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Original article

Increasing rate of lymph node invasion in patients with prostate cancer treated with radical prostatectomy and lymph node dissection

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Abstract

Objectives: To investigate lymph node invasion (LNI) rates in prostate cancer (PCa) patients. Recent studies demonstrated an inverse stage migration in PCa patients toward more advanced and unfavorable diseases. We hypothesized that this trend is also evident in LNI rates, in PCa patients treated with radical prostatectomy (RP) and pelvic lymph node dissection (PLND).

Patients and methods: Within the Surveillance, Epidemiology, and End Results database (2004–2014), we identified patients who underwent RP and PLND. Annual trends of LNI rates and PLND extent were plotted. Univariable and multivariable logistic regression models tested the hypothesis that LNI rates are increasing annually, even after adjustment for clinical or pathological characteristics.

Results: Of 96,874 patients treated with RP and PLND, 4.1% (n = 4,002) exhibited LNI. The rate of LNI (2.5%–6.6%.), the mean (6.5–8.4) and median (5–6) number of removed lymph nodes increased during the study period. In multivariable logistic regression models, more contemporary year of diagnosis was associated with higher LNI rate, when year of diagnosis was modeled as a continuous, categorized or cubic spline variable, with adjustment for either clinical (prostate specific antigen, clinical tumor stage, and biopsy Gleason group) or pathological characteristics (pathologic tumor stage and Gleason group), as well as PLND extent (number of removed lymph nodes).

Conclusion: We confirmed the hypothesis about increasing LNI rate over time in RP patients. This observation implies an increasing rate of unfavorable PCa defined as LNI. This finding is novel for contemporary epidemiological North American or European databases.

Keywords: Lymph node invasion; Prostate cancer; SEER database; Inverse stage migration; Radical prostatectomy

1. Introduction

Lymph node invasion (LNI) represents an adverse pathologic feature and is virtually invariably associated with incurable prostate cancer (PCa) [1–4]. This characteristic carries a particularly poor implication in patients treated with radical prostatectomy (RP) for PCa.

Historically, epidemiological and institutional data suggested a decreasing rate of LNI in patients with PCa [2,5–7]. This phenomenon was partially accounted for by early detection and screening practices, as well as by decreasing rates of pelvic lymph node dissection (PLND) and its extent over time. Despite these encouraging historical LNI facts, the changes in early detection and screening practices that were prompted by the United States Preventive Services Task Force (USPSTF) might have resulted in adverse PCa stage migration, as reported within the Pennsylvania Cancer Registry [8–12]. The same phenomenon was also observed within institutional databases, Gallina et al. [13] reported adverse stage migration and increasing LNI rates in historic North American patients.

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More recently, Budäus et al. [14] also reported increasing LNI rates within an institutional cohort from a German tertiary care PCa referral center. Others also reported adverse stage migration in European RP patients, evidenced by higher rates of locally advanced PCa [15,16].

However, no contemporary large scale North American analysis based on population data addressed the rate of LNI in PCa patients who underwent RP. To address this void, we examined LNI rates in a large contemporary cohort of patients, who underwent radical RP and PLND. Specifically, we hypothesized that a stage migration toward more advanced tumors is evidenced by increasing LNI rates.

2. Patients and methods

2.1. Study population

We relied on the Surveillance, Epidemiology, and End Results (SEER) research data 2004 to 2014, where an extensive data quality review of SEER prostate specific antigen (PSA) values was completed [17].

We identified 584,376 patients (Fig. 1) with histologically confirmed adenocarcinoma of the prostate (International Classification of Disease for Oncology [61.9]; histological code: 8140), aged between 18 and 79 years [18]. Exclusion criteria consisted of PSA >50 ng/ml (i.e., suspected metastatic disease) [19] and confirmed metastatic disease at diagnosis (sixth and seventh edition of American Joint Committee on Cancer [AJCC] Cancer Staging Manual, $n = 11{,}065$). These selection criteria yielded 428,927 patients. Of those, 96,902 represented the focus of the current analyses. All underwent RP and PLND with available data on PLND extent and presence or absence of LNI.

2.2. Statistical analyses

Descriptive statistics included frequencies and proportions for categorical variables. Means, medians, and interquartile ranges (IQRs) were reported for continuously coded variables. The chi-square tested the statistical significance in proportions' differences. The *t*-test examined the statistical significance of means' differences.

The annual rates of LNI as well as PLND extent were displayed graphically. Univariable and multivariable logistic regression models predicted LNI. Two separate multivariable logistic regression models were fitted. The first set of models adjusted for clinical tumor characteristics (baseline preoperative serum PSA value, clinical tumor stage, and biopsy

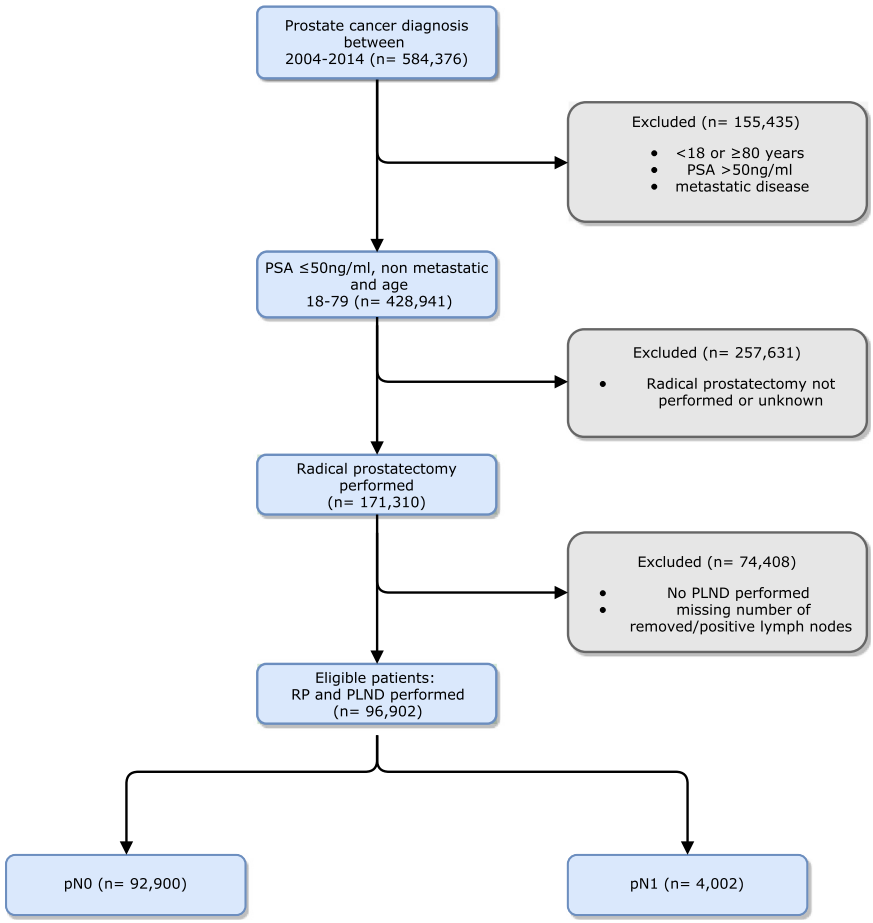

Fig. 1. CONSORT-like diagram depicting inclusion and exclusion criteria. (color figure available online).