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Arterial stiffness in elderly patients with normotension and hypertension in Brazil

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Data on arterial stiffness in older populations, according to blood pressure (BP) levels, are scarce in Brazil. The objective of this study was to establish reference values for core measures of arterial stiffness, including carotid-femoral pulse wave velocity (cf-PWV) and aortic augmentation index (AIx), in a cohort of older individuals with normotension (NT) and hypertension. Cross-sectional analysis was performed with applanation tonometry data from 1192 patients aged 60 years or older. The authors classified patients according to their BP levels as having NT, controlled hypertension (CH), and uncontrolled hypertension (UH). The cf-PWV values were 9.11 ± 0.16 m/s (NT), 9.12 ± 0.18 m/s (CH), and 9.42 ± 2.2 m/s (UH) ($P < 0.005$; UH vs NT and CH). The AIx was 33.3% for the entire cohort and similar across all groups. The cf-PWV increased with age but reached a ceiling at 75 years. Compared with men, women had a higher AIx but similar cf-PWV levels. In conclusion, the markers of arterial stiffness were similar among individuals with NT/CH and higher among individuals with UH.

1 | INTRODUCTION

Evaluation of vascular function is a key element in mapping cardiovascular health. Arterial pulse wave velocity (PWV) is a well-established indirect measure of arterial wall stiffness and an independent predictor of cardiovascular events.[1,2] Human aging is among the most important cardiovascular risk factors and is associated with changes in the function and structure of the heart and vascular network.[3] Changes in the walls of large arteries include calcium deposition, progressive substitution of elastic fibers by collagen, and stiffening of the walls, with segmental dilatation and presence of atherosclerosis.[4,5] These changes lead to an increased pulse pressure, which, in turn, is associated with increased morbidity and mortality in an older population. Aortic wall stiffness changes the PWV and AIx of the central pulse wave generated by the ventricular systole.[6,7] These factors are considered independent predictors of cardiovascular and total mortality, as demonstrated in several studies from different regions of the world.[8–11]

In the literature, reference values for PWV and AIx are mainly from Asia, the United States, Australia, and Europe.[10,12,13] However, compared with European or North American populations, Latin American populations[14–16] differ in the stature, as well as in the arterial stiffness. Latin American countries are traditionally characterized by a high degree of miscegenation between whites and blacks, resulting in a high percentage of "morenos" (brown), which makes the assessment of ethnic differences challenging.

Additionally, there are scarce data on PWV reference values, especially for the elderly population, according to hypertensive status and race. Measuring the carotid-femoral PWV (cf-PWV) is a simple, noninvasive, and reproducible method that is considered by various authors the gold standard for evaluating central artery stiffness.[17–19] The objective of the present analysis was to establish the reference PWV values in a large cohort of elderly persons

with NT and hypertension in both sexes and different races in an urban area of Brazil.

2 | METHODS

The present study is a cross-sectional analysis of the data obtained during the first medical visit of the Study of PWV in Elderly Individuals in Uberlandia, a large urban area of Brazil (EVOPIU [Estudo da Velocidade da Onda de Pulso em Idosos de Uberlandia], Uberlândia, MG; Brazil). EVOPIU is a longitudinal, prospective, observational, multiclinic study with a planned 4-year follow-up. Enrollment occurred from August 2014 to October 2015, and the end of the study is scheduled for 2018. Participants are followed biannually. During the follow-up visits, clinical history, biochemical/hematological tests, electrocardiograms (ECGs), and applanation tonometry are assessed. All collected data are stored electronically and are the responsibility of the Federal University of Uberlândia, MG, Brazil. This study was approved by the research ethics committee under CAAE number 37440114.3.0000.5152 and was financed by the Minas Gerais State Agency for Research and Development (FAPEMIG).

2.1 | Inclusion/Exclusion criteria

A total of 1204 elderly individuals were invited to enroll in the study and were required to meet the following inclusion criteria: age 60 years and older, ambulatory, able to perform activities of daily living without assistance, and not hospitalized. Exclusion criteria were chronic kidney failure (on dialysis), known malignant neoplasms expected to result in death during follow-up, inability to remain in a supine position, and disagreement to participate in the study. The recruitment resulted in a final sample of 1192 patients. The patients came from nine different outpatient clinics (eight public and one private).

2.2 | Anthropometric/biochemical/hematological data and ECG

General demographic and clinical data were collected for each patient. The color/race (white, black or nonblack) of each participant was determined based on skin color, as reported by the researcher. The ethnic classification was performed by interviewers based on skin color, hair pattern, and facial features. These criteria were arbitrarily used as follows: individuals with white skin and light eyes were labeled as white, those with dark skin and curly hair were labeled as black, and those who did not meet the two previous criteria were labeled as nonblack. In the present study, no participants were considered indigenous or Asian. Serum levels of uric acid, urea, and creatinine; blood glucose; and the lipid profile were assessed using colorimetric methods (Cobas® 6000; Roche Hitachi, Brazil), whereas hematological examination was performed with a Sysmex® XED-2100, São Paulo, Brazil. The ECG was obtained with an Innomed Heart Screen device, model EKG HS 60G (Innomed®, São Paulo, Brazil). Glomerular filtration rate was calculated using the Chronic Kidney Disease Epidemiology Collaboration equation.[20] Patients were considered to have hypercholesterolemia when they had total fasting cholesterol >200 mg/dL, high-density lipoprotein cholesterol <40 mg/dL, triglycerides >190 mg/dL, or used statins; diabetes mellitus was considered when fasting plasma glucose was ≥ 126 mg/dL or when patients were using insulin/oral hypoglycemic drugs. Smoking status was defined as never, prior, or current smoker.

2.3 | BP measurements

2.3.1 | Brachial BP

After 10 minutes of rest, brachial blood pressure (bBP) was assessed in a seated position by means of three consecutive measurements at 3-minute intervals. For the first two measurements, an automatic digital oscillometric blood pressure (BP) device (HE 7200 Intelli Sense Omron Hem, Brazil) was used; the third measurement was performed with a SphygmoCor device. Individual values represented the arithmetic means of the three measurements in millimeters of mercury. The sizes of BP cuffs were adjusted to the arm circumference. We used the bBP (systolic/diastolic) levels for the classification of the hypertensive status of the patients. Patients with bBP <140/90 mm Hg were considered to have NT; those with bBP <140/90 mm Hg and using antihypertensive drugs were considered to have controlled hypertension (CH); and those with bBP ≥ 140/90 mm Hg, whether using antihypertensive drugs or not, were considered to have uncontrolled hypertension (UH).

2.3.2 | Central BP, PWV, and AIx

Central BP values, cf-PWV, and the aortic augmentation index (AIx) were obtained by applanation tonometry with a SphygmoCor XCEL device, model EM4C (AtCor Medical, Sydney, NSW, Australia); cf-PWV was measured in meters per second, with the patient in a supine position. The carotid-femoral distance (centimeters) was obtained and multiplied by 0.8 (direct method).[21] The device automatically determines the best wave for the calculation and generates cf-PWV values, central pulse pressure, central systolic BP (cSBP), central diastolic BP (cDBP), and AIx values. The AIx was automatically adjusted for a heart rate of 75 beats per minute since the heart rate is an important modifier of AIx. Applanation tonometry was performed in a single measurement, based on our own pilot study, which demonstrated high measurement reproducibility in this patient population.[22]

2.4 | Sample Size

The sample size was calculated for the analysis of cardiovascular outcomes in this cohort and is therefore not applicable to the present analysis. The present analysis represents the evaluation of the entire cohort at baseline.

2.5 | Statistical analysis

We assessed the normality of the data set using the Kolmogorov-Smirnov test and found that all variables were normally distributed. Thus, the data are expressed as means and standard deviations. Two groups were compared with Student *t* test, whereas three or more groups were compared by analysis of variance and the Bonferroni posttest. The cf-PWV, AIx, and augmentation pressure values were adjusted for sex, age, and mean arterial pressure (MAP). Univariate analyses were performed between cf-PWV and age for the different groups studied (Figure 1). To estimate cf-PWV values at predetermined ages (60, 70, and 80 years), the linear regression was performed, adjusted for sex and MAP, and their respective 95% confidence intervals were determined for the different ages (Figure 3). Significance was set at 0.05 in all analyses. STATA software version 14.0 (StataCorp, College Station, TX, USA) was used for statistical analyses.

3 | RESULTS

Of all participants, 81% were diagnosed with systemic arterial hypertension and 60% were women. Table 1 lists the clinical and laboratory characteristics of the participants according to their BP status. The population was generally overweight and of relatively short stature. In general, both peripheral and central BP values and the measures of arterial stiffness were similar between the patients with NT and those with CH. By contrast, patients with UH were older than both patients with NT and those with CH and had higher values for all BP parameters, as well as for cf-PWV. The distending pressure has a direct effect on cf-PWV (higher pressure, higher PWV); therefore, all analyses of cf-PWV were adjusted for central MAP (cMAP).

The CH group had a higher number of patients using antihypertensive medications than the UH group. The NT group had a lower number of comorbidities than the other groups.

Table 2 lists the BP values in the NT, CH, and UH groups, stratified by sex. In general, women were younger (except in the UH group) and had a higher central BP and higher AIx but not a higher cf-PWV. Table 3 shows the hemodynamic data stratified by color/race. Although nonblack patients were the majority, no significant differences were observed between the listed categories. Table 4 shows the BP values, cf-PWV, AIx, and augmentation pressure according to antihypertensive drug classes. Compared with that of other antihypertensive medications, the use of β-blockers was

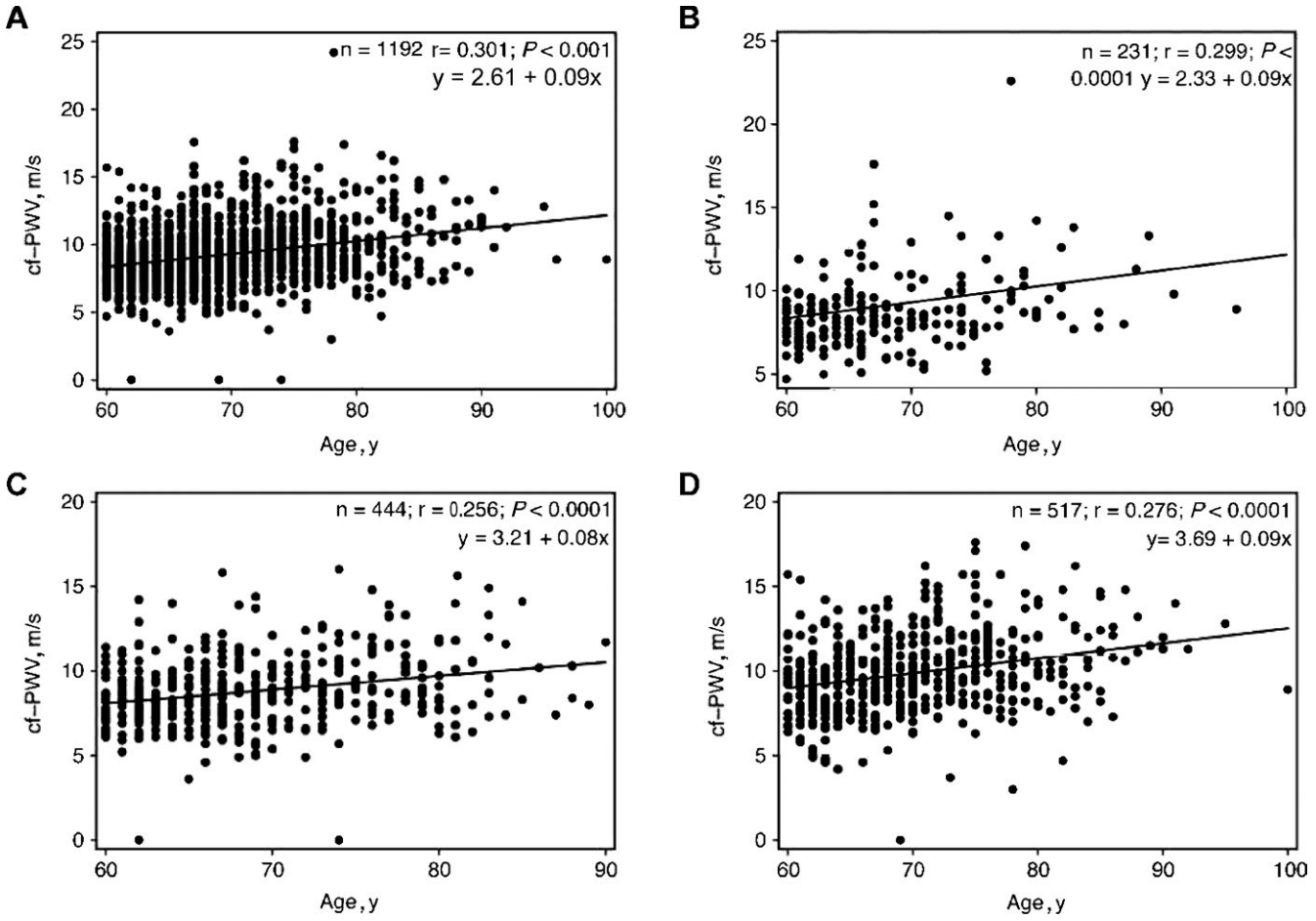

FIGURE 1 Linear regression between age and unadjusted carotid-femoral pulse wave velocity values in all patients (A) and in the normotension (B), controlled hypertension (C), and uncontrolled hypertension D) groups

TABLE 1 Peripheral and central blood pressure, pulse wave velocity, and AIx in patients with NT, CH, and UH

	All patients (N = 1192)	NT (n = 231)	CH (n = 444)	UH (n = 517)	*P* value[a]	*P* value[b]
Age, years	69.2 ± 7.0	68.1 ± 7.0	68.7 ± 6.6	70.2 ± 7.2	0.636	0.002
Male/female sex, %	39.5/60.5	43/57	32/68	39/61	0.0001	0.0001
Race, No./%						
White	99/8.3	22/9.5	38/8.6	39/7.5	0.0001	0.0001
Black	237/20	36/15	95/21.4	106/20.5	0.0001	0.0001
Nonblack	834/70	171/74	301/67.8	362/70	0.0001	0.0001
Height, m	1.57 ± 0.09	1.58 ± .09	1.58 ± .08	1.56 ± .0.9	1	0.015
Weight, kg	70.4 ± 15.2	66.3 ± 13.3	71.8 ± 15.2	70.9 ± 15.8	1	0.258
Abdominal circumference, cm	98.2 ± 13.0	93.1 ± 12.1	99.4 ± 12.3	99.6 ± 13.5	0.347	0.463
BMI, kg/m^2	28.4 ± 6.0	26.6 ± 4.9	28.8 ± 6.2	28.9 ± 6.0	<0.001	1
Heart rate, beats per min	69.2 ± 11.6	68.3 ± 10.1	69.2 ± 11.9	69.6 ± 11.9	0.696	1
Blood pressure, mm Hg						
bSBP	138.7 ± 20.0	124.8 ± 10.1	125.1 ± 10.1[a]	156.6 ± 15.1	1	<0.0001
bDBP	78.1 ± 11.1	78.0 ± 9.9	78.7 ± 10.9	88.2 ± 12.5	1	<0.0001
bPP	55.3 ± 19.3	47.3 ± 13.7	49.4 ± 13.3	64.3 ± 21.8	0.422	<0.0001
bMAP	101.3 ± 12.9	93.6 ± 8.5	94.2 ± 8.8	110.9 ± 11.1	1	<0.0001
cSBP	132.1 ± 19.2	119.2 ± 13.1	123.5 ± 14.3	144.4 ± 17.6	0.004	<0.0001
cDBP	84.0 ± 12.6	78.9 ± 9.9	79.6 ± 10.8	98.8 ± 12.6	0.742	<0.0001
cPP	48.1 ± 14.4	41.0 ± 10.7	43.9 ± 11.6	54.4 ± 15.2	0.018	<0.0001
cMAP	100.1 ± 13.5	92.5 ± 9.9	94.6 ± 10.8	108.1 ± 12.7	0.076	<0.0001
Arterial stiffness[c]						
AP, mm Hg	16.7 ± 0.59	14.8 ± 0.73	16.0 ± 0.53	19.4 ± 0.52	0.165	<0.0001
AIx, %	33.3 ± 0.77	33.0 ± 0.96	33.3 ± 0.69	33.7 ± 0.68	0.803	0.76
cf-PWV, m/s	9.21 ± 0.84	9.11 ± 0.16	9.12 ± 0.18	9.42 ± 2.2	0.924	0.043
Medications in use, No./%						
Diuretic	502/42	0	260/58.5	242/46.8		0.0002
ACEI	347/29	0	194/43.6	153/29.6		0.0001
ARB	321/27	0	163/36.7	161/31.1		0.0649
β-Blocker	297/25	0	147/33.1	149/28.8		0.1502
CCB	179/15	0	78/17.5	101/19.5		0.4446
Direct vasodilators	37/3	0	16/3.1	21/4.0		0.7174
Statins	348/29.1	36/15.5	165/37.1	147/28.4	0.0001	0.0037
Comorbidities, No./%						
Diabetes mellitus	524/44	75/32	213/48	236/46	0.0001	0.4717
Obesity (BMI ≥ 30 kg/m^2)	382/32	20/8.6	161/36.2	201/38.9	0.0001	0.0001
Dyslipidemia	365/31	39/18	173/39	153/30	0.0001	0.4717
Current and ex-smokers	645/54	136/58.8	233/52.4	276/53.3	1	1
Previous CVE	184/15.4	38/16.4	45/10.1	101/19.5	0.0179	0.0001

Values are expressed as mean ± standard error.

ACEI, angiotensin-converting enzyme inhibitor; AIx, augmentation index; AP, augmentation pressure; ARB, angiotensin receptor blocker; bDBP, brachial diastolic blood pressure; bMAP, brachial mean arterial pressure; BMI, body mass index; bPP, brachial pulse pressure; bSBP, brachial systolic blood pressure; CCB, calcium channel blocker; cDBP, central diastolic blood pressure; cf-PWV, carotid-femoral pulse wave velocity; cPP, central pulse pressure; cSBP, central systolic blood pressure; CVE, cardiovascular event.

[a]*P*: normotension (NT) vs controlled hypertension (CH).

[b]*P*: CH vs uncontrolled hypertension (UH).

[c]Adjusted by central mean arterial pressure (cMAP), sex, and age.

TABLE 2 Peripheral and central blood pressure, pulse wave velocity, and AIx in patients with NT, CH, and UH by sex

	NT (n = 231)			CH (n = 444)			UH (n = 517)		
	Male	Female	P value	Male	Female	P value	Male	Female	P value
No.	100	131		170	274		201	316	
Age, y	70.2 ± 7.6	66.3 ± 5.9	<0.0001	70.5 ± 6.4	67.6 ± 6.4	<0.0001	70.3 ± 7.6	70.1 ± 7.0	0.3861
Heart rate, beats per min	67.0 ± 9.7	69.2 ± 10.6	0.9478	65.9 ± 12.0	71.6 ± 11.7	<0.0001	67.4 ± 11.9	70.5 ± 11.8	<0.0001
Race, No./%									
White	10/10	12/9	1	19/11	19/7	1	21/10	18/6	1
Black	20/20	18/14	1	40/24	55/20	1	37/18	69/22	1
Nonblack	70/70	101/77	1	111/65	200/63	1	143/72	229/72	1
Height, m	1.6 ± 0.1	1.5 ± 0.1	<0.0001	1.6 ± 0.1	1.5 ± 0.1	<0.0001	1.6 ± 0	1.5 ± 0	<0.0001
Weight, kg	70.5 ± 1.3	63 ± 0.1	<0.0001	75.1 ± 1.1	69.7 ± 0.9	0.0002	75.2 ± 1.1	68.2 ± 0.8	<0.0001
Abdominal circumference, cm	94.3 ± 1.2	92.4 ± 1.0	0.1043	99.9 ± 0.9	99.1 ± 0.7	0.2603	100.2 ± 1.0	99.2 ± 0.7	0.2115
Body mass index, kg/m^2	26 ± 0.4	27.1 ± 0.4	0.9335	27.3 ± 0.3	29.8 ± 0.4	1	27.9 ± 0.3	29.6 ± 0.3	0.9977
Blood pressure, mm Hg									
bSBP	126 ± 9.0	123 ± 9.7	0.0081	124 ± 11.8	125 ± 8.9	0.2706	154 ± 13.7	156 ± 16.5	0.0216
bDBP	74 ± 7.5	72 ± 7.7	0.0045	72 ± 8.1	72 ± 7.8	0.5877	86 ± 11.6	83 ± 10.3	0.0002
bPP	47 ± 14.4	48 ± 12.8	0.5096	49 ± 13.1	49 ± 12.6	0.4904	60 ± 21.2	64 ± 23.0	<0.0001
bMAP	94 ± 8.1	92 ± 8.9	0.0865	94 ± 8.6	94 ± 8.9	0.7135	111 ± 11.0	110 ± 11.2	0.4331
cSBP	117 ± 12.0	120 ± 13.7	0.0121	121 ± 13.5	125 ± 14.6	0.0049	139 ± 16.2	147 ± 17.7	<0.0001
cDBP	79 ± 9.1	77 ± 10.0	0.6897	79 ± 10.1	80 ± 11.1	0.1867	90 ± 12.6	89 ± 12.6	0.8598
cPP	38 ± 9.0	43 ± 11.4	0.0002	42 ± 11.7	45 ± 11.4	0.0064	48 ± 12.8	58 ± 15.5	<0.0001
cMAP	92 ± 9.4	92 ± 10.3	0.6783	93 ± 10.2	95 ± 11.1	0.0269	107 ± 12.6	108 ± 12.7	0.0779
Arterial stiffness[a]									
AP, mm Hg	11.6 ± 1.0	16.8 ± 0.96	0.0003	13.4 ± 0.84	17.7 ± 0.66	<0.0001	15.4 ± 0.78	22.0 ± 0.64	<0.0001
AIx, %	27.8 ± 12.9	36.5 ± 13.3	<0.0001	28.0 ± 14.2	36.7 ± 14.3	<0.0001	29.2 ± 14.8	36.5 ± 13.5	<0.0001
cf-PWV, m/s	9.04 ± 0.18	9.20 ± 0.20	0.5585	8.96 ± 0.12	9.36 ± 0.16	0.0491	9.33 ± 0.12	9.56 ± 0.14	0.2038

Values are expressed as mean ± standard error.

AIx, augmentation index; AP, augmentation pressure; bDBP, brachial diastolic blood pressure; bMAP, brachial mean arterial pressure; bPP, brachial pulse pressure; bSBP, brachial systolic blood pressure; cDBP, central diastolic blood pressure; cf-PWV, carotid-femoral pulse wave velocity; cPP, central pulse pressure; cSBP, central systolic blood pressure.

[a]Adjusted by central mean arterial pressure (cMAP), sex, and age.

associated with lower cf-PWV values. The most frequent β-blocker used by the patients was atenolol. Figure 1 shows the overall correlation between age and unadjusted cf-PWV in all patients (A) and in the NT (B), CH (C), and UH (D) groups. Despite the wide variability in the distribution, there was a positive linear relationship between age and cf-PWV (r = 0.301; P < 0.001). Figure 2 shows the cf-PWV values adjusted for sex and cMAP and separated by age (in 5-year strata). The values in the highest age groups (75–80 and >80 years) were similar (P = 0.99), thus indicating a "ceiling" for the cf-PWV. Figure 3 shows the cf-PWV slope of predictive margins of cf-PWV, stratified by group (NT, CH, and UH) at 60, 70, and 80 years of age, and the respective confidence intervals, adjusted by MAP and age.

4 | DISCUSSION

This study provides detailed normative data on the central BP and measures of arterial stiffness in a large population of patients with NT, CH, and UH from an older urban-living Brazilian cohort. Arterial stiffness has been evaluated in other large Brazilian cohorts; however, unlike that in the present study, these cohorts were not restricted to the elderly, and the studies focused on other clinical and epidemiological factors, not directly related to hypertension.[23–26] Our data provide relevant novel information on the impact of age, sex, race, and hypertensive status on arterial stiffness in an older population, the major target of arterial stiffening.

TABLE 3 Peripheral and central blood pressure, pulse wave velocity, and AIx by race

	All patients (N = 1192)	White (n = 99)	Black (n = 237)	Nonblack (n = 856)	P value	P value[a]
Age, y	69.2 ± 0.20	70.7 ± 0.75	68.6 ± 0.42	69.2 ± 0.24	0.055	0.701
Male/female sex, %	39.5/60.5	51/49	40/60	39/61	0.0792	0.5179
Weight, kg	70.4 ± 0.41	68.8 ± 1.58	71 ± 0.99	70.2 ± 0.53	0.197	0.3594
Abdominal circumference, cm	98.2 ± 0.38	96.6 ± 1.42	97.3 ± 0.86	98.5 ± 0.45	0.6775	0.2033
Blood pressure, mm Hg						
bSBP	138.7 ± 0.58	138.5 ± 1.93	140.1 ± 1.34	138.1 ± 0.67	1	0.739
bDBP	82.8 ± 0.85	80.5 ± 1.20	85.0 ± 0.81	82.3 ± 0.43	0.009	0.014
bPP	55.5 ± 0.56	55.6 ± 1.91	53.5 ± 1.28	56.0 ± 0.65	1	0.213
bMAP	101.3 ± 0.38	99.8 ± 1.2	103.3 ± 0.86	100.9 ± 0.44	0.078	0.047
cSBP	132.4 ± 0.57	130.2 ± 1.82	133.4 ± 1.30	132.1 ± 0.67	0.478	1
cDBP	84.2 ± 0.37	81.7 ± 1.21	86.4 ± 0.83	83.7 ± 0.44	0.005	0.011
cPP	48.2 ± 0.42	48.4 ± 1.30	47.0 ± 0.93	48.4 ± 0.50	1	0.506
cMAP	100.1 ± 0.39	97.9 ± 1.30	102.1 ± 0.91	99.8 ± 0.47	0.026	0.073
Arterial stiffness[b]						
AP, mm	16.7 ± 0.59	17.4 ± 1.09	15.6 ± 0.70	17.7 ± 0.37	0.178	0.008
AIx, %	33.3 ± 0.77	32.4 ± 1.42	32.7 ± 0.91	33.9 ± 0.48	0.944	0.127
cf-PWV, m/s	9.21 ± 0.84	9.22 ± 0.20	9.42 ± 0.13	9.22 ± 0.07	0.988	0.1821

Values are expressed as mean ± standard error.

AIx, augmentation index; AP, augmentation pressure; bDBP, brachial diastolic blood pressure; bMAP, brachial mean arterial pressure; bPP, brachial pulse pressure; bSBP, brachial systolic blood pressure; cDBP, central diastolic blood pressure; cf-PWV, carotid-femoral pulse wave velocity; cPP, central pulse pressure; cSBP, central systolic blood pressure.

P: white vs black.

[a]*P*: black vs nonblack.

[b]Adjusted by central mean arterial pressure (cMAP), sex, and age.

Evidence from several observational and controlled randomized trials suggests that antihypertensive treatment reduces arterial wall thickening. This effect seems to be attributed to not only reduced brachial systolic BP but also to arterial remodeling. Moreover, cf-PWV data can be considered strong evidence of arterial destiffening.[27–30] Our data suggest that elderly patients with hypertension whose BP is controlled by antihypertensive medication have cf-PWV values similar to those of aged individuals without hypertension. The data shown in Table 4 confirm that patients who used β-blockers for antihypertensive therapy had the lowest cf-PWV values. It should be noted that β-blockers (atenolol) could be combined with other antihypertensive agents and that the observed reduction in cf-PWV has been previously described.[31] The recognized effectiveness of inhibitors of the renin-angiotensin system[31,32] in reducing vascular wall thickening was not demonstrated by our analysis. However, our study was not designed for this specific analysis. Because we did not design our study to compare the effects of individual classes of medications on arterial stiffness, we cannot rule out confounding by indication and other possible confounders relevant to this analysis.

Regarding the race/ethnicity classification, analysis of BP values showed significant differences in cMAP, cDBP, and bDBP between whites and blacks, whereas the vascular thickening markers (cf-PWV and AIx) were not different. Comparison of nonblacks and blacks showed the same results. It is necessary to consider that the classification used in our work was arbitrary and dependent on the interpretation by the researchers. In contrast to the data based on the Brazilian Institute for Geographic Statistics classification, which uses a self-reference for race determination, our percentage of whites was equal to that of blacks, while nonblacks constituted the overwhelming majority. Therefore, we are cautious about making strong comments about the impact of race/ethnicity on our results.

Another interesting observation is that the cf-PWV values (not adjusted for sex and cMAP) progressively increase throughout older age ranges (Figure 1); however, after adjustment, the cf-PWV values seem to reach a plateau after age 75 (Figure 2). We speculate that at the age of 75 years and older, new damage to the arterial wall results in a modest increase in cf-PWV. However, this pattern was not observed for AIx. Of note, the AIx is generally not considered an accurate marker of arterial stiffness because it is strongly influenced by heart rate, height, and contractility and decreases in older age.[3,33]

The cf-PWV values were indistinguishable between the NT and CH groups. Figure 3 shows an overlap in the predictive values of cf-PWV and age between patients with NT and those with CH at age 60, 70, and 80 years. The patients with UH had higher cf-PWV values than patients with NT and CH in all age strata, but the

TABLE 4 Peripheral and central blood pressure, pulse wave velocity, AIx, and antihypertensive drugs

	Diuretic	ARB	ACEI	β-Blocker	CCB
No.	501	324	347	296	179
Age, years	69.8 ± 0.3	69.3 ± 0.3	69.5 ± 0.3	68.8 ± 0.3	70.3 ± 0.5
Heart rate	77.2 ± 1.5	73.8 ± 0.7	74.5 ± 0.7	68 ± 1.4d	75.5 ± 2.0
Blood pressure, mm Hg					
bSBP	139.5 ± 2.57	141.3 ± 1.14	139.3 ± 1.15	138.3 ± 2.21	141.6 ± 3.30
bDBP	86.7 ± 1.60[b]	83.5 ± 0.70	82.5 ± 0.71c	81.2 ± 1.36	82.9 ± 2.03
bPP	54.5 ± 2.44	57.6 ± 1.08	55.6 ± 1.09	57.7 ± 2.09	59.9 ± 3.12
bMAP	104.4 ± 1.66	102.7 ± 0.71	101.5 ± 0.74	100.3 ± 1.4	103.7 ± 1.07
cSBP	132.7 ± 2.49	136.5 ± 1.08	132.3 ± 1.09a	134.2 ± 1.25	133.8 ± 3.11
cDBP	84.2 ± 0.57	85.0 ± 0.73	83.8 ± 0.67	83.8 ± 0.77	85.2 ± 1.03
cPP	49.8 ± 0.67	51.4 ± 0.81	48.6 ± 0.79	53.3 ± 0.89	52.8 ± 1.20
cMAP	102.3 ± 1.75	102.1 ± 0.76	100.0 ± 0.74a	99.7 ± 1.47	102.5 ± 0.73
Arterial stiffness[e]					
AP, mm Hg	14.5 ± 1.0	19.0 ± 0.96	17.5 ± 0.84	21.3 ± 0.66	15.3 ± 0.78
AIx, %	31.7 ± 1.77	34.5 ± 0.78	33.4 ± 0.78	36.9 ± 1.50d	30.7 ± 2.22
cf-PWV, m/s	9.72 ± 0.23	9.48 ± 0.11	9.48 ± 0.11	8.39 ± 0.21d	9.47 ± 0.15

Values are expressed as mean ± standard error.

AP, augmentation pressure; AIx, augmentation index; bDBP, brachial diastolic blood pressure; bMAP, brachial mean arterial pressure; bPP, brachial pulse pressure; bSBP, brachial systolic blood pressure; cDBP, central diastolic blood pressure; cf-PWV, carotid-femoral pulse wave velocity cPP, central pulse pressure; cSBP central systolic blood pressure.

[a]Angiotensin receptor blocker (ARB) vs angiotensin-converting enzyme inhibitor (ACEI): $P = 0.047$.

[b]β-Blocker vs diuretic: $P = 0.0093$.

[c]iECA vs diuretic: $P = 0.016$.

[d]β-Blocker vs diuretic, ACEI, ARB, and calcium channel blocker (CCB).

[e]$P < 0.05$: adjusted by age and central mean arterial (cMAP).

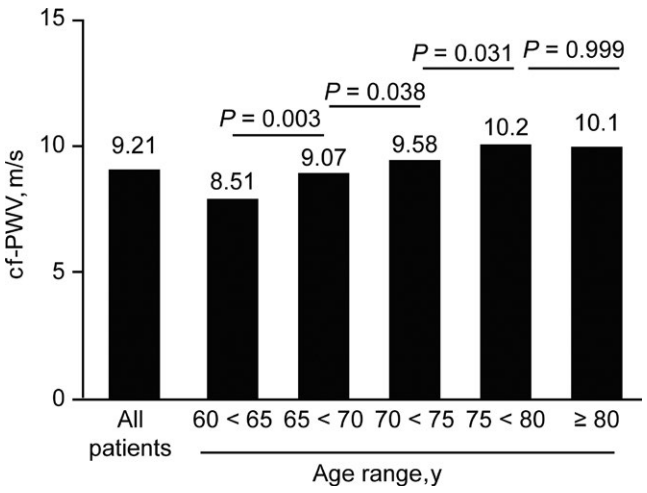

FIGURE 2 Carotid-femoral pulse wave velocity (cf-PWV) values adjusted for sex and central mean arterial pressure and stratified by each 5 y of age

slope of the age-related increase was similar in all three groups. In addition, all components of bBP and central BP in the CH group exhibited values similar to those of the NT group, thus suggesting that antihypertensive therapy maintains the above parameters at levels indistinguishable from those in patients with NT. Because of the cross-sectional nature of our data, we do not know whether control of BP would lead to normalization of arterial stiffness during follow-up. Our longitudinal analysis of patients with UH at baseline will allow us to address this question in the future.

Regarding sex-related differences, hypertensive women had higher systolic values than men, but PWVs were similar between both sexes (Table 2). Among the values observed in elderly men and women, brachial systolic BP, central pulse pressure, brachial pulse pressure, and AIx were higher among women in the UH and CH groups (Table 3). Differences between sexes regarding the central pressure and arterial wall thickening are not completely understood.[34] Furthermore, the higher AIx in women could be attributable to an early return of the wave reflection caused by their shorter height[13] or decreased aortic diameter[35]; it could also be associated with sex-related hormonal differences.[36]

The PWV values in elderly patients from the urban center in Brazil were higher than those obtained in other studies from Latin American countries. In Argentina, Diaz et al[15] reported a PWV value for patients aged 60 to 70 years that was below the overall value obtained in the present study (8.4 vs 9.3 m/s, respectively). The data from the Argentine study were closer to those found in our NT and CH groups. In Uruguay, Farro et al[14] reported a PWV value of 10.4 m/s for a hypertensive population younger than 60 years. In Brazil, for healthy patients aged between 55 and 65 years, Baldo

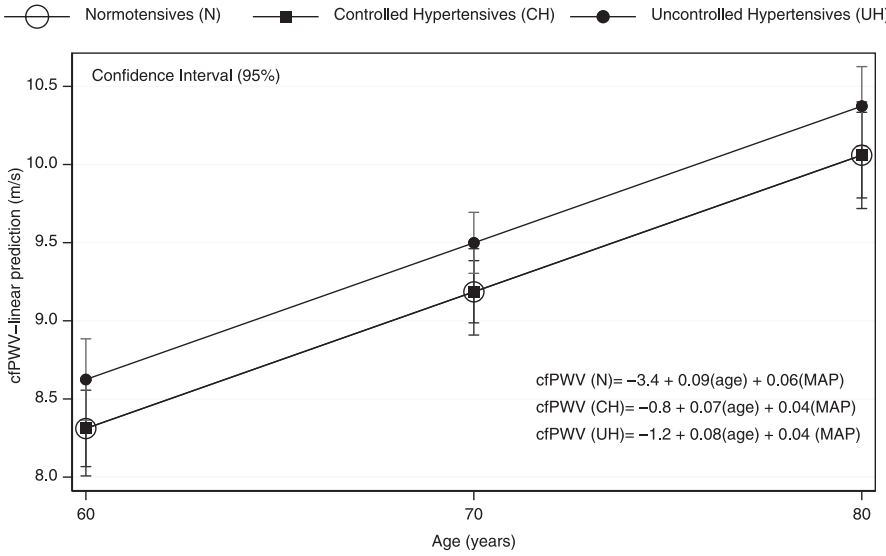

FIGURE 3 Predictive values of adjusted carotid-femoral pulse wave velocity, stratified by group (normotension, controlled hypertension, and uncontrolled hypertension) at 60, 70, and 80 y of age

et al[37] reported a mean cf-PWV value (9.48 ± 1.39 m/s)[37] similar to that found in our study for individuals with NT. Data from Boutouyrie et al[38] from different European centers showed cf-PWV values of 9.3 m/s and 11.1 m/s in elderly patients with NT and hypertension, respectively,[38] and Fu et al[39] have reported a cf-PWV value of 12.5 m/s for Chinese patients with hypertension. Both studies showed values slightly higher than those found in our study.

5 | STUDY LIMITATIONS

The present investigation has limitations typical of cross-sectional studies, such as the measurements of BP and applanation tonometry on a single occasion. These values may differ from those of repeated measurements on different occasions, although the reproducibility of these measurements (at the same BP) is usually adequate.[40]

6 | CONCLUSIONS

In an urban cohort of older Brazilian individuals, central BP and cf-PWV values were higher in patients with UH than in patients with NT and CH. The PWV values increased with age even in this older cohort, reaching a peak at an approximate age of 75 years. Women had a higher AIx, which was possibly attributable to their shorter stature, but their cf-PWV values were similar to those of their male counterparts. Patients with NT and CH exhibited similar cf-PWV values, thus suggesting that effective antihypertensive treatment may delay or reverse the hypertension-associated arterial stiffening.

CONFLICTS OF INTEREST

The authors have no conflicts of interest to declare.

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