Short Communication

Race and Time from Diagnosis to Radical Prostatectomy: Does Equal Access Mean Equal Timely Access to the Operating Room?—Results from the SEARCH Database

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Abstract

Background: **African American men with prostate cancer are at higher risk for cancer-specific death than Caucasian men. We determine whether significant delays in management contribute to this disparity. We hypothesize that in an equal-access health care system, time interval from diagnosis to treatment would not differ by race.**

Methods: **We identified 1,532 African American and Caucasian men who underwent radical prostatectomy (RP) from 1988 to 2007 at one of four Veterans Affairs Medical Centers that comprise the Shared Equal-Access Regional Cancer Hospital (SEARCH) database with known biopsy date. We compared time from biopsy to RP between racial groups using linear regression adjusting for demographic and clinical variables. We analyzed risk of potential clinically relevant delays by determining odds of delays >90 and >180 days.**

Results: **Median time interval from diagnosis to RP was 76 and 68 days for African Americans and Caucasian men, respectively ($P = 0.004$). After controlling for demographic and clinical variables, race was not associated with the time interval between diagnosis and RP ($P = 0.09$). Furthermore, race was not associated with increased risk of delays >90 ($P = 0.45$) or >180 days ($P = 0.31$).**

Conclusions: **In a cohort of men undergoing RP in an equal-access setting, there was no significant difference between racial groups with regard to time interval from diagnosis to RP. Thus, equal-access includes equal timely access to the operating room. Given our previous finding of poorer outcomes among African Americans, treatment delays do not seem to explain these observations. Our findings need to be confirmed in patients electing other treatment modalities and in other practice settings.** (Cancer Epidemiol Biomarkers Prev 2009;18(4):1208–12)

Introduction

Apart from increasing age and family history, the most commonly reported risk factor for prostate cancer is African American ethnicity (1). Furthermore, African Americans with prostate cancer are more likely to have unfavorable tumor characteristics (2) and are at greater risk of prostate cancer mortality (3) than Caucasians.

The exact underlying reasons for prostate cancer racial disparities remain unclear but are likely multifactorial. Proposed mechanisms can be separated into three broad categories: biological (4-8), decreased access to care (i.e., lack of insurance/lower socioeconomic status; refs. 9-12), and attitudes to care among both patients and physicians (13-15). Although all three are likely involved in explaining racial disparity at the population level, the degree to which each mechanism affects prostate cancer outcomes is difficult to assess due to their interrelatedness (16, 17). By studying men within the Veterans Affairs (VA) system, which provides health care coverage for all veterans regardless of ability to pay, access-to-care issues are minimized (11). Within this system, we and others previously found worse prostate cancer outcomes among African Americans undergoing radical prostatectomy (RP) compared with Caucasians (2, 18). In that all men choose a single treatment

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modality, differences in attitudes toward care and patient preferences for one treatment over another are, likewise, minimized. However, it is possible poorer outcomes reflect inherent biases/attitudes within the system that delayed care of African Americans. Given that timely definitive treatment is a hallmark of optimal cancer care, significant delays from diagnosis to intervention could be a potential source of prostate cancer racial disparity. Indeed, whereas delays of a couple of months are not uncommon due to operating room backlogs, need for more diagnostic testing, and patients taking time to weigh their treatment options, some prior studies have shown that delays >90 or >180 days increase the risk of prostate cancer recurrence (19-21). However, racial differences in the time interval between diagnosis and treatment have not been investigated.

In the present study, we determined if there were significant differences in the time from diagnostic biopsy to RP between African American and Caucasian men in the equal-access setting of multi-institutional VA medical centers comprising the Shared Equal-Access Regional Cancer Hospital (SEARCH) database. We hypothesized that in an equal-access setting, time interval from diagnosis to treatment would not differ by race. If no difference is found, then it would be consistent with biology as a potential cause for racial differences in prostate cancer outcome, although other hypotheses are also possible and our study was not designed to specifically test the biology hypothesis. If differences are observed, then assessing the degree to which this contributes to racial disparity in prostate cancer outcomes is warranted. Moreover, if we find racial differences lead to significant delays in treatment, then this finding would have public health implications. Specifically, if reasons behind these delays are identified, changes in current health practices potentially improving care among African Americans may be implemented.

Materials and Methods

Study Population. After obtaining institutional review board approval at each center, demographic and clinicopathologic information from 1,782 patients treated with RP from 1988 to 2007 at the VA hospitals in Durham, North Carolina; West Los Angeles and Palo Alto, California; and Augusta, Georgia, were combined into SEARCH (18).

We excluded men treated with neoadjuvant radiation/hormonal therapy (n = 35) and patients with missing data on race (n = 8) or time from biopsy to RP (n = 92). As our goal was to explore differences between African Americans and Caucasians, we excluded 115 men with unknown or other racial groups, resulting in a study population of 1,532.

Statistical Analysis. The distribution of clinicopathologic characteristics was compared between African Americans and Caucasians using the χ^2 test for categorical variables and Wilcoxon-Mann-Whitney test for continuous variables. We used linear regression to determine associations between race and time from biopsy to surgery independent of demographic and clinical variables. We also analyzed the risk of potential clinically relevant delays by determining odds of delays >90 and >180 days using logistic regression. Variables not exhibiting normal distribution, such as prostate-specific antigen (PSA) and time from biopsy to surgery, were examined as continuous variables after log transformation. In the models, we controlled for the following

Table 1. Demographic and clinicopathologic features of men undergoing radical prostatectomy for prostate cancer

	Ethnicity		P
	Caucasian	African American	
No. patients (%)	849 (55)	683 (45)	
Age at biopsy			<0.001*
Mean ± SD (y)	62.1 ± 6.03	60.3 ± 6.82	
Year of biopsy			<0.001*
Median (IQR)	1999 (1994-2002)	2000 (1996-2003)	
BMI (kg/m^2)			0.42†
<25	198 (28)	159 (25)	
25-29.9	315 (44)	270 (43)	
30-34.9	141 (20)	136 (22)	
≥35	55 (8)	59 (10)	
PSA			0.002*
Median (IQR)	6.9 (4.8-10.6)	7.4 (5.1-11.9)	
Clinical stage (%)			<0.001†
T_1	368 (48)	398 (62)	
T_2/T_3	406 (52)	241 (38)	
Gleason sum at biopsy (%)			0.33†
2-6	521 (63)	415 (62)	
7	228 (27)	202 (30)	
8-10	80 (10)	53 (8)	
Time interval from diagnosis to surgery			0.004*
Median (IQR, d)	68 (45-103)	76 (48-116)	

Abbreviations: IQR, interquartile range; BMI, body mass index.
*Using Wilcoxon-Mann-Whitney test.
† Using χ^2 test.

Table 2. Factors associated with time interval from diagnostic prostate biopsy to radical prostatectomy

Variable	Relative risk (95% confidence interval)	*P*
Race		
Caucasian	(Reference)	
African-American	1.016 (0.998-1.035)	0.09
Age at biopsy	1.001 (0.999-1.002)	0.23
Year of biopsy	1.011 (1.008-1.014)	<0.001
BMI (kg/m^2)		
<25	(Reference)	
25-29.9	0.989 (0.968-1.010)	0.30
30-34.9	0.996 (0.971-1.022)	0.78
≥35	0.994 (0.959-1.031)	0.72
PSA (log-transformed)	0.998 (0.985-1.011)	0.78
Clinical stage		
T_1	(Reference)	
T_2/T_3	1.003 (0.985-1.021)	0.77
Biopsy Gleason sum		
2-6	(Reference)	
7	1.003 (0.983-1.022)	0.79
8-10	0.984 (0.955-1.014)	0.28
Surgical center		
VA Hospital 1	(Reference)	
VA Hospital 2	1.048 (1.018-1.080)	0.002
VA Hospital 3	0.987 (0.961-1.014)	0.334
VA Hospital 4	0.980 (0.956-1.005)	0.117

NOTE: Using linear regression with logarithmically transformed time interval from biopsy to surgery as the outcome variable.

possible confounders: age (continuous), biopsy year (continuous), body mass index (<25.0, 25.0-29.9, 30.0-34.9, or ≥35.0 kg/m^2), clinical stage (T_1 versus T_2/T_3), biopsy Gleason sum (2-6, 7, or 8-10), and surgical center. After determining relationships between race and log-transformed time interval between biopsy and RP, values were back-transformed for proper interpretation of results. To test for interactions between year of biopsy and race, we include both main-effect terms in the model along with a cross-product term and evaluated the *P* value using the Wald test. Associations with *P* values <0.05 were considered statistically significant. All analyses were done with STATA 9.2 (Statacorp).

Results

Baseline Study Population Characteristics. Forty-five percent of participants were African Americans (Table 1). African Americans were younger ($P < 0.001$), had undergone biopsy and surgery more recently (both $P < 0.001$), had higher PSA levels ($P = 0.002$), and were more likely to have T_{1c} disease ($P < 0.001$) than Caucasians.

Race and Time Interval from Diagnosis to Surgery. Median time from diagnostic biopsy to RP was significantly longer ($P = 0.004$) for African Americans (76 days) than Caucasians (68 days). However, after controlling for potential confounders, mean-adjusted time from biopsy to surgery was not significantly different between African Americans (79 days) and Caucasians (74 days; $P = 0.09$; Table 2). To determine which variable had the greatest effect on modifying the positive association on univariate analysis, potential confounding variables were added one at a time to the univariate model. When this was done, adding biopsy year had the greatest effect on affecting the association between race and time delays before surgery: adding biopsy year alone changed the *P* value for race from $P = 0.004$ to $P = 0.36$.

Given this unexpected potential confounding by biopsy year, we performed an unplanned subanalysis by stratifying patients into biopsy year quartiles and analyzed racial differences in the time from diagnosis to RP as a function of biopsy year. In each of the first three/earlier quartiles (<2003), there was no statistically significant association between race and time to RP on multivariate analysis (all $P \geq 0.34$). When these three earlier time points were combined, the mean adjusted racial difference in time to RP was 2 days. However, in the most recent period (2003-2007), the mean adjusted excess time interval between biopsy and RP among African Americans relative to Caucasians was 11 days ($P = 0.05$), although the formal test of interaction between biopsy year as a continuous variable and race was not statistically significant ($P = 0.10$).

To account for men who were on active surveillance then later decided to have surgery, we conducted subanalyses wherein we excluded men who had RP >180 and >360 days after biopsy. These subanalyses yielded results similar to the overall analysis (data not shown). To examine whether race was associated with potential clinically relevant delays, we examined the association between race and delays >90 and >180 days. We found that African Americans did not have an increased risk of delays >90 days (Table 3) or >180 days (Table 4).

Discussion

Underlying causes of racial disparities in prostate cancer outcomes remain the subject of current investigations.

Table 3. Factors associated with delays greater than 90 d from diagnostic prostate biopsy to radical prostatectomy

Variable	Odds ratio (95% confidence interval)	*P*
Race		
Caucasian	(Reference)	
African American	1.10 (0.86-1.41)	0.45
Age at biopsy	1.00 (0.99-1.03)	0.56
Year of biopsy	1.15 (1.11-1.20)	<0.001
BMI		
<25	(Reference)	
25-29.9	0.87 (0.65-1.17)	0.35
30-34.9	0.92 (0.65-1.30)	0.64
≥35	0.63 (0.39-1.02)	0.06
PSA (log-transformed)	1.08 (0.90-1.29)	0.40
Clinical stage		
T_1	(Reference)	
T_2/T_3	1.04 (0.78-1.34)	0.73
Biopsy Gleason sum		
2-6	(Reference)	
7	1.02 (0.78-1.34)	0.88
8-10	0.88 (0.56-1.36)	0.56
Surgical center		
VA Hospital 1	(Reference)	
VA Hospital 2	1.62 (1.07-2.47)	0.02
VA Hospital 3	0.92 (0.64-1.33)	0.66
VA Hospital 4	1.18 (0.85-1.65)	0.33

NOTE: Using logistic regression.

Table 4. Factors associated with delays greater than 180 d from diagnostic prostate biopsy to radical prostatectomy

Variable	Odds ratio (95% confidence interval)	*P*
Race		
Caucasian	(Reference)	
African American	1.23 (0.83-1.82)	0.31
Age at biopsy	1.01 (0.98-1.04)	0.46
Year of biopsy	1.05 (1.00-1.12)	0.105
BMI		
<25	(Reference)	
25-29.9	0.98 (0.62-1.55)	0.93
30-34.9	0.70 (0.39-1.26)	0.23
≥35	1.14 (0.57-2.27)	0.71
PSA (log-transformed)	1.08 (0.81-1.43)	0.60
Clinical stage		
T_1	(Reference)	
T_2/T_3	0.70 (0.46-1.05)	0.08
Gleason sum at biopsy		
2-6	(Reference)	
7	0.87 (0.56-1.34)	0.52
8-10	0.60 (0.28-1.30)	0.20
Surgical center		
VA Hospital 1	(Reference)	
VA Hospital 2	2.09 (1.04-4.08)	0.04
VA Hospital 3	1.60 (0.89-3.03)	0.11
VA Hospital 4	1.74 (0.94-2.93)	0.08

NOTE: Using logistic regression.

One possible contributor would be delay in instigating appropriate aggressive therapy. Although the oncological impact of treatment delays in prostate cancer remains debated (19-21), they can serve as quality control measures to assess systematic biases within the health care delivery system. In the current study, we determined if the time intervals between biopsy and RP in an equal-access setting are different for African Americans and Caucasians. We found, after controlling for demographic and clinical factors at the time of biopsy, that there was no significant difference between the racial groups with regard to the time between biopsy and surgery. Furthermore, race was not significantly predictive of delays >90 or >180 days. Thus, in the equal-access centers within SEARCH, there seemed to be equal timely access to the operating room.

In the general population, financial barriers leading to inaccessibility of health care resources is a major contributor to disparate prostate cancer outcomes between African Americans and Caucasian men. Indeed, low income (13) or lack of health insurance (9) have been identified as risk factors for being diagnosed with advanced prostate cancer. Controlling for socioeconomic factors such as literacy may reduce observed disparity in disease stage at diagnosis (10). Although some studies argue that socioeconomic status cannot fully explain racial disparity in outcomes (11, 22), the impact of unequal access to resources presents a dilemma for African Americans with prostate cancer. In fact, Medicare data suggest that the impact of racial disparity remains undiminished in the past decade (23).

In health care delivery settings identified as equal access, such as the military and VA hospitals, access to resources is assumed to be equal regardless of race (11). Our findings are, therefore, important because it is necessary to characterize what is truly ''equal access'' in an equal-access setting. Specifically, we addressed whether timely access to surgical services is the same regardless of race for a cohort of racially diverse veterans with prostate cancer. We initially found that the median time interval from biopsy to surgery was significantly longer for African Americans. However, after controlling for possible confounders, there was no significant difference in time between biopsy and surgery across racial groups.

Although we found no difference in time between diagnosis and surgery in men from SEARCH, in the same cohort, we found that African Americans were at greater risk for biochemical recurrence, denoted by increasing PSA in the absence of metastatic prostate cancer, compared with Caucasians (24). Thus, other sources of racial disparities need to be elucidated. Possible explanations included residual differences in socioeconomic status across racial groups, differences in comorbidities, biological differences in underlying disease aggressiveness, or other as of yet unclear reasons. With regard to potential biological differences, there are genetic differences involving several mechanisms, including androgen receptor and *CYP17* polymorphisms (6, 7), differences in insulin-like growth factor activity, and epidermal growth factor receptor variations (16), all of which may promote prostate cancer aggressiveness in African Americans. Moreover, African Americans harbor a *CYP3A4* gene variant leading to higher testosterone levels due to slower oxidative deactivation of testosterone (4, 8). Because prostate cancer is androgen responsive, this variant may potentially promote prostate cancer growth in African American men. Thus, all possible genetic sources of racial disparity contributing to worse outcomes in African Americans require further study.

Although not statistically significant, there seemed to be an interesting interplay between race and biopsy year. First, adjusting for biopsy year had the greatest effect on negating the initially observed positive association between race and time from diagnosis to surgery. Second, the mean adjusted racial difference in time interval between diagnosis and treatment increased from 2 days in men biopsied before 2003 to 11 days in more contemporary patients. Although the clinical and epidemiologic importance of these nominal *P* values in an unplanned secondary analysis is unclear, it does suggest that this issue should be examined in other settings to verify these results. If confirmed (i.e., a significant delay in more recent times, but not historically), then research must be conducted to identify the reasons for this discrepancy and how to modify practice patterns to prevent this. Regardless of the contemporary findings, the lack of significant racial difference in delays for patients treated in earlier years (<2003) cannot explain ethnic disparities in prostate cancer outcomes that we observed in 2002 (24). Thus, these findings are consistent with a potential biological explanation, at least in part, for the poorer outcomes among African American men; however, alternative explanations exist and further studies are needed to specifically test these various hypotheses.

Our study has several limitations. First, the study was based on surgical patients, a source for selection bias. Whether these findings apply to men electing other treatment modalities must be investigated. Second, it is possible our findings only pertain to the VA system.

Thus, similar analyses should be done in other equal-access settings, such as active military hospitals. Finally, we did not account for comorbid conditions other than obesity (body mass index), which may cause delays before surgery as these comorbidities require extensive medical work-up.

Conclusions

In a cohort of men undergoing RP in an equal-access setting, African American men did not have a significantly longer time interval between diagnostic biopsy to RP controlling for other demographic and clinical factors. Thus, for racially diverse veterans in the VA health care system, equal access includes equal timely access to the operating room. Whether similar findings would be observed in tertiary-care and community hospitals remains to be determined. If significant racial differences in time to RP are seen in other settings, implementation of health care delivery policies to reduce these disparities should be considered.

Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

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