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Increase in the Annual Rate of Newly Diagnosed Metastatic Prostate Cancer: A Contemporary Analysis of the Surveillance, Epidemiology and End Results Database

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Abstract

Background: Reported recommendations against prostate specific antigen (PSA) screening may have negatively affected the rates of newly diagnosed metastatic prostate cancer (mPCa).

Objectives: To investigate the annual rate of newly diagnosed mPCa and changes in disease characteristic at presentation over time in a large North American patient cohort.

Design, setting, and participants: Within the Surveillance, Epidemiology and End Results database (2004–2014) we identified 12 939 patients newly diagnosed with mPCa.

Outcome measurements and statistical analysis: We used LOWESS to plot the annual trends for age, PSA (<50, 50–98, and >98 ng/ml), clinical T stage (T1, T2, and T3-4), biopsy Gleason score ([GS] ≤6, 7, and 8–10), and M1a, M1b, and M1c substages. Multivariable logistic regression was used to test the effect of more contemporary year of diagnosis (YOD; 2014) on PSA, cT stage, GS, and M substage distributions. Multivariable linear regression was used to test the effect of more contemporary YOD on patient age.

Results and limitations: Between 2004 and 2014, the age-adjusted incidence of newly diagnosed mPCa increased from 1.9 to 2.4 cases per 100 000 population (odds ratio [OR] 1.30, 95% confidence interval [CI] 1.18–1.44; $p < 0.0001$). Rates of cT1 (from 23% to 37%; OR 1.85; $p < 0.0001$), GS 8–10 (from 67% to 85%; OR 2.62;

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$p < 0.0001$), and M1a disease (from 4.5% to 6.0%; OR 2.16; $p = 0.006$) increased. Conversely, patient age at initial mPCa diagnosis decreased from 71 to 68 yr (coefficient −0.14; $p < 0.001$). The PSA level at diagnosis remained stable over time. A limitation is the lack of detail on the distribution of metastatic disease.

Conclusions: The rate of newly diagnosed mPCa increased by 25% over the past decade and the age at initial presentation decreased. These observations may be indicative of diagnostic delays related to less frequent PSA screening.

Patient summary: The US Preventive Services Task Force recommendations against prostate cancer screening might have indirectly caused an increase in the rate of newly diagnosed metastatic prostate cancer.

1. Introduction

The introduction of prostate-specific antigen (PSA)-based prostate cancer (PCa) screening in the late 1980s dramatically altered the PCa landscape in North America [1]. Shortly after, an increase in the incidence of newly diagnosed PCa was observed that was accompanied by a stage migration towards early stage and less aggressive disease at presentation [2]. These changes dramatically decreased the proportion of newly diagnosed metastatic PCa (mPCa), which reached approximately 4% in 2004 [3].

During the past decade, the US Preventive Services Task Force (PSTF) has repeatedly recommended against PSA testing for PCa screening [4–6]. Specifically, in 2002 Harris et al [5] reported that PSA screening was associated with potential harms, while no related benefit could be determined when the screening was applied to the overall male population. Similarly, in 2008 the United States PSTF published the first statement in which they recommended against screening for PCa among men aged ≥75 yr (grade I recommendation). Finally, in 2012 the US PSTF extended the recommendation of 2008 to men in the general US population, regardless of age (grade D recommendation). This policy might have resulted in an increase in the rate of mPCa at initial diagnosis. Indeed, an inverse stage migration towards more aggressive localized PCa has been reported [7,8] after these recommendations.

On the basis of this premise, we examined stage migration among patients with newly diagnosed mPCa over the last decade. Specifically, we tested for changes in baseline PSA, biopsy Gleason score (GS), clinical T stage, metastatic substages, and age at presentation in a contemporary cohort of patients with newly diagnosed mPCa patients during 2004–2014.

2. Methods

2.1. Data source and study cohort

Our data source was the Surveillance, Epidemiology and End Results (SEER) database (2004–2014), which samples 26% of the USA and approximates the US population in terms of demographic composition and cancer incidence [9].

In the SEER database, we focused on subjects aged >18 yr who were diagnosed between 2004 and 2014 with histologically confirmed adenocarcinoma of the prostate (International Classification of Disease for Oncology code 8140 for the prostate, site code C61.9) as previously reported [10]. We only considered patients with newly diagnosed mPCa ($n = 21\,542$). Exclusion criteria consisted of patients with unknown PSA ($n = 2303$), GS ($n = 4162$), clinical T stage ($n = 1366$), and M substage ($n = 772$). Final selection yielded 12 939 assessable individuals. We relied on the SEER research data for 1973–2014, for which an extensive data quality review of SEER PSA values from 2004 to 2014 was completed [11].

2.2. Statistics

Descriptive statistics focused on the frequency and proportion for categorical variables (year of diagnosis [YOD], race, marital status, insurance status, PSA, clinical T stage, biopsy GS, and M substages). The median and range are reported for continuous variables (age and YOD).

The age-adjusted incidence of newly diagnosed mPCa per 100 000 population was graphically depicted using a locally weighted scatterplot smoothing (LOWESS) function [12]. We graphically represented the incidence of newly diagnosed mPCa using the SEER population file representing the age-adjusted incidence (https://seer.cancer.gov/seerstat/tutorials/aarates/step1.html). Similarly, annual trends defined according to YOD were plotted for baseline PSA (<50, 50–98, and >98 ng/ml), biopsy GS (GS ≤6, GS 7, GS 8–10), cT stages (cT1, cT2, and cT3–4), M substages (according to the 6th [2004–2009] and 7th [2010–2014] editions of American Joint Committee on Cancer staging manual: M1a, M1b, M1c), and age at diagnosis. We used ten sets of multivariable (MVA) logistic regression models to test the relationship between more contemporary YOD (2014) and ten specific endpoints. These were rates of cT1, cT2, cT3–4, GS ≤6, GS 7, GS 8–10, M1a, M1b, M1c, and overall mPCa. All MVA models were adjusted for PSA, biopsy GS, cT stage, M substages, age at diagnosis, marital status, insurance status, and race. In all sets of models, YOD was treated as a categorical variable. Finally, multivariable linear regression analyses were carried out to test for the relationship between YOD and age.

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