The Relationship of Baseline Prostate Specific Antigen and Risk of Future Prostate Cancer and Its Variance by Race

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Abstract: Purpose: Several studies suggest that a baseline prostate specific antigen (PSA) measured in young men predicts future risk of prostate cancer. Considering recent recommendations against PSA screening, high-risk populations (e.g. black men, men with a high baseline PSA) may be particularly vulnerable in the coming years. Thus, we investigated the relationship between baseline PSA and future prostate cancer in a black majority–minority urban population.

Materials and methods: A retrospective analysis was performed of the prostate biopsy database ($n = 994$) at the Brooklyn Veterans Affairs Hospital. These men were referred to urology clinic for elevated PSA and biopsied between 2007 and 2014. Multivariate logistic regression was used to predict positive prostate biopsy from log-transformed baseline PSA, race (black, white, or other), and several other variables.

Results: The majority of men identified as black (50.2%). Median age at time of baseline PSA and biopsy was 58.6 and 64.8, respectively. Median baseline PSA was similar among black men and white men (2.70 vs 2.91 for black men vs white men, $p = 0.232$). Even so, black men were more likely than white men to be diagnosed with prostate cancer (OR 1.62, $p < 0.0001$). Black men less than age 70 were at particularly greater risk than their white counterparts. Baseline PSA was not a statistically significant predictor of future prostate cancer ($p = 0.101$).

Conclusions: Black men were more likely to be diagnosed with prostate cancer than were white men, despite comparable baseline PSA. In our pre-screened population at the urology clinic, a retrospective examination of baseline PSA did not predict future prostate cancer.

Keywords: Prostate cancer■Prostate-specific antigen■Screening■Preventive care■Minority population■Urology

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INTRODUCTION

The issue of prostate cancer (CaP) screening remains fraught with controversy. In 2012, the United States Preventive Services Task Force (USPSTF) assigned a "Grade D" to CaP screening, recommending against the use of prostate specific antigen (PSA) screening in men of all ages.[1] In contrast, other notable organizations such as the American Urological Association (AUA) and American Cancer Society (ACS) continue to support individualized discussions with men regarding the benefits and harms of PSA screening, with special consideration of high-risk populations (e.g. positive family history, African-American race).[2,3]

In the United States, CaP incidence and mortality in black men are 1.7 times and 2.4 times higher, respectively, than those in white men.[4] Significant research has explored whether this disparity is due to differences in tumor biology or disease management.

Many studies have demonstrated that black men with CaP have lower overall survival and cancer-specific survival when compared with white men.[5–7] A large systematic review found, however, that after adjusting for disease severity and socioeconomic status, there was no longer a difference in survival.[5] A review of CaP in equal-access healthcare systems (e.g. Veterans Affairs) found that survival was similar in black men and white men.[8] These studies suggest that the observable reduced survival in black men may be attributable to differences in socioeconomic status and access to care.

Data from radical prostatectomy specimens indicate that black men are more likely to have rapidly growing cancer, adverse pathological findings, metastatic disease, and biochemical recurrence after treatment.[9,10] Considering that black men may have more aggressive tumors and less access to care in some settings, it is not surprising that they present with more advanced CaP and higher PSA levels at the time of diagnosis.[6,7,11,12]

Clearly, black men suffer disproportionately from CaP. It is thus necessary to adequately study the utility of PSA screening specifically in this population. Furthermore, there is a need to identify men that are at high risk for CaP to best guide appropriate preventive screening. Several studies have found that a baseline PSA value measured in men younger than 50 predicts long-term risk of developing CaP.[13–16] Lilja et al suggested that "a single PSA test in the mid to late 40s could stratify the population according

to risk for intensity of subsequent prostate cancer screening."[13] Critics of these studies cited limited generalizability of these findings due to ethnic homogeneity of the study populations.

Our inner-city facility serves a majority−minority population, in which black men comprise greater than 50% of the patient population. Therefore, we sought to study the relationship of baseline PSA and risk of future CaP in a majority−minority cohort and whether there was a difference in risk between black men and white men.

MATERIALS AND METHODS

We performed a retrospective review of our prostate biopsy database at the Brooklyn campus of the VA NY Harbor Healthcare System. From 2007 to 2014, 994 men that were initially referred to the urology clinic for elevated PSA underwent transrectal ultrasound and 12-core needle biopsy of the prostate. A positive prostate biopsy was defined as a biopsy diagnostic of CaP. Baseline screening PSA was defined as the first identified PSA value found in the electronic medical record, implying that these values could have been measured months to years prior to the time of prostate biopsy. Additional pre-biopsy PSA values were also included in our analysis.

Multivariate logistic regression was used to predict positive prostate biopsy from log-transformed baseline PSA, race (black, white, or other), age at biopsy, presence or absence of prostatitis, histology, and PSA velocity from baseline to the time of biopsy. The Hosmer−Lemeshow method was used to test fit of the data. Odds ratios (OR) and 95% confidence intervals are reported. Baseline demographics and characteristics in the cohort were compared using Chi-square and independent samples median test. The trend in Gleason grades with repeat biopsies was analyzed using the Kruskal−Wallis test. Statistical significance was defined as $p < 0.05$. Statistical analyses were performed using Stata (StataCorp, Release 13, College Station, TX).

Initial multivariate analysis also included the presence or absence of family history of CaP. However, this produced unlikely odds ratios: OR of a positive prostate biopsy in black men vs white men was 89 (95% CI 22−364) and in other men vs white men was 25 (95% CI 5.7−110). These OR values are not supported by any other publication in the literature and thus likely represented outlier values. A return to our data set and further analysis revealed that zero percent of black men had reported a positive family history for prostate cancer. As this finding is unlikely when compared to other studies in the literature, the family history category was excluded on repeat analysis.

THEORY

Recent changes in PSA screening guidelines were largely based on results from the Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial (PLCO) and the European Randomized Study of Screening for Prostate Cancer (ERSPC). However, these trials underrepresented black men, with only 4% identifying as non-Hispanic black in the PLCO trial.[17] Even more alarming is the recent finding that the PLCO trial suffered from severe contamination in its control arm that was randomized to no PSA screening; more than 80% of men in the control arm reported undergoing PSA testing during the course of the study.[18] This raises concerns regarding the generalizability of these data and subsequent recommendations against CaP screening to the black population.

Prior to the 2012 USPSTF recommendations, data from the Surveillance, Epidemiology, and End Results (SEER) database showed that black men had longer PSA screening intervals than did white men.[12] Methods found to increase rates of PSA screening among black men include engaging, encouraging, and informative discussions with healthcare providers regarding CaP prevention and fostering patients' understanding of the disease.[19,20] Even prior to the 2012, it appears we were ineffectively extending CaP screening to black men. As the new recommendations do not explicitly account for the higher risk in black men, there is a danger of continuing or even worsening this disparity in preventive care.

Since the 2012 USPSTF recommendations, the rate of PSA screening has decreased to the same extent in black men and white men, despite the former representing a high risk group.[21,22] Compared to men prior to the 2012 guidelines, men are now more likely to be diagnosed with high risk disease (e.g. stage T2c or T3a, Gleason 8 to 10, PSA $>$ 20 ng/mL).[23]

Although routine PSA screening has fallen out of favor, it remains prudent to identify patients at particularly high risk for CaP. Several studies have suggested the value of measuring a baseline PSA value in men younger than 50.[13−16] Using data from the Malmo Preventive Project, Lilja et al found that men under 50 years old with a baseline PSA $\leq$ 0.5 ng/mL were at lower risk of later developing CaP than the general population.[13] Higher baseline PSA values that were still within normal range were increasingly predictive of future CaP as far as 20 years later. Similarly, Loeb et al found that men aged 40−49 with baseline PSA values greater than their age-specific median but still within normal range had 14.6