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Practice Patterns and Impact of Postchemotherapy Retroperitoneal Lymph Node Dissection on Testicular Cancer Outcomes

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Abstract

Background: Owing to surgical complexity and controversy regarding indications, there are wide practice variations in the use of postchemotherapy retroperitoneal lymph node dissection (PC-RPLND).

Objective: To evaluate patterns of PC-RPLND use in the USA and evaluate the association between PC-RPLND and survival in advanced nonseminomatous germ cell tumors (NSGCTs).

Design, setting, and participants: A retrospective, observational study using National Cancer Data Base (NCDB) data from 2004–2014 for 5062 men diagnosed with stage II/III NSGCT.

Outcome measurements and statistical analysis: In a comparative analysis based on receipt of PC-RPLND, the primary outcome of interest was factors associated with omission of PC-RPLND as explored via logistic regression. As a secondary outcome, we evaluated the association between PC-RPLND and overall survival (OS) via multivariable Cox regression and propensity score matching (PSM).

Results and limitations: Patients undergoing PC-RPLND were more likely to be younger, white, privately insured, and reside in more educated/wealthier regions ($p < 0.001$). Insurance status was independently associated with receipt of PC-RPLND; compared to patients with private insurance, those without insurance were significantly less likely to receive PC-RPLND (odds ratio 0.49; $p < 0.001$). After multivariate adjustment, age, comorbidity, non-private insurance, distance from hospital, clinical stage, and risk group were independently associated with all-cause mortality. In addition, omission of PC-RPLND remained associated with all-cause mortality (hazard ratio 1.98; $p < 0.001$). After PSM, the 5-yr OS was significantly lower among those not undergoing PC-RPLND (72% vs 77%; $p = 0.007$).

Conclusions: PC-RPLND represents a critical part of the multidisciplinary management of NSGCT. Patients with non-private insurance are less likely to undergo PC-RPLND, and omission of PC-RPLND is associated with lower OS.

Patient summary: We evaluated the practice patterns for advanced testicular cancer management and found that patients who did not undergo a postchemotherapy retroperitoneal lymph node dissection were more likely to have worse survival outcomes. Patients with unfavorable insurance were less likely to receive this surgical treatment.

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1. Introduction

Primary metastatic or relapsed advanced nonseminomatous germ cell tumors (NSGCTs) are typically managed with upfront platinum-based chemotherapy followed by assessment of radiographic response to chemotherapy and measurement of serum tumor markers (STMs). For many patients, the next step in management is a postchemotherapy retroperitoneal lymph node dissection (PC-RPLND), which has the potential to be diagnostic of residual retroperitoneal mass, to treat residual disease, and is the only treatment for chemoresistant teratoma. For patients with residual masses >1 cm and normal STMs, the standard of care is PC-RPLND. Although advocated by many centers as a standard of care following chemotherapy, the indications for PC-RPLND are controversial in certain cases, in particular in cases with a complete response (CR), subcentimeter residual masses, or resistance to chemotherapy [1]. Furthermore, there is wide practice pattern variation in the use of PC-RPLND. We previously found that lower-volume hospitals are significantly less likely to perform PC-RPLND, and postulated that some of the variability may be because of concerns about the complexity of the operation and morbidity, as well as a lack of understanding regarding the biology of NSGCT [2].

Given the rarity of the disease, most publications on testicular germ cell tumor (TGCT) are single-center retrospective reviews, which are not necessarily reflective of nationwide practice patterns or socioeconomic factors that play a role in disease management. We used the National Cancer Data Base (NCDB) to study factors associated with the performance of PC-RPLND and the association between performance of PC-RPLND and survival in NSGCT.

2. Patients and methods

2.1. Data source

The NCDB is a national cancer registry sponsored by the American College of Surgeons (ACS) and the American Cancer Society that collects data on malignancies from ACS-Commission on Cancer (CoC) accredited facilities. It includes approximately 70% of all malignant cancers diagnosed in the USA from more than 1500 facilities [3]. The NCDB was queried for patients with TGCT diagnosed from 2004 to 2014.

2.2. Study population

There were 62 727 reported cases of testis cancer screened for inclusion. Fig. 1 illustrates the case selection process. The International Classification of Disease for Oncology (3rd edition) was used to identify men diagnosed with NSGCT. Patients with non-testicular cancers, spermatocytic seminoma, sex cord/stromal tumors, seminoma, or unspecified germ cell tumors were excluded. Patients with unspecified American Joint Committee on Cancer (AJCC) clinical staging or stage 0–I disease were excluded. The CoC classifies patients according to the facility at which the malignancy was diagnosed and where the first-line treatment was provided. Patients who were not treated at the reporting facility (class of case "00") were excluded. For patients treated at multiple CoC facilities, the NCDB reports the most recent treatment facility and/or the facility with the most complete records. Further information on CoC case classification and comparison of baseline demographics between patients included and those excluded because of missing or unknown selection parameters is provided in Supplementary Tables 1 and 2.

2.3. Definition of PC-RPLND

Receipt of PC-RPLND is not explicitly listed in the NCDB, but it can be inferred. Patients with nonlocalized disease are typically managed with upfront chemotherapy. Patients given chemotherapy within 60 d of NSGCT diagnosis were categorized as having received primary chemotherapy. Within this group, patients recorded as having undergone regional lymph node surgery (RPLND) after chemotherapy were classified as having undergone PC-RPLND.

2.4. Covariates

Covariates included age, AJCC clinical stage, Charlson-Deyo comorbidity index, race/ethnicity, insurance coverage, distance from hospital, socioeconomic factors in the form of income and education in the patient's region and a measure of urban versus rural geography [4], and International Germ Cell Cancer Collaborative Group (IGCCCG) risk classification [5]. The IGCCCG risk group was calculated by assessing metastatic location and postorchiectomy tumor marker status [5]. The CoC classifies hospitals according to facility type (eg, academic vs community) and geographic region; however, these variables are censored for patients younger than 39 yr. Given the young age at presentation of most men with testicular cancers, these variables were not included in the analysis.

2.5. Outcome

The primary outcome of interest was the association of PC-RPLND with overall survival (OS) measured from the time of diagnosis. As secondary outcomes, we analyzed patient and tumor factors associated with performance of PC-RPLND. In addition, we assessed the impact of PC-RPLND pathologic nodal staging on OS.

2.6. Statistical analysis

The mean ± standard deviation (SD) and median and interquartile range (IQR) are reported for normally and non-normally distributed continuous variables, respectively. Categorical and ordinal variables are presented as proportions. Baseline covariates were compared using the χ^2 test for categorical variables and the Mann-Whitney U test for continuous and ordinal variables. A binomial logistic regression analysis was performed to ascertain the effects of covariates on the likelihood that PC-RPLND would be performed on a patient. Patients in the last year of the study (2014) were excluded from survival analysis, as directed by the NCDB. Survival was estimated using univariate analysis according to the Kaplan-Meier method, and comparisons were performed using the log-rank test and unadjusted Cox regression analysis.

To minimize selection bias, we performed propensity score matching (PSM) to account for differences in covariates between patients who received PC-RPLND and those who did not. Matching was performed in a nearest 1:1 fashion according to the propensity to receive PC-RPLND according to multivariate logistic regression analysis of all observed covariates used in the multivariate analysis. The goal of this technique is to balance the covariates between those who did and did not receive PC-RPLND. Survival analysis was performed using Kaplan-Meier estimates of OS between the groups and univariate Cox regression analysis. Landmark analysis was performed at 6 mo after the time of diagnosis to account for the potential effect of immortal time bias, which may favor patients who went on to receive PC-RPLND.

Statistical analysis was performed using SPSS 22.0 (IBM, Armonk, NY, USA) and the MatchIt R package was used to perform PSM [6]. Bone-

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