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# Lymph node yield during radical prostatectomy does not impact rate of biochemical recurrence in patients with seminal vesicle invasion and node-negative disease

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**Abstract**

**Objectives:** Seminal vesicle invasion (SVI) is a risk factor for poor oncologic outcome in patients with prostate cancer. Modifications to the pelvic lymph node dissection (PLND) during radical prostatectomy (RP) have been reported to have a therapeutic benefit. The present study is the first to determine if lymph node yield (LNY) is associated with a lower risk of biochemical recurrence (BCR) for men with SVI.

**Methods:** A total of 220 patients from 2 high-volume institutions who underwent RP without adjuvant treatment between 1990 and 2015 and had prostate cancer with SVI (i.e., pT3b) were identified, and 21 patients did not undergo lymph node dissection. BCR was defined as a postoperative PSA $>$ 0.2 ng/mL, or use of salvage androgen deprivation therapy (ADT) or radiation. Multivariable Cox proportional hazards models were used to determine whether LNY was predictive of BCR, controlling for PSA, pathologic Gleason Score, pathologic lymph node status, NCCN risk category, etc. The Kaplan-Meier method was used to determine 3-year freedom from BCR.

**Results:** Median number of lymph nodes sampled were 7 (IQR: 3–12; range: 0–35) and 90.5% underwent PLND. The estimated 3-year BCR rate was 43.9%. Results from multivariable analysis demonstrated that LNY was not significantly associated with risk of BCR overall (HR $=$ 1.00, 95% CI: 0.98–1.03; $P = 0.848$) for pN0 (HR $=$ 0.99, 95% CI: 0.97–1.03; $P = 0.916$) or pN1 patients (HR $=$ 0.96, 95% CI: 0.88–1.06; $P = 0.468$). Overall, PSA (HR $=$ 1.02, $P < 0.001$) and biopsy Gleason sum $\geq 8$ (HR $=$ 1.81, $P = 0.001$) were associated with an increased risk of BCR, and increasing LNY increased the likelihood of detecting $>2$ positive lymph nodes (OR $=$ 1.27, 95% CI: 1.06–1.65, $P = 0.023$).

**Conclusion:** Seminal vesicle invasion is associated with an increased risk of BCR at 3 years, primarily due to pathologic Gleason score and PSA. Although greater lymph node yield is diagnostic and facilitates more accurate pathologic staging, our data do not show a therapeutic benefit in reducing BCR. 

*Keywords:* Pelvic lymphadenectomy; Lymph node yield; Advanced prostate cancer; Biochemical recurrence

## 1. Introduction

The presence of seminal vesicle invasion (SVI) is a poor prognostic factor for patients with prostate cancer (PC) undergoing radical prostatectomy (RP) [1]. Further, 5-year biochemical recurrence (BCR) rates have been reported to range from 53% to 86% [2,3] and, at 10-years, 65% in men with SVI and N0 disease [4,5]. Additionally, men with SVI at the time of RP are more likely to have other poor pathologic features, such as extracapsular extension and positive surgical margins, also known to independently increase BCR [6,7]. As patients with these pathologic features are closely followed and often offered salvage therapy, a modification in surgical technique that reduces risk of BCR would reduce the need for secondary interventions. Further, the presence of lymph node involvement found in roughly 24% of SVI patients is associated with

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even worse BCR outcomes, and lymph node resection may potentially further reduce the need for salvage intervention [6–8].

Greater freedom from BCR has been variably noted in patients undergoing PLND during RP [9–11]. In 2006, Joslyn and Konety [10] used the SEER database to report that increasing lymph node yield (LNY) reduced the 10-year prostate cancer specific mortality (PCSM). The study was limited due to the inability to adjust for hormonal therapy intervention. Subsequently, Briganti and associates [12] reported clear evidence of oncologic benefit to PLND. In distinction, Masterson and associates found no evidence of a therapeutic benefit of reducing BCR with more extensive PLND [11]. Kim et al. demonstrated a lack of benefit of LNY on BCR in intermediate- and high-risk patients. [13] Evidence of therapeutic benefit remains divided.

Because of their increased risk for BCR, we propose that men with SVI are a good population to model [14,15] whether increasing lymph node yield could have a therapeutic benefit. The present study is the first to analyze whether greater LNY during RP in men with SVI results in improved BCR rates.

## 2. Materials and methods

### 2.1. Study data and population

Between 1990 and 2015, 289 patients with SVI (pT3b) PCa underwent RP at 2 academic institutions. High-volume institutions were selected such that variation between surgeon and surgical technique would be mitigated. Standard clinical and pathological characteristics were prospectively collected and entered into electronic databases at their respective institutions, under approved institutional review board protocols. Prior to transmission to the principal investigator (KB), datasets were de-identified such that the case-series was considered nonhuman participants research under the US Department of Health and Human Services′ Office for Human Research Protection and did not require institutional review board (IRB) review or informed consent. Patients without follow-up data ($n = 8$) or who received adjuvant treatment, including chemotherapy, radiation, or androgen deprivation therapy ($n = 61$), were excluded, leaving 220 patients for retrospective cohort analysis.

### 2.2. Study variables

Fifteen data points per patient were requested: age (years), year of surgery, preoperative prostate-specific antigen (PSA) level (ng/mL), National Comprehensive Cancer Network (NCCN) risk category, clinical t-stage, clinical Gleason score (cGS), pathological t-stage, pathological Gleason score (pGS), prostate volume (ml), lymph node involvement (LNI) status, lymph node yield (LNY), bladder neck invasion (BNI) status, surgical margin (SM) status, unilateral or bilateral seminal vesicle invasion (SVI) status, and time to biochemical recurrence (BCR).

Biochemical recurrence (BCR) was defined as a post-operative prostate-specific antigen (PSA) $> 0.2$ ng/mL, or use of salvage androgen deprivation therapy (ADT) or radiation in response to clinical suspicion of disease progression. Because the primary outcome was the potential impact of lymph node removal on reducing BCR, we used lymph node yield as opposed to standard vs. extended pelvic lymph node dissection.

### 2.3. Pathologic staging

Following surgical extirpation of the prostate, all specimens were fixed in formalin, processed per each institution's standard protocol, and evaluated for pathologic review. The pathologic staging was reported as per the 1997 5th edition TNM classification; patients reported to have either pT3b or pT3c disease were included. SVI is defined as invasion of the seminal vesicle muscular wall via invasion through the vas deferens, through the capsule, or as a metastatic focus [16]. Lymph node packets were fully embedded and lymph node counts were determined by the uropathologist.

### 2.4. Statistical analysis

Clinical and pathological features were compared with a BCR endpoint per the Mann-Whitney U test for continuous variables and a chi-squared test for categorical variables. The Kaplan-Meier method was used to estimate 3-year BCRFS, with separate Kaplan-Meier estimates used for the overall cohort and in the N0 vs. N1 subgroups. Multivariable Cox-Proportional Hazard models were used to assess whether LNY is associated with BCR, after adjusting for covariate such as year of surgery, NCCN risk categories, preoperative PSA, pathologic GS $\geq 9$, prostate volume, BNI, and PSM. LNY was included as both a continuous and categorical ($<5$, 5–10, $>10$) variable.

Multivariable analysis was conducted with a BCR endpoint for the overall cohort and separately for patients with pathologic N1 vs. N0 disease. Covariates consisted of PSA at diagnosis, biopsy Gleason score, and LNY. To evaluate whether LNY had been influenced by preoperative variables, we tested for interactions between LNY and PSA, and between LNY and biopsy Gleason score.

Patients who did not undergo PLND ($n = 21$) were excluded in all analysis assessing the influence of LNY on BCR and the detection of N1 disease. The institution performing the RP was also included as a covariate in all analyses. Statistical analysis was performed using SPSS, version 20 (Chicago, IL).