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Racial/Ethnic Differences in the Relative Risk of Receipt of Specific Treatment among Men with Prostate Cancer

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Abstract

Objective—African-American (AA) men have excess mortality from prostate cancer (PCa) compared to White men, which has remained unchanged over several decades. The purpose of this study is to determine if race/ethnicity is an independent predictor of receipt of any definitive treatment vs watchful waiting/active surveillance (WW/AS).

Methods and Materials—Men diagnosed with PCa from 2004 to 2011 were identified from the Surveillance, Epidemiology and End-Results (SEER) program. Multinomial logistic regression analysis was performed to determine the relative risk ratio (RRR) of receipt of radical prostatectomy (RP), external beam radiation therapy (RT), brachytherapy, cryotherapy, or combination therapy vs WW/AS.

Results—Compared to White men, AA men were significantly less likely to receive RP (RRR 0.53, $p<0.001$), brachytherapy (RRR 0.72, $p<0.001$), cryotherapy (RRR 0.84, $p=0.001$), and combination therapy (RRR 0.70, $p<0.001$), and more likely to receive RT (RRR 1.03, $p=0.041$) versus AS/WW. Hispanic men were significantly less likely to receive RP (RRR 0.84, $p<0.001$) and brachytherapy (RRR 0.77, $p<0.001$), and more likely to receive RT (RRR 1.08, $p<0.001$) and cryotherapy (RRR 1.19, $p=0.005$) versus AS/WW compared to White men.

Conclusions—The disparate risk of receiving definitive treatment among AA and Hispanic men represents a significant public health issue that requires efforts to improve physician education, increase cultural competency, and ensure equitable access.

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Keywords

prostate cancer; racial disparity; treatment

1- Introduction

Treatment options for men diagnosed with prostate cancer (PCa) include radical prostatectomy (RP), external beam radiation therapy (RT), brachytherapy, cryotherapy, and combination therapy (defined herein as RP with RT, or two forms of RT). Certain populations of men are at greater risk for undertreatment, which can lead to poorer outcomes such as biochemical recurrence, metastasis and death from PCa. African-American (AA) men, in particular, have a higher incidence of PCa, present with higher grade and stage disease, and have greater risk of mortality from PCa compared to White men.[1–3] Studies investigating the role of socioeconomic factors, screening patterns and genetic risk factors do not completely explain the disparity, thus implicating differences in treatment received as a major factor.[4–6] To that end, there are over 30 years of data demonstrating variation in the type of treatment received by AA men compared to White men, with consistent utilization of RT or ADT rather than RP, despite convincing data which show a survival benefit to utilization of RP in AA men.[7–9]

Despite the consistently reported preferential utilization of RT over RP among AA men, some have suggested that there may not be an overall treatment disparity since AA who receive RT are receiving guideline-based definitive treatment.[10] The purpose of this study is to determine whether there are differences in receipt of each definitive therapy (RP, RT, brachytherapy, cryotherapy, or combination therapy) vs WW/AS for PCa among AA, Hispanic, White, and Asian/Other men. It is important to elucidate these treatment trends to determine if practice patterns have evolved regarding higher risk populations, or if persistent treatment disparities need to be addressed more urgently. To address these issues, we utilized SEER data from 2004–2011, controlling for various factors that have been implicated in poorer outcomes from PCa.

2- Materials and Methods

2.1- Data Sources and Study Cohort

The study was conducted using Surveillance, Epidemiology, and End Results (SEER) Registry 17. The study cohort consisted of 327,641 men diagnosed 2004–2011 with clinically localized PCa. SEER data from 2012 was excluded due to lack of PSA data. Men excluded from the study included those with “death certificate and autopsy” only detected PCa, pre-treatment data indicating advanced stage, non-localized PCa (clinical T3b and PSA >40ng/ml) and missing data on variables of interest (race/ethnicity, age, grade, American Joint Committee on Cancer (AJCC) stage, prostate specific antigen (PSA), SEER site, and treatment received). Less than 4% of men were excluded due to missing data on variables of interest. Men were grouped into the following racial groups using SEER race code variables AA (Non-Hispanic black/AA), Hispanic Origin Recode NHIA recode, White (Race code Non-Hispanic Whites) and Asian/Other (race code combined Asian Pacific

Islanders and Alaskan natives). Men were grouped using Gleason sum, PSA category (≤ 1 ng/ml, $>1-2$ ng/ml, $>2-4$ ng/ml, $>4-10$ ng/ml, $>10-20$ ng/ml, $>20-40$ ng/ml) and AJCC tumor classification. Marital status was reclassified as married (including cohabitating) and non-married (single, divorced or widowed). The treatment categories were classified using SEER treatment variables and were classified as receiving definitive therapy as receiving a RP, RT, brachytherapy, cryotherapy, or combination therapy. Men were classified as not receiving definitive therapy (WW/AS) if not receiving either of the aforementioned treatments.

2.2- Statistical Analysis

The means for continuous variables were analyzed using *t-test* with unequal variances for between group comparisons. Chi square tests were used to assess between group differences for categorical variables (race/ethnicity, PSA, age, treatment, Gleason score, marital status, year of diagnosis, SEER site, AJCC Classification and D'Amico risk classification). Multinomial regression analysis was performed to determine the relative risk ratio (RRR) for the dependent variable receiving a specific treatment over WW/AS by race/ethnicity (AA, Hispanic, and Asian/Other) over White adjusting for Gleason sum, AJCC tumor classification, age category, PSA, year of diagnosis, marital status and SEER registry site. Reference is White, Gleason 6, Age 60–69, PSA ≤ 1 , year of diagnosis 2004, not married, and San Francisco-Oakland registry site. All statistical analyses were performed using STATA Statistical software version 12, StataCorp LP College Station, TX.

3- Results

There were 327,641 men included for analysis, of which 14.0% were AA, 8.2% were Hispanic, 72.8% were White, and 5.0% were Asian/Other (Table 1). Overall, AA men were younger, whereas Asian/Other men had higher mean PSA, were significantly older, and had the highest percentage of D'Amico high-risk PCa.

There were significant differences in the type of treatment received between racial/ethnic groups (Table 2). A significantly lower percentage of AA men received RP (31.1%) compared to Hispanic (38.3%), White (38.2%), and Asian/Other men (34.3%) (all $p < 0.001$). A similar percentage of Hispanic men received RP compared to White men (38.3% vs 38.2%), but a higher percentage received RT (25.5% vs 22.7% White, $p < 0.001$). A significantly higher percentage of AA men received RT (26.8%) compared to Hispanic (25.5%) and White (22.7%) men (both $p < 0.001$), but a similar percentage compared to Asian/Other men (27.5%). A significantly lower percentage of White men received RT compared to all other groups. There were no differences in receipt of cryotherapy between any of the racial groups.

Multinomial logistic regression was performed to test the relative risk (RR) of receiving RP, RT, brachytherapy, cryotherapy or combination therapy vs WW/AS (Table 3). The model was adjusted for Gleason sum, D'Amico classification, age, year of diagnosis, marital status and registry site. Compared to White men receiving the same treatment modality, AA men were 47% less likely to receive RP (RRR 0.53; 95% CI: 0.52, 0.55, $p < 0.001$), 3% more likely to receive RT (RRR 1.03; 95% CI: 1.001, 1.07, $p = 0.041$), 28% less likely to receive

brachytherapy (RRR 0.72; 95% CI: 0.69,0.75), 16% less likely to receive cryotherapy (RRR 0.84; 95% CI: 0.76,0.93, $p<0.0001$), and 30% less likely to receive combination therapy (RRR 0.70; 95% CI: 0.68,0.73, $p<0.001$) than WW/AS. In fact, AA men were less likely to receive RP compared to all other racial groups, and AA men were less likely to receive RP over radiation compared to White men (RRR 0.52, $p<0.001$, data not shown). Compared to White men, Hispanic men were 16% less likely to receive RP (RRR 0.84; 95% CI: 0.81,0.88, $p<0.001$), 8% more likely to receive RT (RRR 1.08; 95% CI: 1.04,1.12, $p<0.001$), and 23% less likely to receive brachytherapy (RRR 0.77; 95% CI: 0.73,0.81, $p<0.001$) over WW/AS. Compared to White men, Asian/Other men were 10% less likely to receive RP (RRR 0.90; 95% CI: 0.86,0.95, $p<0.001$), 12% more likely to receive RT (RRR 1.12; 95% CI: 1.06,1.18, $p<0.001$), and 21% less likely to receive brachytherapy (RRR 0.79; 95% CI: 0.74,0.85, $p<0.001$) over WW/AS.

4- Discussion

The results of this study demonstrate that AA men are less likely to receive almost every definitive treatment modality over receiving WW/AS compared to White men and only 3% more likely to receive RT, controlling for multiple factors including tumor grade, stage and PSA. Additionally, Hispanic men demonstrate a lower rate of receipt of RP and brachytherapy over receiving WW/AS compared to White men. The 3% increase in risk of receipt of RT among AA men likely does not make up for the 16–47% risk of not receiving RP, cryotherapy, brachytherapy, or combination therapy vs WW/AS compared to White men. These data stand in contradistinction to reports that AA men receive guideline based therapy[10] and represent a significant treatment disparity.

A significant finding of this study is the emerging disparity in receipt of definitive treatment among Hispanic men. Hispanic men are less likely to receive RP compared to White men, though not to the degree of AA men, as well as brachytherapy. These data reflect a change in patterns of treatment initially reported from SEER 1992–1999 which showed that Hispanic men had similar likelihood of receiving definitive therapy.[8] As seen in AA men, Hispanic men have a significantly increased likelihood of receipt of RT compared to White men. This particular finding among Asian/Other men may be more understandable due to the significantly older age at diagnosis and higher percentage of Gleason 8–10 disease. However, among younger men (AA and Hispanic), this consistent trend towards utilization of RT vs RP seems inconsistent with data showing improved outcomes of RP among younger men, particularly with intermediate or high-risk disease.[11] With an ever increasing Hispanic population in the US, it will be important for the public health community to address disparities in treatment for PCa.

We show that AA men are significantly less likely to receive RP, brachytherapy or combination therapy after a diagnosis of PCa, with a slightly increased risk of receiving RT compared to White men. In a recent study from the SEER-Medicare database, Presley et al also showed that AA men had lower odds of receiving treatment for PCa.[12] Furthermore, among men determined to have intermediate- to high-benefit disease, AA men were less likely to receive treatment, with the greatest disparity seen among men with high-benefit disease (Gleason sum 7–10 or T2b-T2c disease and life expectancy ≥ 10 years).[12] Thus,

AA men, who would appear to have the greatest need for definitive treatment, are significantly less likely to receive such treatment than their White counterparts. Pollack et al also found that AA men overall were less likely to receive definitive treatment than Whites. [13] In part, this was attributable to AA men having been more likely to be treated at a hospital with a high proportion of AA patients, and men treated at these hospitals were significantly less likely to receive definitive treatment. The authors were able to demonstrate that hospitals with a higher proportion of AA patients had higher rates of Medicaid, and that higher rates of Medicaid were associated with lower odds of treatment. However, they did not have the demographic information of the treating physicians or the availability of subspecialists such as urologists or medical/radiation oncologists within these institutions. It is possible that high minority population hospitals reliant on Medicaid reimbursement may not have access to subspecialty care, and difficulties in referral to hospitals with a broader range of services may negatively impact rates of treatment. These variations in practice patterns among treating physicians and hospitals are excellent targets for public health entities that create and fund programs to reduce disparity in PCa treatment.

The fact that AA men are less likely to receive most modalities of treatment is not unique to PCa. AAs have increasing excess mortality from colorectal cancer compared to Whites, and data abstracted from Medicare has shown that AAs are less likely to receive adjuvant therapy after colon cancer diagnosis.[14, 15] Additionally, data from equal-access care hospitals demonstrate that when AA receive equivalent surgical and adjuvant care for stage-matched disease, survival outcomes are improved and are similar to their White counterparts.[16] This mirrors similar findings in the PCa literature which have shown that AA men who receive RP may experience similar biochemical-recurrence free survival despite worse presenting disease, and underscores the importance of equal application of stage-appropriate standard treatment.[17]

Breast cancer is another malignancy with a widening survival disparity between AA and White women, with data from the equal-access Department of Defense healthcare system suggesting that access to care may not be the only barrier to optimal outcomes.[18] In a recent analysis of SEER-Medicare data, AA women who were matched on presentation characteristics to White women were significantly less likely to receive treatment, had longer time from diagnosis to treatment, and lower receipt of adjuvant chemotherapy.[19] These results were mostly driven by the greater proportion of higher stage at presentation among AA women; however, in another study by Sail et al analyzing women with early stage, operable disease AA women were less likely to receive adjuvant chemotherapy after breast conserving surgery, regardless of node status.[20]

The current study highlights the glaring disparity in the receipt of definitive treatment for PCa. However, it is no longer enough to identify the sources of disparity in outcomes from PCa, or any other disease process. It is incumbent upon the medical community to take the information that has been gleaned from decades of population-based research and implement strategies to combat these persistent disparities.

One of the first steps in reducing treatment disparity in PCa is provision of consistent access to subspecialty care and information about PCa risk and treatment options, particularly for

men in lower sociodemographic strata. A second step would be to prioritize diversification of the physician workforce to address the needs of the US population. A third opportunity for improvement is to address barriers to quality care and improve cultural competence within the healthcare system. Betancourt et al conducted a systematic review of the literature and identified three areas where cultural competence could be improved at the organizational, structural and clinical level.[21] The common theme in all three areas is the lack of minority representation in leadership positions of medical and public health school faculties and healthcare management organizations, and under-representation of physicians of color within the healthcare workforce. The lack of members of under-represented groups at leadership levels translates to lack of understanding of the cultural needs of communities of color and thus, reduced implementation of programs to address these needs.[22] It has been demonstrated that despite an overall physician shortage in AA and Hispanic communities, AA and Hispanic physicians are more likely to care for AA and Hispanic patients in medically underserved areas, provide more effective care due to lack of cultural or language barriers, and more likely to care for patients with Medicaid or no insurance.[23, 24] However, efforts to increase AA and Hispanic representation in medical and public health schools so that they reflect the general population have been thwarted by attacks on affirmative action programs.[25] These attacks have a direct, negative impact on the most economically and medically vulnerable populations who will continue to have poor outcomes unless institutional diversity is addressed in health policy, health delivery and medical education systems.[26] Despite the obstacles to diversify the medical trainee population, there are some programs that have been successfully implemented to increase the number of graduates who go on to serve medically underserved populations.[27, 28] Efforts to recruit physicians of color and White physicians interested in providing healthcare to economically disadvantaged populations should be encouraged and supported.

There are some limitations that must be taken into consideration when interpreting our findings. We were not able to determine which of the patients who did not receive treatment underwent AS for low-risk disease vs WW, particularly since SEER data captures treatment within a four month window from diagnosis. The likelihood that AS is a significant confounder is small in that our findings were consistent across all treatment modalities. Additionally, some have called into question the utility of AS in AA men due to the higher risk of upstaging and adverse pathologic features among those who have RP, but would have otherwise qualified for inclusion in most AS protocols.[29] Second, we were not able to assess comorbidity within our cohort. This, too, likely has limited effect on the results as the AA population was significantly younger, and there is no significant data showing that AA men with PCa present with significantly higher comorbidity, which would preclude them from treatment.[9] Clearly there are significant socioeconomic and health status indicators that affect length and quality of life among AAs; however, data have shown that both AA and White men can expect an average life expectancy greater than 25 years after reaching age 50.[30, 31]

5- Conclusions

AA and Hispanic men are less likely to receive treatment for PCa compared to White and Asian/Other men; in particular, AA and Hispanic men were less likely to receive RP and

brachytherapy than White men. The lack of definitive treatment represents a significant factor likely contributing to higher mortality in minority populations. These findings represent a major public health issue that requires addressing diverse representation in healthcare leadership positions, recruiting physicians of color to specialty areas such as Urology and Medical Oncology, and implementing strategies to improve PCa knowledge, screening behaviors, and access to treatment in communities of color.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Highlights

- African-American men have worse mortality from prostate cancer compared to Whites
- We determined the relative risk of receipt of treatment modalities vs no treatment
- African-American men are less likely to receive any treatment except radiation
- Hispanic men also have an emerging disparity in treatment
- A shift in public policy is needed regarding management of prostate cancer

Table 1

Clinical and Demographic Data (n=327,641)

	African-American	Hispanic	White	Asian
Race/Ethnicity No. (%)	45,864 (14.0%)	26,904 (8.2%)	238,632 (72.8%)	16,241 (5.0%)
Mean Age (y) ± SD	63.1 ± 8.97	65.5 ± 9.06	66.0 ± 8.92	67.4 ± 8.76
Mean PSA (ng/ml) ± SD	8.64±6.62	8.58±6.44	7.58±5.71	9.04±6.50
Gleason Sum	<6	1.4%	1.3%	1.3%
	6	44.2%	47.1%	42.3%
	7	42.1%	39.1%	39.0%
	8–10	12.3%	12.5%	17.4%

Table 2
Comparison of Overall Treatment Received by Individual Racial/Ethnic Pairings

	WW/AS	RP	Brachytherapy	RT	Combination	Cryotherapy
AA vs Hispanic	24.0% vs 23.9%, NS	31.1% vs 38.3%, *	9.1% vs 7.0%, *	26.8% vs 25.5%, *	9.1% vs 5.3%, *	1.2% vs 1.3%, NS
Hispanic vs White	23.9% vs 21.4%, *	38.3% vs 38.2%, NS	7.0% vs 10.9%, *	25.5% vs 22.7%, *	5.3% vs 6.9%, *	1.3% vs 1.3%, NS
AA vs White	24.0% vs 21.4%, *	31.1% vs 38.2%, *	9.1% vs 10.9%, *	26.8% vs 22.7%, *	9.1% vs 6.9%, *	1.2% vs 1.3%, NS
AA vs Asian	24.0% vs 22.5%, *	31.1% vs 34.3%, *	9.1% vs 8.5%, ^	26.8% vs 27.5%, NS	9.1% vs 7.3%, *	1.2% vs 1.1%, NS
White vs Asian	21.4% vs 22.5%, *	38.2% vs 34.3%, *	10.9% vs 8.5%, *	22.7% vs 27.5%, *	6.9% vs 7.3%, #	1.3% vs 1.1%, NS
Hispanic vs Asian	23.9% vs 22.5%, *	38.3% vs 34.3%, *	7.0% vs 8.5%, *	25.5% vs 297.5, *	5.3% vs 7.3%, *	1.3% vs 1.1%, NS

* p-value <0.001,

^ p-value=0.014,

p-value=0.044, NS-not significant (p-value >0.05)

AA- African-American, RP- radical prostatectomy, RT- external beam radiation therapy, WW- watchful waiting; Combination treatment is defined as surgery and radiation, or two forms of radiation.

Table 3

Relative risk ratios (RRR) of Definitive Treatment vs WW/AS (95% Confidence Interval)

	White	African-American	Hispanic	Asian/Other
RP	Reference	0.53 (0.52,0.55) p<0.001	0.84 (0.81,0.88) p<0.001	0.90 (0.86,0.95) p<0.001
RT	Reference	1.03 (1.001,1.07) p=0.041	1.08 (1.04,1.12) p<0.001	1.12 (1.06,1.18) p<0.001
Brachytherapy	Reference	0.72 (0.69,0.75) p<0.001	0.77 (0.73,0.81) p<0.001	0.79 (0.74,0.85) p<0.001
Cryotherapy	Reference	0.84 (0.76,0.93) p=0.001	1.19 (1.05,1.34) p=0.005	1.01 (0.85,1.19) p=0.94
Combination	Reference	0.70 (0.68,0.73) p<0.001	1.02 (0.96,1.09) p=0.45	1.04 (0.96,1.12) p=0.36

Multinomial logistic regression model adjusted for race/ethnicity, Gleason sum, D'Amico classification, age, year of diagnosis, marital status and registry site. Reference is White, Gleason 6, low risk, age 60–69, year of diagnosis 2004, married, and San Francisco-Oakland registry site.

WW- watchful waiting, RP- radical prostatectomy, RR- relative risk, RT- radiation therapy

Combination treatment is defined as surgery and radiation, or two forms of radiation.