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Heterogeneous methodology of racial/ethnic classification may be responsible for the different risk assessments for prostate cancer between Black and White men in Brazil

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ABSTRACT

Objectives: To evaluate if the different results of prostate cancer risk between black and white Brazilian men may be associated with the varying methodology used to define participants as either Blacks or Whites.

Patients and Methods: We evaluated median PSA values, rate of PSA level ≥4.0 ng/mL, indications for prostate biopsy, prostate cancer detection rate, biopsy/cancer rate, cancer/biopsy rate, and the relative risk of cancer between blacks versus whites, blacks versus non-blacks (browns and whites), non-whites (browns and blacks) versus whites, African versus non-African descendants, and African descendants or blacks versus non-African descendants and non-blacks.

Results: From 1544 participants, there were 51.4% whites, 37.2% browns, 11.4% blacks, and 5.4% African descendants. Median PSA level was 0.9 ng/mL in whites, browns, and non-African descendants, compared to 1.2 ng/mL in blacks, and African descendants or blacks, and 1.3 ng/mL in African descendants. Indications for prostate biopsy were present in 16.9% for African descendants, 15.9% of black, 12.3% of white, 11.4% for non-African descendants, and 9.9% of brown participants. Prostate cancer was diagnosed in 30.3% of performed biopsies: 6.2% of African descendants, 5.1% of blacks, 3.3% of whites, 3.0% of non-African descendants, and 2.6% of browns.

Conclusions: Median PSA values were higher for Blacks versus Whites in all classification systems, except for non-white versus white men. The rate of prostate biopsy, prostate cancer detection rate, and relative risk for cancer was increased in African descendants, and African descendants or blacks, compared to non-African descendants, and non-African descendants and non-blacks, respectively.

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INTRODUCTION

Prostate cancer is the most common visceral malignant neoplasm in men. The incidence of prostate cancer varies according to racial differences in several countries, as well as the estimated lifetime risk of disease and the mortality rate for cancer (1-3).

Black men have the highest reported incidence of prostate cancer in the World, with a relative risk of 1.6 compared with white men in the United States (US) (1, 2). Furthermore, age-adjusted

prostate cancer mortality is 2.4 times higher for Black patients than for Whites (2, 3).

In Brazil, most studies demonstrated a similar risk of prostate cancer between Black and White men (4-11), while only some verified an increased prevalence of prostate cancer in Black participants, compared to White ones (12-14). These results have been frequently attributed to the high race mixture index in the Brazilian population as a consequence of centuries of interethnic crosses between Europeans, Africans, and Amerindians, but they may as well be the result of the different methodology used to define participants as either Blacks or Whites in each study, because there is still no consensus in the Brazilian society (15, 16).

In Brazil, unlike US and Europe, race is frequently associated to the skin color and physical appearance of the individual, rather than ethnic origin or ancestry, with a number of classification systems available to characterize the vast majority of Brazilians along a white-to-black color continuum, each with a set of categories that vary in number and degree of complexity (15).

To evaluate if the heterogeneous methodology of racial/ethnic classification may be responsible for the different risk assessments for prostate cancer in Black and White Brazilian men, we stratified a single cohort of men undergoing prostate cancer screening within five working systems of classification, and compared the median PSA values, rate of PSA level ≥4.0 ng/mL, indications for prostate biopsy, prostate cancer detection rate, biopsy/cancer rate, cancer/biopsy rate, and the relative risk of cancer between Black and White groups within each racial/ethnic classification system.

PATIENTS AND METHODS

All men attending a prostate cancer education program in our Institution that accepted to be tested for prostate cancer underwent a free prostate cancer screening that included medical history, digital rectal examination (DRE), and serum PSA determination. The program was conducted in the city of Curitiba, PR, located in the south region of Brazil, as part of the city employees' health care system. The study protocol was reviewed and approved by the Institutional Ethics Committee on Human Research (registry number 2253.147/2010-06).

At evaluation, all participants were categorized by a single examiner as white, brown (pardo) or black (hetero-identification), and responded an open-ended question regarding their origin or ancestry (self-identification).

Individuals were classified as blacks when they presented typical physical features of the black race, including dark skin on clothing-covered areas, and characteristic hair texture and shape of the lips and nose; whites when they had white to pale pink skin color on covered areas; and browns when they did not fit the black or white variables. Participants were also included in two groups: African descendants, when they reported any African origin or ancestry in the family, regardless of their skin color; or non-African descendants.

A Microsoft® Excel® database was specifically design for the study purposes. Outcomes of interest included the number of participants, proportion of black, brown, and white men, percentage of African descendants, and non-African descendants, median (range, mean±SD) PSA value, rate of participants with a PSA level ≥4.0 ng/mL, indications for prostate biopsy, prostate cancer detection rate, biopsy/cancer rate, cancer/biopsy rate, and the relative risk of cancer between Blacks and Whites in the different racial/ethnic classification systems. For comparison means, participants were grouped as blacks versus whites, blacks versus non-blacks (browns and whites), non-whites (browns and blacks) versus whites, African versus non-African descendants, and African descendants or blacks versus non-African descendants and non-blacks.

Statistical analyses were performed using univariate (non-adjusted), and multivariate (adjusted) analysis. In the first, Pearson's chi-square test or Fisher exact test were used for categorical variables and student's t-test for continuous variables. In the latter, linear or logistic regression were performed, whichever appropriate, adjusted for age (≥60 years versus <60 years), education (incomplete elementary school level or lower versus complete elementary school level or higher), family history of prostate cancer, and personal history of increased blood pressure, diabetes melli-

tus, vasectomy, and sexually transmitted urethritis (yes versus no, to all). Computations were performed using IBM® SPSS Statistics®, version 20.0.0. Statistical significance was considered for $p<0.05$.

RESULTS

Among 1544 participants included in the study, 794 (51.4%) men were identified as whites, 574 (37.2%) as browns, and 176 (11.4%) as blacks. African ancestry was reported by 5.4% of participants: 23.3% of blacks, 4.6% of browns, and 1.9% of whites. Demographics of the racial groups are summarized in Table-1.

The PSA level was ≥4 ng/mL in 12.0% of African descendants, 11.4% of blacks, 8.6% of whites, 8.0% of non-African descendants, and 7.0% of browns. The median PSA level was 0.9 ng/mL in white men, brown individuals, and non-African descendants, compared to 1.2 ng/mL in blacks, and African descendants or blacks, and 1.3 ng/mL in African descendants. Median PSA level was higher for Blacks versus Whites in all classification systems, except for non-white versus white individuals (Table-2).

Indications for prostate biopsy were present in 183 (11.9%) participants, including a PSA level at or above 4.0 ng/mL in 59.6%, a suspicious

Table 1 - Demographics.

Racial Classification System	Black[1] versus White[2]	Black versus non-black[3]	Non-white[4] versus white	African descendant[5] versus non-African descendant[6]	African descendant or black versus non-African descendant and non-black
Black group – No. (%)	176 (18.1)	176 (11.4)	750 (48.6)	83 (5.4)	218 (14.1)
White group – No. (%)	794 (81.9)	1368 (88.6)	794 (51.4)	1443 (94.6)	1326 (85.9)

[1] Participants with typical physical features of the black race, including dark skin on clothing-covered areas, and characteristic hair texture and shape of the lips and nose; [2] Participants with white to pale pink skin color on covered areas; [3] White and brown participants together; [4] Brown and black participants together; [5] Participants with any African origin or ancestry in the family, regardless of their skin color; [6] Participants with no African origin or ancestry in the family

Table 2 - Median PSA values between different racial classification systems.

Racial Classification System	Median PSA value (range, mean±SD)	Univariate analysis(*)	Multivariate analysis(**)
Black	1.2 (0.0-134.5, 2.8±10.7)	0.007	0.004
White	0.9 (0.0-28.3, 1.6±2.2)	0.001	0.003
Black	1.2 (0.0-134.5, 2.8±10.7)		
Non-black[1]	0.9 (0.0-61.0, 1.6±2.7)	0.339	0.062
Non-white[2]	0.9 (0.0-134.5, 1.9±6.0)		
White	0.9 (0.0-28.3, 1.6±2.2)	<0.001	<0.001
African descendant	1.3 (0.2-134.5, 3.4±15.3)		
Non-African descendant	0.9 (0.0-61.0, 1.6±2.8)		
African descendant or black	1.2 (0.0-134.5, 2.6±9.6)	0.006	0.015
Non-African descendant and non-black	0.9 (0.0-61.0, 1.6±2.7)		

SD = Standard deviation; **[1]** White and brown participants together; **[2]** Brown and black participants together; * T-Student test; ** Linear regression, including race/ethnicity, age, education, family history of prostate cancer, and personal history of increased blood pressure, diabetes mellitus, vasectomy, and sexually transmitted urethritis.

DRE in 30.0%, or both in 10.4%. The indication rate for prostate biopsy was 16.9% for African descendants, 15.9% for blacks, 12.3% for whites, 11.4% for non-African descendants, and 9.9% for browns, being higher for African descendants versus non-African descendants (16.9% versus 11.4%, $p<0.05$ in multivariate analysis), and for African descendants or blacks versus non-African descendants and non-blacks (16.5% versus 11.1%, $p<0.05$ in univariate and multivariate analyses).

Among 165 performed biopsies, prostate cancer was detected in 50 (30.3%) subjects. Cancer rate was 6.2% in African descendants, 5.1% in black men, 3.3% in white men, 3.0% in non-African descendants, and 2.6% in brown men. The detection rate of prostate cancer was increased in African descendants versus non-African descendants (6.2% versus 3.0%, $p<0.05$ in multivariate analyses), and in African descendants or blacks versus non-African descendants and non-blacks (5.2% versus 3.0%, $p<0.05$ in univariate and multivariate analyses).

The number of biopsies required for the diagnosis of each prostate cancer increased from 2.8 in African descendants and 3.1 in blacks, to 3.8 in browns, and 3.9 in whites and non-African descendants, resulting in a prostate cancer/biopsy rate of 41.7% in African descendants, 36.0% in black, 30.0% in brown, 28.2% in non-African descendants, and 27.8% for white participants.

The relative risk of prostate cancer between black and white groups in each racial/ethnic classification system is summarized in Table-3.

DISCUSSION

PSA levels and the risk of prostate cancer are increased in Black men compared to White men in several regions around the world, including the US, Canada, Caribbean, and England (12, 17-20). In Brazil, most studies evaluating the correlation between prostate cancer and different racial/ethnic groups did not demonstrate a significant difference in the prevalence of prostate cancer between Black and White individuals (4-11). These results have been frequently attributed to the high race mixture index in the Brazilian population, but other potential source of bias may include the use of different methodology to classify individuals into racial groups.

The racial/ethnic classification model in Brazil is more complex than the bifurcated US and European model. Brazilian classification is usually based on skin color and other physical characteristics such as facial features, hair texture, and the shape of lips and nose, with a diversity of systems currently in use (15, 16).

Within the several systems of racial/ethnic classification evaluated in this study, we observed that the proportion on men grouped as Blacks varied from 5.4% to 48.6%, suggesting that the methodology of racial classification substantially modifies the racial/ethnic pattern of the population in study, with potential implications on the results.

Median PSA levels were higher in all definitions of Black group, similarly to other studies (19, 20), except for non-white versus white men.

Evaluating prostate cancer detection rates, although the relative risk of cancer was increased by 56% to 2-fold in all Black versus White groups, excluding the non-white versus white classification system, the results were statistically significant only in multivariate analysis for the groups defined as African versus non-African descendants, and African descendants or blacks versus non-African descendants and non-blacks. The groups of blacks versus whites, blacks versus non-blacks, and non-whites versus whites did not reach statistically significant difference.

The relatively wide range in the risk of prostate cancer among the different racial/ethnic classification systems reported in the present study, as well as the non significant results reported in other Brazilian studies (4-11), may reflect the relatively poor accuracy in the assignment of race/ethnicity based exclusively on anthropometric features, since these traits are believed to be a combination of genetic inheritance and adaptations to geographical factors such as solar radiation and heat (20).

Another difficulty includes the uncertainty about assigning individuals from the brown category into a separate classification group, within the White group, or within the Black group. While whites and blacks refer to the ends of the spec-

Table 3 - 95% CI relative risk between different ethnic/race/color classification groups.

Univariate analysis (*)		
Racial Classification System	RR (95% CI)	p value
Black versus white	1.56 (0.74-3.27)	0.082
Black versus non-black[1]	1.71 (0.84-3.45)	0.056
Non-white[2] versus white	0.98 (0.57-1.69)	0.934
African versus non-African descendant	2.06 (0.84-5.08)	0.070
African descendant or black versus non-African descendant and non-black	1.60 (0.94-2.75)	0.096
Multivariate analysis (**)		
Racial Classification System	RR (95% CI)	p value
Black versus white	1.90 (0.83-4.33)	0.129
Black versus non-black[1]	2.08 (0.96-4.50)	0.064
Non-white[2] versus white	0.81 (0.43-1.53)	0.520
African versus non-African descendant	3.11 (1.13-8.55)	0.027
African descendant or black versus non-African descendant and non-black	2.23 (1.09-4.59)	0.029

[1] White and brown participants together; [2] Brown and black participants together; * Fisher exact test or Pearson's Chi-square; ** Logistic regression, including race/ethnicity, age, education, family history of prostate cancer, and personal history of increased blood pressure, diabetes mellitus, vasectomy, and sexually transmitted urethritis.

trum, the Brown group serves as an umbrella category for various mixed-race terms such as mulattos (descendants of Blacks and Whites), caboclos (Amerindians and Whites), and cafuzos (Amerindians and Blacks) (15). Paschoalin et al. (13) demonstrated by genetic studies that, in Brazil, a higher proportion of Amerindian alleles may be associated with a lower prevalence of prostate cancer, while a higher proportion of African alleles is significantly related to a higher predisposition for cancer. Therefore, studies that group together brown men either with blacks as non-whites, or with whites as non-blacks, may join distinct groups of race admixture that counterbalance each other in their susceptibility to prostate cancer.

There is also disagreement about the ideal methodology of data collection for racial/ethnic classification in Brazil. Self-identification refers to a race/ethnic choice made by the respondent, and hetero-identification to a race/ethnic attribution assigned by the interviewer to the respondent (15, 16). In the present study, we used hetero-identification to classify individuals in different color groups (black, brown, or white), and self-identification to stratify participants by their origin/ancestry (African, or non-African descendants).

It is interesting to note that, although it is known there are a large number of people with at least partial African origin in Brazil, 76.7% of black participants self-reported to be non-African descendants. A large previous study showed similar results, with only about 10% of blacks considering themselves as African descendants (17). The apparent low identity of Brazilians with African ancestry may be explained because mixing usually occurred during the slavery period or in a state of degradation of the mother, resulting in a widespread social prejudice that can be observed even in present-day. This may explain why people with a darker complexion associated their skin color preferably with Amerindian (or Brazilian) ancestry, rather than African origin (16).

Some limitations of our study should be noted. Even though we adjusted PSA levels to age and other confounding variables, we did not include prostate volume and prostate symptoms

score in the multivariate analysis. Furthermore, our sample included a relatively small proportion of blacks and African descendants, and a small number of prostate cancers in each subgroup, which can result in relatively wide confidence intervals and limit the statistical power of the study.

In summary, the racial/ethnic classification system most accepted recently by government, Black movement, and media, which uses only two terms (non-white or *negro*, and white), is apparently the least adequate model for prostate cancer risk stratification. The assignment of race/ethnicity based either on anthropometric features (black, brown, and white), or on ethnic origin/ancestry (African descendant, and non-African descendant) are practical, although they are less accurate when used separately. Therefore, anthropometric features should be preferably used in combination with origin/ancestry to increase the accurateness of racial/ethnic classification in the risk assessment of prostate cancer, especially in populations with a high miscegenation index like the Brazilian people.

CONCLUSIONS

Based on several classifications systems used to stratify a single cohort of Brazilian men in different groups of Blacks and Whites, median PSA values were higher in Black versus White groups classified as blacks versus whites, blacks versus non-blacks, African descendants versus non-African descendants, and African descendants or blacks versus non-African descendants and non-blacks. Median PSA values were similar between the groups categorized as non-whites versus whites.

Black groups defined as African descendants, and as African descendants or blacks, had an increased rate of prostate biopsy, prostate cancer detection rate, and relative risk for cancer, compared to the white groups categorized as non-African descendants, and non-African descendants and non-blacks, respectively. The indication rate for prostate biopsy, prostate cancer detection rate, and relative risk for cancer were comparable between blacks versus whites, blacks versus non-blacks, and non-whites versus whites.

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CONFLICT OF INTEREST

None declared.

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