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## **Research Article**

Correlation between age and pulse wave velocity in adults, salvador, bahia, brazil in a populationbased study: Design, methods and preliminary results

#### Abstract

Cardiovascular diseases are the leading cause of death in Brazil. The pulse wave velocity (PWV) is an independent cardiovascular risk factor detecting arterial stiffness, correlated to age, among other variables.

**Objective:** Analyze age (i) and PWV correlation on individuals aged ≥ 18 years.

**Methods:** A cross-sectional exploratory study on a representative population of a community in Salvador-Bahia-Brazil. The data were obtained from a simple random sample, including 301 individuals, over 12 census sectors. 95 individuals of both sexes were initially assessed, from November 2016 to February 2018. Home visits were carried out to fill out individual and home records and to schedule examinations, including PWV measurement, in an outpatient clinic. The carotid-femoral PWV was measured as the velocity between the carotid and femoral wave coupled to the electrocardiogram, considering the beat-to-beat pulse wave base, adjusted for a .8 ratio. Femoral carotid length is measured in millimeters. An AT Cor SphygmoCor applanation tonometer was used. Central and dispersion trend measures were analyzed and stratified by sex, age and PWV. Frequency and descriptive measures, Spearman's linear correlation coefficient between PWV and age and Prevalence Ratio per sex were obtained with the respective confidence intervals, estimated as a function of the Odds Ratio. STATA v.12 software was used. The level of statistical significance was 5%. The standards of the human research ethics board were observed.

**Results:** There was a prevalence of women (65.3%); mean PWV was higher among men (9.5±2.5) compared to women (8.9±2.5); 68.7% of women and 31.3% of men presented normal PWV values. Statistically significant trends (ES) of PWV mean gradient increase over age groups (p = 0.000) were found. There are no changes in the mean value of PWV among participants that are less than 30 years old. The prevalence of adjusted abnormal PWV was 29.5%, 36.4% among males and 25.8% among females. The chance of women, when compared to men, to present PWV abnormality was 1.64 times (95% CI: 0.66-4.07). There was a positive and statistically significant among women (r=0.63, p=0.0000), weak positive and statistically significant among men (r=0.41, p=0.0167).

Conclusion: The correlation between PWV and age progression in both sexes was verified, with higher correlations found for women.

# Introduction

Cardiovascular diseases are the main cause of death in Brazil and Bahia, accounting for 28% and 24.2% of all deaths in both sexes, respectively [1]. Increased arterial stiffness has been associated as an independent risk factor for fatal cerebrovascular accident, coronary events, and general and cardiovascular mortality in hypertensive patients and in the general population [2-5].

Aging itself has been pointed as the main cause of increased arterial stiffness, either as a physiological process or as an early underlying pathological mechanism. With age, arteries are more likely to have their structure and function changed.

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The wall stiffening is a natural, expected event, but genetic and environmental factors can also interfere with this structure at an early stage, including nutritional features, lifestyle, smoking, physical inactivity, dyslipidemia, dysglycemia. Multiple mechanisms are involved in this process, the most obvious being the remodeling of the middle tunica, comprising the loss of elastin and its replacement with collagen fibers, and calcium deposition, resulting in loss of elasticity and decreased arterial compliance [6–8].

The carotid-femoral pulse wave velocity (Cf-pwv) is currently considered the gold standard for measuring arterial stiffness, being a non-invasive, simple and easily reproducible method [2-4,6,8,9]. The Cf-pwv can be obtained by the equation V = D/T, where V is the pulse wave velocity (PWV), D is the distance covered between (carotid and femoral) artery pulses, and T is the time the flow (pulse) covers this path. Increased arterial stiffness is directly related to increased PWV [7,8,10,11].

The pulse wave velocity is an important tool to evaluate arterial stiffness, it can help to determine and estimate early cardiovascular risk and assist in the definition of therapeutic procedures and their efficacy. More recent hypertension guidelines use PWV as a risk predictor, increasing the accuracy cardiovascular risk stratification [12–16].

The increasing number of studies identified in the literature on this subject involves Caucasian populations in Europe and North America [9,10,17]. In Latin America, especially in Brazil, literature is still incipient. Accordingly, the objective is to evaluate the association between pulse wave velocity and patient age in a markedly mixed Brazilian population and an attached community.

## **Objective**

To describe design and methods and to analyze the correlation between age and pulse wave velocity in adults >18 years of age, in a Brazilian population based study.

## Methodology

#### Design and type of study

This is a cross-sectional, exploratory, population-based study conducted in a neighborhood of Salvador-Bahia, from November 2016 to February 2018, whose duration was extended for another 2 years.

This study is part of a larger project named VASCOR, carried out by Faculdade de Tecnologia e Ciências (FTC), in a partnership with Fiocruz-Bahia and Universidade de Minho in Portugal, the main purpose of which is to investigate the association between visceral obesity syndrome or metabolic syndrome, low-intensity chronic inflammation and arterial stiffness.

#### Area of coverage

The Ogunjá Valley is part of the Acupe de Brotas neighborhood, in the metropolitan region of Salvador, capital of Bahia, Brazil. The region is subdivided into 12 Census Sectors (SC), each with its own streets, which were used as an aggregate in the survey. According to 2010 IBGE Brazilian Geografic and Stastistic Institute Census data [18], the estimate is 7,450 individuals ≥18 years, corresponding to 4,181 women (56%) and 3,269 men (44%).

#### **Target population**

The study included individuals of both sexes residing in the Ogunjá Valley region, aged ≥18 years. Pregnant, bedridden, people with locomotion difficulties and domestic servants, were excluded.

#### Sample calculation

A simple random sample (SRS) was obtained, considering a sampling error of 4.5%, a prevalence of Metabolic Syndrome of 20%, a 5% (alpha) error, a 25% loss was estimated, for a total of 301 individuals. For the calculation of individuals by census sector in the selected region, the proportional distribution criterion was used, whereby a sampling fraction per stratum (SC) similar to overall sampling fraction [19,20] is secured.

The area described was mapped according to its main roads (aggregate), secondary roads, ways, alleys and smaller alleys, and divided into census sectors, as shown in Figure 1. The sample was distributed to keep representativeness for the

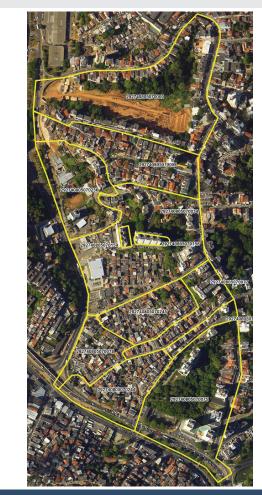


Figure 1: Delimitation of the area used for collecting sample data (areas of the study delimitated by Google Maps).

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different regions, with a random sampling procedure. Only one individual was drawn in each household.

### **Data collection**

The data were obtained through structured interviews at home, filling in individual and home records, scheduling complementary examinations at the Clinic School at Faculdade de Tecnologia e Ciência (FTC). Before the interview, participants were informed on the study's objectives and after accepting it, the informed consent form (TCLE) was read and signed.

The work team consists of 30 people (students and researchers) allocated to the following sectors: field, appointment sector, laboratory, anthropometric measurements, electrocardiogram, data and evaluation of pulse wave velocity (PWV) and central pressure (CP). Researchers received training in meetings scheduled periodically with the whole team; and based on visits to the community during the first two months of researcher's admission. They only made group visits with. The training for Pulse Wave Velocity and Central Pressure measurement occurred from December 2016 to January 2017 with people qualified to use SphygmoCor.

**Socioeconomic covariates:** Age (18–50, >50); gender; selfdeclared race (black, brown, white, asian and indigenous); marital status (married, single, widower, divorced); education (not education, < fundamental, fundamental, <secondary, secondary, undergraduate, postgraduate); per capita family income in USD dollars (USD) (no income, ≤250.00, 250.00 to 500.00, 501.00 to 1000.00, >1000.00).

Covariates to familiar antecedents of 1<sup>st</sup> grade for cardiovascular diseases: all of this with medical diagnosis – yes/no. If yes, identify (parents, brothers and children); type of cardiovascular disease (acute myocardial infarction, stroke, heart surgery, stent in heart); diabetes mellitus; hypertension; overweight; dead of cardiovascular disease.

**Others covariates:** Smoking (time of and numbers of cigarrets); alcoholism (AUDIT criteria); physical activity (IPAC criteria).

During the consultations, each participant was registered with name, date of birth, gender and an identification code. Age calculation was based on the date of birth collected at the time of PWV evaluation. At the FTC School Clinic, blood and urine were collected; anthropometric measurements, electrocardiogram, peripheral blood pressure and pulse wave velocity and central pressure were performed. The Pulse wave velocity (PWV) was assessed by a SphygmoCor applanation tonometer equipment (At Cor M Pty Ltd, New South Wales, Australia), calibrated with the software that comes with the equipment. For this measure was considered: PWV normal: < 10m/seg and abnormal: ≥ 10m/ seg. Three measurements of the peripheral blood pressure were performed with an onrom 1100 HBP pressure monitor with recognized validation [21,22], with the first measurement discarded and the average of the other two measurements recorded in the PWV system (systolic and diastolic). The

peripheral pressure was measured with the individual lying at zero degree, on the naked left arm, at 1-minute measurement intervals and 5 minutes of waiting before the 1<sup>st</sup> measurement. No cigarette, alcohol or caffeinated beverage consumption were allowed thirty minutes before measurement of arterial pressure and PWV and CP. All measurements were made with subjects on an empty bladder.

In case of any difficulty to evaluate the PWV, including patients with anatomical variations, high adipose tissue, or operator's failure, an attempt was made to reschedule the participants, to minimize possible bias.

Variables other definition: glicemia: above > 100mg/ dl; arterial hypertension:  $\geq$ 130/85 mm/Hg or normal blood pressure with regular treatment of hypertension; Dyslipidemia (ATP III criteria definition): triglicerídeos  $\geq$ 150 mg/dl or colesterol-HDL <40 mg/dl for men and <50 mg/dl for woman or colesterol-LDL  $\geq$ 130 mg/dl; Abdominal obesity: CC >84 cm for woman and > 88 cm for men; and body mass index: kg/m<sup>2</sup>:  $\geq$ 25 [23].

The value recorded in the software was multiplied by the 0.8 adjust ratio [24]. A stadiometer was used to avoid measurement bias in patients with increased abdominal circumference and/ or very bulky breasts. The maximum normality value after adjusting was 10m/sec [24]. Each patient had their examination recorded in the software and subsequently printed and attached to their clinical file. The PWV examination was identified only by the patient's research record number, securing the ethical requirements.

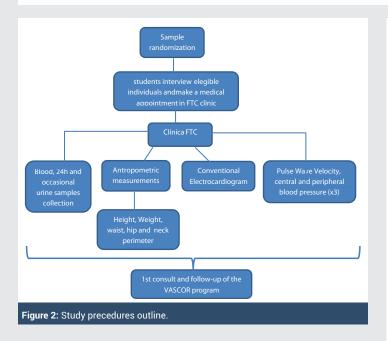
The next procedure was installing the electrocardiogram with three leads placing the electrodes on the thorax of the individuals. With an inelastic tape measure a direct measurement from the point of greatest carotid incursion on the right side of the neck to the point of greatest incursion of the femoral pulse near the groin was obtained. This technique defines the direct cf-PWV measure. The value was entered in millimeters in the software. Immediately after these procedures, the carotid wave was measured and after a satisfactory amplitude, the PWV was performed in the femoral, after the same requirements, then the reading is finished and the cf-PWV appears on the display. If the standard deviation of this velocity was greater than 10%, the measure would be discarded. Measure PWV per pacient several times until the stand deviation was reached [24].

After the collection, each participant receives a card with all the results of the physical and laboratory exams, and a report with their clinical condition. After this procedure, the individual is referred to a baseline health unit for follow-up with a team clinic (Figure 2).

#### **Data analysis**

EPIINFO for Windows (version 7.0) was used to build the database. For the exploratory analysis of results, univariate and bivariate frequency distributions and measures of central tendency stratified by sex were used. The frequency and

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descriptive measures (mean, mode, median and standard deviation), Spearman linear correlation coefficient between the pulse wave velocity and age, and the Prevalence Ratio (RP) by sex and respective confidence intervals estimated as a function of Odds Ratio through binary logistic regression were obtained. STATA v.12 software was used for treatment and generation of results. The level of statistical significance was set at 5%.

### **Ethical considerations**

This study follows the definitions set forth in the Declaration of Helsinki VII and was submitted to and approved by the FTC's Research Ethics Committee (CEP), in accordance with the ethical precepts of Resolution 466/2012 of the National Health Council (No1827621), which consists of guidelines and norms governing researches with humans.

The data were collected with the guarantee of confidentiality that ensures the privacy and anonymity of the subjects regarding the confidential data involved in the research, without any situations that could cause any kind of biological, physical and/or psychological damage. The Informed Consent Form was read and signed by all participants in this study.

#### **Findings**

Data were collected from 95 individuals, which correspond to 31.6% of the total sample (n=301). Preliminary datas show: female of 65.3%, with age between 18 and 59 years (57,9%) e no smoking (75,3%). Only 4.2% has glicemia above > 100 mg/ dl and arterial hypertension ( $\geq$  130/85 mm/Hg or normal blood pressure with regular treatment of hypertension) of 14,3%. Attract attention for dyslipidemia (87,2%) and the abdominal obesity (72,6%). The body mass index was 27,7kg/m<sup>2</sup>.

The prevalence among the population of non-normal adjusted PWV was 31,5.5% (28/95), 36,4% (12/33) among men, and 25,8% (16/62) among women. The chance of women to present PWV abnormality, when compared to men, was 1.64

times (IC95%:0.66-4.07), which result is not statistically significant.

Mean pulse wave velocity was higher among males  $(9.5\pm2.5)$  compared to females  $(8.9\pm2.5)$ . Likewise, 68.7% of women presented normal PWV values, whereas in men this corresponded to 31.3% (Table 1).

When analyzing the age distribution of the participants, there are statistically significant trends of gradual average increase in the wave pulse between age groups (p = 0.000). It is verified that, between the 60 to 69 years and 70 or more years, there was a higher frequency of individuals with PWV values exceeding the mean pulse wave velocity values expected for their age / above 10m/s. It is important to emphasize the absence of changes in the mean PWV value among participants that are less than 30 years old (Table 2). It is important to emphasize that on age groups 30 - 39 and 40 - 49, approximately 15% of young adults have PWV above 10 m/s.

Figure 3, shows a moderate positive correlation between adjusted PWV values and age (r=0.54; p=0.0000). The correlation is moderate and statistically meaningful among

#### Table 1: Description of general clinical parameters.

	. g					
	n (%)	Pulse Wave Velocity (PWV) with Reset (m/s)				
Variables		Mean (±dp)	Normal n (%)	Not normal n (%)	p-value	
Gender						
Male	33 (34.7)	9.5 (±2.5)	21 (31.3)	12 (42.9)	0.283ª	
Female	62 (65.3)	8.9 (±2.5)	46 (68.7)	16 (57.1)		
Mean PWV ((± dp)		9.1 (± 2.5)	7,8 (±1.3)	12,3 ((±1.6)		
Age category (years)						
< 30	14 (14.7)	6.9 (±1.2)	14 (20.9)	0 (0.0)		
30 - 39	26 (27.4)	8.4 (±2.1)	22 (32.8)	4 (14.3)		
40 - 49	15 (15.8)	9.0 (±2.7)	11 (16.4)	4 (14.3)		
50 - 59	17 (17.9)	9.4 (±2.3)	12 (17.9)	5 (17.9)	0.000 <sup>b</sup>	
60 - 69	14 (14.7)	10.8 (±2.0)	5 (7.5)	9 (32.1)		
70 e +	9 (9.5)	11.6 (±2.4)	3 (4.5)	6 (21.4)		
Note: "Depress's shi aguarad test: b Chi aguarad trand						

Note: a Pearson's chi-squared test; b Chi-squared trend.

#### Table 2: Based characteristic of population study.

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Variables	n	%
Gender		
Male	33	34.7
Female	62	65.3
Age group (n=76)		
18 a 50 years	44	57.9
> 50 years	32	42.1
Current smoker (n=77)	19	24.7
Diabetes Mellitus (n=71)	3	4.2
Dyslipidaemia (n=94)	82	87.2
Arterial hypertension	11	14.3
Abdominal obesity	69	72.6
Body mass index (Kg/m <sup>2</sup> )	28.1±6,0	
		064

females (r=0.63; p=0.0000), weak positive and statistically meaningful among males (r=0.41; p=0.0167).

### Discussion

Cf-PWV has been used as a gold standard for assessing arterial stiffness, which is used in most studies in several specialized centers [2-4,24-28].

Tillin [25] found that the carotid-femoral site was a better indicator for assessing atherosclerosis than the posterior carotid-radial and femoral-tibial sites. This is due to a greater rigidity between the heart and the periphery, resulting in values that are higher than those measured at the carotidfemoral site. This study used the carotid-femoral site, where carotid and femoral pulse waves were measured shortly after the electrocardiogram QRS complex and the time from carotid to femoral in consecutive waves measured automatically with a SphygmoCor. In addition to assessing arterial stiffness, the automated software can also estimate the aortic root pressure, i.e., the central pressure (which has a direct impact on the left ventricle) and the augmentation index. Thus, evaluating several specific aspects of the arterial waveform at (carotid) proximal central and femoral distal central levels. The assessment of arterial stiffness was measured by cf-PWV with a SphymoCor following the 2012 consensus [24].

Logan [26] analyzed the effect of age and sex on arterial stiffness and blood pressure levels in 102 Korean Americans aged 21 to 60 years. By measuring carotid-femoral pulse wave velocity, age was an important determinant, with a high correlation (r=0.61, p<0.0001). Although not significantly different, it was also observed that the effect of age on arterial stiffness was higher in females, where individuals aged 51 to 60 presented PWV values of 7.87±1.11 and 8.68±1.09 in males and females, respectively (p 0.227).

Several other studies have studied the significant influence of age in PWV. and demonstrated the age and pulse wave velocity correlation; The European Reference Values Collaboration studied more than 18.000 subjects, showing that there was a clear correlation of age with increasing values of PWV; unlike the results that we found in our preliminary study, no difference betwenn genders was identified in the European Reference Values Work [29]. In a Population based study in Portugal, age was found to be the major determinant of PWV values, especially in men [29]. In individuals of South African origin, Shiburi [27] analyzed 185 subjects without hypertension, diabetes or cardiovascular disease, divided into three age groups (<30, from 30 to 49 and ≥50 years). There was a mean PWV of 5.8±1.7 m/sec, with progressive increase with age, with 5.0±1.2; 6.2±1.2 and 7.6±2.5, respectively. Diaz [28] studied pulse wave velocity in 780 individuals from the urban and rural populations of Argentina, who were asymptomatic, normotensive, and had no first-degree family history of hypertension. It found a PWV mean of 6.84±1.65, with progressive increase with age, of 6-8% for each decade of life. The increase was more pronounced over 50 years (8.52) versus 5.92 (p <0.05). There was no difference between men and women, with 6.81 versus 6.89, respectively.

In this study, similarly to the studies shown, there are statistically significant trends of mean incremental increase in pulse wave velocity with age (p=0.000). However, although not significant, the mean was higher in males when compared to females, with PWV values of  $9.5\pm2.5$  versus  $8.9\pm2.5$ , respectively (p=0.283).

In the analysis of this study, some points can be evaluated. First, the highest percentage of the population studied was female, reflecting a more active acceptance of participating in the study and a possible increased concern with the prevention of cardiovascular diseases, which are known to present a higher life expectancy in women when compared to men [20]. Second, the mean PWV was higher among men, but with a lower number of individuals studied.

It is well known according to the 7<sup>th</sup> Brazilian Guideline on Arterial Hypertension that 60% of the elderly of the elderly have Arterial Hypertension, contributing directly or indirectly to 50% of deaths due to cardiovascular diseases [13]. The PWV analysis would be a marker in the noninvasive diagnostic stratification on these patients.

On the other hand, and most importantly, the fact that approximately 15% of the population below 50 years of age has "not-normal" PWV is of major relevance, as it identifies subjects at risk of CVD that will benefit from a more aggressive and precocious intervention, in an a attempt to prevent the development of CVD.

The analysis of the results of this study shows that the PWV of men and women adjusted for age was statistically significant, but a study with a larger male population is required for this data to present in a more robust way.

# Conclusion

There was a correlation between a change in the PWV and increased age in both sexes. Significant prevalence of "not-normal" PWV was found in young adults (curtailing higher cardiovascular risk at a very young age). For a higher accuracy of the data presented, studies with larger samples are necessary, especially with males.

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