Trade-Off between Treatment of Early Prostate Cancer and Incidence of Advanced Prostate Cancer in the Prostate Screening Era

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Purpose: Prostate specific antigen screening has led to the early detection of prostate cancer. However, there has also been concern about the over diagnosis and overtreatment of patients with indolent cancers. We performed a population based analysis to evaluate the trade-off between excess treatment and prevention.

Materials and Methods: We used the CDC (Centers for Disease Control and Prevention) Behavioral Risk Factor Surveillance System survey from 2001 to 2010 to determine rates of prostate specific antigen screening. We used the SEER database to identify all patients diagnosed with prostate cancer from 1988 (pre-prostate specific antigen screening) to 2010. Demographic, staging and treatment data were collected. Cases were classified as early (low/intermediate risk), high risk, node positive or metastatic disease.

Results: Prostate specific antigen screening rates in the last 2 years were 54% for men older than 40 years, including 71% for those older than 60, and did not vary during 2001 to 2010. Comparing 1988 and 2000 to 2010, per 100,000 men the incidence of early prostate cancer increased (61.7 to 113.7), while high risk cancer increased (20.7 to 28.2), node positive cancer decreased (3.7 to 1.8) and metastatic cancer decreased (13.6 to 6.2). The rate of definitive primary treatment (radical prostatectomy or radiation therapy) for men with early cancer increased from 47% to 67% ($p < 0.001$).

Conclusions: Prostate specific antigen screening has led to an additional diagnosis of 5.8 cases of early stage cancer and 3.9 cases receiving treatment for early cancer for every 1 less case of stage IV disease at initial diagnosis. This ratio represents the worst-case scenario for overtreatment and provides a quantitative basis for studying the effect of prostate specific antigen screening.

Key Words: prostatic neoplasms, early detection of cancer, medical overuse

Abbreviations and Acronyms

BRFSS™ = Behavioral Risk Factor Surveillance System

PSA = prostate specific antigen

SEER = Surveillance, Epidemiology and End Results

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PROSTATE cancer is the most common solid malignancy and the second most common cause of cancer death in American men.[1] Prostate specific antigen has been widely used as a screening tool for early detection of prostate cancer. Since its introduction in the late 1980s, PSA testing has become routinely used in primary care, leading to fundamental changes in the composition of prostate cancer incidence.

Due to the long natural history of many prostate cancers, some patients will never experience clinical symptoms of prostate cancer before they die of competing causes. Critics of PSA screening argue that such cases

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of over diagnosis lead to overtreatment with resultant morbidity[2,3] and increased cost of care.[4]

Two large scale randomized clinical trials have attempted to address the effect of screening. The ERSPC (European Randomized Study of Screening for Prostate Cancer) found an improvement in survival from prostate cancer[5] while the PLCO (Prostate, Lung, Colorectal, and Ovarian) Cancer Screening Trial found an increased incidence but no survival benefit with PSA screening.[6] The PIVOT (Prostate Cancer Intervention Versus Observation Trial) study of radical prostatectomy vs observation in men with early prostate cancer diagnosed by PSA screening failed to demonstrate any survival benefit to treatment.[7] Together these results led to significant policy change in the United States, including the influential USPSTF (U.S. Preventive Services Task Force) recommending against routine PSA screening.[8]

Given the long survival of men with prostate cancer, including those with metastatic prostate cancer, the benefit of screening may not be apparent when considering trials with short to intermediate followup time. In particular, while screening may lead to the overtreatment of some patients with early stage cancer, other patients may be spared from lifelong androgen deprivation therapy, as well as morbidity from complications of diagnosis at an advanced stage of disease. Therefore, we performed a population based study to evaluate the effect of PSA screening as a trade-off between treatment of early stage prostate cancer (as a proxy for overtreatment) and reduction in the incidence of late stage prostate cancer.

MATERIALS AND METHODS

PSA Screening Use

The CDC BRFSS database was used to measure PSA screening from 2000 to 2010. The BRFSS is a national yearly telephone based survey used to evaluate health behaviors since 1984 and includes PSA screening questions since 2001. Collected data include any history of PSA screening and PSA screening within 2 years by age group. The weighted average was determined using the PSA screening rate for each age group crossed to the proportion of men by age group as reported in the 2005 U.S. Census data.

Prostate Cancer Incidence and Treatment

The incidence of prostate cancer by stage from 1988 to 2010 was determined using the National Cancer Institute SEER database. Data were collected on all adult men diagnosed with prostate cancer from 1988 to 2010 in the original 9 SEER regions (SEER-9). Tumor characteristics including Gleason grade or score, clinical stage and pathological stage were used to group patients into one of 4 clinical groups of early (T1-T2, Gleason 7 or less), high risk (T3 or Gleason 8 or greater), lymph node positive and metastatic. In cases for which clinical and pathological staging were available, pathological stage was used. Cases for which staging could not be determined were grouped with early stage. Our early stage classification generally included patients with low and intermediate risk cancer. For analysis the lymph node positive and metastatic cases were considered advanced cancer. The incidence rate per 100,000 adult males was determined by dividing total cases per population of males (age greater than 18) in each SEER region using U.S. Census state and county population data. The use of definitive treatment was defined as prostatectomy and/or radiation therapy.

Trends in Screening, Incidence and Treatment 2000 to 2010

Linear regression was used to evaluate for trend in PSA screening rate, incidence for each clinical group, and treatment rate between 2001 and 2010. Equilibrium was defined as the finding of no significant change in the rate of each measurement.

RESULTS

PSA Testing 2001 to 2010

Between 2000 and 2010 the self-reported overall rate of any history of PSA testing was 56% to 61% for men older than 40 years, 70% to 78% for men older than 50 and 76% to 83% for men older than 60. Self-reported PSA testing within the previous 2 years was 48% to 51% for men older than 40, 62% to 64% for men older than 50 and 68% to 74% for men older than 60 (see table).

Incidence of Prostate Cancer 1988 to 2010

The overall incidence of prostate cancer increased from 100 per 100,000 adult men in 1988 to a peak of 182 per 100,000 in 1992. Subsequently there was a decrease to a stable level of approximately 150 per 100,000 from 2000 to 2010. Early and high risk localized prostate cancers followed a similar pattern of increase to a peak in 1992, followed by a decrease and plateau in subsequent years. In contrast, node positive and metastatic cancers did not experience any initial increase in incidence but had an early decrease and subsequent stabilization (fig. 1, *A*).

PSA screening rates within last 2 years

Yr	% Age 40–49	% Age 50–59	% Age 60–69	% Age 70+	% Weighted Av Age 50+
2001	26.6	54.9	68.8	67.2	62.0
2002	28.3	56.4	68.0	66.8	62.4
2003	26.2	55.4	71.1	72.4	64.3
2004	23.8	53.5	68.0	68.6	61.5
2005	23.8	57.3	74.1	74.0	66.4
2006	25.1	54.5	70.2	69.7	62.9
2007	26.2	52.9	72.0	74.7	64.0
2008	26.1	55.0	72.2	72.1	64.3
2009	26.8	54.0	73.0	73.5	64.4
2010	25.3	52.6	70.7	70.4	62.3