Annals of Epidemiology 72 (2022) 40–47

Contents lists available at ScienceDirect

Annals of Epidemiology

journal homepage: www.annalsofepidemiology.org

Original article

Racial discrimination is associated with greater arterial stiffness and carotid intima-media thickness: the ELSA-Brasil study

Lidyane V. Camelo, PhD[a,*], Amanda Viana Machado, MPH[b], Dóra Chor, PhD[c], Rosane Harter Griep, PhD[d], José Geraldo Mill, PhD[e], Luisa Campos Caldeira Brant, PhD[f], Sandhi Maria Barreto, PhD[a]

[a] Department of Preventive and Social Medicine, Faculdade de Medicina, Universidade Federal de Minas Gerais, Minas Gerais, Brazil
[b] Postgraduate Program in Public Health, Faculdade de Medicina, Universidade Federal de Minas Gerais, Minas Gerais, Brazil
[c] Escola Nacional de Saúde Pública, Fundação Oswaldo Cruz, Rio de Janeiro, Brazil
[d] Laboratory of Health and Environment Education, Instituto Oswaldo Cruz, Fundação Oswaldo Cruz, Rio de Janeiro, Brazil
[e] Department of Physiological Sciences, Universidade Federal do Espírito Santo, Vitoria, Espírito Santo, Brazil
[f] Department of Internal Medicine, Faculdade de Medicina, Universidade Federal de Minas Gerais, Belo Horizonte, Minas Gerais, Brazil

ARTICLE INFO

Article history:
Received 26 October 2021
Revised 14 March 2022
Accepted 18 March 2022
Available online 26 March 2022

Keywords:
Racial discrimination
Racial inequalities in health
Racism
Pulse wave velocity
Carotid intima-media thickness
Arterial Stiffness
Cohort Studies
ELSA-Brasil

ABSTRACT

Purpose: The association between racial discrimination and subclinical cardiovascular markers remains under-examined. We aimed to investigate the association of race/skin color and racial discrimination with pulse wave velocity (PWV) and carotid intima-media thickness (c-IMT) in the Brazilian context.

Methods: We used data from 13,284 participants from the Brazilian Longitudinal Study of Adult Health (ELSA-Brasil) baseline with information of PWV and 9850 for c-IMT. Self-reported race/skin color and perceived racial discrimination were the exposures. PWV and c-IMT were used continuously and categorizing according to cutoff that indicates increased cardiovascular risk. Linear and logistic regression models were used.

Results: Experience of racial discrimination was reported by 7% of total participants, but this prevalence was much higher among Blacks than Browns (PWV sample: 31,9% vs. 6,1%; c-IMT sample: 33,7% vs. 6,8%). After adjustments for age, sex, and research center, Blacks and Browns presented higher means of PWV and c-IMT and had greater chances of PWV>10 m/s and c-IMT≥75th percentile than Whites. The magnitude of all these associations were higher among Blacks and Browns with racial discrimination. In final models adjusted for education this pattern of association remained the same, although an attenuation in the magnitude of the association has been observed.

Conclusions: Blacks and Browns presented worse profiles of subclinical cardiovascular markers compared to Whites and those exposed to racial discrimination seem to have an additional cardiovascular risk.

Introduction

Racial inequalities in cardiovascular diseases (CVD) are profound, and Blacks have major disadvantages compared to Whites in the incidence, progression, and mortality from these causes [1–3]. The adverse effects of racial inequality on the cardiovascular system seem to be present in the early stages of the natural history of CVD since Blacks generally present worse profiles of subclinical markers for these diseases [4–9], such as the pulse wave velocity (PWV) [4–7,9] and the carotid intima media thickness (c-IMT) [8].

The mechanisms involved in the association between race/skin color and CVD remain incompletely elucidated. The experience of racial discrimination by Blacks and other stigmatized race/skin

Abbreviations: CVD, cardiovascular diseases; PWV, pulse wave velocity; c-IMT, carotid intima media thickness; ELSA-Brasil, Brazilian longitudinal study of adult health; IBGE, instituto brasileiro de geografia e estatística; CRF, corticotropin-releasing factor; BMI, body mass index; HPA axis, hypothalamic-pituitary-adrenal axis.

Conflicts of interest: The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

* Corresponding author. Department of Preventive and Social Medicine, Faculdade de Medicina, Universidade Federal de Minas Gerais, Av. Alfredo Balena, 190, 30130-100, Minas Gerais, Brazil. Tel.: +55-31-3409-9014.
E-mail address: lidyanecamelo@gmail.com (L.V. Camelo).

https://doi.org/10.1016/j.annepidem.2022.03.009
1047-2797/

color individuals may explain, at least in part, this inequality [10,11]. In fact, the experience of discrimination has been associated with high blood pressure [12], cardiovascular risk factors [10], and incident cardiovascular events [13]. However, the association between racial discrimination and subclinical cardiovascular outcomes [14–16] remains under-examined. This investigation is relevant because it allows us to verify whether discrimination is involved in the pathophysiology of CVD and not just as triggers of final outcomes. Although studies carried out using subclinical cardiovascular outcomes, such as c-IMT and PWV, are scarce, the few identified ones have shown provocative results in small samples. Racial discrimination was marginally associated to c-IMT in African-American women in a cross-sectional study (OR: 4.02, 95%CI:0.94–17.14) [14], and it was also associated with increased arterial stiffness among young adults in a longitudinal study (β:0.30, 95%CI: 0.02–0.58) [15]. On the other hand, the association between c-IMT and racial discrimination was not found in cross-sectional study carried out with middle-aged and older north-American adults [16].

Although Brazil is a society strongly marked by racism [17], studies investigating the association between racial discrimination with cardiovascular outcomes are still incipient [18]. Studies carried out in ELSA-Brasil cohort found that individuals self-declared as Black have higher values of c-IMT when compared to Whites and Browns [19], and that Blacks and Browns have greater arterial stiffness when compared to Whites [20]. However, we do not know whether exposure to racial discrimination can help explain racial differences in PWV and c-IMT in this population. Therefore, this study aimed to investigate the combined effect of race/skin color and racial discrimination on PWV and c-IMT in Brazilian context.

Materials and methods

This study is a cross section analysis that used baseline data (2008–2010) from the Brazilian Longitudinal Study of Adult Health (ELSA-Brasil), a multicenter cohort study involving 15,105 active or retired civil servants from universities or research institutions located at six Brazilian capitals (Belo Horizonte, Porto Alegre, Rio de Janeiro, Salvador, São Paulo and Vitória) aged 35–74 years.

The ELSA-Brasil aims to investigate biological, behavioral, environmental, occupational, psychological and social factors related to incidence and progression of diabetes and cardiovascular disease. For this reason, a great diversity of data was placed in the baseline, including detailed interviews and measurements to access social determinants of health, clinical and subclinical conditions related to diabetes, cardiovascular diseases and mental health. All the data were collected by trained and certified interviewers at each of the six research centers. Ethics committees of all institutions involved approved the study, and volunteers gave written consent to participate. Further details on study design have been described elsewhere [21,22].

We excluded from these analysis participants with missing data on race/skin color ($N = 184$) and racial discrimination ($N = 29$), individuals who reported themselves as Asian descents ($N = 373$) or Brazilian indigenous ($N = 157$), as they were underrepresented in the ELSA-Brasil cohort. We also excluded Whites who mentioned race/skin color as the reason for discrimination ($n = 64$) because there is evidence that racial discrimination reported by Whites captures different experiences in comparison to Blacks and Browns [23]. The participants who reported a diagnosis of cardiovascular disease (acute myocardial infarction, cardiac revascularization surgery, heart failure and stroke) were also excluded ($n = 686$) to ensure the inclusion of subclinical atherosclerosis and arterial stiffness cases only. Thus, 13,612 participants were eligible to participate in this study.

From the 13,612, we also excluded participants with non-validated data of PWV ($N = 328$) in the analyses involving PWV as outcome resulting in a total sample of 13,284 participants for this analysis. In the c-IMT analyses, from the 13,612, we excluded participants who either did not undergo c-IMT measurements or whose c-IMT image did not achieve the adequate quality ($N = 3762$) resulting in a total sample of 9850 participants for this analysis. Considering that the loss of information for IMT was substantial, we analyzed the differences of included *versus* excluded participants and we did not observe statistically significant differences with regard to the racial discrimination (7.0% vs. 7.4%, $P = .375$) and age (mean: 51.4 vs. 52.1 years, $P = .316$). Nevertheless, the included participants in the IMT sample presented higher proportion of Whites (58% vs. 43%, $P < .001$) and women (56% vs. 52%, $P < .001$); and lower proportion of Browns (26% vs. 37%, $P < .001$), Blacks (15% vs. 19%, $P < .001$) and participants with university degree (52% vs. 55%, $P = .048$).

Outcome assessment: PWV and c-IMT

PWV was performed with the participants in the supine position using a validated automatic device (Complior, Artech Medicale, Patin, France), as previously described [24]. Blood pressure was measured on the right arm using an oscillometer device (Omron HEM 705 CP), with the subject in the supine position. To capture the pulse waveform a sensor was placed at the carotid and femoral arteries, and the distance from the suprasternal notch to the right femoral site, where the pulse was recorded, was measured with an inextensible tape. For PWV calculation we divided the distance between recordings by the difference between the time delay of simultaneously recorded pulse waves in the carotid and the femoral arteries, expressed in m/s. The results were recorded as the average of all measurements obtained in 10 consecutive cardiac cycles under regular cardiac rhythm. The PWV was considered as a continuous variable as well as a categorical variable using the cut-off value of 10 m/s ($\leq$10 m/s *versus* $>$10 m/s), which is related to increased cardiovascular risk [51].

To measure c-IMT images of the common carotid artery were acquired within a region free of plaque in the outer wall of a pre-defined carotid segment of 1 cm in length from 1 cm below the carotid bifurcation during three cardiac cycles using a device (Aplio XG (tm), Toshiba) with a 7.5 MHz linear transducer. The images were collected and recorded at study sites and then sent to the centralized reading center for analysis using MIA, an automated computer program [19]. The IMT measurements were summarized in this analysis as the mean of the right and left mean values (mean-mean).

The IMT was considered as a continuous variable as well as a categorical variable using the 75th percentile of IMT in the ELSA-Brasil population as a cut-off value ($<$75th percentile vs. 75th percentile), because values of IMT greater than or equal to 75th percentile are considered high and indicative of increased cardiovascular risk [25].

Exposure variable

Our exposure variable was constructed combining the variables self-declared race/skin color (White, Brown, Black) and racial discrimination (Yes or No), and classified into 5 categories: White (reference), Brown without report of racial discrimination, Brown with report of racial discrimination, Black without report of racial discrimination, Black with report of racial discrimination.

In ELSA-Brasil the classification according to race/skin color was based on the following question: "The Brazilian Census (IBGE) uses the terms 'Black' ('*Preto*'), 'Brown' ('*Pardo*'), 'White' ('*Branco*'), 'Asian descendent' and 'Brazilian indigenous' to describe people's color or

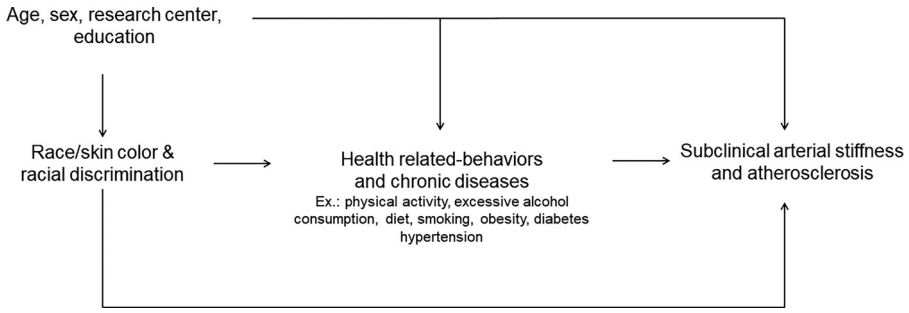

Fig. 1. Directed acyclic graph (DAG) showing the association between race/skin color & racial discrimination with subclinical arterial stiffness and atherosclerosis.

race. If you were to answer the IBGE census today, how would you declare yourself with regards to color or race?"

Lifetime discrimination was assessed using a modified version of the *Major Experiences of Discrimination* [26] also known as the *Lifetime Major Events Scale*. This tool captures unfair treatment at public places, at work, at police stations, at schools or colleges, and regarding housing rights. Respondents reporting unfair treatment in any of these domains and attributed race/skin color as the reason for unfair treatment were coded as having experienced racial discrimination. The reliability of this modified version of the scale obtained a Kappa coefficient of 0.85 (95% CI 0.72–0.98) in a population similar to that of ELSA-Brasil [28].

Covariates

We constructed a directed acyclic graph (DAG) of proposed associations between the compound measure of racial discrimination and race/skin color with PWV and c-IMT to guide our selection of the potential confounders to be included in the model adjustments (Fig. 1). The construction of this DAG was based on the evidences available of the relationship between race/discrimination and health [11,34]. Following this DAG, to investigate the associations between the compound measure of racial discrimination and race/skin color with PWV and c-IMT we must adjust the analyses for age (continuous, in years) and sex. Moreover, considering that ELSA-Brasil is a multicenter study involving individuals living in six cities located in different Brazilian capitals, the research center (São Paulo, Belo Horizonte, Porto Alegre, Rio de Janeiro, Salvador, and Vitória) was also defined as a potential confounding factor, since varying proportions of self-declared White, Brown and Black individuals in different sites may impact racial self-classification as well as perception of racial discrimination [49]. Moreover, the occurrence of cardiovascular outcomes varies according country region [27].

Education (university degree, high school, complete elementary school, incomplete elementary school) was also considered as confounder because there is evidence that education can impacts in the unfair treatment perception (i.e., individuals with higher education would perceive it more often) [30,31]. However, we also are aware that education is also a mediator in the association race/skin color and health-related outcomes because race/skin color is a determinant of years and quality of education achieved by individuals [29]. Considering this characteristic, we performed the analysis with and without the adjustment for education in order to better see the impact of this variable in the associations.

According with the DAG we could not condition our analyses on variables that represent health-related behaviors and/or chronic diseases (ex. physical activity, excessive alcohol consumption, smoking, obesity, diabetes, hypertension) because all of these variables are mediators of the associations between the compound measure of racial discrimination and race/skin color with PWV and c-IMT.

Heart rate and mean arterial pressure were also considered as adjusting variables in the models using PWV as outcome, because these adjustments are necessary for the comprehension of PWV due to the dependence of PWV on these two variables [52]. Considering this characteristic heart rate and mean arterial pressure were not considered in the DAG. The mean arterial pressure {diastolic blood pressure+ [(*systolic blood pressure−diastolic blood pressure*)/3]} was calculated using blood pressure levels obtained after a 5-minute rest, with the subject in the supine position, and using an oscillometric device (Omron HEM 705 CP) on the subject's right arm. The heart rate was assessed with participants sitting up, using the same oscillometric device. Three recordings were performed, and the mean of the second and third measurements was used.

Data analysis

Descriptive analyses were conducted to display the characteristics of the study population considering the PWV and c-IMT samples. The association of the compound measure of racial discrimination and race/skin color with PWV and c-IMT was investigated using linear regression models. Logistic regression models were also used to investigate the association of the compound measure of racial discrimination and race/skin color with high PWV and high c-IMT. After obtaining the crude analysis, the age, sex, research center variables were then added in the models (Model 1). In the models using PWV as outcome, we also included in the Model 1 the mean arterial pressure and heart rate. Secondly, in order to better see the impact education in these associations we included education separately in the Model 2.

The results of the fully adjusted linear regression models of the analyzes involving PVW and c-IMT as continuous variables were plotted on a graph showing the predicted adjusted means of PVW and c-IMT according to the compound measure of racial discrimination and race/skin color.

The interaction of the compound measure of racial discrimination and race/skin color with sex was evaluated by adding a bivariate interaction term to fully adjusted regression models, but evidence of interaction was not found. Analyses were conducted using Stata 14.0 (Stata Corporation, College Station, United States) and the level of significance was set at 5%.

Results

Descriptive characteristics of participants in the PWV and c-IMT samples are presented in Table 1. In both samples, most participants were female, reported White race/skin color, and presented university degree. Experience of racial discrimination was reported by 7% of total participants, but this prevalence was much higher among Blacks than Browns (PWV sample: 31,9% vs. 6,1%; c-IMT sample: 33,7% vs. 6,8%).

In the minimally adjusted model (Model 1), Blacks and Browns presented higher mean of PWV and greater chances of high PWV

Table 1
Descriptive characteristics of participants in the pulse wave velocity (PWV) sample and carotid intima-media thickness (c-IMT) sample

Variables	PWV Sample(N = 13,284)	c-IMT Sample(N = 9850)
Sociodemographic characteristics		
Age, mean (SD)	51.6 (8.9)	51.4 (8.9)
Gender, Female, N (%)	7268 (54.7)	5507 (55.9)
Race/skin color, N (%)		
White	7206 (54.2)	5732 (58.2)
Brown	3876 (29.2)	2597 (26.4)
Black	2202 (16.6)	1521 (15.4)
Education, N (%)		
University degree	7030 (52.9)	5135 (52.1)
High school	4680 (35.2)	3515 (35.7)
Complete elementary school	870 (6.5)	653 (6.6)
Incomplete elementary school	704 (5.3)	547 (5.5)
Racial discrimination		
Racial discrimination, N (%)		
Yes	941 (7.1)	690 (7.0)
Compound measure of racial discrimination and race/skin color, N (%)		
White	7206 (54.2)	5732 (58.2)
Brown without report of racial discrimination	3638 (27.4)	2420 (24.6)
Brown with report of racial discrimination	238 (1.8)	177 (1.8)
Black without report of racial discrimination	1499 (11.3)	1008 (10.2)
Black with report of racial discrimination	703 (5.3)	513 (5.2)
Outcomes		
Pulse wave velocity (m/s), mean (SD)	9.3 (1.8)	–
High pulse wave velocity (>10 m/s), N (%)	3434 (25.8)	–
Avg-Avg IMT (mm), mean (SD)	–	0.60 (0.13)
High IMT (≥75 percentile), N (%)	–	2464 (25.0)
Other covariates		
Mean arterial pressure, mean (SD)	91.1 (12.2)	90.6 (12.0)
Heart rate, mean (SD)	70.3 (10.2)	70.5 (10.3)

The Brazilian Longitudinal Study of Adult Health-ELSA-Brasil, (2008–2010).
c-IMT = carotid intima-media thickness; PWV = pulse wave velocity.

Table 2
Associations of racial discrimination with carotid femoral pulse wave velocity (PWV) as continuous variable and with high PWV (PWV>10 m/s)

PWV‡	**Crudeβ (95% CI)***	**Model 1β (95% CI)***	**Model 2β (95% CI)***
Race/skin color – Racial discrimination			
White	Ref	Ref	Ref
Brown without racial discrimination	**0.075 (0.003; 0.146)***	**0.085 (0.026; 0.144)****	0.046 (−0.015; 0.108)
Brown with racial discrimination	**0.455 (0.222; 0.687)*****	**0.401 (0.218; 0.583)*****	**0.365 (0.181; 0.548)*****
Black without racial discrimination	**0.418 (0.318; 0.518)*****	**0.183 (0.101; 0.264)*****	**0.124 (0.039; 0.209)****
Black with racial discrimination	**0.297 (0.157; 0.436)*****	**0.251 (0.141; 0.361)*****	**0.223 (0.112; 0.333)****
High PWV‡	**Crude OR (95% CI)**†	**Model 2 OR (95% CI)**†	**Model 3 OR (95% CI)**†
Race/skin color – Racial discrimination			
White	Ref	Ref	Ref
Brown without racial discrimination	**1.11 (1.01–1.22)***	**1.22 (1.09–1.38)****	**1.14 (1.01–1.29)***
Brown with racial discrimination	**1.72 (1.31–2.25)*****	**2.13 (1.53–2.98)*****	**2.01 (1.43–2.81)*****
Black without racial discrimination	**1.58 (1.40–1.78)*****	**1.37 (1.18–1.60)*****	**1.24 (1.05–1.45)***
Black with racial discrimination	**1.34 (1.13–1.59)****	**1.47 (1.19–1.81)*****	**1.39 (1.12–1.72)****

The Brazilian Longitudinal Study of Adult Health (2008–2010) (ELSA-Brasil).
Model 1: age, sex, research center, mean arterial pressure and heart rate
Model 2: Model 1+ education.
* Regression coefficients β represent the difference in cf-PWV in m/s. Bold values denote statistical significance at the p < 0.05 level. One asterisk denote a significance level of 0.05, two asterisks 0.01 and three asterisks 0.001. CI= confidence interval.
† OR = odds ratio. Bold values denote statistical significance at the p < 0.05 level. One asterisk denote a significance level of 0.05, two asterisks 0.01 and three asterisks 0.001. CI= confidence interval.
‡ PWV = pulse wave velocity.

in comparison to Whites, and such differences were even greater among those with racial discrimination (Table 2). This pattern of association remained after adjustment for education, although an attenuation in the magnitude of the association has been observed (Table 2 and Fig. 2). This attenuation resulted in the loss of statistical significance of the association of Browns without racial discrimination with higher mean of PWV (Table 2).

Concerning c-IMT, in the minimally adjusted model (Model 1), Blacks and Browns with racial discrimination showed higher mean of c-IMT and higher chances of high c-IMT than Whites (Table 3). Blacks without racial discrimination also presented higher mean of c-IMT and higher chance of high c-IMT than Whites, but the magnitude of this association was lower than the observed among those with racial discrimination. Further adjustment for education

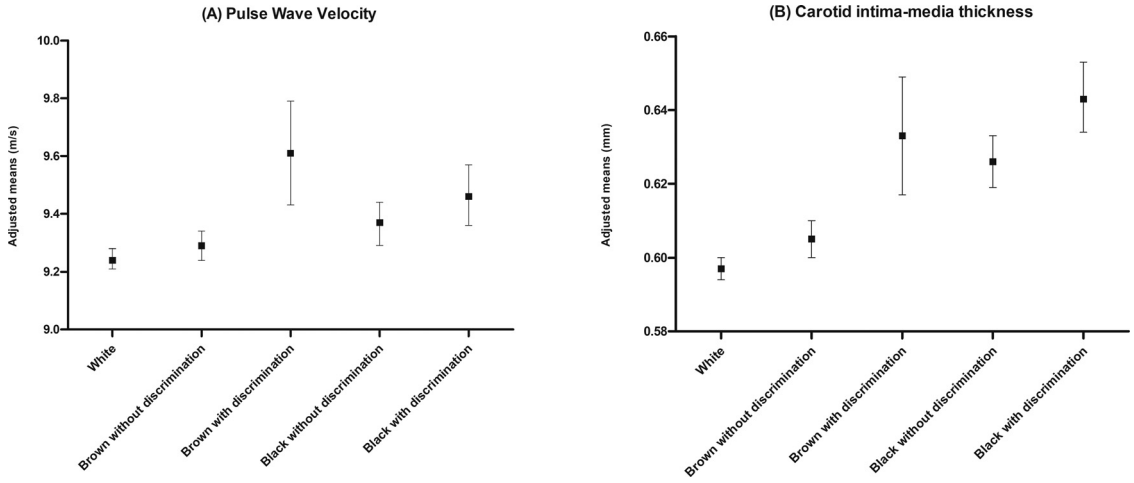

Fig. 2. Adjusted means (95% confidence interval) of pulse wave velocity (A)[1] and carotid intima-media thickness (B)[2] according to race/skin color and perceived racial discrimination. The Brazilian Longitudinal Study of Adult Health (2008–2010).
[1] Means of pulse wave velocity was adjusted by age, sex and research center, education, systolic blood pressure and heart rate.
[2] Means of carotid intima-media thickness was adjusted by age, sex and research center and education.

Table 3
Associations of racial discrimination with carotid intima-media thickness(c-IMT) as continuous variable and with high c-IMT (≥ 75th percentile)

c-IMT[3]	**Crudeβ (95% CI)**[1]	**Model 1β (95% CI)**[1]	**Model 2β (95% CI)**[1]
Race/skin color – Racial discrimination			
White	Ref	Ref	Ref
Brown without racial discrimination	−0.002 (−0.008; 0.004)	**0.015 (0.009; 0.020)****	**0.008 (0.003; 0.014)****
Brown with racial discrimination	**0.020 (0.001; 0.040)***	**0.041 (0.024; 0.057)****	**0.036 (0.019; 0.052)****
Black without racial discrimination	**0.028 (0.019; 0.036)****	**0.039 (0.031; 0.046)****	**0.029 (0.021; 0.037)****
Black with racial discrimination	**0.032 (0.020; 0.044)****	**0.051 (0.041; 0.061)****	**0.046 (0.036; 0.056)****
High c-IMT[3]	**Crude OR (95% CI)**[2]	**Model 1 OR (95% CI)**[2]	**Model 2 OR (95% CI)**[2]
Race/skin color – Racial discrimination			
White	Ref	Ref	Ref
Brown without racial discrimination	0.97 (0.87–1.08)	**1.36 (1.20–1.55)****	**1.19 (1.04–1.36)***
Brown with racial discrimination	1.24 (0.89–1.73)	**1.91 (1.31–2.78)****	**1.73 (0.19–2.52)****
Black without racial discrimination	**1.42 (1.22–1.64)****	**1.99 (1.68–2.35)****	**1.66 (1.39–1.99)****
Black with racial discrimination	**1.27 (1.04–1.56)***	**2.00 (1.60–2.50)****	**1.80 (1.43–2.26)****

The Brazilian Longitudinal Study of Adult Health (2008–2010) (ELSA-Brasil).
Model 1: age, sex and research center
Model 2: Model 1+ education.
* Regression coefficients β represent the difference in c-IMT in mm. Bold values denote statistical significance at the p < 0.05 level. One asterisk denote a significance level of 0.05, two asterisks 0.01 and three asterisks 0.001. CI= confidence interval.
† OR = odds ratio. Bold values denote statistical significance at the p < 0.05 level. One asterisk denote a significance level of 0.05, two asterisks 0.01 and three asterisks 0.001. CI= confidence interval.
‡ c-IMT = carotid intima-media thickness.

attenuated these associations, but the pattern remained the same for c-IMT (Table 3 and Fig. 2).

Discussion

In a large multiracial cohort of Brazilian civil servants, we found that Blacks and Browns presented higher means of PWV and c-IMT than Whites, especially those with racial discrimination. Compared to Whites, we also observed that Blacks and Browns, particularly those with racial discrimination, presented high PWV and c-IMT using cut-offs, indicating impaired vascular health, even after considering the effects of age, sex, research center and education.

We presented results of great public health relevance, as it demonstrated a significant association between racial discrimination, PWV and c-IMT using cutoff points that are considered at risk for cardiovascular disease, in addition to the association with these markers continuously. Unfortunately, few studies evaluated the relationship between subclinical markers of cardiovascular disease and race-specific discrimination, and most were conducted in very small samples [14–16]. Furthermore, we did not find any study that evaluated the combined effect of race/skin color and racial discrimination with PWV and c-IMT in the Brazilian population.

The greater arterial stiffness identified in Blacks and Browns with racial discrimination vis-a-vis those without racial discrimination was also observed in a study that evaluated the association between discrimination and PWV in a multiethnic sample of children enrolled in London schools. Cruickshank and cols [15] followed children aged between 11 and 13 years for 10 years and found that perceived racial discrimination was related to increased arterial stiffness in young adults [15]. We did not find other previous studies that has evaluated the association of racial discrimination and PWV.

Regarding c-IMT, our results were consistent with a previous study carried out with 334 White and Black north-American women from the Study of Women's Health Across the Nation [14], which found a marginal association between racial discrimination

and c-IMT [14]. This marginal result may be explained by the reduced power of the study to assess this association. Differently of our results, previous study that included middle-aged and elderly north-American adults, the racial discrimination was not associated with c-IMT [16].

Our findings showed that the adjustment for education only attenuated the associations of the compound measure of racial discrimination and race/skin color with PVW and c-IMT, but the pattern of the association remained essentially the same. Therefore, our results suggest that regardless of the level of education attained by individuals, race/skin color and the experience of discrimination seem to be implicated in higher levels of PWV and c-IMT. These findings are probably reflecting the structural racism prevalent in the society that interferes with the placement of individuals in the labor market, as well as access to housing, quality education, and various goods and services, meaning that, even if Brown and Black individuals attain the same level of education observed in Whites, they still tend to have less prestigious occupations and positions and lower income level than Whites [48]. Moreover, the experience of discrimination affects Blacks and Browns in all levels of education, and can be even higher among those with high education [31].

As in Brazil the racial classification is different from that adopted in other societies and there is a significant number of individuals who declare themselves as Brown (43.1% according to the last demographic census) [32], we investigated the association between racial discrimination, PWV and c-IMT also among Browns. Our results demonstrate that the associations of racial discrimination with PWV and c-IMT were identified in both Browns and Blacks, even considering that a smaller number of Browns reported racial discrimination when compared to Blacks. We also found that racial discrimination was more strongly associated with c-IMT among Blacks than Browns, but contrary to our expectations, the opposite was observed for PWV. It is important to note that in both analysis there were an overlap in the confidence intervals of the regression coefficients and ORs observed in Blacks and Browns with discrimination. Thus, we cannot say with certainty that these two groups are in fact different. On the other hand, we can safely say that these results suggest that the reporting of experience of discrimination seems to have a negative effect on PWV and c-IMT regardless of whether the individual is Brown or Black.

In this study we used as exposure a compound measure that included the exposure to both self-reported race/skin color and lifetime racial discrimination. Health inequities related to self-reported race/skin color are considered societal markers of cultural and structural racism at the individual level. The cultural racism, refers to the incorporation into the system of beliefs, images and cultural norms, of the idea of inferiority of Black and non-White individuals [11]. The structural racism, refers to development and maintenance of social policies and structures, allowing dominant groups to unevenly distribute resources and social opportunities to stigmatized groups. Both cultural and structural racism restricts access to goods and services (including medical care), housing, education, employment and income, which leads to a great disparity in socioeconomic level [34] increasing the exposure to psychosocial stress and risk health conditions such as violence and unhealthy working conditions. On the other hand, lifetime racial discrimination is an indicator of interpersonal racism, that can bring additional adverse effects on health, by generating more suffering and stress to those exposed and further reduce their access to social opportunities and resources [11,35]. To consider race/skin color as an indicator of racism is important to allow an adequate interpretation of the reasons why we found higher levels of PWV and c-IMT even in Blacks and Browns who did not report racial discrimination when compared to Whites. Even Blacks and Browns who do not report discrimination are victims of the racist way in which society is structured, which has negative repercussions on health.

The cultural, structural and interpersonal racism generate adaptive responses to stress leading to greater engagement in health-risk behaviors as a way to alleviate the stress, and increasing cardiovascular risk directly through hyperactivity of the hypothalamic-pituitary-adrenal axis (HPA axis), reactivity of the autonomic nervous system and inflammation [36]. Stressful situations lead to the autonomic nervous system activation, which triggers responses from the sympathetic and parasympathetic nervous systems [36]. The release of adrenaline and noradrenaline increases heart rate, reduces heart rate variability, optimizes blood flow to the muscle, increases pulse pressure, arterial stiffness, peripheral vasoconstriction, removal of vagal tone and energy mobilization [35–37]. Exposure to psychosocial stress can also lead to hyperactivity of the HPA axis and the consequent synthesis of corticotropin-releasing factor (CRF) and vasopressin [38]. CRF stimulates the anterior pituitary to release adrenocorticotropic hormone, which induces the adrenal cortex to produce glucocorticoids, which contribute to increased adiposity, hypertension and insulin resistance [38]. Changes in the autonomic nervous system combined with the response of the HPA axis lead to increased platelet activation, fibrinogen levels, viscosity, coagulation factors, and a chronic inflammation [36]. In long term, these changes can accelerate atherosclerosis and arterial stiffness by increasing blood pressure and endothelial dysfunction [36]. In addition, racial discrimination has been related to shorter telomere length [39–44] a biological aging marker [45]. Thus, exposure to racial discrimination may lead to premature aging contributing to occurrence of atherosclerosis and arterial stiffness [46,47].

The large number of participants and the characteristic multiracial and multicentric of the cohort of ELSA-Brasil are important strength of this analysis compared to previous studies, providing greater statistical power and population diversity. Moreover, the use of subclinical cardiovascular outcomes is also an advantage of this study. Firstly, because it contributes to the understanding that the racial inequities seem to be involved in the pathophysiology of CVD and not just as triggers of final outcomes. Secondly, because it is unlikely that subclinical cardiovascular changes can influence racial self-classification and reporting of racial discrimination. Therefore, although this study is a cross-sectional analysis, reverse causality is probably not a limitation of this paper.

Our study has also limitations that need to be highlighted. The ELSA-Brasil is a cohort of civil servants from Brazilian education and research institutions who have higher average income and education than that found in the Brazilian population as a whole. The prevalence of racial discrimination found in Blacks and Browns in ELSA-Brasil (Blacks: 33.3%; Browns: 6.6%) was lower than the prevalence observed in a representative study of the Brazilian population aged 16 years or more carried out in 2008 (Blacks: 41.1%; Browns: 14.7%) [33]. This might be explained by differences in age range between the cohort and the national survey, and also by the fact that ELSA-Brasil does not include the very poor nor the very rich, and there is compelling evidence showing that the perception of race discrimination vary according to these factors [30,31,33]. It is also possible that the report of racial discrimination is underestimated in the present study. If this is the case, there is no reason to suppose that underreporting was affected by the outcomes. Thus, in this latter case, the magnitude of the association between racial discrimination and PWV/c-IMT in the present study would have been underestimated, especially among Browns. However, despite the small proportion of Browns who reported racial discrimination, our study was able detect a statistical association between racial discrimination and c-IMT/PWV in this group.

We also observed some differences when comparing included participants *versus* excluded participants due to missing data for c-

IMT, since our analytical sample for c-IMT analyses included lower proportion of Browns, Blacks, and participants with university degree. Whereas the lower proportion of Browns and Blacks could have led to lower proportion of individuals who reported racial discrimination, the lower proportion of participants with university degree could have led to the opposite. As the effects of these differential losses were in the opposite direction, it is probable that their effects canceled each other out. In fact, we did not find any difference with regard to the report of racial discrimination in the group excluded versus included. Therefore, we believe that these differences did not significantly impact our final findings.

The results of our study are relevant because we verified that the racism can be a contributing factor for increased arterial stiffness and c-IMT in Blacks and Browns. Future research with a longitudinal design may help to understand the complex relationship between race/skin color, racial discrimination, and cardiovascular health, adding more robust evidence to support public policies to promote racial equity in health.

Acknowledgments

This study was funded by the Brazilian Ministry of Health (Department of Science and Technology) and the Brazilian Ministry of Science, Technology and Innovation (FINEP, Financiadora de Estudos e Projetos and CNPq, National Research Council), Grant No 01 06 0010.00, 01 06 0212.00, 01 06 0300.00, 01 06 0278.00, 01 06 0115.00 and 01 06 0071.00. This study was financed in part by the Coordenação de Aperfeiçoamento de Pessoal de Nível Superior, Brasil (CAPES) Finance Code 001. SMB, DC and RHG are research fellows of the National Research Council (CNPq). SMB is supported by a research grant (Pesquisador Mineiro) from the Fundação de Amparo à Pesquisa do Estado de Minas Gerais (FAPEMIG), Brazil. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

The authors thank all ELSA-Brasil participants for their invaluable contribution to this study.

References

[1] Justin Thomas S, Booth JN, Dai C, Li X, Allen N, Calhoun D, et al. Cumulative incidence of hypertension by 55 years of age in blacks and whites: the cardia study. J Am Heart Assoc 2018;7. doi:10.1161/JAHA.117.007988.
[2] Benjamin EJ, Muntner P, Alonso A, Bittencourt MS, Callaway CW, Carson AP, et al. Heart disease and stroke statistics-2019 update: a report from the American heart association. Circulation 2019;139:e1–473. doi:10.1161/CIR.0000000000000659.
[3] Center for Disease Control. Health, United States Spotlight: racial and ethnic disparities in heart disease 2019.
[4] Duprez DA, Jacobs DR, Lutsey PL, Herrington D, Prime D, Ouyang P, et al. Race/ethnic and sex differences in large and small artery elasticity - results of the multi-ethnic study of atherosclerosis (MESA). Ethn Dis 2009;19:243–50.
[5] Ferreira AVL, Viana MC, Mill JG, Asmar RG, Cunha RS. Racial differences in aortic stiffness in normotensive and hypertensive adults. J Hypertens 1999;17:631–7. doi:10.1097/00004872-199917050-00006.
[6] De Lima Santos PCJ, De Oliveira Alvim R, Ferreira NE, De Sá Cunha R, Krieger JE, Mill JG, et al. Ethnicity and arterial stiffness in Brazil. Am J Hypertens 2011;24:278–84. doi:10.1038/ajh.2010.244.
[7] Goel A, Maroules CD, Mitchell GF, Peshock R, Ayers C, McColl R, et al. Ethnic difference in proximal aortic stiffness: an observation from the Dallas heart study. JACC Cardiovasc Imaging 2017;10:54–61. doi:10.1016/j.jcmg.2016.07.012.
[8] D'Agostino RB, Burke G, O'Leary D, Rewers M, Selby J, Savage PJ, et al. Ethnic differences in carotid wall thickness: the insulin resistance atherosclerosis study. Stroke 1996;27:1744–9.
[9] Zaniqueli D, Alvim RO, Luiz SG, Oliosa PR, De Sá Cunha R, Mill JG. Ethnicity and arterial stiffness in children and adolescents from a Brazilian population. J Hypertens 2017;35:2257–61. doi:10.1097/HJH.0000000000001444.
[10] Lewis TT, Williams DR, Tamene M, Clark CR. Self-reported experiences of discrimination and cardiovascular disease. Curr Cardiovasc Risk Rep 2014;8:1–15. doi:10.1007/s12170-013-0365-2.
[11] Williams DR, Lawrence JA, Davis BA, Vu C. Understanding how discrimination can affect health. Health Serv Res 2019;54:1374–88. doi:10.1111/1475-6773.13222.
[12] Dolezsar CM, McGrath JJ, Herzig AJM, Miller SB. Perceived racial discrimination and hypertension: a comprehensive systematic review. Heal Psychol 2014;33:20–34. doi:10.1037/a0033718.
[13] Everson-Rose SA, Lutsey PL, Roetker NS, Lewis TT, Kershaw KN, Alonso A, et al. Perceived discrimination and incident cardiovascular events: the Multi-Ethnic Study of Atherosclerosis. Am J Epidemiol 2015;182:225–34. doi:10.1093/aje/kwv035.
[14] Troxel WM, Matthews KA, Bromberger JT, Sutton-Tyrrell K. Chronic stress burden, discrimination, and subclinical carotid artery disease in African American and Caucasian women. Heal Psychol 2003;22:300–9. doi:10.1037/0278-6133.22.3.300.
[15] Cruickshank JK, Silva MJ, Molaodi OR, Enayat ZE, Cassidy A, Karamanos A, et al. Ethnic differences in and childhood influences on early adult pulse wave velocity: the determinants of adolescent, now young adult, social wellbeing, and health longitudinal study. Hypertension 2016;67:1133–41. doi:10.1161/HYPERTENSIONAHA.115.07079.
[16] Beatty Moody DL, Leibel DK, Pantesco EJ, Wendell CR, Waldstein SR, Evans MK, et al. Interactive relations across dimensions of interpersonal-level discrimination and depressive symptoms to carotid intimal-medial thickening in African Americans. Psychosom Med 2020;82:234–46. doi:10.1097/PSY.0000000000000765.
[17] TELLES EE. Racismo à brasileira: uma nova perspectiva sociológica. Rio de Janeiro: Relume Dumará; 2003.
[18] Htun M. From "racial democracy" to affirmative action: changing state policy on race in Brazil. Lat Am Res Rev 2004;39:60–98.
[19] Santos IS, Bittencourt MS, Oliveira IRS, Souza AG, Meireles DP, Rundek T, et al. Carotid intima-media thickness value distributions in the Brazilian longitudinal study of adult health (ELSA-Brasil). Atherosclerosis 2014;237:227–35. doi:10.1016/j.atherosclerosis.2014.09.004.
[20] Baldo MP, Cunha RS, Ribeiro LP, Lotufo PA, Chor D, Barreto SM, et al. Racial differences in arterial stiffness are mainly determined by blood pressure levels: results from the ELSA-Brasil study. J Am Heart Assoc 2017;6:1–11. doi:10.1161/JAHA.117.005477.
[21] Schmidt MI, Duncan BB, Mill G, Lotufo PA, Barreto SM, Aquino EML, et al. Cohort profile: longitudinal Study of adult health (ELSA-Brasil). Int J Epidemiol 2015;44:68–75. doi:10.1093/ije/dyu027.
[22] Aquino EML, Barreto SM, Bensenor IM, Carvalho MS, Chor D, Duncan BB, et al. Brazilian longitudinal study of adult health (ELSA-Brasil): objectives and design. Am J Epidemiol 2012;175:315–24. doi:10.1093/aje/kwr294.
[23] Cunningham TJ, Berkman LF, Gortmaker SL, Kiefe CI, Jacobs DR, Seeman TE, et al. Assessment of differential item functioning in the experiences of discrimination index: the coronary artery risk development in young adults (CARDIA) Study. Am J Epidemiol 2011;174:1266–74. doi:10.1093/aje/kwr253.
[24] Mill JG, Pinto K, Griep RH, Goulart A, Foppa M, Lotufo PA, et al. Aferições e exames clínicos realizados nos participantes do ELSA-Brasil. Rev Saude Publica 2013;47:54–62. doi:10.1590/S0034-8910.2013047003851.
[25] Stein JH, Korcarz CE, Hurst RT, Lonn E, Kendall CB, Mohler ER, et al. Use of carotid ultrasound to identify subclinical vascular disease and evaluate cardiovascular disease risk: a consensus statement from the American society of echocardiography carotid intima-media thickness task force endorsed by the society for vascular. J Am Soc Echocardiogr 2008;21:93–111. doi:10.1016/j.echo.2007.11.011.
[26] Williams DR, Gonzalez HM, Williams S, Mohammed SA, Moomal H, Stein DJ. Perceived discrimination, race and health in South Africa. Soc Sci Med 2008;67:441–52. doi:10.1016/j.socscimed.2008.03.021.Perceived.
[27] Ribeiro AL, Duncan BB, Brant LC, Lotufo PA, Mill JG, Barreto SM. Cardiovascular health in Brazil: trends and perspectives. Circulation 2016;133(4):422–33 PMID: 26811272. doi:10.1161/CIRCULATIONAHA.114.008727.
[28] Faerstein E, Chor D, Werneck GL, Lopes C de S, Kaplan G. Race and perceived racism, education, and hypertension among Brazilian civil servants: the Pró-Saúde Study. Rev Bras Epidemiol 2014;17:81–7. doi:10.1590/1809-4503201400060007.
[29] Kawachi I, Daniels N, Robinson DE. Health disparities by race and class: why both matter. Health Aff 2005;24:343–52. doi:10.1377/hlthaff.24.2.343.
[30] Dailey AB, Kasl SV, Holford TR, Lewis TT, Jones BA. Neighborhood- and individual-level socioeconomic variation in perceptions of racial discrimination. Ethn Heal 2010;15:145–63. doi:10.1080/13557851003592561.Neighborhood.
[31] Burgard S, Castiglione D de P, Lin KY, Nobre AA, Aquino EML, Pereira AC, et al. Differential reporting of discriminatory experiences in Brazil and the United States. Cad Saude Publica 2017;33:1–14. doi:10.1590/0102-311x00110516.
[32] Instituto Brasileiro de Geografia e Estatística. Censo demográfico 2010: características da população e dos domicílios. 2011.
[33] Daflon VT, Carvalhaes F, Junior Feres J. Deeper than skin: browns' and Blacks' perceptions of discrimination in Brazil. Dados - Rev Ciências Sociais 2017;60:293–330.
[34] Williams DR, Mohammed SA. Racism and Health I: pathways and scientific evidence. Am Behav Sci 2013;57:1152–73. doi:10.1177/0002764213487340.
[35] Steptoe A, Kivimäki M. Stress and cardiovascular disease. Nat Rev Cardiol 2012;9:360–70. doi:10.1038/nrcardio.2012.45.
[36] Kivimäki M, Steptoe A. Effects of stress on the development and progression of cardiovascular disease. Nat Rev Cardiol 2018;15:215–29. doi:10.1038/nrcardio.2017.189.
[37] Wilkinson IB, MacCallum H, Hupperetz PC, Van Thoor CJ, Cockcroft JR, Webb DJ. Changes in the derived central pressure waveform and pulse pressure in response to angiotensin II and noradrenaline in man. J Physiol 2001;530:541–50. doi:10.1111/j.1469-7793.2001.0541k.x.

[38] Osborne MT, Shin LM, Mehta NN, Pitman RK, Fayad ZA, Tawakol A. Disentangling the links between psychosocial stress and cardiovascular disease. Circ Cardiovasc Imaging 2020:1–13. doi:10.1161/CIRCIMAGING.120.010931.
[39] Chae DH, Wang Y, Martz CD, Slopen N, Yip T, Adler NE, et al. Racial discrimination and telomere shortening among African Americans: the coronary artery risk development in young adults (CARDIA) study. Heal Psychol 2020;39:209–19. doi:10.1037/hea0000832.
[40] Rej PH, Gravlee CC, Mulligan CJ. Shortened telomere length is associated with unfair treatment attributed to race in African Americans living in Tallahassee, Florida. Am J Hum Biol 2020;32:1–13. doi:10.1002/ajhb.23375.
[41] Sullivan S, Hammadah M, Al Mheid I, Shah A, Sun YV, Kutner M, et al. An investigation of racial/ethnic and sex differences in the association between experiences of everyday discrimination and leukocyte telomere length among patients with coronary artery disease. Psychoneuroendocrinology 2019;106:122–8. doi:10.1016/j.psyneuen.2019.03.021.
[42] McFarland MJ, Taylor J, McFarland CAS, Friedman KL. Perceived unfair treatment by police, race, and telomere length: a Nashville community-based sample of black and white men. J Health Soc Behav 2018;59:585–600. doi:10.1177/0022146518811144.
[43] Lee DB, Kim ES, Neblett EW. The link between discrimination and telomere length in African American adults. Heal Psychol 2017;36:458–67. doi:10.1037/hea0000450.
[44] Pantesco EJ, Leibel DK, Ashe JJ, Waldstein SR, Katzel LI, Liu HB, et al. Multiple forms of discrimination, social status, and telomere length: interactions within race. Psychoneuroendocrinology 2018;98:119–26. doi:10.1016/j.psyneuen.2018.08.012.
[45] Blackburn EH, Epel ES, Lin J. Human telomere biology: a contributory and interactive factor in aging, disease risks, and protection. Science 2015;350:1193–8 (80). doi:10.1126/science.aab3389.
[46] Juonala M, Kähönen M, Laitinen T, Hutri-Kähönen N, Jokinen E, Taittonen L, et al. Effect of age and sex on carotid intima-media thickness, elasticity and brachial endothelial function in healthy adults: the cardiovascular risk in young Finns study. Eur Heart J 2008;29:1198–206. doi:10.1093/eurheartj/ehm556.
[47] Cecelja M, Chowienczyk P. Dissociation of aortic pulse wave velocity with risk factors for cardiovascular disease other than hypertension: a systematic review. Hypertension 2009;54:1328–36. doi:10.1161/HYPERTENSIONAHA.109.137653.
[48] Bailey ZD, Krieger N, Agénor M, Graves J, Linos N, Bassett MT. Structural racism and health inequities in the USA: evidence and interventions. Lancet 2017;389:1453–63.
[49] Chor D, Pereira A, Pacheco AG, et al. Context-dependence of race self-classification: results from a highly mixed and unequal middle-income country. PLoS ONE 2019;14:1–17.
[51] Van Bortel Luc M, et al. Expert consensus document on the measurement of aortic stiffness in daily practice using carotid-femoral pulse wave velocity. J Hypertens 2012;30(3):445–8. doi:10.1097/HJH.0b013e32834fa8b0.
[52] Townsend Raymond R, et al. Recommendations for improving and standardizing vascular research on arterial stiffness: a scientific statement from the American heart association. Hypertension 2015;66(3):698–722. doi:10.1161/HYP.0000000000000033.