

Original article

Lymphadenectomy in Gleason 7 prostate cancer: Adherence to guidelines and effect on clinical outcomes

Thenappan Chandrasekar, M.D.^{a,*}, Hanan Goldberg, M.D.^a, Zachary Klaassen, M.D.^a,
Rashid K. Sayyid, M.D.^a, Robert J. Hamilton, M.D., M.P.H., F.R.C.S.C.^a,
Neil E. Fleshner, M.D., M.P.H., F.R.C.S.C.^a, Girish S. Kulkarni, M.D., Ph.D., F.R.C.S.C.^{a,b}

^a Department of Surgical Oncology, University Health Network, University of Toronto, Toronto, Ontario, Canada

^b Institute for Health Policy, Management and Evaluation, University of Toronto, Toronto, Ontario, Canada

Received 11 June 2017; received in revised form 24 July 2017; accepted 22 August 2017

Abstract

Background: To examine usage trends, guideline adherence, and survival data for patients undergoing lymphadenectomy (LND) at the time of radical prostatectomy (RP) for Gleason 7 prostate cancer (PCa).

Methods: The SEER database was queried for all patients with nonmetastatic biopsy Gleason 7 PCa from 2004 to 2013. Distribution and trends of LND were analyzed. The Memorial-Sloan Kettering Cancer Center nomogram was applied to stratify patients based on risk of nodal disease at time of RP (<5% risk or ≥5% risk). Analyses were performed to determine covariates associated with LND receipt at time of RP and cancer-specific mortality (CSM).

Results: A total of 78,641 patients with either G34 or G43 PCa underwent RP (59,194 and 19,447, respectively). Of these patients, 61.2% of G34 and 73.5% of G43 patients underwent LND. During this 10-year period, the proportion of G43 patients undergoing LND remained relatively stable, whereas the proportion of G34 patients undergoing LND ranged between 55.9% and 67.9%. Regional differences were a predictor of LND receipt regardless of risk stratification, but did not translate to higher risk of CSM. Receipt of LND was not predictive of improved CSM in any of the cohorts analyzed.

Conclusions: The role of LND for Gleason 7 prostate adenocarcinoma is not yet standardized, as indicated by the variability of LND dissection rates. Receipt of LND did not improve CSM, and in G43 patients, it predicted higher CSM. As the effect of LND on CSM is uncertain, further evaluation of oncologic benefit in this patient population is warranted. © 2018 Elsevier Inc. All rights reserved.

Keywords: Prostate cancer; Lymphadenectomy; Utilization; Guidelines; Cancer-specific survival

1. Introduction

Prostate cancer (PCa) has now surpassed lung cancer as the most common solid malignancy in men in the United States, with 180,890 new cases in 2016 alone [1]. Despite significant changes in the management of both advanced/metastatic PCa and localized low-risk PCa, the standard of care for Gleason 7 PCa remains radical prostatectomy (RP) or external beam radiation therapy with a short course of androgen deprivation therapy, with or without brachytherapy [2–4].

In the setting of RP for intermediate-risk Gleason 7 PCa, the role for lymphadenectomy (LND) remains uncertain. There has never been a large prospective randomized clinical trial assessing the clinical effect of LND on RP survival outcomes in intermediate- or high-risk patients [5]. Ji et al. [6] completed a small randomized prospective trial of 360 consecutive patients with localized PCa undergoing RP at a single institution in Japan, and they found that extended pelvic LND (ePLND) was an independent predictor of biochemical progression-free survival, but did not assess cancer-specific or overall survival. However, benefit is often inferred based on numerous retrospective series, which suggest potential curative response with RP and LND alone in patients with low-volume nodal disease [7–10],

* Corresponding author. Tel.: +1-647-701-6025; fax: +1-844-351-9508.
E-mail address: thenappan.chandrasekar@gmail.com (T. Chandrasekar).

improved staging [5], or improved progression-free survival and overall survival [11–13].

Based on this lack of definitive data, the international guidelines defer to the use of nomograms as an indication for LND completion. The National Comprehensive Cancer Network (NCCN) recommends LND for any man with $\geq 2\%$ risk of pathologic node-positive (pN+) disease, the European Association of Urology (EAU) recommends LND for $\geq 5\%$ risk of pN+ disease [2,3], whereas the American Urological Association guidelines only state that LND is reserved for patients with higher risk of nodal involvement [4], highlighting the uncertainty of the role of LND.

Herein, we use a population-based database to assess the usage of LND at the time of RP for the patient with biopsy proven Gleason 7 PCa in the United States. We then assess the predictors of receiving a LND at the time of RP and the effect of LND on cancer-specific outcomes.

2. Materials and methods

2.1. Study population

Patients diagnosed with biopsy proven Gleason 7 PCa from 2004 to 2013 were identified in the Surveillance, Epidemiology, and End Results (SEER) database, which reports cancer-specific outcomes from specific geographic areas representing 28% of the US population. Inclusion criteria were: Primary PCa, Gleason 3 + 4 or 4 + 3 disease on biopsy, localized disease, receipt of RP, and no preoperative radiation therapy. Patients were crossvalidated based on 2 separate variables to determine receipt of LND and final pathologic N-stage (pN). Patients were then classified by initial Gleason grade (Gleason 3 + 4 = “G34” and Gleason 4 + 3 = “G43”) and by receipt of LND.

2.2. Preoperative risk stratification

Current guidelines recommend using nomograms to predict the risk of pN+ at the time of RP. The NCCN guidelines use a cutoff of 2% as an indication for LND at the time of RP [2], whereas the EAU uses 5% as the cutoff [3]. The key variables of the Memorial Sloan Kettering Cancer Center (MSKCC) nomogram are primary and secondary Gleason score, preoperative prostate-specific antigen (PSA), clinical T-stage, percentage of positive cores and age [14]. Biopsy core data is not available in the SEER database, thus we used a 30% rate of core positivity based on widely published median percentage of positive cores at biopsy between 25% and 33% [15–18]. Based on this, essentially all patients with Gleason 7 PCa exceeded the NCCN cutoff of 2%. Patients with PSA and clinical T-stage data were stratified per the 5% cutoff indication for LND at the time of RP. Varying the clinical parameters to achieve a $\geq 5\%$ probability of pN+ disease at the time of RP, the only

patients who would not warrant a LND at the time of RP are those with cT1c G34 disease and PSA <15 (Supplementary Table 1). Of note, only men treated after 2010 have accurate PSA data available, so only these men were stratified [19].

2.3. Description of covariates

Covariates assessed were age at diagnosis, sex, race, insurance status (uninsured, insured, and Medicaid), marital status (married, single, divorced/separated, and widowed), and receipt of postsurgical radiation. Based on prior literature [20,21], a county-level socioeconomic (SES) measure was created, based on the percentage of individuals with less than a high school education, percentage of individuals below the poverty line, percentage of individuals unemployed, percentage of individuals who were foreign-born, and median household income.

2.4. Statistical analysis

Descriptive statistics for demographic and SES variable comparisons were performed by the Student *t*-test for continuous variables and the chi-square test for categorical variables. Distributions and trends of LND were assessed. A multivariable logistic regression model was performed to generate odds ratios for the identification of factors associated with receiving LND at time of RP and factors associated with receiving post-RP radiation therapy. A competing risks regression analysis assessing cancer-specific mortality (CSM) was performed using the entire cohort (2004–2013) stratified by Gleason score; a separate analysis of the MSKCC subset was completed using MSKCC stratification as a covariate owing to the limited number of events. All statistical tests were 2-tailed and a $P < 0.05$ was considered statistically significant. Statistical tests were performed using R statistical package—R Core Team (2012) and SAS 9.4 (SAS Institute, Cary, NC).

3. Results

3.1. Demographics

A total of 78,641 patients were included; Table 1 highlights the key demographics of the cohort. Patients with G43 disease or those undergoing LND presented with higher rates of cT3+ disease, had higher PSA at diagnosis, and were more likely to receive post-RP radiation therapy. The rate of LND at RP for the G43 cohort was higher than the G34 cohort (73.5% vs. 61.2%) as was the rate of pathologic node-positive disease (pN+) (4.3% vs. 1.3%). Mean follow-up (mo) was longer in the G34 cohort (59.1 mo vs. 54.2 mo).

Download English Version:

<https://daneshyari.com/en/article/8790202>

Download Persian Version:

<https://daneshyari.com/article/8790202>

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