Racial Disparities in Prostate Cancer–Specific Mortality in Men With Low-Risk Prostate Cancer

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Abstract

This study examined the association of race and prostate cancer–specific mortality (PCSM) in 51,315 men with low-risk prostate cancer, using the Surveillance, Epidemiology, and End Results (SEER) database. African American men were found to have a higher risk of PCSM compared with white men, suggesting that further studies are needed to determine whether guidelines for active surveillance should take race into account.

Background: Men with low-risk prostate cancer (CaP) are considered unlikely to die of CaP and have the option of active surveillance. This study evaluated whether African American (AA) men who present with low-risk disease are at higher risk for death from CaP than white men. **Patients and Methods:** The authors identified 56,045 men with low-risk CaP (T1-T2a, Gleason score ≤ 6, prostate-specific antigen ≤ 10 ng/mL) diagnosed between 2004 and 2009 using the Surveillance, Epidemiology, and End Results (SEER) database. Fine-Gray competing-risks regression analyses were used to analyze the effect of race on prostate cancer–specific mortality (PCSM) after adjusting for known prognostic and sociodemographic factors in 51,315 men (43,792 white; 7523 AA) with clinical follow-up information available. **Results:** After a median follow-up of 46 months, 258 patients (209 [0.48%] white and 49 [0.65%] AA men) died from CaP. Both AA race (adjusted hazard ratio [AHR], 1.45; 95% CI, 1.03-2.05; $P = .032$) and noncurative management (AHR, 1.49; 95% CI, 1.15-1.95; $P = .003$) were significantly associated with an increased risk of PCSM. When analyzing only patients who underwent curative treatment, AA race (AHR, 1.62; 95% CI, 1.04-2.53; $P = .034$) remained significantly associated with increased PCSM. **Conclusion:** Among men with low-risk prostate cancer, AA race compared with white race was associated with a higher risk of PCSM, raising the possibility that clinicians may need to exercise caution when recommending active surveillance for AA men with low-risk disease. Further studies are needed to ultimately determine whether guidelines for active surveillance should take race into account.

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Introduction

In 2013, nearly 238,590 men received a new diagnosis of prostate cancer and 29,720 deaths were attributed to prostate cancer (CaP) in the United States.[1] Men have a 17% lifetime risk of being diagnosed with CaP, with over 20% of those diagnoses representing low-risk disease. Recent evidence from the Prostate Cancer Intervention Versus Observation Trial (PIVOT) did not show significant differences in prostate cancer–specific mortality (PCSM) or all-cause mortality among patients with localized CaP who underwent either radical prostatectomy or active surveillance/observation.[2] Furthermore, the PIVOT trial, which included a large proportion of African American (AA) men (nearly one-third

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of the cohort was AA), did not show any differences in outcomes between AA men and white men.[2] Other studies have also found that among patients with low-risk CaP, survival outcomes do not differ between patients managed definitively (with radiation or radical prostatectomy) or conservatively (watchful waiting/active surveillance).[3-8] Although these results are encouraging, most studies (other than the PIVOT trial) include cohorts with a small number of AA patients, and therefore it is difficult to determine whether the results can be generalized to AA populations.

AA men are at a higher risk of developing CaP, present with more aggressive disease, and have poorer oncologic outcomes when compared with white men.[1,9-11] Furthermore, Sundi et al[12,13] recently found that AA men with very low-risk CaP who met criteria for active surveillance but who underwent radical prostatectomy had higher rates of adverse pathology and upgrading compared with white men. Similarly, Ha et al[14] found that AA men who were candidates for active surveillance but who underwent radical prostatectomy had worse clinicopathologic features on final surgical pathology than white men. It has also been found that AA race is associated with a higher risk of progression while on active surveillance and also a higher rate of discontinuing active surveillance.[15,16] Nevertheless, there is a paucity of data examining the effect of AA race on mortality in low-risk prostate cancer, and it is unknown whether AA race should be taken into consideration when making treatment recommendations for men with low-risk CaP.

The Surveillance, Epidemiology, and End Results (SEER) database was used to determine the effect of race on PCSM among patients with low-risk CaP.

Patients and Methods

Patient Population and Study Design

The SEER database was used to identify 56,045 men (44,642 white; 7702 AA; 3701 other) with low-risk prostate cancer,[17] defined by a clinical classification of T1-T2a, a Gleason score $\leq$ 6, and a pretreatment prostate-specific antigen (PSA) level $\leq$ 10 ng/mL, diagnosed between 2004 and 2009. Gleason scores, as provided by the SEER program, represent the highest Gleason score identified at either biopsy or surgery. Stage was determined using the American Joint Committee on Cancer guidelines, sixth edition, as provided by the SEER program.[18] The inclusion period was limited to 2004 through 2009, as 2004 represents the year that several of the covariates included in the present multivariable analysis were introduced to SEER and 2009 represents the most recent year for which full information is available.[18] The SEER program, sponsored by the US National Cancer Institute, collects and publishes cancer incidence, survival, and treatment data from population-based cancer registries; the program captures approximately 97% of incident cancers, and the 17 tumor registries cover about 26% of the US population.[18]

Initial management approaches were defined as either curative or noncurative. Curative approaches included radical prostatectomy, with or without the use of radiation therapy, or radiation therapy (either brachytherapy or external beam radiation), in accordance with the National Comprehensive Cancer Network (NCCN).[17] Patients with unknown treatment status (n = 1029) were excluded from analyses. Of note, the SEER database does not contain information regarding androgen deprivation therapy.

Race was classified as white and African American (AA), as designated by the SEER program.[18] Patients of other races were excluded given the small number (n = 3701) of these patients in the present cohort. Income (computed as median household income) and educational status (computed as the percentage of residents $\geq$ 25 years of age with at least a high school education) were determined at the county level by linking to the 2000 United States Census.[19] Residence type was also determined at the county level by linking to the 2003 United States Department of Agriculture rural-urban continuum codes.[20]

Statistical Analysis

Baseline patient characteristics were compared using the *t* test and χ^2 test, as appropriate. PSA level was log-transformed to ensure that PSA values followed a normal distribution.

After adjusting for demographic factors (age, race, marital status, income, education, residence [urban vs. rural]), initial management approach (curative vs. noncurative), cancer stage (T1 vs. T2a), and log-PSA, a Fine-Gray univariable and multivariable competing-risks regression was used to assess the effect of race on PCSM in 51,315 men (43,792 white; 7523 AA) with complete clinical information available.[21] Multivariable logistic regression was used to assess for an association between race and initial management approach after adjustment for the previously listed covariates. A Fine-Gray univariable and multivariable competing-risks regression was repeated for patients who underwent curative treatment to determine the effect of race on PCSM in the curative setting, with adjustments for sociodemographic factors, radical prostatectomy as curative treatment type, log-PSA, and cancer stage. Multivariable logistic regression was again used to determine the association between race and use of radical prostatectomy as the initial curative approach after adjustment for the previously listed covariates.

Cumulative incidences of PCSM stratified by race were generated from the aforementioned competing-risks regression models and displayed graphically.[22] Point estimates and associated CIs were generated and compared using the Gray k-mean *P* value.

All *P* values were 2-sided. The threshold of .05 was used to determine statistical significance. Statistical analyses were performed by authors B.M. and A.A. using R software, version 2.12.0 (R Foundation for Statistical Computing, Vienna, Austria) for calculations relating to the Gray k-mean *P* value and using Stata, version 11.1 (StataCorp, College Station, TX) for all remaining analyses. This study was approved by the institutional review board; informed consent was waived.

Results

Patient Characteristics

Baseline patient clinical and demographic characteristics are shown in Table 1. Although there were significant differences in age, income, education, marital status, residence, PSA, stage, and receipt of curative treatment when comparing between AA and white patients, the magnitude of most of the differences was small. Notably, whereas white patients were more likely to present with cT2a (vs. cT1) disease, AA patients were more likely to present with slightly higher PSA.