Evaluation of the Current Prostate Cancer Staging System Based on Cancer-Specific Mortality in the Surveillance, Epidemiology, and End Results Database

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Abstract

Stage IV prostate cancer is a heterogeneous group. Considering the favorable outcomes of T4 or N1 non-metastatic prostate cancer relative to those with M1 disease in this analysis of data from the Surveillance, Epidemiology, and End Results database, the authors propose that T4 or N1 M0 prostate cancer should be reclassified into a new stage IIIB and that patients with such disease should be offered curative-intent therapy whenever possible.

Background: Prostate cancer is the most common noncutaneous malignancy diagnosed in men. From a large population-based database, this study aimed to report prostate cancer–specific mortality (PCSM) rates of men diagnosed with various presentations of prostate cancer and to examine the adequacy of the current American Joint Committee on Cancer (AJCC) staging system. **Patients and Methods:** The Surveillance, Epidemiology, and End Results (SEER) database was queried for all patients diagnosed with prostate cancer from 1997 to 2005. PCSM was reported by the classification of extent of disease provided by the SEER database, for clinically staged and pathologically staged cohorts. **Results:** Using the cumulative incidence method, PCSM at 10 years for all patients (n = 354,326) was 5% for clinically localized (CL) lesions, 7% for T3aN0M0, 14% for T3bN0M0, 26% for T4N0M0, 27% for $T_{any}N1M0$, and 66% for $T_{any}N_{any}M1$. Within the pathologically staged subgroup (n = 108,135), PCSM at 10 years was 1% for CL lesions, 4% for T3aN0M0, 9% for T3bN0M0, 9% for T4N0M0, and 19% for $T_{any}N1M0$. **Conclusion:** Staging of any disease site aims to accurately communicate, prognosticate, and guide management for that particular level of disease. Stage IV prostate cancer is a diverse group, with PCSM in the subgroups ranging from 9% to 68% in this study. Considering the favorable outcomes of those with T4 or N1 nonmetastatic prostate cancer relative to those with M1 disease, the authors propose that T4 or N1 M0 prostate cancer should be reclassified into a new stage IIIB and that patients with such disease should be offered curative-intent therapy whenever possible.

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Introduction

Prostate cancer is the most common noncutaneous malignancy diagnosed in men, with the National Cancer Institute (NCI) estimating 238,590 new cases in 2013. Despite the high incidence rate, prostate cancer–specific mortality (PCSM) remains relatively low, with an estimated 29,720 deaths.[1] When prostate cancer presents with localized disease, it is highly curable with a variety of available treatment options. A smaller proportion of patients present with locally advanced or regional nodal disease in the era of prostate-specific antigen (PSA) screening.

Locally advanced disease is classified by the seventh edition of the American Joint Committee on Cancer (AJCC) staging system as either T3a (extraprostatic extension), T3b (seminal vesicle invasion), T4 (invasion of adjacent organs), or N1 (pelvic lymph node involvement). These patients carry a significantly higher risk of

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death and may stand to benefit the most from aggressive therapy.[2-6] Select reports suggest that some men with locally advanced, nonmetastatic prostate cancer may be undertreated, many often receiving androgen deprivation alone.[7-9]

Stage IV prostate cancer as defined by the AJCC at the time of this report comprises cases with T4, N1, or M1 disease, with M1 defined as distant metastases to lymph nodes beyond the true pelvis or to other organs. In general, the stage IV designation is often associated with incurable cancer, in which local therapy may not be recommended or offered to patients; however, there may be subsets of patients who could benefit from locoregional therapy with curative intent. From a large population-based database, this study aimed to report the PCSM rates of men diagnosed with various presentations of prostate cancer and to examine the adequacy of the current AJCC staging system.

Patients and Methods

The NCI's Surveillance, Epidemiology, and End Results (SEER) database collects and reports data from 17 population-based cancer registries representing about 28% of the United States population. The SEER database was queried to find all cases of men diagnosed with prostate adenocarcinoma between the years 1997 and 2005 using the International Classification of Disease for Oncology (ICD-O-3) site code C61.9 (prostate) and histology codes 8140 to 8389 (adenomas and adenocarcinomas) in SEER*Stat 7.1.0 software (NCI, Silver Spring, MD) (case listing function). Excluded were cases diagnosed at autopsy, those with in situ disease only, and those with incomplete or unavailable staging information, yielding 354,326 analyzable cases.

Within this overall group, the authors identified a subset of 108,135 patients who underwent prostatectomy alone, without any neoadjuvant or adjuvant treatments, using site-specific surgery codes 30 to 80 to generate a group of patients with pathologically based staging.

For the 246,191 patients who did not undergo prostatectomy as primary therapy, it was assumed that the extent of disease (EOD) coded in the SEER database represented clinical staging, given that pathologic staging information was not available in this group. Because clinical staging is often discordant with pathologic findings, clinically staged patients were analyzed separately. The clinically staged cohort included men treated with external beam radiotherapy (EBRT), prostate brachytherapy, cryotherapy, transurethral resection, no treatment, or various combinations of those. Information regarding the use of androgen suppression (AS) and chemotherapy is not available in the SEER database.

For each individual case listed, SEER provides local, regional, and distant EOD at diagnosis. Based on EOD information found in manuals available on the SEER website (http://www.seer.cancer.gov/data/documentation.html), cases were categorized as "clinically localized" (CL) if the cancer was confined to the prostate or if there was capsular invasion alone without extension through the capsule. This corresponds to stage T1N0M0 or T2N0M0 disease per AJCC criteria. Extension of cancer through the prostatic capsule and into periprostatic tissue, but without involvement of the seminal vesicles, was categorized as "extracapsular disease" (T3aN0M0, hereafter designated T3a). Extension beyond the prostatic capsule with extension to the seminal vesicles was categorized as "seminal vesicle invasion" (T3bN0M0, hereafter designated T3b). Extension to or fixation of adjacent structures other than seminal vesicles was characterized as "extended direct extension" (T4N0M0, hereafter designated T4). Involvement of regional nodes was categorized as "regional nodal disease" (TxN1M0, hereafter designated N1), and metastases to bone, distant soft tissue, other organs, and nonregional nodes were categorized as "metastatic disease" (TxNxM1, hereafter designated M1).

Grade of disease is provided in the SEER database. Grade I is well differentiated, Gleason scores of 2 to 4, or both; grade II is moderately differentiated, Gleason scores of 5 to 7, or both; grade III is poorly differentiated, Gleason scores of 8 to 10, or both; and grade IV is undifferentiated or anaplastic. Starting on January 1, 2003, Gleason score 7 was moved from moderately differentiated (grade II) to poorly differentiated (grade III). Those cases with unknown grade (n = 9483) were excluded from the grade analysis. Grades I-II and III-IV were combined in this analysis, owing to relatively small numbers in the reporting of grade I and grade IV.

PCSM was defined as the time from cancer diagnosis until death due to prostate cancer, which was provided by the SEER cause-specific death classification variable. PCSM was compared by EOD classification (CL, T3a, T3b, T4, N1, M1) for the clinically staged and pathologically staged cohorts and was subsequently stratified by grade (I-II, III-IV) within each EOD category.

All statistical analyses were conducted with R statistical software, version 2.15.2 (R Core Team, 2012, http://www.r-project.org) with add-on packages of survival and cmprsk.[10] Statistical significance was set at $P < .05$. All tests were 2-tailed. Actuarial all-cause mortality (ACM) and PCSM were estimated using the Kaplan-Meier and cumulative incidence methods, respectively. The mortality differences across groups were compared by log-rank test and Gray K-sample test for ACM and PCSM, respectively.[11,12]

Results

A total of 354,326 cases were identified from the 1997-2005 period using the aforementioned inclusion and exclusion criteria. The pathologically staged subset contained 108,135 cases. The clinically staged cohort contained 246,191 cases. Descriptive characteristics for each cohort are shown in Table 1. The median follow-up time was 79, 87, and 76 months for all patients, surgically staged patients, and clinically staged patients, respectively. CL disease made up most cases at 318,506 (90%). The median age at diagnosis for the overall group was 68 years, with the M1 group having the highest median age of 71. White men comprised most cases (80%), followed next by African American men (13%). Approximately equal proportions of white and African American men were diagnosed within each EOD stage. The median age in the surgically staged group was 7 years lower (62 vs. 69) than in the clinically staged group (not shown in Table 1).

For all patients, PCSM at 10 years was 5% for CL, 7% for T3a, 14% for T3b, 26% for T4, 27% for N1, and 66% for M1 ($P < .001$). Within the prostatectomy cohort, PCSM at 10 years was 1% for CL, 4% for T3aN0M0, 9% for T3bN0M0, 9% for T4N0M0, and 19% for $T_{any}N1M0$ ($P < .001$), as depicted in Figure 1 and Table 2. There were only 159 out of 5002 cases of TxNxM1 that received prostatectomy. Because the treatment paradigm for M1 disease does not include surgery, PCSM and ACM for this group are