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Differences in Clinical Characteristics and Disease-free Survival for Latino, African American, and Non-Latino White Men with Localized Prostate Cancer

Data from CaPSURE™

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BACKGROUND. Few studies of ethnicity and prostate cancer have included Latino men in analyses of baseline clinical characteristics, treatment selection, and disease-free survival (DFS). The present study examines the impact of Latino ethnicity on these parameters in a large, multiinstitutional database of men with prostate cancer.

METHODS. We compared baseline disease characteristics and clinical outcomes for Latino ($N = 138$), non-Latino White (NLW, $N = 5619$), and African-American (AA, $N = 608$) men with localized prostate cancer by using chi-square and ANOVA for baseline variables and survival analysis to examine differences in time to recurrence.

RESULTS. Latino men resembled AA men more than NLW on sociodemographic characteristics. AA men had higher Gleason scores and prostate-specific antigen (PSA) at diagnosis than Latino or NLW men (both $P < 0.01$). 10% of both Latino and AA men presented with advanced disease (T3b/T4/N+/M+) versus 4% of NLW ($P < 0.01$). Latino men did not receive different treatments than NLW or AA men after controlling for clinical and demographic factors; however, AA men were more

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likely to receive external beam radiation (OR = 1.51, 95% confidence interval [CI] = 0.99–2.31) and hormone treatment (OR = 1.56, 95% CI = 1.05–2.32) then NLW men. For prostatectomy patients, 3-year actuarial DFS rates were 83% for NLW men and 86% for Latino men versus 69% for AA men ($P < 0.01$). After controlling for clinical and sociodemographic variables, AA men were somewhat more likely than NLW to experience disease recurrence after radical prostatectomy (RP) (HR = 1.38, 95% CI = 0.98–1.94, $P = 0.06$).

CONCLUSIONS. Latinos are more similar to African Americans on sociodemographic characteristics but more similar to NLW on clinical presentation, treatments received, and DFS. ***Cancer. Cancer* 2006;106:789–95.**

KEYWORDS: prostatic neoplasms, ethnicity, longitudinal analysis.

The influence of ethnicity on prostate cancer presentation and outcome is receiving growing attention in research literature. However, most research on prostate cancer and ethnicity has focused on the greater incidence among African Americans[1] or on comparing clinical and quality of life (QOL) outcomes for Whites and African Americans,[2–4] even though Latinos have prostate cancer rates close to that of non-Latino Whites (NLW). Prostate cancer strikes more than 8500 Latino men each year, accounting for 27% of new cancer diagnoses and 10% of cancer deaths among Latino men.[5] From 1997–2001, the age-adjusted incidence rate of prostate cancer was 140.0 per 100,000 for Latinos, compared with 167.4 for Whites and 271.3 for African-American (AA) men.[6] The mortality rates during that time period for Latino men were 23.5 per 100,000, versus 28.8 for White men and 70.4 for AA men.[6]

Previous studies have shown that Latino men present with clinical characteristics more similar to those of AA than NLW. In a study of external beam radiation patients, the baseline and posttreatment clinical characteristics of 54 Latino men with prostate cancer were compared with AA and NLW men with prostate cancer. Latino men presented with higher prostate-specific antigen (PSA) results at baseline than NLW and had a nonsignificant trend toward lower 5-year disease-free survival (DFS) than NLW.[7] Hoffman and his colleagues found that 12.3% of AA and 10.5% of Latinos presented with advanced-stage prostate cancer, compared with 6.3% of NLW.[8]

Whereas some studies have examined differences between AA and White men in biochemical recurrence, less is known about differences in clinical outcomes between Latinos and other men with prostate cancer. Given the similarity in clinical presentation between Latinos and AA, it may be hypothesized that disease recurrence and other clinical outcomes would be similar for the two groups. Whether this hypothesis is true or not is unclear, as studies that have included Latino men have focused on baseline disease characteristics only or on baseline disease and treatment choice. In the current study, we extend the discussion of ethnicity and prostate cancer by including Latino men in a comparison of baseline and follow-up characteristics of men with clinically localized disease. We describe baseline clinical and sociodemographic characteristics of Latino men with prostate cancer and compare them with NLW and AA men. We also compare the 3 ethnic groups on initial treatment. For men who received a radical prostatectomy (RP), we examine DFS by ethnicity.

MATERIALS AND METHODS

Participants

We drew men from the CaPSURE™ (Cancer of the Prostate Strategic Urologic Research Endeavor) study, a longitudinal, observational, disease registry for men with biopsy-proven prostate cancer. In CaPSURE, more than 1000 variables are collected from participants and their urologists. Sociodemographic and QOL data are collected from patients at enrollment and at 6-month intervals thereafter. Participating practices provide clinical data at enrollment and each time the patient returns for care, including history of prostate cancer diagnosis, number and results of biopsies, pathology reports, staging tests, primary and subsequent prostate cancer treatments, Karnofsky performance status scores, and medications. Follow-up PSA results are also reported. The institutional review board at the University of California, San Francisco and contributing sites approved data collection protocols and other study methods.

As of December 2004, more than 11,000 patients were enrolled in this study. The group of men currently being followed numbers more than 6800. Participants are actively enrolled from a core group of 31 urologic practice sites (40 sites have ever enrolled patients into CaPSURE). The sample is primarily from community-based practices, with only about 8% of

participants drawn from academic or Veterans Administration practices. A more detailed description of the CaPSURE project methods is available.[9,10]

To be included in the current analysis, men had to be 1) diagnosed with prostate cancer between January 1989 and December 2004; 2) self-identified as Latino, AA, or NLW; and 3) enrolled from a study site at which Latino patients comprise $\geq$ 1% of patients at the site. The resulting sample of 6365 men (138 Latino, 608 AA, 5619 NLW) was used in the analysis of baseline clinical and sociodemographic characteristics. Men in this analysis sample came from 25 practices, with 31% of the Latino men from one Texas site, 42% from 6 other sites in California, Florida, Illinois, New York, Virginia, and Wisconsin, and the remaining 28% from 18 other sites.

Of the 11,583 CaPSURE patients, 24% were not included in this analysis because they were seen at study sites that did not treat any Latino men or treated very few Latino men. In order not to introduce bias based on site practices and uneven distribution of ethnic groups within sites, we chose to exclude all patients from these sites. An additional 25% of CaPSURE patients were excluded from our analysis because they reported another ethnic identity, a mixed ethnic identity, or did not report ethnicity. Finally, an additional 3% were diagnosed outside the study period (1989–2004) and were excluded.

In the main study cohort of 6365 men, 5643 were diagnosed with localized disease (clinical Stage T1 to T3a) and had initial treatment information. Therefore, these men could be included in the analysis of treatment choice. There were no differences by ethnicity for inclusion in this analysis (90% of Latinos, 88% of AA, and 89% of NLW).

To examine DFS in men receiving surgical treatment, we looked at men who had received radical prostatectomy without any neoadjuvant or adjuvant treatments, had baseline clinical data necessary to categorize clinical risk (i.e., had clinical T stage, Gleason grade, and PSA test results), and had at least 2 follow-up serum PSA results to assess disease recurrence. Surgery patients were selected for the recurrence analysis because they represented the largest treatment group in the study cohort. This resulted in a subset of 1842 men who could be included in the analysis of time to disease recurrence. Again, there were no differences by ethnicity for inclusion in this analysis (28% of Latinos, 25% of AA, and 29% of NLW included in this analysis).

Statistical Analysis

Baseline clinical and sociodemographic characteristics for the 3 ethnic groups were compared by using the chi-square test for discrete variables and analysis of variance for continuous variables. Clinical risk was based on a modification of risk groups defined by D'Amico et al.[11] Patients were low risk if they had PSA $\leq$ 10 ng/mL, Gleason sum $<$ 7 with no primary or secondary Gleason score of 4 or 5, and clinical T-stage T1–T2a; intermediate risk if they had PSA 10.1–20 ng/mL or Gleason sum 7 or Gleason secondary 4 or 5, or T-stage cT2b–2c; and high risk if they had PSA $>$ 20 ng/mL, or Gleason sum $>$ 7 or Gleason primary 4 or 5, or T-stage cT3a.

To understand the relation between ethnicity and primary treatment, we first carried out a chi-square test. Then, we created a multinomial logistic regression model with primary treatment as the outcome (i.e., a multilevel categorical variable) to determine if Latino men are more or less likely to receive certain treatments than other ethnicities. We statistically controlled clinical and sociodemographic factors in the model, and we also included study site and year of diagnosis in the model to control potential confounding by local practice patterns and changes in treatment mix over time.[10]

We used survival analysis techniques to assess the impact of patient ethnicity on disease recurrence after RP. Disease recurrence was defined as 2 consecutive PSA measures $\geq$ 0.2 ng/mL following RP. Because serial PSA data were not complete for all patients, recurrence for some patients was also defined by delivery of a second prostate cancer treatment more than 6 months after prostatectomy. In an observational registry, such as CaPSURE, a patient may not meet full criteria for biochemical recurrence when clinical treatment for recurrence is evident. Thus, a 6-month cutoff was used to effectively differentiate between adjuvant treatment and a second treatment due to disease recurrence. We have previously demonstrated that using such a cutoff can identify treatments that are surrogate markers of disease recurrence in this population.[12,13] Whichever event occurred first was considered the date of disease recurrence. First, we conducted a life table analysis and produced Kaplan–Meier graphs by ethnicity. We next created a Cox proportional hazards regression model to determine if ethnicity was an independent predictor of DFS controlling for clinical and sociodemographic factors.

When performing pair-wise comparisons of the 3 ethnic groups, we considered a more conservative *P*-value of 0.01 to be statistically significant. For all other analyses, we considered *P*-values $<$ 0.05 to be statistically significant. All analyses were performed with version 9.1 SAS Software (SAS Institute, Cary, NC).

TABLE 1
Sociodemographic Characteristics by Ethnicity

	Latino (*N* = 138)	African American (*N* = 608)	White (*N* = 5619)	
	n (%)	*n* (%)	*n* (%)	*P*
Age at diagnosis				< 0.01[a]
< 55	17 (12)	67 (11)	480 (9)	
55-64	50 (36)	224 (37)	1662 (30)	
65-74	58 (42)	239 (39)	2395 (43)	
≥ 75	13 (9)	78 (13)	1082 (19)	
Age at diagnosis Mean ± SD	64.5 ± 7.5	64.6 ± 8.1	66.8 ± 8.5	< 0.01[b]
Education				<0.01[a]
No college	88 (66)	394 (69)	2145 (39)	
Some college	17 (13)	106 (18)	1127 (21)	
College graduate	28 (21)	75 (13)	2196 (40)	
Yearly household income				<0.01[a]
< $30,000	76 (63)	315 (62)	1524 (32)	
$30-50,000	29 (24)	97 (19)	1191 (25)	
> $50,000	16 (13)	98 (19)	2057 (43)	
Type of insurance				<0.01[a]
Medicare plus supplement	27 (20)	141 (23)	2286 (41)	
Medicare alone	18 (13)	116 (19)	722 (13)	
Private	74 (54)	238 (39)	2307 (41)	
Other or none	19 (14)	113 (19)	304 (5)	
Relationship status				<0.01[a]
Married or together	115 (89)	454 (81)	4819 (91)	
Single	14 (11)	105 (19)	500 (9)	

May not sum to total "*N*" because of missing values. SD: standard deviation.
[a]*P*-value from chi-square test.
[b]*P*-value from ANOVA.

TABLE 2
Baseline Clinical Characteristics

	Latino (*N* = 138)	African American (*N* = 608)	White (*N* = 5619)	
	n (%)	*n* (%)	*n* (%)	*P*
PSA, ng/mL				< 0.01[a]
< 4	17 (14)	34 (6)	719 (14)	
4.1-10	55 (46)	250 (45)	2986 (57)	
10.1-20	27 (23)	128 (23)	907 (17)	
> 20	21 (18)	142 (26)	590 (11)	
Median	6.9	9.8	6.7	< 0.01[b]
Gleason sum				< 0.01[a]
2-4	14 (11)	44 (8)	408 (8)	
5-6	75 (60)	284 (49)	3112 (59)	
7	23 (18)	167 (29)	1210 (23)	
8-10	14 (11)	81 (14)	509 (10)	
Disease stage				< 0.01[a]
T1–T3a	113 (90)	504 (90)	5054 (96)	
T3b/T4/N+/M+	13 (10)	59 (10)	229 (4)	
Clinical risk				< 0.01[a]
Low	39 (32)	148 (27)	1897 (37)	
Intermediate	52 (42)	168 (30)	1863 (36)	
High	32 (26)	242 (43)	1400 (27)	
BMI				< 0.01[a]
Not overweight	27 (21)	144 (26)	1635 (31)	
Overweight	69 (54)	275 (50)	2605 (49)	
Obese	31 (24)	132 (24)	1036 (20)	
No. of comorbidities				0.29[a]
None	34 (25)	117 (20)	1028 (19)	
1-2	61 (44)	297 (50)	2865 (52)	
3+	43 (31)	185 (31)	1657 (30)	

May not sum to total "*N*" because of missing values. PSA: prostate-specific antigen; BMI: body mass index. [a]*P*-value from chi-square test. [b]*P*-value from Wilcoxon test.

TABLE 3
Treatment Choice by Ethnicity

	Latino (*N* = 124)	African American (*N* = 533)	White (*N* = 4986)	
	n (%)	*n* (%)	*n* (%)	*P*
Primary treatment				< 0.01
RP	57 (46)	234 (44)	2440 (49)	
Brachytherapy	30 (24)	36 (7)	643 (13)	
XRT	16 (13)	87 (16)	698 (14)	
Hormone therapy	17 (14)	153 (29)	875 (18)	
WW	4 (3)	23 (4)	330 (7)	

RP: radical prostatectomy; XRT: external beam radiation; WW: watchful waiting.

RESULTS

Baseline Characteristics

The 3 groups differed significantly on a number of sociodemographic and clinical characteristics (Tables 1 and 2). Latino men were different from NLW men in age, education, household income, type of health insurance, and advanced disease stage (all $P < 0.01$ for pair-wise comparisons). Latino men were different from AA men in serum PSA levels and clinical risk at presentation (all $P < 0.01$ for pair-wise comparisons). Furthermore, AA men were different from NLW men on all characteristics except number of comorbidities (all $P < 0.01$ for pair-wise comparisons).

Primary Treatment Selection

RP was the most common treatment for all 3 ethnic groups. However, brachytherapy was next most common in Latino men, and hormone therapy was next most common in AA men. NLW men had the highest proportion of men selecting watchful waiting (Table 3; all $P < 0.01$ for pair-wise comparisons). In a multinomial logistic regression model that controlled for clinical risk, age, education, marital status, type of insurance, comorbidities, diagnosis year, and study site, ethnicity was significantly related to treatment selection ($P = 0.01$). This difference primarily resulted from AA men being more likely to receive hormonal therapy rather than RP compared with NLW men (odds ratio [OR] = 1.56, 95% confidence interval [CI] = 1.05–2.32)

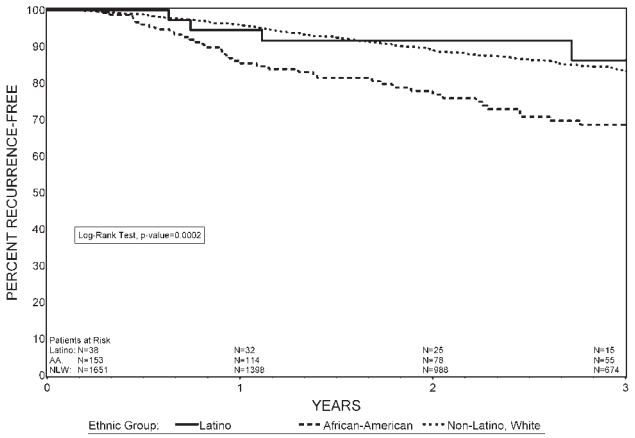

FIGURE 1. This figure illustrates recurrence-free survival by ethnicity ($N = 1842$).

and Latino men (OR = 2.08, 95% CI = 0.93–4.66). AA men were also somewhat more likely to receive external beam radiotherapy than NLW men (OR = 1.51, 95% CI = 0.99–2.31). There were no differences between Latino and NLW men in primary treatment after adjusting for other variables in this study.

Disease-Free Survival

For men treated with RP, we compared DFS by ethnicity. Of the 1842 men included in this analysis, 370 (20%) recurred: 242 (65%) of recurring patients based on PSA criteria and 128 (35%) based on second treatment. The median follow-up time for men who failed was 24 months (range, 2–139 mos). For the 1472 men who did not fail during the observation period, the median follow-up was 31 months (range, 1–189 mos).

The subset of men included in this analysis had ethnic differences similar to those of the entire cohort. In this subset, AA men presented with higher-risk disease and were most likely to be single. Latinos and AA had lower levels of education and income compared with NLW.

At 3 years post-RP, the actuarial DFS rate was 69% (95% CI: 58–77%) for AA; 86% (95% CI: 60–96%) for Latinos; and 83% (95% CI: 81–86%) for NLW (Fig. 1). The log-rank test for difference in survival distribution by ethnicity was significant at $P < 0.01$ (AA vs. NLW, $P < 0.01$; AA vs. Latino, $P = 0.07$; Latino vs. NLW, $P = 0.71$). To further understand the relation between ethnicity and time to disease recurrence, we performed a Cox proportional hazards regression with ethnicity predicting survival time. Other significant predictors in the model were prostate cancer risk and education. NLW were not significantly different from Latinos ($P = 0.73$) nor were AA men different from Latinos ($P = 0.29$) in disease recurrence. However AA men were somewhat more likely to experience disease recurrence than NLW men (hazard ratio [HR] = 1.38, 95% CI = 0.98–1.94, $P = 0.06$).

The largest number of Latino men came from 1 site in Texas. To understand whether differences between ethnic groups for the entire analysis sample were being driven by the large number of Latinos from the Texas site, we carried out a number of additional comparisons. First, we compared Latinos at the Texas site ($n = 43$) against other Latino men ($n = 95$) in the sample. There were no differences in baseline clinical characteristics and only 2 significant differences in sociodemographic characteristics. Latinos at the Texas site were more likely to have private insurance (67% vs. 47%), whereas Latinos at other sites were more likely to have no insurance or "other" forms of insurance (19% vs. 2%; $P < 0.03$). In addition, Latinos at the Texas site were more likely to have been diagnosed earlier in the study period—51% were diagnosed during1989–1994 versus 16% from the other sites ($P < 0.01$). Furthermore, there were no differences between this site and other sites in disease recurrence for all men ($P = 0.81$) or within the Latino men ($P = 0.85$).

DISCUSSION

In this article, we have broadened the discussion of ethnicity and prostate cancer both by including Latino men in our analyses and by focusing not just on baseline clinical characteristics but also on treatment selection and on clinical outcomes for men receiving RP as treatment for their prostate cancer. We found that Latino men in our sample were generally similar to NLW in their baseline clinical presentation. Latino and NLW had significantly lower PSA and Gleason scores at diagnosis than AA men, although Latino and AA men were significantly more likely to present with more advanced disease stage than NLW. However, Latino men more closely resembled AA men on their sociodemographic characteristics. Latino and AA men were significantly more likely than NLW to report incomes < $50,000 per year, to have not attended college, and to be younger at diagnosis. Among men who received RP, AA men may be more likely than NLW men to experience disease recurrence, but this difference was of borderline significance once we controlled for clinical disease risk and education.

Previous research has shown that AA men have a significantly higher incidence of prostate cancer than White men.[1] Some reports have indicated that AA men present with significantly more advanced disease than White men and have poorer outcomes.[4,8,14] Robbins et al. suggest that differences between AA and NLW may be because of greater tumor virulence in AA men.[4] However, other studies have shown that ethnicity is not an independent predictor of disease stage and grade when investigators control for sociodemo-

graphic characteristics.[2] Another explanation recently put forward for ethnic differences in prostate cancer recurrence is the difference in rates of obesity for different ethnic groups.[15] However, in our study, both Latinos and AA men were significantly more likely to be overweight than NLW men.

Previous studies of Latinos with prostate cancer have focused on baseline characteristics. Some reports show Latino men presenting with more advanced disease, similar to AA, whereas others show Latinos with a clinical presentation more like NLW.[16] In a study of radiation oncology facilities with 40% or more minority men as patients, 10% of Latino men had T3–4 disease, 37% had PSA of 10 or greater, and 21% had a Gleason score of 8–10.[17] The Latino men in our sample were similar: 13% had T3–4 disease, 40% had PSA of 10 or greater, and 13% had a Gleason score of 8–10.

Our analyses show that Latino and AA men present with similar sociodemographic characteristics but that their clinical presentation differs, with Latino men presenting with lower-risk disease than AA men. This seeming incongruence—where worse socioeconomic status is *not* associated with worse health outcomes—has been identified for other health conditions among Latinos and has come to be referred to as the "Latino paradox".[18] More recent research has shown that once researchers control for clinical characteristics, the differences between Latinos and others in cardiovascular health and low birth weight disappear.[19,20] Authors of other recent studies maintain this paradoxical relation exists,[21] with various theories of its cause such as genetics, diet, or other cultural features.

Attempts to explain the paradox have focused on variables not included in most studies that find this relation, including differences among Latino subgroups.[22] In 1 report, Cuban-American men had a slightly higher rate of prostate cancer than NLW.[23] The same article showed significant differences in presentation between Black Latinos and White Latinos with prostate cancer.

Health literacy—"the ability to which individuals have the capacity to obtain, process, and understand health information services needed to make appropriate health decisions"[24]—has been shown to be strongly related to health status and health outcomes.[25–27] Health literacy is a particular concern for men with prostate cancer because AA men, a group with a significantly higher prevalence of prostate cancer, are overrepresented among lower literacy men with prostate cancer.[26] Persons with lower health literacy skills are significantly less likely to take preventive actions to improve their health.[28,29] Lower health literacy may account for some of the differences in clinical presentation for AA and Latino men reported here and in other studies. Predominantly Spanish-speaking Latino men may face a particular burden in trying to navigate a complex health care system in a language foreign to them.

To better understand prostate cancer in Latinos, further research is needed that enrolls larger numbers of Latino men in prostate cancer outcome studies and collects sociodemographic and cultural variables that better characterize participants. For example, information on acculturation, which is a multidimensional construct,[30] is usually not collected or reported in published studies of Latinos and prostate cancer. In the CaPSURE database, no acculturation measures were collected other than the language in which the patient filled out the patient questionnaire. Only 10 of the 138 Latino men in this analysis requested a Spanish-language questionnaire. Information is needed not just on language use and whether a patient is of Mexican, Cuban, Puerto Rican, or other descent but should be collected on other aspects of acculturation, such as years in the United States for foreign-born men, birthplace of parents and grandparents, and personal values. Language use needs to be further specified to include not just the language in which the patient was interviewed but also his language use at home and in other common situations.[31] However, efficient collection of important sociodemographic and cultural variables must bear in mind budget limitations of projects and participant burden.

Limitations to the current study should be considered when interpreting the results reported here. The number of Latino participants in CaPSURE is small, relative to the number of NLW. CaPSURE participants may not be representative of Latino men with prostate cancer as a whole, even though this database contains more Latinos with more finely detailed information about clinical presentation and outcomes than most other studies in the literature. Latino men in the database are drawn primarily from practices in the western United States. Thus, these men are likely to be primarily of Mexican descent and may not be representative of other subgroups of Latinos. Another potential concern might be the large proportion of Latino men from one site in Texas, since differences between Latinos and other groups might simply be differences between that site and others. However, when we examined this concern by comparing Latinos at the Texas site to other Latinos in the sample, few differences were found.

In addition, work needs to be done to describe the experiences of men with prostate cancer who are of other ethnicities. Because of small numbers, Asian, Pacific Islander, Native American, and multiracial participants were excluded from this analysis.

Conclusions

This study represents the first attempt to characterize baseline clinical presentation of Latino men with prostate cancer and to examine differences in disease recurrence for Latinos. Further research is needed, particularly studies that enroll larger numbers of Latino men from different subgroups, to collect detailed information about sociocultural characteristics that may help explain the paradoxical relation between sociodemographic and clinical variables.

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