authors identified a figure of >50% positive biopsies involved with cancer as an independent predictor for LNM and disease recurrence after RP. However, this finding became statistically nonsignificant when the model was restricted to patients with PSA <10 ng/mL which might be the result of a heterogenous patient cohort, a low number of patients with LNM, and a limited PLND. This approach was recently addressed by Briganti *et al.* [20] who demonstrated that easily available parameters such as PSA, clinical stage, and detailed biopsy information can accurately predict lymph node involvement. The authors evaluated the prognostic significance of the percentage of positive cores in a heterogeneous cohort of 278 men with clinically localized or locally advanced PCA. In their study, the authors found a predictive accuracy of 83.7% which is somewhat inferior to our findings of an accurate prediction in 87% of the patients with LNM.

Briganti *et al.* [20] also developed a nomogram to predict LNM in patients with clinically organ-confined PCA which had a predictive accuracy of 83%. Herein, we report the results of a validation study on external and homogenous data originated from a group of patients with low-risk PCA treated at a single-center. The comparison of the predicted outcome and the actual observation of LNM differed by less than 3% and it demonstrates the general applicability of the nomogram, even in patients with low-risk PCA who undergo both nerve-sparing RP and EPLND. The data derived from our study have significant implications for the practising urologist who might individually counsel patients with regard to the necessity of EPLND. A limitation of our study is that a mean of only 8 biopsies have been taken in the entire cohort. However, the other series evaluating the predictive accuracy of the percentage of positive biopsies also reported on a mean number of 7–8 biopsies [18–20]. In addition, although the nomogram has been validated internally and externally, it still lacks prospective, multicenter validation which is under way in an initiated prospective randomized clinical phase-III trial of the Association of Oncological Urology of the German Cancer Society. Furthermore, we still do not have proven evidence that EPLND has a positive impact on progression-free and cancer-specific survival [10]. Considering the potentially increased morbidity [25,26], EPLND should be limited to high-risk groups until the data of the initiated prospective randomized clinical phase-III trial are available.

CONCLUSION

The risk of pelvic LNM is 5.8% in a homogenous cohort of patients with low-risk PCA. The percentage of positive cores involved with cancer represents the most reliable predictor of LNM. The Briganti nomogram has been validated externally and a general applicability to predict the presence of LNM was proven.

ACKNOWLEDGEMENTS

We are grateful to Professor Francesco Montorsi and Dr Alberto Briganti for their critical review of the manuscript.

CONFLICT OF INTEREST

None declared.

REFERENCES

1 **Heidenreich A, Varga Z, von Knobloch R.** Extended pelvic lymphadenectomy in patients undergoing radical prostatectomy in prostate cancer: high incidence of lymph node metastases. *J Urol* 2002; **167**: 1681–6
2 **Schuhmacher 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**: 272–9
3 **Weckermann D, Goppelt M, Dorn R, Wawroschek F, Harzmann R.** Incidence of positive pelvic lymph nodes in patients with prostate cancer, a prostate-specific antigen (PSA) level of ≤10 ng/mL and biopsy Gleason score ≤6, and their influence on PSA progression-free survival after radical prostatectomy. *BJU Int* 2006; **97**: 1173–8
4 **DiMarco DS, Zincke H, Sebo TJ, Slezak J, Bergstralh EJ, Blute ML.** The extent of pelvic lymphadenectomy for pTxPn0 prostate cancer does not influence prostate cancer outcomes in the prostate specific antigen era. *J Urol* 2005; **173**: 1121–5
5 **Heidenreich A, Aus G, Bolla M *et al.*** EAU guidelines on prostate cancer. *Eur Urol* 2008; **53**: 68–80
6 **Harisinghani MG, Barentsz J, Hahn PF *et al.*** Noninvasive detection of clinically occult lymph node metastases in prostate cancer. *N Engl J Med* 2003; **348**: 2491–9
7 **De Jong IJ, Pruim J, Elsinga PH, Vaalburg W, Meninsk HJ.** Preoperative staging of pelvic lymph nodes in prostate cancer by 11C-choline PET. *J Nucl Med* 2003; **44**: 331–5
8 **Heidenreich A, Ohlmann CH, Polyakov S.** Anatomical extent of pelvic lymphadenectomy in patients undergoing radical prostatectomy. *Eur Urol* 2007; **52**: 29–37
9 **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
10 **Joslyn SA, Konety BR.** Impact of extent of lymphadenectomy on survival after radical prostatectomy for prostate cancer. *Urology* 2006; **68**: 121–5
11 **Berglund RK, Sadetsky N, DuChane J, Carroll PR, Klein EA.** Limited pelvic

lymph node dissection at the time of radical prostatectomy does not affect 5-year failure rates for low, intermediate and high risk prostate cancer: results from CaPSURE. *J Urol* 2007; **177**: 526–9

12 **Weight CJ, Reuther AM, Gunn PW, Zippe CR, Dhar NB, Klein EA.** Limited pelvic lymph node dissection does not improve biochemical relapse-free survival at 10 years after radical prostatectomy in patients with low-risk prostate cancer. *Urology* 2008; **71**: 141–5

13 **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**: 1320–4

14 **D'Amico AV, Whittington R, Malkowicz SB *et al.*** Biochemical outcome after radical prostatectomy, external beam radiation therapy, or interstitial radiation therapy for clinically localized prostate cancer. *JAMA* 1998; **280**: 969–74

15 **Conrad S, Graefen M, Pichlmeier U, Henke RP, Hammerer PG, Huland H.** Systematic sextant biopsies improve preoperative prediction of pelvic lymph node metastases in patients with clinically localized prostatic carcinoma. *J Urol* 1998; **159**: 2023–9

16 **Haese A, Epstein JI, Huland H, Partin AW.** Validation of a biopsy based pathologic algorithm for predicting lymph node metastases in patients with clinically localized prostatic carcinoma. *Cancer* 2002; **95**: 1016–21

17 **Graefen M, Ohori M, Karakiewicz PI *et al.*** Assessment of the enhancement in predictive accuracy provided by systematic biopsy in predicting outcome for clinically localized prostate cancer. *J Urol* 2004; **171**: 200–4

18 **Freedland SJ, Aronson WJ, Csathy GS *et al.*** Comparison of percentage of total prostate needle biopsy tissue with cancer to percentage of cores with cancer for predicting PSA recurrence after radical prostatectomy: results from the SEARCH database. *Urology* 2003; **61**: 742–7

19 **Quinn DI, Henshall SM, Brenner PC *et al.*** Prognostic significance of preoperative factors in localized prostatic carcinoma treated with radical prostatectomy: importance of percentage of biopsies that contain tumor and the presence of biopsy perineural invasion. *Cancer* 2003; **97**: 1884–93

20 **Briganti A, Karakiewicz PI, Chun FKH *et al.*** Percentage of positive biopsy cores can improve the ability to predict lymph node invasion in patients undergoing radical prostatectomy and extended pelvic lymphadenectomy. *Eur Urol* 2007; **51**: 1573–81

21 **Graefen M, Walz J, Huland H.** Open retropubic nerve-sparing radical prostatectomy. *Eur Urol* 2006; **49**: 38–48

22 **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

23 **Kawakami J, Meng MV, Sadetsky N *et al.*** Changing patterns of pelvic lymphadenectomy for prostate cancer: results from CaPSURE. *J Urol* 2006; **176**: 1382–6

24 **Briganti A, Blute ML, Eastham JH *et al.*** Pelvic lymph node dissection in prostate cancer. *Eur Urol* 2009; **55**: 1251–65

25 **Clark T, Parkeh 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**: 145–8

26 **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

Correspondence: Axel Heidenreich, Department of Urology, RWTH University Aachen, Pauwelsstr. 30, 52074 Aachen, Germany.
e-mail: aheidenreich@ukaachen.de

Abbreviations: **LMN**, lymph node metastases; **PCA**, prostate cancer; **RP**, radical prostatectomy; **EPLND**, extended pelvic lymphadenectomy; **PLND**, pelvic lymphadenectomy.