

Original article

# Does increasing the nodal yield improve outcomes in contemporary patients without nodal metastasis undergoing radical prostatectomy?

Luis A. Kluth, M.D.<sup>a,c,1</sup>, Evangelos Xylinas, M.D.<sup>a,d,1</sup>, Malte Rieken, M.D.<sup>a,e</sup>,  
Felix K.-H. Chun, M.D.<sup>c</sup>, Harun Fajkovic, M.D.<sup>f</sup>, Andreas Becker, M.D.<sup>c,g</sup>,  
Pierre I. Karakiewicz, M.D.<sup>g</sup>, Niccolo Passoni, M.D.<sup>h</sup>, Michael Herman, M.D.<sup>a</sup>,  
Yair Lotan, M.D.<sup>i</sup>, Christian Seitz, M.D.<sup>j</sup>, Paul Schramek, M.D.<sup>j</sup>, Mesut Remzi, M.D.<sup>k</sup>,  
Wolfgang Loidl, M.D.<sup>l</sup>, Bertrand Guillonnet, M.D.<sup>m</sup>, Morgan Rouprêt, M.D., Ph.D.<sup>a,n</sup>,  
Alberto Briganti, M.D.<sup>h</sup>, Douglas S. Scherr, M.D.<sup>a</sup>, Markus Graefen, M.D.<sup>o</sup>,  
Ashutosh K. Tewari, M.D.<sup>a</sup>, Shahrokh F. Shariat, M.D.<sup>a,b,j,\*</sup>

<sup>a</sup> Department of Urology, Weill Cornell Medical College, New York Presbyterian Hospital, New York, NY

<sup>b</sup> Division of Medical Oncology, Weill Cornell Medical College, New York Presbyterian Hospital, New York, NY

<sup>c</sup> Department of Urology, University Medical-Center Hamburg-Eppendorf, Hamburg, Germany

<sup>d</sup> Department of Urology, Cochin Hospital, Assistance Publique-Hopitaux de Paris, Paris Descartes University, Paris, France

<sup>e</sup> Department of Urology, University Hospital of Basel, Basel, Switzerland

<sup>f</sup> Department of Urology, Landeskrankenhaus St. Poelten, Sankt Poelten, Austria

<sup>g</sup> Cancer Prognostics and Health Outcomes Unit, University of Montreal Health Center, Montreal, Quebec, Canada

<sup>h</sup> Department of Urology, Vita-Salute University, Milan, Italy

<sup>i</sup> Department of Urology, University of Texas Southwestern Medical Center, Dallas, TX

<sup>j</sup> Department of Urology, Medical University of Vienna, Vienna, Austria

<sup>k</sup> Department of Urology, Landeskrankenhaus Korneuburg, Korneuburg, Austria

<sup>l</sup> Prostate cancer center, Krankenhaus Barmherzige Schwestern Linz, Linz, Austria

<sup>m</sup> Department of Urology, Diaconesses Hospital, Paris 6 University, Paris, France

<sup>n</sup> Academic Department of Urology of la Pitié-Salpêtrière, Assistance Publique-Hôpitaux de Paris, University Paris VI, Faculté de médecine Pierre et Marie Curie, Paris, France

<sup>o</sup> Prostate cancer center, Martini-Clinic, Hamburg, Germany

Received 21 May 2013; received in revised form 22 June 2013; accepted 24 June 2013

## Abstract

**Objectives:** To determine if the number of lymph nodes (LNs) removed is an independent predictor of biochemical recurrence (BCR) in patients without LN metastases undergoing radical prostatectomy (RP).

**Material and methods:** Retrospective analysis of 7,310 patients treated at 7 centers with RP and pelvic LN dissection for clinically localized prostate cancer between 2000 and 2011. Patients with LN metastases ( $n = 398$ ) and other reasons (stated later in the article) ( $n = 372$ ) were excluded, which left 6,540 patients for the final analyses.

**Results:** Overall, median biopsy and RP Gleason score were both 7; median prostate specific antigen level was 6 ng/ml (interquartile range [IQR]: 5); and median number of LNs removed was 6 (IQR: 8). A total of 3,698 (57%), 2,064 (32%), and 508 (8%) patients had  $\geq 6$ ,  $\geq 10$ , and  $\geq 20$  LNs removed, respectively. Patients with more LNs removed were older, had a higher prostate specific antigen level, had higher clinical and pathologic T stage, and had higher RP Gleason score (all  $P < 0.002$ ). Within a median follow-up of 21 (IQR: 16) months, more LNs removed was associated with an increased risk of BCR (continuous:  $P = 0.021$ ; categorical:  $P = 0.014$ ). In multivariable analyses that adjusted for the effects of standard clinicopathologic factors, none of the nodal stratifications predicted BCR.

<sup>1</sup>Both authors contributed equally to this work.

\* Corresponding author. Tel.: +431-4-040-02616; fax: +431-4040-02332.

E-mail address: sfshariat@gmail.com (Shahrokh F. Shariat).

**Conclusions:** The number of LNs did not have any prognostic significance in our contemporary cohort of patients with LN-negative prostate cancer. This suggests that the risk of missed clinically significant micrometastasis may be minimal in patients currently treated with RP and having a lower LN yield. © 2014 Elsevier Inc. All rights reserved.

**Keywords:** Prostate cancer; Pelvic lymph node dissection; Lymph node metastasis; Nodal yield; Biochemical recurrence

## 1. Introduction

Pelvic lymph node dissection (PLND) is the only reliable technique to ensure an accurate nodal status in prostate cancer (PCa) [1,2]. PLND is not without morbidity and its extent and therapeutic benefit is still a matter of debate [3–5]. More extensive PLND has been shown to improve survival in patients with lymph node (LN)-positive or LN-negative bladder cancer or both [6,7].

Regarding PCa, several studies have suggested that a more extensive PLND has a staging and therapeutic benefit in patients with LN-positive PCa [8–11]. In patients with LN-negative PCa, few studies found that more extensive PLND is associated with a survival advantage owing to the removal of clinically significant micrometastases [4,12]. However, in patients treated with radical prostatectomy (RP) nowadays who have a lower-risk disease, a more extensive PLND may not improve outcomes [5,13].

The notion that only a very few LNs are needed to be removed to define low-risk patients as node negative is mainly driven by the extremely low rate of LN involvement (LNI) in this patient group. Indeed, even extending the nodal yield to all anatomical nodal pelvic areas would result in a LN metastasis rate of <2% in these patients [14]. Conversely, one of the hypotheses that a higher nodal yield is required to achieve accurate node-negative staging in men at higher risk of LN disease is based on the highly complex anatomical pathway of LN metastasis in PCa. LN dissemination in PCa, indeed, does not follow a predefined pathway of metastatic spread but rather different lymphatic routes tributary to several primary lymphatic landing sites [15,16].

The aim of this study was to determine if the number of LNs removed, especially in patients with LN-negative PCa with unfavorable clinicopathologic features, is associated with the risk of biochemical recurrence (BCR) in a contemporary RP cohort.

## 2. Material and methods

### 2.1. Patients and data collection

This was an institutional review board–approved study, with all participating sites providing the necessary institutional data sharing agreements before the initiation of the study. Seven academic centers from Europe, Canada, and the United States provided data. The study comprised 7,310 patients who underwent RP with bilateral PLND for PCa between 2000 and 2011. No patient received preoperative radiotherapy, hormonal treatment, or chemotherapy. None of the patients received adjuvant hormonal therapy, and 164

(2.5%) patients received postoperative radiotherapy within 12 months of RP at prostate specific antigen (PSA) levels less than 0.2 ng/ml (i.e., adjuvant radiotherapy).

No patient had distant metastatic disease at the time of RP. Indication for RP was biopsy-proven PCa. All patients without follow-up (FU) ( $n = 281$ ), missing RP Gleason score ( $n = 25$ ), missing PSA value ( $n = 23$ ), or PSA > 50 ng/ml (i.e. possible metastatic disease) [17] ( $n = 43$ ) were excluded from analyses. Patients with LN metastasis ( $n = 398$ ) were also excluded from the analyses. LNs were examined grossly, and all of lymphoid tissue was submitted for histologic examination. The extent of LN dissection was at the surgeon's discretion, and extended LN dissection was not routinely performed.

### 2.2. Clinical and pathologic evaluation

All surgical specimens were processed according to standard pathologic procedures as outlined elsewhere [18]. Dedicated genitourinary pathologists assigned pathologic stage, which was reassigned according to the 2007 American Joint Committee on Cancer Tumor, Node, Metastasis staging system when necessary.

### 2.3. FU

FU was conducted according to institutional protocols. Generally, patients were seen postoperatively quarterly within the first year, semiannually in the second year, and annually thereafter. Digital rectal examination and PSA evaluation were performed at each visit. The primary end point was defined as PSA > 0.2 ng/ml on 2 occasions.

### 2.4. Statistical analysis

Nodal yield was analyzed as continuous variable, tertiles, and using the cutoffs of  $\geq 6$ ,  $\geq 10$ , and  $\geq 20$  removed LNs. Using the cutoff of 6 LNs is based on the median number of 6 LNs removed in the whole cohort of patients. The cutoff 10 is based on previous reports indicating that more than 10 LNs is the minimum number required for standard LN dissection [11,19]. The cutoff of 20 LNs is based on previous reports indicating an extended LN dissection [2,20]. The Kolmogorov-Smirnov test was used to assess the distribution of variables. The Fisher exact and chi-squared tests were used to evaluate the associations between categorical variables. Differences in variables with a continuous distribution across categories were assessed using Mann-Whitney U (2 categories) and Kruskal-Wallis tests (3 and more categories). The correlation between 2 continuous and ranked variables

Download English Version:

<https://daneshyari.com/en/article/6194529>

Download Persian Version:

<https://daneshyari.com/article/6194529>

[Daneshyari.com](https://daneshyari.com)