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'Race' and Prostate Cancer Mortality in Equal-access Healthcare Systems

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Abstract

BACKGROUND—Reports suggest worse health-related outcomes among black (vs white) men diagnosed with prostate cancer, but appropriate cause–effect inferences are complicated by the relationship of race and other prognostic factors.

METHODS—We searched the literature to find contemporary articles focusing on mortality among black and white men with prostate cancer in equal-access healthcare systems. We also directly assessed the association of race and prostate cancer mortality by conducting an observational cohort analysis of 1270 veterans diagnosed with prostate cancer and followed for 11 to 16 years at 9 medical centers within the Veterans Health Administration.

RESULTS—Among 5 reports providing quantitative results for the association of race and mortality among men with prostate cancer in equal-access systems, outcomes were similar for black and white men. Race also was not a prognostic factor in the observational cohort analysis of US veterans, with an adjusted hazard ratio for black (vs white) men and prostate cancer mortality of 0.90 (95% confidence interval, 0.58–1.40; $P = .65$).

CONCLUSIONS—Mortality among black and white patients with prostate cancer is similar in equal-access healthcare systems. Studies that find racial differences in mortality (including cause-specific mortality) among men with prostate cancer may not account fully for socioeconomic and clinical factors.

Keywords

Delivery of health care; Ethnic groups; Healthcare disparities; Prostatic neoplasms; Race

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Prostate cancer is the most common malignancy among American men and has the second highest cancer-related mortality rate. The burden of prostate cancer apparently varies according to race, however, with black men reported to have a higher incidence, more advanced anatomic stage at diagnosis, and higher mortality.[1–4] Potential intrinsic (biological) explanations for these disparities include "racial" differences in tumor biology and responsiveness to treatments[5–7]; potential extrinsic (societal) explanations include differences in access to care, patterns of screening, and treatments received.[8,9]

Determining the true impact of race is challenging. Race is related to other prognostic variables, regardless of whether race itself is a cogent factor affecting outcome or only a culturally constructed label. For example, given the interplay of race and socioeconomic status in analyses of health outcomes,[10,11] the observed impact of race could change depending on whether race is studied with or without considering socioeconomic status. Of note, the literature on race, socioeconomic status, and health outcomes uses a wide range of study designs and analytic strategies, including a focus on overall or cause-specific mortality —and the corresponding complexity of methods used is considerable.

However, a methodological opportunity exists in considering situations for which baseline characteristics that are associated with race, as susceptibility (confounding) factors, are less likely to vary. In general, the independent impact of biological aspects of race might be determined more readily in a relatively homogeneous setting regarding the societal factor of socioeconomic status and access to health care. Specifically, the impact of race on mortality among men with prostate cancer would be more evident in equal-access healthcare systems.

Our goal was to clarify the association of race with mortality among men with prostate cancer, using 2 approaches. First, to better understand existing evidence in equal-access healthcare systems, we reviewed published studies of men with prostate cancer receiving healthcare from the Departments of Defense or Veterans Affairs in the United States, the National Health Service in the United Kingdom, or the Health Canada provincial/territorial healthcare system. These equal-access systems would promote an unbiased comparison based on race. Second, to generate new evidence on this topic, we conducted an observational cohort analysis of race and prostate cancer mortality among men receiving care in the New England region of the Veterans Health Administration. The results represent an additional report from an equal-access system, and the socioeconomic status of veterans receiving their health care from the Veterans Affairs tends to be restricted in comparison with the general US population.[12,13]

MATERIALS AND METHODS

Literature Review

A search using MEDLINE—even when limited to the English language and publication dates from January 1, 1990, to December 31, 2012—returned thousands of articles for *prostate cancer* combined with *mortality* or *survival* as multipurpose search terms (eg, in title, abstract, subject heading). We recognized and avoided the methodological complexity of accounting adequately for relevant clinical features, such as patterns of screening and selection of treatment options; we also recognized and avoided the methodological

complexity of evaluating different analytic approaches, such as how to adjust optimally for baseline characteristics or discern cause of death. Instead, we intentionally restricted our review to the few articles that examined (1) *race* and (2) *equal access* or *socioeconomic status* (or pertained to *Soldiers*, *Veterans*, *United Kingdom*/*England*, or *Canada*, indicative of equal-access healthcare systems).

Observational Cohort Analysis

Data were obtained from a source population of 64,545 health care beneficiaries at 9 medical centers in the Veterans Health Administration, and analyses were based on an intensive medical record review of 1270 men diagnosed with prostate cancer during 1991–1995. Follow-up for cause-specific mortality was available through 2006. Details of the study population and methods have been reported.[14–16] Appropriate statistical tests (chi-square, chi-square for linear trend, Wilcoxon rank-sum) were used to compare pretreatment characteristics for groups classified by race. The primary analysis compared black with non-black (white and "other") patients; data extraction allowed for Hispanic patients to be black or white, and Native Americans or Asians were subsequently designated as non-black.

The impact of race on prostate cancer mortality was assessed with a proportional hazards model, first accounting only for age. A subsequent proportional hazards model accounted for age, comorbidity, and tumor-related variables.[17] Our focus did not include conducting an evaluation of therapy, but we confirmed our results regarding race in a sensitivity analysis that included the type of treatment as an additional factor potentially affecting outcome. In a separate sensitivity analysis, we assessed whether our results differed when "other" (eg, Hispanic) patients were excluded or reclassified as black or white.

RESULTS

Literature Review

The final search (see "Materials and Methods" section) yielded 85 citations potentially focusing on race and mortality in equal-access healthcare systems. Many articles assessed nonmortality outcomes or did not analyze data based on race (albeit mentioning the terms *mortality* and *race*). Other articles had a broad scope with limited data on prostate cancer, studied restricted patient or treatment groups, or were otherwise not pertinent. From a combined clinical-methodological perspective, 5 articles[18–22] from equal-access healthcare systems provided quantitative results based on race and involving mortality among unselected patients with prostate cancer.

Beyond whether unadjusted or incompletely adjusted (eg, age- but not stage-adjusted) differences were observed on the basis of race, none of the 5 studies concluded that black race was associated independently with increased cause-specific mortality among patients with prostate cancer in equal-access settings (Table 1). Reports from the Department of Defense[18] and the Veterans Affairs healthcare system[19,20] found similar overall survival among blacks and whites with prostate cancer. A report comparing Veterans Affairs and private sector health care[21] found that black race was associated with cause-specific mortality in the private sector, but not in the Veterans Affairs. A report from the United

Kingdom found "no significant difference [in prostate cancer-specific survival] between Black and White men."[22] Of note, most studies classified patients as black or African American versus white or European American or Caucasian; one study[20] mentioned specifically excluding Hispanic patients, and another study[22] reported on Indian or Pakistani men (data not shown).

Observational Cohort Analysis

Among 1270 veterans, the distribution of patient demographic and tumor characteristics for 139 black veterans (10.9%) and 1131 white or other veterans (89.1%) who were diagnosed with prostate cancer between 1991 and 1995 is presented in Table 2. In regard to "other" races, 7 patients (<1%) were identified as Hispanic or Native American in the medical records (data not shown). In unadjusted comparisons, black (vs white) patients tended to be younger and to have higher anatomic stage, more poorly differentiated tumors, and higher baseline prostate-specific antigen levels. After 11 to 16 years of follow-up, 17.3% (n = 24) of black men and 15.5% (n = 175) of white men died of prostate cancer (P = .58).

Among the 1249 patients (98.3%) with complete data for multivariable analyses, the age-adjusted association of race and prostate cancer mortality was not statistically significant: The adjusted hazard ratio for black race was 1.30 (95% confidence interval, 0.84–2.00; P = .24). As shown in Table 3, the association of race and prostate cancer mortality was not statistically significant after further adjustment for comorbidity and tumor-related characteristics, with an adjusted hazard ratio for race of 0.90 (95% confidence interval, 0.58–1.40; P = .65).

The results regarding race were similar—specifically neither quantitatively nor statistically significant—when treatment was added to the multivariable model (data not shown). Results also were similar (data not shown) when excluding or reclassifying Hispanic or Native American patients. As expected, increasing age, severe comorbidity, and more aggressive tumor characteristics were independently associated with an increased risk of prostate cancer mortality (Table 3).

DISCUSSION

In a selected review of the medical literature and in a de novo analysis, black and white patients diagnosed with prostate cancer in equal-access healthcare systems had similar overall or disease-specific mortality. This evidence is consistent with reports of comparable biological disease characteristics in blacks and whites.[23,24] Our results also support the premise that differences in outcomes based on race are reduced or eliminated when patients have access to similar opportunities for treatment. Thus, race may be a marker for other prognostic factors.

Our main goal was to avoid methodological complexity—essentially minimizing the impact of socioeconomic status and patient- or investigator-based decisions—in assessing whether race affects prostate cancer mortality. Studies in equal-access systems allow for the independent impact of race to become evident. Likewise, examining the full spectrum of patients with prostate cancer, even if at a single institution, helps to avoid complex or

incorrect inferences made when comparing race-based outcomes among subgroups identified by the results of clinical tests or by selection of therapeutic interventions.

The inferences arising from our results depend on the impact of social factors on health outcomes being more influential and problematic methodologically in "non"–equal-access contexts. As a simple overview, individual-level measures of education, income, and occupation (as well as measures of social class in the United Kingdom) are traditional components of socioeconomic status that can affect health, and other characteristics also are relevant.[25,26] As mentioned previously, however, identifying, measuring, and accounting for such factors are challenging.[27,28] In addition, and with regard to prostate cancer in particular, personal attitudes and behaviors toward screening tests and treatment options can vary substantially according to race, contributing to observed differences in mortality.[11,29]

Study Limitations

We did not examine all reports that mention black–white differences in prostate cancer, yet our results are consistent with a systematic review finding "most studies investigating racial differences in prostate cancer treatment outcomes over the past years found no differences between races after controlling for tumor and patient characteristics."[30] In addition, the observational cohort analysis of veterans is from only 9 medical centers, and Hispanic or Native American (and other) veterans were not well represented or not always identified in medical records, but the study encompassed a wide geographic region and the African-American representation approximated prevalence in the US population. The focus on cause-specific death is another strength of the analysis, and the validity of results is supported by rigorous primary data collection of clinical variables in an equal-access setting. Finally, all potentially eligible beneficiaries may not have actually enrolled in or used their corresponding equal-access healthcare system, yet the minimization or removal of financial barriers provides a substantial contrast to private-payer healthcare systems.[12,13]

CONCLUSIONS

Future studies, including genomic analyses, will provide more insight on what does and *does not* define "race." In the interim, studies in patient-oriented research should recognize that the reasons for black versus white outcome differences in the United States are complex. In healthcare settings that do not involve equal access—with corresponding disparities in access, diagnosis, and treatment—a rigorous approach is warranted in terms of how race is conceptualized, measured, and analyzed. In regard to prostate cancer, the current findings confirm results from a report,[18] using Department of Defense data, indicating that racial disparities in outcomes for prostate cancer are eliminated or diminished in an equal-access system.

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CLINICAL SIGNIFICANCE

- Mortality among men with prostate cancer varies according to race, but the underlying reasons are unclear.
- Differences in mortality based on race would not be attributable to biological factors unless sociodemographic factors (affecting access, diagnosis, and treatment) are accounted for.
- In equal-access healthcare systems, race was not associated independently with mortality due to prostate cancer.

Table 1

Selected Articles Focusing on Race and Prostate Cancer in Equal-access Healthcare Systems

Setting of Study (Citation)	Race Variables	Main Finding*
Department of Defense[18]	Black; white	"[Overall] survival among blacks is similar to that among whites"
Veterans Health Administration[19]	Black; white	"Stratified for grade and stage, [overall] survival was similar in both races"
Veterans Health Administration[20]	Black; white	"When all patients were compared, the [overall] survival plots of black and white men were similar"
Veterans Health Administration[21]	Black; white	"No racial differences in [overall] survival were found"†
National Health Service[22]	Black; white; Indian/Pakistani	"No difference in prostate cancer-specific survival between black and white men"

*Main finding for current study, as found in Abstract or Results section of cited article.

†Result ("no difference") from Veterans Affairs portion of analysis, but "Blacks in the private sector fared significantly worse than did whites."

Table 2

Comparison of Baseline Characteristics Among White and Black Veterans in Observational Cohort Analysis (N = 1270)

Factor	White	Black	*P* Value*
Age (median in years)	72.2	69.1	<.001
	N (%)	N (%)	
First-degree relative:			.52
No	1058 (93.6)	132 (95.0)	
Yes	73 (6.5)	7 (5.0)	
Comorbidity:			.37
0	302 (26.7)	42 (30.2)	
1	333 (29.4)	42 (30.2)	
2	248 (21.9)	26 (18.7)	
≥3	248 (21.9)	29 (20.9)	
Anatomic stage:			.007
I or II	1014 (89.7)	115 (82.7)	
III	52 (4.6)	8 (5.8)	
IV	65 (5.8)	16 (11.5)	
Histologic grade:			.27
well differentiated	264 (23.4)	34 (24.5)	
moderately differentiated	686 (60.8)	73 (52.5)	
poorly differentiated	178 (15.8)	32 (23.0)	
Baseline PSA:†			.001
0–4	162 (14.8)	20 (14.5)	
4–10	402 (36.7)	34 (24.6)	
10–20	268 (24.5)	25 (18.1)	
20+	264 (24.1)	59 (42.8)	
D'Amico score:‡			.001
Low	375 (30.2)	32 (2.6)	
Moderate	348 (27.9)	38 (3.0)	
High	387 (31.0)	69 (5.5)	
Treatment:			.04
Watchful waiting/none	337 (29.8)	30 (21.6)	
Prostatectomy	210 (18.6)	30 (21.6)	
Beams/"seeds"	386 (34.1)	45 (32.4)	
Neoadjuvant only	198 (17.5)	34 (24.5)	
Prostate cancer mortality:			.58
Yes	175 (15.5%)	24 (17.3%)	
No	956 (84.5%)	115 (82.7%)	

PSA = prostate-specific antigen.

**P* values determined, as appropriate, by chi-square test, chi-square test for linear trend, or Wilcoxon rank-sum test.

[†] N = 1234 after accounting for missing values from 36 patients.

[‡] N = 1249 after accounting for missing values from 21 patients; the D'Amico score[17] was used as a composite variable representing prostate cancer prognosis.

Table 3

Impact of Prognostic Factors on Prostate Cancer Mortality Over 11 to 16 Years Among Veterans in Observational Cohort Analysis (N = 1249)

Prognostic Factor	Adjusted Hazard Ratio*	95% Confidence Interval	*P* Value
Age (per year)	1.03	1.01–1.06	.01
Comorbidity:			
0	[ref]	–	–
1	1.03	0.70–1.53	.87
2	1.31	0.86–1.98	.21
≥3	2.36	1.59–3.51	<.001
D'Amico score:[23]			
low risk	[ref]	–	–
intermediate risk	3.06	1.58–5.92	.0009
high risk	14.2	7.86–25.7	<.001
Race:			
white	[ref]	–	–
black	0.90	0.58–1.40	.65

*Adjusted for characteristics listed in this table, including D'Amico score[17] as a composite variable representing prostate cancer prognosis.