Echocardiography and Analysis of Subclinical Cardiovascular Diseases in Indigenous People Living in Different Degrees of Urbanization: Project of Atherosclerosis Among Indigenous Populations (Pai)

Ecocardiografia e Análise de Doenças Cardiovasculares Subclínicas em Povos Indígenas que Vivem em Diferentes Graus de Urbanização: Projeto de Aterosclerose nas Populações Indígenas (Pai)

Pedro Vinícius Amorim de Medeiros Patriota[1]; Ana Marice T. Ladeia[2]; Juracy Marques[3]; Ricardo Khoury[4]; Aldina Barral[4]; Alvaro A. Cruz[5]; Luis Claudio L. Correia[2]; Manoel Barral-Netto[4]; Joao A. C. Lima[6]; Anderson C. Armstrong[1]

[1]Federal University of São Francisco Valley, Petrolina, Brazil; [2]Bahiana School of Medicine and Public Health, Salvador, Brazil; [3]Bahia State University, Juazeiro, Brazil; [4]Oswaldo Cruz Foundation, Salvador, Brazil; [5]ProAR - Federal University of Bahia, Salvador, Brazil; [6]Johns Hopkins Hospital, Baltimore, MD, USA.

Abstract

Background: The urbanization process impacts the burden of cardiovascular disease (CVD). Indigenous populations can undergo a devastating epidemiological transition.

Objective: The present study aimed to describe the Project of Atherosclerosis among Indigenous Populations (PAI) study protocol for assessing echocardiographic images and subclinical CVD in indigenous populations according to the degree of urbanization and report its preliminary results.

Methods: The PAI is a cross-sectional study that includes volunteers aged 30–70 years among Brazilian indigenous groups exposed to low and advanced stages of urbanization (Fulni-ô and Truká, respectively) and an urban control group. Individuals with known CVD or who were on hemodialysis were excluded. The pilot study began in Fulni-ô territory in September 2016. The participants underwent clinical and laboratory evaluations, electrocardiography, carotid artery ultrasound, and a comprehensive echocardiography protocol including global longitudinal strain (GLS) assessed by speckle tracking. The preliminary results are described by participant sex in univariate analysis.

Results: The pilot study evaluated the protocol used in 55 Fulni-ô individuals (mean age, 48.7 ± 12.0 years; 80% women). Traditional risk factors such as hypertension, diabetes, and dyslipidemia were found in 40%, 36%, and 54% of participants, respectively, without significant statistical differences between the sexes. Tobacco use was extremely prevalent, reported in 91% of participants. Most echocardiographic parameters were within the normal range; however, mean GLS was 17.3 ± 3.4% (p = 0.73 between sexes).

Conclusion: We described the PAI study protocol for assessing subclinical CVD and risk factors in indigenous populations by urbanization stage. Its preliminary results suggest a high prevalence of these factors in the indigenous population exposed to a lower degree of urbanization.

Keywords: Cardiovascular Disease; Indigenous Population; Urbanization.

Resumo

Fundamento: *O processo de urbanização tem impacto na carga de doenças cardiovasculares. As populações indígenas podem sofrer uma transição epidemiológica devastadora.*

Objetivos: *Descrever o protocolo de estudo do Projeto de Aterosclerose nas Populações Indígenas (PAI) para avaliar a análise ecocardiográfica e as doenças cardiovasculares (CV) subclínicas em populações indígenas de acordo com o grau de urbanização e mostrar resultados preliminares do estudo piloto.*

Métodos: *O PAI é um estudo transversal, com voluntários com idade entre 30 e 70 anos, em grupos indígenas brasileiros expostos a estágios baixos e avançados de urbanização (Fulni-ô e Truká, respectivamente) e um grupo controle urbano, excluindo indivíduos com doenças CV*

conhecidas ou em hemodiálise. O estudo piloto começou no território de Fulni-ô em setembro de 2016. Os participantes foram submetidos a avaliação clínica e laboratorial, eletrocardiograma (ECG), ultrassonografia de carótidas e um protocolo ecocardiográfico abrangente, incluindo strain longitudinal global (SLG) avaliado por speckle tracking. Os resultados preliminares são descritos de acordo com o sexo em uma análise univariada.

Resultados: O estudo piloto avaliou o protocolo descrito em 55 indivíduos do grupo indígena Fulni-ô (48,7 ± 12,0 anos, 80% mulheres). Foram encontrados fatores de risco tradicionais como hipertensão, diabetes e dislipidemia em 40%, 36% e 54%, respectivamente, sem diferenças estatísticas significativas entre os sexos. O uso de tabaco mostrou-se extremamente prevalente, referido em 91% dos participantes. Os parâmetros derivados da ecocardiografia estavam, em média, dentro da faixa normal. No entanto, a média do SLG foi de 17,3 ± 3,4% (p 0,73 por sexo).

Conclusão: Descrevemos o protocolo do estudo PAI para avaliar doenças cardiovasculares subclínicas e fatores de risco em populações indígenas de acordo com o estágio de urbanização. Resultados preliminares sugerem alta prevalência desses na população indígena em menor grau de urbanização.

Palavras-chave: Doença Cardiovascular; População Indígena; Urbanização.

Introduction

Cardiovascular diseases (CVDs) play an important role in noncommunicable diseases, the most common causes of mortality worldwide.[1] In recent decades, the transition from a principally rural economy to a predominantly urban economy has led to a substantial change in the global environment, with a negative impact on population health mediated by multiple factors that vary according to the reality of each region.[2]

Urbanization, industrialization, and other signs of economic development and social organization are related to global environmental changes that generate an epidemiological transition in diverse areas of the world. Developing countries have changed their health profiles, decreasing mortality rates caused by infectious diseases and nutritional deficiencies while increasing mortality rates from CVDs.[3,4] However, different levels of epidemiological transitions can occur within a country,[4] with numerous behavioral and cultural particularities involved in different indigenous communities.

In fact, the burden of CVDs has proven to be more devastating in poor countries than in wealthy countries. In this regard, the lack of public resources and insufficient number of trained health professionals contribute to suboptimal assistance.[1,3] The nutritional particularities of each culture, as well as the lack of population-based health education in poor countries, also play a major role in CV morbidity and mortality. These aspects have an even stronger influence because of the late urbanization process that has recently affected indigenous populations.

Few data are available on CV risk factors in indigenous populations. In Brazil, a study of adult Xavante participants showed a significant association between anthropometric measures and socioeconomic indexes in a comparison of data from 1962 and 2006, demonstrating weight gain among young people and those with higher income status.[5] Individuals with a higher body mass index (BMI) and waist circumference also had higher blood pressure levels than their counterparts.

The vastness of Brazil's territory creates contrasts that are seen in urban areas and, importantly, can be identified among indigenous communities in different regions. Indigenous communities in Northeastern Brazil, where most of the European colonization efforts started in the 1500s, often experienced greater territorial losses and disadvantageous policies of their land rights.[6] Moreover, a more recent wave of urban development has generated large dams, canals, and hydroelectric power plants, greatly affecting not only the landscape but also the lifestyle of numerous native communities in the area.

Here, we aimed to describe the Project of Atherosclerosis among Indigenous Populations (PAI) study protocol for assessing echocardiographic images and subclinical CVD in indigenous populations according to the degree of urbanization. Furthermore, we showed the preliminary results of the pilot study of the least urbanized indigenous community in Northeast Brazil. This study only proposes a statistical analysis of participants in the pilot study, and much more testing of various test protocols will be required to obtain data for difficult-to-access populations. The authors did not intend to draw conclusions that will only be possible with the analysis of the study data with the entire sample already reached. These data will be sent for publication shortly.

Methods

Design and Eligibility

The PAI is an observational cross-sectional study that was designed to access volunteers of both sexes aged 30–70 years from three communities with different levels of urbanization. Patients with heart failure, a history of hospitalization for acute coronary syndrome or cerebrovascular disease, or a history of surgery for heart disease or peripheral arterial disease; who were undergoing hemodialysis; or who did not agree to participate in the study were excluded.

The PAI study was approved by institutional local and national ethics committees (CONEP number 1.488.268). It was also approved by the Brazilian agency that regulates indigenous affairs (Fundação Nacional do Índio, FUNAI; process number 08620.028965/2015-66). Finally, the study was approved by the tribal authorities of each indigenous group. All participants provided informed consent before taking part in the study.

Degree of Urbanization and Community Selection

The goal of recruitment was to obtain a representative sample of residents of the São Francisco Valley in Northeast Brazil who were exposed to different degrees of urbanization that contained indigenous and non-indigenous participants and aimed to distribute participants equally by age (30–50 years old vs. 51–70 years old) and sex (male vs. female). For this purpose, we included two indigenous groups and a non-indigenous group from a related urban area.

Establishing the degree of urbanization of a given community is challenging because of the lack of standardized criteria and the regional particularities that should be considered when defining urbanization. In fact, indigenous populations usually have cultural and religious aspects that are directly related to their idea of territory. Therefore, a concept of urbanization that considers only physical characteristics would be false and artificial for an indigenous group.[7] Thus, the PAI study aimed to integrate both cultural and physical parameters to establish a more accurate definition of urbanization throughout the study. We combined official urban density concepts with anthropological parameters related to the use of native language and adherence to a more traditional lifestyle.[8,9]

With the application of these criteria, three groups were selected for the PAI study: (1) the Fulni-ô people, considered the least urbanized group in Northeast Brazil, mostly because they practice periodic isolation from non-indigenous people and maintain daily use of native language in addition to inhabiting an area with a low density of urban constructions; (2) the Truká people, who are in a more advanced stage of urbanization, historically affected by territorial losses and environmental changes resulting from major national infrastructural constructions such as dams, canals, and power plants; and (3) an urban control population from the city of Juazeiro, Bahia, Brazil, also located on the São Francisco River. The latter was chosen by the authors according to to criteria established by IBGE - Brazilian Institute of Geography and Statistics - the city of Juazeiro is a densely urbanized territory.[8]

Data Collection

Recruitment began in September 2016, with the pilot study in the Fulni-ô territory designed to include at least 50 participants. The Fulni-ô were selected for the pilot assessment because they were located in the most remote area, thus comprising the most challenging part of the study. Volunteers underwent a screening interview to establish eligibility. As part of the main study protocol, the included participants underwent clinical assessments, laboratory tests, ECG, carotid duplex scans, ankle-brachial index assessment, and echocardiography.

Clinical Parameters

Comprehensive medical history was assessed and physical examinations were performed. Alcohol consumption and smoking were self-reported. In this study, we did not aim to assess alcohol consumption patterns; rather, we registered a positive alcohol intake if the participant reported any alcohol consumption. To assess the amount of tobacco from traditional use (with traditional pipes known as *chanduca*), the number of daily refills was used to calculate average consumption.

Weight was measured in kilograms using digital scales. Height was measured with validated equipment. BMI was calculated as weight/height^2 (kg/m^2). Overweight and obesity were classified as BMI $\geq$ 25 kg/m^2 and BMI $\geq$ 30 kg/m^2, respectively. Neck, hip, and waist circumferences were measured according to National Institutes of Health recommendations.[10]

Heart rate and oxygen saturation were recorded using automated equipment after at least a 5-minute rest with the participants seated. Three blood pressure measurements were performed (conventionally twice in the right arm and once in the left arm) using an Omron® BP785 IntelliSense® Automatic Blood Pressure Monitor in accordance with the recommendations of the Brazilian Society of Cardiology.[11] Hypertension was defined a systolic blood pressure $\geq$ 140 mmHg, diastolic blood pressure $\geq$ 90 mmHg, or use of medications for hypertension.

All clinical data were collected using RegaDB,[12] a database with software tools developed by the Rega Institute (Catholic University of Leuven; Leuven, Belgium) and MyBioData Biomedical (Leuven, Belgium). In this study, the software was further adapted as "RegaDB PAI" to store the clinical research data and configured to run simultaneously on all study computers using an intranet system.

Laboratory Testing

Approximately 10 mL of blood was drawn into adequate Vacutainer® tubes. The spun serum was aliquoted and shipped to a central laboratory (FIOCRUZ, Salvador, Brazil) for storage and subsequently tested for creatinine, HbA1c, total cholesterol, low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), triglycerides, and ultra-sensitive C-reactive protein. Diabetes was identified if the participant was using any hypoglycemic medication or if HbA1c was $\geq$ 6.5%, while pre-diabetes was identified if the HbA1c was 5.7–6.4%. Dyslipidemia was established if the participant was using hypolipidemic medication or if at least one of the following criteria was met: reduced HDL-C, a level lower than 40 mg/dL in men or 50 mg/dL in women; hypertriglyceridemia, a triglyceride level > 150 mg/dL; and hypercholesterolemia, an LDL-C > 160 mg/dL. When the triglyceride level was $\geq$ 400 mg/dL, the calculation of LDL-C by the Friedewald formula was not adequate; thus, hyperlipidemia was identified if the total cholesterol level was $\geq$ 200 mg/dL.

Echocardiography Protocol

The echocardiography exam was conducted with a GE Vivid Q Portable Scanner (General Electric Medical Systems, Milwaukee, WI, USA) to obtain and store echocardiography-derived images in digital files. The images were acquired by echocardiography experts in accordance with a standardized protocol following the recommendations of the American Society of Echocardiography and the European Association of Cardiovascular Imaging.[13] Carotid duplex ultrasonography was used to assess cervical carotid artery disease, and intima-media thickness was computed following current recommendations.[14]

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Pai Study Protocol and Preliminary Results

Original Article

Transthoracic echocardiography was acquired from apical four-, three-, and two-chamber acoustic windows as well as from the parasternal longitudinal view and at the level of the papillary muscles in a short-axis view, including two-dimensional imaging, M-mode, tissue Doppler, and pulsed and continuous Doppler. An offline analysis was performed blindly following international recommendations.[13]

Left ventricular ejection fraction (LVEF) was calculated using the modified Simpson's rule. Left ventricular mass (LVM) was calculated with linear measurements and indexed by body surface area (BSA). Left ventricular hypertrophy was defined as LVM index > 115 g/m^2 in men or > 95 g/m^2 in women. Left atrial volume was acquired using the biplane area-length technique and then indexed by BSA. Transmitral Doppler–derived E and A waves and transaortic velocities were acquired. Tricuspid annular plane systolic excursion was assessed by M-mode in a four-chamber view. Tissue Doppler imaging computed velocities in the right ventricular free wall, interventricular septal wall, and left ventricular lateral wall in a four-chamber view. In the pilot study, echocardiographic parameters for the evaluation of diastolic function, such as E and e' velocities, were not obtained, but they will be presented and analyzed in future publications describing the other participants.

Speckle tracking echocardiography acquisition and interpretation techniques followed a standardized protocol similar to that of the CARDIA study.[15] In summary, left ventricular images were acquired in two-, three-, and four-chamber views, ensuring a frame rate of > 40 fps and documenting three consecutive cardiac cycles. Blind analysis was used to compute the global longitudinal strain (GLS) and the average of the longitudinal strain of the two-, three-, and four-chamber assessments.

Results of the carotid artery ultrasound analysis and the evaluation of the left ventricular diastolic function will be documented in another article to be submitted soon for publication. We believe that the analysis of clinical, laboratory, and CV images will be more succinct in this article since its main objective is to describe the PAI study methods.

Additional Assessments

Ankle-brachial index was obtained using portable Doppler ultrasound machine and manual sphygmomanometer following recommendations from the American College of Cardiology and American Heart Association.[16] The ankle-brachial index result was abnormal if <0.9 or >1.3. Twelve-lead electrocardiography (ECG) was recorded using portable digital equipment with the patient at rest in the dorsal decubitus position at a standard speed of 25 mm/s and amplitude of 10 mV. Each ECG was acquired and blindly analyzed according to the recommendations of the Brazilian Society of Cardiology.[17] To enhance sensitivity, we considered participants positive for chamber overload if the ECG showed at least one abnormal parameter: left atrial enlargement if the P wave duration in lead II was >120 ms, P wave notching in the interval duration between the atrial components was >40 ms (P mitrale), and/or the terminal negative component of a biphasic P wave in precordial lead V1 was >0.04 mm/s

or area was >1 mm^2 (Morris index). Left ventricular overload was defined as the ECG criteria were expressed by sum of the S wave of the V1 derivation with the largest R wave of the V5 or V6 being ≥35 mm (Sokolow-Lyon index) and/or sum of the R wave in aVL and S wave in V3 derivation being ≥22 mm in women and >28 mm in men (Cornell index). Right ventricular overload was identified with the presence of axis deviation to the right and a sum of the S wave in V5 or V6 with the R wave in the V1 lead of >10.5 mm. Right atrial enlargement was defined as the presence of an amplitude > 2.5 mm in lead II.

Statistical Analysis

For the entire PAI study, we estimated a total sample of 957 participants (319 from each of the three groups) considering a statistical power of 90% and an alpha of 0.05 to detect statistically significant differences based on a previous World Health Organization report for the prevalence of hypertension according to urbanization.[18] In the current report, we present the preliminary results obtained after assessing a pilot study. The data are described for the population assessed in the pilot study according to participant sex. Categorical variables are presented as percentages at the 95% confidence interval, with p values for the intergroup comparisons calculated by Fisher's exact test. For continuous variables, normal distribution was assessed by comparing quantiles of variables against quantiles of normal distribution. According to the distribution, the data are summarized as mean and standard deviation or median and interquartile range (IQR), and differences were assessed by a t-test or 2-sample Wilcoxon rank-sum. STATA v. 14 was used for the statistical calculations and p values < 0.05 were considered statistically significant.

Results

For the PAI pilot study, a total of 55 participants were enrolled from the Fulni-ô territory. The majority of participants were middle-aged women (Table 1). The prevalence of hypertension was higher among women, although men showed a trend toward higher systolic and diastolic blood pressures (Table 1). Of those classified as having hypertension, 23.9% (n = 11) were using blood lowering medication. Of them, 45.4% (n = 5) showed uncontrolled systolic or diastolic blood pressure. All participants using blood pressure medication were women (29.7%).

Glucose serum levels as assessed by HbA1c were, on average, higher than normal (Table 1). Diabetes had a general prevalence of 36%, with no sex-related differences. Of those classified as having diabetes, 17% (n = 8) were using blood sugar lowering medication. Of those using medication, 87.5% (n = 7) had uncontrolled serum glucose levels defined as an HbA1c level ≥ 7.0%.

More than half of the participants were classified as having at least one type of dyslipidemia (Table 1), with lower serum triglyceride levels and higher LDL-C and HDL-C levels among women than among men.

Table 1 also shows that the majority of participants were active smokers and classified as overweight or obese with a similar prevalence between the sexes. The men had higher ankle-

Table 1. Description of clinical parameters of participants of the pilot study.

Parameter	Men (n = 11) Proportion (95% CI)	Women (n = 44) Proportion (95% CI)	All (n = 55) Proportion (95% CI)	P value (comparison of sexes)
Age, years	48.0 (10.2)	49.0 (12.6)	48.7 (12.0)	0.815
Hypertension	33% (8:74)	43% (27:60)	40% (27:56)	0.449
Diabetes	33% (8:74)	37% (22:55)	36% (23:52)	0.571
Pre-diabetes	55% (19:86)	60% (42:75)	59% (43:73)	
Dyslipidemia	44% (13:80)	57% (40:73)	54% (39:69)	0.430
Overweight	33% (8:74)	45% (29:63)	43% (29:58)	0.938
Obesity	22% (4:67)	20% (9:37)	20% (11:35)	
Tobacco use	100%	88% (72:95)	91% (77:96)	0.219
Alcohol consumption	22% (4:67)	8% (3:24)	11% (5:25)	0.440
	Média (DP)	Média (DP)	Média (DP)	
SBP, mmHg	141.9 (18.5)	128.3 (22.4)	131.2 (22.1)	0.085
DBP, mmHg	82.2 (9.9)	78.2 (10.8)	79 (10.6)	0.300
ABI	1.26 (0.12)	1.11 (0.18)	1.14 (0.18)	0.018
HbA1c*, %	6.26 (0.71)	6.32 (0.74)	6.31 (0.63)	0.78
Total cholesterol, mg/dL	192.9 (47.6)	217.3 (44.4)	212.1 (45.7)	0.136
LDL-C, mg/dL	92.2 (25.8)	123.9 (37.7)	118.3 (37.6)	0.041
HDL-C, mg/dL	35.6 (11.3)	50.8 (12.6)	47.5 (13.7)	0.001
Triglycerides, mg/dL	363.4 (296.1)	217.8 (139.4)	248.8 (189.7)	0.023
BMI, kg/m^2	26.3 (3.0)	27.1 (5.9)	26.9 (5.4)	0.938

*ABI, ankle-brachial index; BMI, body mass index; DBP, diastolic blood pressure; HbA1c, glycated hemoglobin; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; SBP, systolic blood pressure. P values were determined using a t-test except for HbA1c, which was determined using a two-sample Wilcoxon rank-sum test. *HbA1c is shown as median (IQR).*

Table 2. Description of electrocardiography-derived parameters by sex in the pilot study.

Parameter	Men (n = 9)	Women (n = 35)	All (N = 44)	P value (comparison of sexes)
Heart rate, beats per minute	68 (8)	75 (11)	73 (11)	0,06
Left atrial enlargement	55% (5)	34% (12)	38% (16)	0,25
Left ventricular overload	11% (1)	2.8% (1)	4.5% (2)	0,30

P values were determined using a t-test.

Table 3. Echocardiography-derived parameters of participants of the pilot study.

Parameter	Men (n = 10)	Women (n=32)	All (n = 42)	P value (comparison of sexes)
LV mass	166.3 (40)	121.6 (37.6)	132.3 (42.2)	0.002
LV mass index, g/m^2	91.5 (21.4)	70.5 (19.0)	75.5 (21.4)	0.005
Ao diameter, mm	30.0 (4.3)	28.5 (4.2)	28.8 (4.3)	0.35
LA volume, mL	51.3 (13.2)	42.9 (13.5)	44.8 (13.7)	0.09
LA volume index, mL/m^2	28.3 (7.6)	24.8 (6.3)	25.6 (6.7)	0.15
RA volume, mL	47.3 (15.7)	31.6 (9.7)	35.2 (12.9)	0.0004
RA volume index, mL/m^2	26.1 (8.7)	18.4 (4.8)	20.3 (6.7)	0.001
TAPSE, mm	22.4 (2.5)	22.3 (4.7)	22.3 (4.3)	0.96
LVEF, %	63.6 (7.8)	63.8 (10.6)	63.8 (9.9)	0.94
GLS, %	-17.6 (3.0)	-17.2 (3.6)	-17.3 (3.4)	0.73

Ao, aorta; GLS, global longitudinal strain; LA, left atrium; LV, left ventricle; LVEF, left ventricle ejection fraction; RA, right atrium; TAPSE, tricuspid annular plane systolic excursion. P values were determined using a t-test. Data are shown as mean (standard deviation).

brachial index levels than the women. Alcohol consumption tended to be more frequent among men than women.

ECG-derived variables were in generally within the normal range with no differences between sexes (Table 2). All participants had sinus rhythm with a mean heart rate of 73 beats per minute (SD, 11 bpm; range, 55–103 beats per minute). One woman had a complete left bundle branch block. Another woman presented with a first-degree atrioventricular block. No participants showed any signs of ischemia or abnormal Q waves, right atrial enlargement, right ventricular overload, or complex arrhythmias.

Table 3 summarizes the echocardiography-derived parameters and intima-media thicknesses of the carotid arteries. LVM and right atrial volumes were higher among men than among women. Other echocardiography-derived parameters and intima-media thicknesses did not differ between Fulni-ô men and women.

Discussion

The PAI study is an original study aiming to demonstrate the prevalence of CV risk factors and subclinical cardiac disease in indigenous people exposed to different levels of urbanization. This paper presents the PAI study protocol and shows preliminary data on CV risk factors and subclinical disease collected during the pilot study that assessed the Fulni-ô people, an indigenous community from Northeast Brazil with a low degree of urbanization. Although the initial project design is cross-sectional, we will secure funding to follow up all subjects longitudinally and explore the most common comorbidities observed, including chronic respiratory diseases.

The pilot study proved that use of the PAI protocol is feasible in remote indigenous territories. The researchers are responsible for proving the viability of their projects, particularly when assessing traditionally neglected communities such as Native American tribes. Additionally, the PAI pilot study provided early identification of the CV risk burden of the Fulni-ô people, who underwent a comprehensive survey in CV health for the first time. The originality and, in particular, importance of the high-risk profile found in this preliminary assessment underscores the need for further investigations.

In the PAI pilot study, we examined a middle-aged group of adults with a high prevalence of CV risk factors, particularly indigenous women. We also report a high prevalence of subclinical disease compared to what would be expected in a general population as evidenced by a mean GLS < -18%.[13] In fact, although the participants' average traditional echocardiography-derived parameters (including

LV ejection fraction) were within the normal range, the assessed Fulni-ô people showed signs of subclinical LV dysfunction (Figure 1).

Our group's previous epidemiological reviews showed increasing rates of CV mortality among indigenous people in the São Francisco Valley that appeared to be related to the degree of urbanization.[19] In fact, urbanization has been associated with an epidemiological transition in indigenous groups characterized by a reduction in death rates related to infections or nutritional deficiency disorders and an increase in mortality from CVDs.[4,20,21] In the consideration of traditional people in the process of environmental changes, CV mortality rates have been related to lifestyle changes impacting the CV risk burden. Importantly, CV deaths in traditional groups have been associated with low socioeconomic status, low access to health care, and a breakdown in social structure such as the loss of social support and cohesion.[4,20]

The pilot findings demonstrated a higher proportion of indigenous Fulni-ô people with hypertension than previous reports on indigenous groups at earlier stages of urbanization.[4,22,23] There is significant variation in the reported prevalence of hypertension among indigenous Brazilian groups. The rural Xukuru community had a prevalence of hypertension near 30%,[22] whereas the Suruí people from Amazonia, at the initial stages of urbanization, are currently dealing with their first cases of hypertension.[23] Conversely, our reported prevalence of hypertension was similar to that in urban areas in Brazil and other low-income countries.[24]

Our group of Fulni-ô women tended to have a higher prevalence of hypertension than the men. Interestingly, compared to men, hypertensive Fulni-ô women were more prompted to use medication and adequately control their blood pressure. This may explain our finding of a higher proportion of LV hypertrophy among Fulni-ô men than among women. LV hypertrophy is a well-known CV risk marker, particularly in hypertensive patients.[25,26]

We reported an alarming prevalence of diabetes and uncontrolled glucose levels among Fulni-ô men and women. Similarly, the Xavante people, an indigenous tribe from Central Brazil, have a reported diabetes prevalence of 28.2%.[25,26] In fact, other Native American groups have shown a high prevalence of diabetes.[27-29] To emphasize this diabetes burden in native groups, the ORBITA trial investigating urban European participants with known coronary artery disease reported a prevalence of diabetes at a magnitude of about half that of our findings in the Fulni-ô pilot group.[30] Genetic predisposing factors and lifestyle changes related to the urbanization process may play an important role in the prevalence of diabetes among American indigenous communities.

We also found a high prevalence of dyslipidemia and a prevalence of overweight/obesity of > 60% among the assessed Fulni-ô participants. These findings appear to be directly affected by a modern urban lifestyle and relate to the worldwide pandemic obesity burden.[10] Traditional indigenous groups may be following the Western tendency regarding the most current challenges in body weight control. In fact, the Embera-Chami indigenous people from Colombia, who resemble the Fulni-ô people in many aspects, reportedly had a similar unfavorable cardiometabolic profile.[31] Public social policies are necessary to minimize this growing health problem.

Tobacco smoking is an increasing social problem in many indigenous communities globally.[32] In the Fulni-ô people assessed in this pilot study, the prevalence of tobacco smoking is remarkably higher than that in other communities, indigenous or non-indigenous.[1,32] Smoking is highly prevalent in men and women, found in almost the entire observed population in the Fulni-ô pilot study. Worldwide data show that the prevalence of tobacco smoking is much higher in men (37%) than in women (7%), Europe being the region with the highest rate of smokers (30%).[1] In the general population of Brazil, the prevalence of smoking is declining rapidly.[33] Social unacceptability is an important factor observed in urban areas where tobacco smoking has been decreasing.[6] However, for most of the Fulni-ô people, smoking is seen as culturally essential, especially with traditional pipes (*chanduca*).

Similar to worldwide findings in indigenous and non-indigenous groups,[1,32] the Fulni-ô pilot study showed that more men reported alcohol consumption than women. Alcohol consumption appears to be an increasing social problem in many indigenous communities, but our study design may not allow for comparisons in alcohol consumption patterns to those of other reported studies.

As can be expected from a study designed for a group of generally healthy participants, we found a low prevalence of abnormal parameters strongly related to clinically manifested CVD, such as ECG measures, and traditional echocardiographic functional parameters, such as LV mass and LVEF. However, GLS tended to be reduced in the assessed Fulni-ô men and women. GLS predicts cardiac outcomes beyond the traditional LVEF,[33] even with a lack of other echocardiographic or clinical evidence of heart failure.[34] GLS can also identify early subclinical cardiac dysfunction.[35,36] This pilot study population, despite including only 55 participants, demonstrated a high prevalence of CV risk factors and a possible considerable number of subclinical CVDs, as suggested by reduced values of global strain. However, these are preliminary data from a much smaller sample with no objective of reaching conclusions that will be of greater statistical importance when the analysis of the entire sample is published.

Conclusions

Here we described the PAI study protocol for assessing subclinical CVD and CV risk factors in indigenous populations according to the degree of urbanization. The pilot study proved the feasibility of the PAI study protocol. We also showed the preliminary data of the Fulni-ô study population, the least urbanized indigenous group that features a high prevalence of important atherosclerosis risk factors and the presence of subclinical cardiac disease as assessed by LV longitudinal deformation.

Contribution of authors

Research design and design: Armstrong AC, Patriota

PVAM, Lima JAC. Obtaining data: Patriota PVAM, Ladeia AM, Marques J, Armstrong AC. Data analysis and interpretation: Armstrong AC, Patriota PVAM, Correia LCL. Statistical analysis: Armstrong AC, Patriota PVAM. Obtain financing: Armstrong AC. Writing of the manuscript: Armstrong AC, Patriota PVAM. Critical review of the manuscript for important intellectual content: Patriota PVAM, Ladeia AM, Marques J, Khoury R, Barral A, Cruz AA, Correia LCL, Barral-Netto M, Lima JAC, Armstrong AC.

References

1. Mendis S, Armstrong T, Bettcher D, Branca F, Lauer J, Mace C, Poznyak V, et al. Global Status Report: on noncommunicable diseases. WHO, 2014. Accessed: May 1, 2017. Available at: http://www.who.int/nmh/publications/ncd-status-report-2014/en/

2. Teo K, Chow CK, Vaz M, Rangarajan S, Yusuf S. The Prospective Urban Rural Epidemiology (PURE) study: examining the impact of societal influences on chronic noncommunicable diseases in low-, middle-, and high-income countries. Am Heart J [electronic article]. 2009;158(1):1–7.e1.

3. Deaton C, Froelicher ES, Wu LH, Ho C, Shishani K, Jaarsma T. The global burden of cardiovascular disease. J Cardiovasc Nurs. 2011;26(4 Suppl):S5-14.

4. Yusuf S, Reddy S, Ounpuu S, Anand S. Global burden of cardiovascular diseases: general considerations, the epidemiologic transition, risk factors, and impact of urbanization. Circulation. 2001 Nov 27;104(22):2746-53.5. Welch JR, Ferreira AA, Santos RV, Gugelmin SA, Werneck G, Coimbra CEA. Nutrition transition, socioeconomic differentiation and gender among adult Xavante Indians, Brazilian Amazon. Hum Ecol. 2009;37:13–26.

6. Coimbra CEA, Santos RV, Welch JR, Cardoso AM, de Souza MC, Garnelo L, et al. The first national survey of indigenous people's health and nutrition in Brazil: rationale, methodology, and overview of results. BMC Public Health. 2013;13:52.

7. Fany R. Terras indígenas & unidades de conservação da natureza: o desafio das sobreposições. São Paulo: Instituto Socioambiental, 2004. 37–41p. Accessed: August 3, 2017. Available at: https://www.socioambiental.org/banco_imagens/pdfs/10144.pdf.

8. IBGE. Áreas urbanizadas. (Electronic) Available at: http://www.ibge.gov.br/home/geociencias/geografia/geografia_urbana/areas_urbanizadas/default.shtm?c=8. Accessed: August 2, 2017.

9. Dos Santos J M. Cultura material e etnicidade dos povos indígenas do São Francisco afetados por barragens: um estudo de caso dos Tuxá de Rodelas, Bahia, Brasil. Salvador. 2008. Available at: https://repositorio.ufba.br/ri/bitstream/ri/10835/1/tese_Juracy Marques1.pdf. Accessed: April 7, 2017.

10. Becker DM, Bouchard C, Carleton RA, Colditz GA, Dietz WH, Foreyt JP, et al. Practical guide to the Identification, evaluation, and treatment of overweight and obesity in adults. NIH, 2000. Available at: https://www.nhlbi.nih.gov/files/docs/guidelines/prctgd_c.pdf. Accessed: August 1, 2017.

11. Malachias MV, de Souza W, Plavnik FL, Rodrigues C, Brandão AA, Neves M, et al. 7ª diretriz brasileira de hipertensão arterial. Arq Bras Cardiol. 2016;107(3).

12. Katholieke Universiteit te Leuven. RegaDB. (Electronic) Available at: https://rega.kuleuven.be/cev/regadb. Accessed: August 2, 2017

13. Lang RM, Badano LP, Mor-Avi V, Afilalo J, Armstrong A, Ernande L, et al. Recommendations for cardiac chamber quantification by echocardiography in adults: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. J Am Soc Echocardiogr. 2015;28:1-39.

14. Stein JH, Korcarz CE, Hurst RT, Lonn E, Kendall CB, Mohler ER, et al. American Society of Echocardiography Carotid Intima-Media Thickness Task Force. 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 Medicine. J Am Soc Echocardiogr. 2008;21(2):93-111.

15. Armstrong AC, Ricketts EP, Cox C, Adler P, Arynchyn A, Liu K, et al. Quality control and reproducibility in M-mode, two-dimensional, and speckle tracking echocardiography analysis: the CARDIA Study, year 25 examination experience. Echocardiography. 2015;32(8):1233-40.

16. Hirsch AT, Haskal ZK, Hertzer NR, Bakal CW, Creager MA, Halperin JL, et al. ACC/AHA 2005 Practice guidelines for the management of patients with peripheral arterial disease. Circulation. 2006;113 (11):e463-654.

17. Pastore CA, Pinho JA, Pinho C, Samesima N, Pereira-Filho HG, Kruse JCL, et al. III Diretrizes da Sociedade Brasileira de Cardiologia sobre Análise e Emissão de Laudos Eletrocardiográficos. Arq Bras Cardiol. 2016; 106(4Supl.1):1-23.

18. World Health Organization. World Health Statistics 2012. Accessed: April 8, 2017.Available at: http://apps.who.int/iris/bitstream/handle/10665/44844/9789241564441_eng.pdf?sequence=1

19. Armstrong, AC, Ladeia, AMT, Marques J, Armstrong DMFO, Silva AMLD, Morais Junior JC, et al. Urbanization is Associated with Increased Trends in Cardiovascular Mortality Among Indigenous Populations: the PAI Study. Arq Bras Cardiol. 2018; 110(3):240-5.

20. Reddy KS, Yusuf S. Emerging Epidemic of Cardiovascular Disease in Developing Countries. Circulation. 1998;97(6):596–601.

21. Sanderson JE, Mayosi B, Yusuf S, Reddy S, Hu S, Chen Z, et al. Global burden of cardiovascular disease. Heart. 2007; 93(10):1175.

22. Barbosa JMVB. Prevalência e fatores associados à pressão arterial elevada no povo Indígena Xukuru do Ororubá, Pesqueira-PE, 2010. 2013. Dissertação (Mestrado em Saúde Publica) – Centro de Pesquisas Aggeu Magalhães, Fundação Oswaldo Cruz, Recife, 2013.

23. Tavares FG, Coimbra CEA, Cardoso AM. Níveis tensionais de adultos indígenas Suruí , Rondônia , Brasil Blood pressure levels of Suruí indigenous adults in Rondônia, Brazil. 2012:1399–1409. Available at: https://pdfs.semanticscholar.org/730d/772bc2db01acc6d94e3ba4f957935d820446.pdf. Accessed: August 7, 2017.

24. Chow CK, Teo KK, Rangarajan S, Islam S, Gupta R, Avezum A, et al. Prevalence, awareness, treatment, and control of hypertension in rural and urban communities in high-, middle-, and low-income countries. JAMA. 2013;310(9):959-68.

25. Armstrong AC, Gidding S, Colangelo LA, Lima J. Influence of early adult modifiable cardiovascular risk factors on left atrial index: the CARDIA study. In: American College of Cardiology Meeting, 2012. JACC, 2012. v. 59. p. A283.

26. Armstrong AC, Jacobs DR, Gidding SS, Colangelo LA, Gjesdal O, Lewis CE, et al. Framingham score and LV mass predict events in young adults: CARDIA study. Int J Cardiol. 2014;172(2):350-5.

27. United Nations Office of the Special Adviser on Gender Issues and Advancement of Women and the Secretariat of the United Nations Permanent Forum on Indigenous Issues. Gender and indigenous peoples. (Electronic) New York, February 2010. Available at: <http://www.un.org/esa/socdev/unpfii/documents/Briefing%20Notes%20Gender%20and%20Indigenous%20Women.pdf>. Accessed: 14 November 2017.

28. Epidemiologia e prevenção do diabetes mellitus. Available at: http://www.diabetes.org.br/profissionais/images/pdf/diabetes-tipo-2/001-Diretrizes-SBD-Epidemiologia-pg1.pdf. Accessed: August 11, 2017.

29. Knowler WC, Saad MF, Pettitt DJ, Nelson RG, Bennett PF. Determinants of diabetes mellitus in the Pima Indians. Diabetes Care. 1993;16(1):216-27.

30. Al-Lamee R, Thompson D, Dehbi H, Sen S, Tang K, Davies J, et al. Percutaneous coronary intervention in stable angina (ORBITA): a double-blind , randomised controlled trial. Lancet. 2018 Jan 6;391(10115):31-40.

31. Bedoya, JUC, Botero JD, González CAN, Molina DCR, Gracia JR, Pineda AFG, et al. Prevalencia de factores de riesgo cardiovascular en indígenas embera-chamí de Cristianía (Jardín), Antioquia. Iatreia. 2015;28(1):5–16.

32. United Nations. State of the world's indigenous peoples: indigenous Peoples' access to health services. 2016. Available at: http://www.who.int/hhr/activities/indigenous/en/. Accessed: August 8, 2017.

33. Malta DC, Stopa SR, Santos MAS, Andrade S, Oliveira TP, Cristo EB, Silva MM. Evolution of tobacco use indicators according to telephone surveys, 2006-2014. Cad Saude Publica. 2017;33Suppl 3(Suppl 3):e00134915

34. De Almeida ALC, Gjesdal O, Mewton N, Choi E, Teixido-Tura G, Yoneyama K, et al. Speckle-tracking pela ecocardiografia bidimensional: aplicações clínicas. Rev bras ecocardiogr imagem cardiovasc. 2013;26(1):38-49.

35. Pellicori P, Kallvikbacka-Bennett A, Khaleva O, Carubelli V, Costanzo P, Castiello T, et al. Global longitudinal strain in patients with suspected heart failure and a normal ejection fraction: does it improve diagnosis and risk stratification?; Int J Cardiovasc Imaging. 2014;30(1):69-79.

36. Gonçalves S, Cortez-Dias N, Nunes A, Belo A, Cabrita Z, Sousa C, et al. Disfunção sistólica ventricular esquerda detetada por speckle tracking em hipertensos com fração de ejeção preservada. Rev Port Cardiol. 2014; 33(1):27-37.