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Urologic Oncology: Seminars and Original Investigations ▮ (2014) ▮▮▮–▮▮▮

UROLOGIC ONCOLOGY

Original article

Population-based assessment of prostate-specific antigen testing for prostate cancer in the elderly[1]

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Received 9 May 2014; received in revised form 3 June 2014; accepted 5 June 2014

Abstract

Objectives: To perform a population-based analysis to characterize the effect of prostate-specific antigen (PSA) testing on oncologic outcomes in men diagnosed with prostate cancer.

Materials and methods: We used the Surveillance, Epidemiology, and End Results–Medicare–linked data to identify 98,883 men diagnosed with prostate cancer from 1996 to 2007. We stratified frequency of PSA testing as none, 1 to 2, 3 to 5, and ≥6 tests in the 5 years before prostate cancer diagnosis. We used propensity scoring methods to assess the effect of frequency of PSA testing on likelihood of (1) metastases at diagnosis and (2) overall mortality and prostate cancer–specific mortality.

Results: In adjusted analyses, the likelihood of being diagnosed with metastatic prostate cancer decreased with greater frequency of PSA testing (none, 10.6; 1–2, 8.3; 3–5, 3.7; and ≥6, 2.5 events per 100 person years, $P < 0.001$). Additionally, greater frequency of PSA testing was associated with improved overall survival and prostate cancer–specific survival ($P < 0.001$ for both).

Conclusions: Greater frequency of PSA testing in men 70 years of age or older in the 5 years before prostate cancer diagnosis is associated with lower likelihood of being diagnosed with metastatic prostate cancer and improved overall and prostate cancer–specific survival.

Keywords: Prostate-specific antigen; PSA; Elderly; Survival; Mortality

1. Introduction

Prostate cancer remains the most commonly diagnosed solid organ tumor among U.S. men, with an estimated 241,740 new cases and 28,170 deaths in 2012 [1]. Prostate cancer has been singled out as a litmus test for health care reform, with a lack of consensus regarding optimal screening or treatment strategies [2]. Prostate-specific antigen (PSA) screening has led to a significant increase in detection of clinically localized T1c prostate cancer with concomitant stage migration [3]. It is widely believed that PSA screening adds net costs to the health care system without overwhelming support from randomized controlled trials demonstrating improved survival. The randomized controlled trials of PSA screening vs. no screening have

[1] This work is supported by a Department of Defense Prostate Cancer Physician Training Award (W81XWH-08-1-0283) presented to Dr. Hu. This study used the linked SEER-Medicare database. The interpretation and reporting of these data are the sole responsibility of the authors.

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http://dx.doi.org/10.1016/j.urolonc.2014.06.003
1078-1439/

yielded conflicting results. Although the European Randomized Study of Screening for Prostate Cancer demonstrated that PSA screening in a largely PSA-naïve population reduced prostate cancer–specific mortality by 20% [4], the U.S. Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial did not demonstrate a survival benefit of annual PSA screening compared with a control arm in which 52% of subjects had undergone PSA testing before randomization or outside of the trial or both [5]. After a systematic review of the evidence largely weighted by these studies, the U.S. Preventative Services Task Force recommended against PSA screening owing to moderate to high certainty the service has no net benefit and the harms outweigh the benefits [6].

Although clinical trials overcome concerns of internal validity, there are often concerns regarding external validity and generalizability—clinical trial enrollees tend to be younger and healthier than most patients with cancer and often times represent highly selected patient subgroups [7–9]. Therefore, the purpose of our population-based study was to determine whether use and frequency of PSA testing in the 5 years before prostate cancer diagnosis affects prostate cancer stage and overall and prostate cancer–specific mortality in a contemporary cohort of elderly Americans.

2. Materials and methods

2.1. Data

Our study was approved by the University of California, Los Angeles institutional review board; patient data were deidentified, and the requirement for consent was waived. We used the Surveillance, Epidemiology, and End Results (SEER)–Medicare–linked data for analyses, comprising the linkage of population-based cancer registry data from 16 SEER regions covering approximately 26% of the U.S. population with Medicare administrative data. The Medicare program provides benefits to 97% of Americans aged $\geq$65 years [10].

2.2. Study cohort

We identified 267,052 men from the SEER-Medicare–linked data diagnosed with prostate cancer between 1996 and 2007 with follow-up of Medicare services through 2009. As we evaluated PSA testing in the 5 years before diagnosis, 182,190 men aged $\geq$70 years at the time of prostate cancer diagnosis were identified. We excluded 73,134 men who also had health maintenance organization coverage and were not enrolled to Medicare throughout the study period, as medical services for these men may be incompletely captured. Moreover, we excluded 5,345 men owing to missing tumor stage at diagnosis and 4,828 men because of missing demographic or comorbidity characteristics, resulting in a final cohort of 98,883 men.

We identified PSA tests before prostate cancer diagnosis using Healthcare Common Procedure Coding System codes 84153, 84154, and G0103. Against the backdrop of the U.S. Preventative Services Task Force's recent recommendation against any PSA screening and the inherent differences in patient characteristics of men who never receive any PSA testing from those who obtained at least one PSA test in the 5 years before prostate cancer diagnosis, we categorized men who did not have any PSA testing separate from those who had at least 1 PSA test. These men were categorized into groups according to 1 to 2, 3 to 5, and $\geq$6 PSA tests in the 5 years before prostate cancer diagnosis. However, in sensitivity analyses, we also combined men with 0 and 1 to 2 PSA tests, and results were similar.

2.3. Control variables

Age was obtained from the Medicare file; tumor characteristics, race, census tract measures of median household income and high school education, region, population density (urban vs. rural), and marital status were obtained from SEER registries. Comorbidity was assessed using the Klabunde modification of the Charlson index during the year before surgery [11]. Use of other preventive procedures covered by Medicare for men was identified using corresponding Healthcare Common Procedure Coding System codes: (1) influenza vaccination 90732, 90724, 90659, 90658, 90669, and G0008; (2) cholesterol testing 82465, 83718, 83721, 83719, and 80061; and (3) colorectal cancer testing 82270, 82272, 82274, 82270, G0328, and G0107.

2.4. Statistical analysis

Because men with varying use of PSA testing differed in terms of demographic characteristics and use of other preventative tests covered by Medicare, we used weighted propensity score methods to adjust for these differences [12,13]. Propensity score methods permit control for observed confounding factors that may influence both group assignment and outcome using a single composite measure, and they attempt to balance patient characteristics between groups. To conduct the propensity score adjustment, we used a logistic regression model to calculate the propensity (probability) of being in 1 of the 4 PSA testing frequency groups based on all aforementioned covariates and then weighted each subject's data based on the inverse propensity of being in 1 of the 4 PSA screening frequency groups [14]. To compare unadjusted proportions across PSA testing groups, we used Pearson chi-squared test, and to compare propensity-adjusted proportions across PSA testing groups, we used a Rao-Scott chi-squared test [14], which accounts for the propensity weighting. To compare unadjusted rates, we fit a Poisson log-linear regression model [15] with PSA testing groups as the only covariate. To compare propensity-adjusted rates, we fit a Poisson log-linear regression model [16], with PSA testing groups as the only covariate, but also weighting each