Original Article

Study of Risk Factors Associated with Peripheral Arteriopathy in Japanese-Brazilians from Bauru (SP)

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Abstract

Background: Cardiovascular diseases are the major cause of morbidity and mortality in developed and emerging countries. Their main etiology, atherosclerosis, is a disseminated disease that affects the coronary, cerebral and peripheral territories. The peripheral arterial disease (PAD), as well as its consequences, indicates the involvement of the coronary territory. Therefore, its better understanding enables proper treatment, delaying local and long-term complications, reducing the cost to the health system.

Objective: This study estimates the percentage of PAD in Japanese-Brazilians from Bauru (SP), recognized by the high prevalence of metabolic disorders such as hypertension (43%), diabetes mellitus (33%) and hypercholesterolemia (60%), and examines the association with risk biomarkers.

Methods: This cross-sectional population study evaluated 1,330 Japanese-Brazilians of both genders aged ≥ 30 who underwent a complete physical examination, anthropometric measurements, laboratory tests and ankle-brachial index (ABI). Participants with ABI ≤ 0.90 were diagnosed as having PAD. After applying the exclusion criteria, 1,038 individuals were part of the analysis. We used Poisson regression to analyze associations with PAD.

Results: The mean age was 56.8 years and the percentage of PAD was 21.1%, equal among the genders. PAD was associated with smoking (PR 2.16 [1.33 to 3.48]) and hypertension (PR 1.56 [1.12-2.22]).

Conclusion: The percentage of PAD in Japanese-Brazilians was similar to other populations of adverse cardiometabolic profile (US PARTNERS and POPADAD). The independent association of PAD with smoking and hypertension, but not with other classical risk factors, may depend on the very high frequencies of metabolic disorders in this population. (Arq Bras Cardiol. 2014; 102(2):143-150)

Keywords: Risk factors; Peripheral arterial disease; Migration; Atherosclerosis; Diabetes mellitus; Coronary diseases.

Introduction

Despite changes in lifestyle and a growing therapeutic arsenal, cardiovascular diseases are still the leading cause of morbidity and mortality in developed and emerging countries. Data from the Ministry of Health showed that they are the leading cause of death in Brazil. In 2006, they accounted for 29.4% of deaths in the country, while neoplasias accounted for 15.1%[1].

PAD (peripheral arterial disease) of atherosclerotic etiology is increasingly prevalent in modern society, partly due to increased life expectancy, affecting 202 million people worldwide in 2010. In the last decade, there was an increase of 28.7% in its prevalence in countries of low

and middle per capita income, and 13.1% in high-income countries[2]. The growing interest in the early diagnosis of PAD is occurring not only for its increased prevalence associated with an aging population, but also because it is related to atherosclerotic disease in other territories, such as coronary and cerebral[3].

Being a chronic disease, the resources needed for treatment are high. In the U.S. population, the estimated cost per year was US$ 5,955 per patient with PAD[4].

Moreover, the progression of PAD is associated with coronary artery disease. We found an increased risk of cardiovascular events of 2.8 times in three years in patients with PAD compared to those without the disease[3]. A study conducted in patients undergoing coronary angiography found concomitance between PAD and coronary artery disease in 90.7% of patients[5].

Immigrants of Japanese descent in the Americas have high rates of diabetes mellitus and other metabolic disorders[6]. It is believed that exposure to the Western environment should have exacerbated a genetic tendency to accumulate body fat, increasing cardiovascular risk. Genetically homogenous populations with an adverse

cardiometabolic profile represent an opportunity to study the PAD, as well as other atherosclerotic manifestations and their relationship with risk factors[6,7].

In view of this scenario, it can be argued that it is worth studying this population, the traditional and non-traditional risk factors for PAD, which are similar to those of coronary artery disease, enabling a better treatment of the disease, delaying complications and reducing the cost to the health system.

Methods

This cross-sectional study was based on the Japanese-Brazilian population living in Bauru (SP). The data used in this analysis belong to the second phase of the main study conducted in 2000. Individuals of both genders, aged ≥ 30, of Nipponese origin, first and second generations, were invited to participate. Methodological details were previously described[7]. The study was approved by the institutional ethics committee, and consent was signed by all participants. A total of 1,330 individuals, which corresponded to one third of the local Nipponese population, agreed to participate in the study and were interviewed using standardized questionnaires on clinical status (smoking and history of previous diseases) and nutrition. The participants were invited to undergo clinical examination (including anthropometric measurements, blood pressure and Doppler ankle-brachial index - ABI) and blood collection. Exclusion criteria for this analysis were incomplete questionnaire data and clinical and laboratory evaluation (255 participants), ABI > 1.40 (one participant) and concentration of C-reactive protein (hs-CRP) > 10 mg/L (36 participants). Therefore, 1,038 individuals were studied.

Weight (Filizola® scale) and height were determined with minimal clothing and no shoes for the calculation of body mass index (BMI)[8]. Waistline circumference[8] was measured with a nondistensible measuring tape at the midpoint between the last floating rib and the iliac crest parallel to the ground, and hip measurement was determined by the buttock level, through the pubic symphysis. The waist-hip[9] ratio was determined by the ratio between these circumferences. For diagnosing obesity and central obesity, the values recommended by the Japan Society for the Study of Obesity[8] were employed, and for the waist-hip ratio, those of the World Health Organization were used[9].

Blood pressure was measured in an automatic device (Omron HEM-712C, Omron Health Care, USA) after five minutes in the sitting position. The mean of the two last measurements was considered the final value of systolic and diastolic pressure. Hypertension was diagnosed in those with blood pressure values > 140 × 90 mmHg or those who reported drug treatment[10].

After fasting for 12 hours and prior tracking with blood glucose, the participants underwent oral glucose tolerance testing with 75 g. Besides those who reported drug treatment, those who met the American Diabetes Association (ADA) criteria were diagnosed as diabetics[11]. The participants with fasting glucose < 100 mg/dL and two hours after overload < 140 mg/dL were considered normal. Those with fasting glucose ranging from 100 to 125 mg/dL and two-hour fasting

< 140 mg/dL were considered as having impaired fasting glucose (IFG). Impaired glucose tolerance (IGT) was diagnosed when fasting glucose was ≥ 100 mg/dL, but with glucose after overload between 140-199 mg/dL. Diabetes was diagnosed by fasting glucose ≥ 126 mg/dL or overload ≥ 200 mg/dL.

For the diagnosis of dyslipidemia, the criteria of the Executive Summary of the Third Report of the National Cholesterol Education Program - Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adults Treatment Panel III) were employed[12]. Participants with total cholesterol ≤ 200 mg/dL, LDL-cholesterol ≤ 130 mg/dL, HDL cholesterol ≥ 35 mg/dL for men and ≥ 45 mg/dL for women, and triglycerides ≤ 200 mg/dL were considered normal as to the lipid profile. Those with abnormalities in at least one of these parameters were considered dyslipidemic.

Uric acid concentrations of up to 6 mg/dL for women and of up to 7 mg/dL for men were considered normal[13]. For homocysteine, the cutoff value was 15 μmol/L[14]; for hs-CRP, the cutoff value corresponded to the median of the population: 1.1 mg/L.

Plasma glucose and lipoproteins were determined by enzymatic methods. The determination of homocysteine was based on the methodology described by Pfeiffer et al[15] CRP concentrations were determined by chemiluminescence.

Diagnosis of PAD

This diagnosis was done using continuous wave 8 MHz Imbracios® Doppler. The ABI value was calculated by the quotient of the pressure auscultated in the ankle arteries by the highest pressure determined in the brachial arteries. As recommended by the Transatlantic Society Consensus[16], an index of ≤ 0.9 and > 1.40 was considered abnormal. The PAD was diagnosed in the participant who presented an index of ≤ 0.9 in at least one of the arteries analyzed (posterior tibial artery or the dorsalis pedis artery) in one of the ends.

Statistical Analysis

Data are presented as percentages or means and standard deviations. Participants were stratified according to the presence of PAD or according to the ABI values (≤ 0.70; 0.71 to 0.90; ≥ 0.90)[17].

Frequencies were compared by chi-square, and prevalence ratios (PR) are presented by point and interval with 95% confidence. In the comparison of means, Student's t test or Bonferroni's analysis of variance was used.

We used the Poisson regression model to determine the RP of PAD according to the risk factors. The initial model included all the variables associated with PAD with $p < 0.15$ in the crude analysis. One by one, these variables were removed from the model, considering the statistics of maximum verisimilitude. A similar procedure was adopted to determine the odds ratios in the ordered logistic regression analysis according to the ABI values (≤ 0.70; 0.71 to 0.90; ≥ 0.90).

The analyses used the software Stata 8.0 (Statacorp, 2004. Stata statistical software release 7.0 College Station, TX Stata Corporation). A p value < 0.05 was considered significant.

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Results

The average age of the 1,038 participants (46% male) was 56.8 (± 12.9 years). The men had higher values of BMI, waist-hip ratio, blood pressure, fasting glucose, triglycerides, uric acid and homocysteine, whereas the women had higher concentrations of total cholesterol, LDL-cholesterol, HDL-cholesterol and CRP (Table 1).

The total population presented high levels of abdominal obesity (51.4%), hypertension (45.4%), diabetes mellitus (34.9%), hypercholesterolemia (62.2%), increased LDL-cholesterol (48.4%), increased triglycerides (64.3%). The percentages of risk factors stratified by sex are shown in Table 2. Especially among men, there was a high frequency of smoking (p = 0.01). The hypertension did not differ between the genders. Regarding glucose tolerance disorders, the percentage of DM was significantly higher in men (38.7% versus 31.7%, p = 0.008). They also presented more frequently hypertriglyceridemia, low HDL-cholesterol, hyperuricemia and hyperhomocysteinemia, but high levels of LDL-cholesterol and hs-CRP were more frequent in women.

The PAD percentage was 21.1% (95% CI 18.4-24.1; n = 219) with no difference between the genders (19.2% versus 22.7%). Stratifying by gender, the results of participants with and without PAD maintained the same pattern, and were, therefore, presented together. The average age of participants with PAD was higher compared to those without the disease (60 versus 56 years, p < 0.001).

About 53% of patients with PAD were hypertensive and their average systolic blood pressure was statistically higher than those without the disease (data not shown). Similarly, the participants presented higher average homocysteine values (12.2 versus 11.1 mg/dL, p = 0.004).

The percentages of PAD were significantly higher in the older age group, in hypertensive patients and in those with hyperhomocysteinemia (Table 3). There were no differences in the distribution of participants with and without PAD in the categories of smoking, adiposity, glucose tolerance and dyslipidemia. The same happened with the categories of hs-CRP and uric acid.

The adjusted analysis of the data detected associations of PAD with smoking and hypertension (Table 4).

When we stratify the ABI into three categories (≤ 0.70, 0.71-0.90 and > 0.90), the behavior of these results was maintained (data not shown). The average age of participants with ABI ≤ 0.70 was statistically higher than in other categories (p <0.001). Regarding the disorders of glucose tolerance, the highest fasting glucose and two-hour glucose averages were observed in patients with ABI ≤ 0.70 (p = 0.002 and p = 0.001, respectively), and 70% of those with ABI ≤ 0.70 had diabetes mellitus. The smokers had the highest proportion of ABI ≤ 0.70 (3.9%). Those who had the lowest ABI values (≤ 0.70) were those who smoked the highest number of cigarettes per day (22.5 cigarettes). As to the WHR, 70% of those with ABI ≤ 0.70 presented increased values of this variable. Average systolic blood pressure and average homocysteine were higher in participants with ABI ≤ 0.70 (p < 0.001 and p = 0.031, respectively) and 85% of these had hypertension (data not shown).

Table 1 - Média (DP) de variáveis demográficas, antropométricas, clínicas e bioquímicas segundo o sexo de uma amostra de 1.038 nipo-brasileiros da cidade de Bauru (SP)

	Men N = 473	Women N = 565	Total N = 1.038	p
	Mean (SD)	Mean (SD)	Mean (SD)	
Age (years)	56.7 (12.9)	56.9 (12.4)	56.8 (12.6)	0.364
Cigarettes per day*	18.1 (7.5)	16.8 (7.7)	17.7 (7.6)	0.138
Body mass index (kg/m2)	25.2 (3.8)	24.5 (3.8)	24.8 (3.8)	0.001
Waist-hip ratio	0.91 (0.06)	0.84 (0.07)	0.88 (0.08)	< 0.001
Diastolic blood pressure (mmHg)	81.5 (13.5)	77.5 (13.0)	79.3 (13.4)	< 0.001
Systolic blood pressure (mmHg)	135.5 (23.0)	131.7 (25.5)	133.4 (24.5)	0.006
Fasting glucose level (mg/dL)*	127.2 (31.3)	122.3 (36.8)	124.5 (34.4)	< 0.001
2-hour glucose (mg/dL)*	168.5 (85.8)	159.9 (68.8)	163.9 (77.2)	0.169
Total cholesterol (mg/dL)	211.9 (41.8)	216.9 (42.9)	214.6 (42.5)	0.030
Triglycerides (mg/dL)*	279.9 (244.0)	198.7 (139.6)	231.6 (197.5)	< 0.001
HDL-cholesterol (mg/dL)*	49.7 (12.5)	52.4 (10.3)	51.2 (11.4)	< 0.001
LDL-cholesterol (mg/dL)	127.3 (37.8)	132.9 (38.0)	130.4 (38.0)	0.009
Homocysteine (mg/dL)*	13.1 (7.5)	9.9 (4.1)	11.4 (6.1)	< 0.001
Hs-CRP (mg/L)*	1.6 (1.7)	1.9 (1.8)	1.8 (1.8)	0.015
Uric acid (mg/dL)*	7.0 (1.8)	5.3 (1.3)	6.1 (1.8)	< 0.001

Values transformed into logarithms for analysis.

Table 2 - Percentages of the main cardiovascular risk factors in a sample of 1,038 Japanese-Brazilians from Bauru (São Paulo) according to gender

		Men n = 473		Women n = 565		p value
		N	%	N	%	
Age	≤ 60 years	284	60.0	335	59.3	0.806
	< 60 years	189	40.0	230	40.7	
Smoking	No	218	46.2	499	88.8	< 0.001
	Yes (past)	91	19.3	39	6.9	
	Yes (current)	163	34.5	24	4.3	
Central obesity	No	350	74.3	153	27.1	< 0.001
	Yes	121	25.7	411	72.9	
Body mass index	< 23 kg/m^2	131	27.8	213	37.7	0.001
	23.0-24.9 kg/m^2	107	22.6	130	23.0	
	≥ 25 kg/m^2	234	49.6	222	39.3	
Hypertension	No	250	52.8	317	56.1	0.295
	Yes	223	47.2	248	43.9	
Glucose tolerance	Normal	16	3.4	42	7.5	0.008
	IFG	170	35.9	207	36.7	
	IGT	104	22.0	136	24.1	
	DM	183	38.7	179	31.7	
Hypercholesterolemia	No	189	40.0	203	35.9	0.182
	Yes	284	60.0	362	64.1	
Low HDL	No	395	83.5	514	91.0	< 0.001
Increased LDL	Yes No	78 269	16.5 56.9	51 267	9.0 47.3	0.002
	Yes	204	43.1	298	52.7	
Hypertriglyceridemia	No	131	27.7	236	41.8	< 0.001
	Yes	342	72.3	329	58.2	
hs-CPR	≤ 1.1 mg/L	252	53.3	257	45.5	0.012
	1.1-9.9 mg/L	221	46.7	308	54.5	
Homocysteine	≤ 15 mg/dL	286	77.3	414	92.2	< 0.001
	> 15 mg/dL	84	22.7	35	7.8	
Hyperuricemia	No	216	45.7	139	24.6	< 0.001
	Yes	257	54.3	426	75.4	

IFG: impaired fasting glucose; IGT: Impaired glucose tolerance; DM: Diabetes mellitus.

Discussion

In this population-based study, 21.1% of Japanese-Brazilians living in Bauru had PAD. Considering the unfavorable cardiometabolic profile previously described[18], this high percentage was expected. Although higher frequencies of cardiovascular risk factors among men were found, the PAD was similar between the genders.

As in our study, other studies in populations at high cardiovascular risk found high PAD values. The US PARTNERS program, designed to study the prevalence of PAD and other cardiovascular diseases, found a prevalence of PAD of 29% in individuals aged > 70 or > 50 with comorbidities (diabetes and smoking)[19]. The POPADAD program evaluated 8,000 diabetic patients aged ≥ 40 and found PAD prevalence of 20.1%[20].

In our community, a multicenter study on the prevalence of PAD conducted in the general population of 72 urban centers (n = 1170) found a prevalence of only 10.5%. It is important to note that the age group was lower (≥ 18 years) and the sample represented best the Brazilian population for neither including individuals genetically homogeneous nor those at high cardiovascular

Table 3 - Number, percentage and prevalence ratios (95% confidence intervals) of categories of demographic and clinical variables of a sample of 1,038 Japanese-Brazilians from Bauru (São Paulo) stratified according to the presence of PAD

		With PAD n = 219		Without PAD n = 819		Total n = 1.038		Chi-square	PR	CI95%
		N	%	N	%	N	%			
Gender	Women	128	22.7	437	77.3	565	100	1.80	1	
	Men	91	19.2	382	80.8	473	100		0.85	0.67-1.08
Age	≤ 60 years	110	17.8	509	82.2	619	100	10.2	1	
	> 60 years	109	26.0	310	74.0	419	100		1.46	1.16-1.85
Smoking	No	150	20.9	567	79.1	717	100	0.39	1	
	Yes (past)	38	20.3	149	79.7	187	100		0.97	0.71-1.33
	Yes (current)	30	23.1	100	76.9	130	100		1.10	0.78-1.56
Waist-hip ratio	No	101	20.1	402	79.9	503	100	0.57	1	
	Yes	117	22.0	415	78.0	532	100		1.10	0.86-1.39
Body mass index	< 23 kg/m^2	76	22.1	268	77.9	344	100	3.10	1	
	23.0-24.9 kg/m^2	57	24.1	180	75.9	237	100		1.09	0.81-1.47
	≥ 25 kg/m^2	85	18.6	371	81.4	456	100		0.84	0.64-1.11
Hypertension	No	101	17.8	466	82.2	567	100	8.1	1	
	Yes	118	25.1	353	74.9	471	100		1.41	1.11-1.78
Glucose tolerance	Normal	8	13.8	50	86.2	58	100	4.40	1	
	IFG	73	19.4	304	80.6	377	100		1.40	0.71-2.76
	IGT	59	24.6	181	75.4	240	100		1.78	0.90-3.52
	DM	79	21.8	283	78.1	362	100		1.58	0.81-3.10
Hypercholesterolemia	No	81	20.7	311	79.3	392	100	0.07	1	
	Yes	138	21.4	508	78.6	646	100		1.03	0.81-1.32
Low HDL	No	190	20.9	719	79.1	909	100	0.17	1	
	Yes	29	22.5	100	77.5	129	100		1.08	0.72-1.52
High LDL	No	112	20.9	424	79.1	536	100	0.03	1	
	Yes	107	21.3	395	78.7	502	100		1.02	0.81-1.29
Hypertriglyceridemia	No	76	20.7	291	79.3	367	100	0.05	1	
	Yes	143	21.3	528	78.7	671	100		1.03	0.80-1.32
hs-CRP	≤ 1.1 mg/L	100	19.6	409	80.4	509	100	1.26	1	
	1.1-9.9 mg/L	119	22.5	410	77.5	529	100		1.15	0.90-1.45
Homocysteine	≤ 15 mg/dL	140	20.0	560	80.0	700	100	5.36	1	
	> 15 mg/dL	35	29.4	84	70.6	119	100		1.47	1.07-2.02

PR: prevalence ratio. CI95%: confidence interval; PAD: peripheral arterial disease; IFG: impaired fasting glucose; IGT: Impaired glucose tolerance ; DM: Diabetes mellitus.

risk[21]. Publications of our group confirmed that the Japanese-Brazilians from Bauru are at high risk, based on the levels of obesity, diabetes mellitus, hypertension and dislipidemia[22].

Classical risk factors were independently associated with PAD, such as smoking (current) and hypertension in the population studied. Smoking has been considered the most important preventable risk factor for PAD[23]. This risk factor is more strongly associated with PAD than the coronary artery disease[24,25]. The adjusted risk of PAD reported for age and sex is 1.9 for

moderate smokers and 3.9 for heavy smokers, in contrast to the risk of coronary heart disease of 1.6 and 1.7, respectively[25].

Hypertension was present in more than half the population of Japanese-Brazilians from Bauru affected by PAD and was associated with this complication regardless of other risk factors. Our findings agreed with Lip et al[26] who found hypertension in 55% of arteriopathic patients studied in a systematic review. Evaluating in isolation our hypertensive population, we found 25% of arteriopathic patients, which was statistically higher than

Table 4 - Prevalence ratios (PR) of PAD and their intervals with 95% confidence intervals (CI95%) in a sample of 1,038 Japanese-Brazilians from Bauru (São Paulo) according to the presence of selected variables (initial and final model)

Variable		Initial model		Adjusted model	
		PR	CI95%	PR	CI95%
Gender	Women	1		1	
	Men	0.66	0.42-1.02	0.66	0.44-1.01
Age	≤ 60 years	1		1	
	> 60 years	0.98	0.71-1.36	0.94	0.69-1.23
Smoking	No	1		1	
	Yes (past)	1.45	0.91-2.31	1.44	0.92-2.33
	Yes (current)	2.14	1.32-3.50	2.16	1.34-3.48
Hypertension	No	1		1	
	Yes	1.61	1.12-2.31	1.56	1.12-2.22
Glucose tolerance	Normal	1			
	IFG	0.67	0.38-1.21	0.71	0.40-1.32
	IGT	0.76	0.42-1.38	0.65	0.43-1.44
	DM	0.66	0.37-1.17	0.65	0.39-1.23
Homocysteine	≤ 15mg/dL	1		1	
	> 15mg/dL	1.25	0.88-1.77	1.26	0.89-1.78

PR: prevalence ratio; IC95%: confidence interval; IFG: impaired fasting glucose; IGT: Impaired glucose tolerance; DM: Diabetes mellitus.

that of non-hypertensive patients (25% versus 17%, p < 0,05). In the same line, Wiinberg et al[27] evaluating a population of 1,044 individuals from 20 centers (591 women, mean age 71 years) also found higher percentage of PAD in hypertensive patients (10.5% versus 6.2%; p <0.05).

The diagnosis of diabetes mellitus itself was not associated with PAD in this study. However, mean fasting glucose level and two-hour post-overload glucose were significantly higher in individuals with ABI ≤ 0.70, and 70% of them were diabetic. For the American Diabetes Association, diabetes and smoking represent the most important risk factors for PAD; if diabetes is present, this risk increases with age, with disease duration and the presence of diabetic neuropathy[28]. In our study, 32.3% of Japanese-Brazilians from Bauru, affected by diabetes, knew they had the disease (n = 117), and the average time of diagnosis was 11.8 years. It is possible that the duration of the disease in the population studied has not caused a greater impact on this complication, since an average time of 16.2 years of diabetes has been described for the development of PAD[29].

An interesting finding was the increased WHR in 70% of Japanese-Brazilians from Bauru with ABI ≤ 0.70, unlike the BMI, which was not associated with PAD. Our findings agreed with those of Planas et al[30] who found a positive association between PAD and WHR, but not with BMI in Europeans. These authors considered that the BMI is not a good indicator of atherosclerotic disease, especially in the older population, because the body fat may increase without changing or even reducing body weight due to loss of lean body mass. In our population, participants with ABI ≤ 0.70 in fact were the oldest ones, supposedly with some reduction of lean mass.

Homocysteine concentrations were associated with PAD in the crude analysis and were also higher in patients with ABI ≤ 0.70. Several studies have shown this association, including our group. We had also detected in male Japanese-Brazilians living in Bauru a positive and independent association between these variables[14]. A meta-analysis concluded that patients with PAD had higher homocysteine levels than controls without the disease, although a causal relationship cannot be ensure yet[31].

An association of lipid abnormalities with PAD would be expected. However, a previous publication from our group showed how high is the frequency of dyslipidemia in this population of Japanese-Brazilians from Bauru, which may have made it difficult to reach statistical significance[32]. The literature is scant as to evidence regarding the relationship of lipid variables with the peripheral territory. Murabito et al[33] found a positive relationship of PAD only with low HDL-cholesterol concentrations.

hs-CRP was not associated with PAD in our study. Only patients with ABI ≤ 0.70 presented higher values, but without statistical significance. hs-CRP has been used as a marker of chronic subclinical inflammation, which is present early in the natural history of atherosclerosis and diabetes mellitus, hypertension, dyslipidemia and other diseases. There is much controversy about the relationship between hs-CRP and PAD in the literature. The individuals included in this study are mostly in the advanced stage of evolution of these diseases, therefore its prognostic value may be small. The vast majority of literature studies that evaluate the relationship of hs-CRP with atherosclerotic disease has focused on the coronary arteries. A study conducted at Clínica Mayo in 247 individuals referred

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for investigation of asymptomatic PAD using ABI also found no association between high levels of hs-CRP and PAD[34].

There is evidence that the concentration of CRP has an hereditary component. It was found that certain polymorphisms in the PCR gene were able to influence their blood concentrations[35]. Genetic epidemiology has assisted in obtaining evidence about the involvement of CRP in atherosclerosis because, since PCR is causally involved in atherosclerosis, individuals carrying alleles that promote high plasma concentrations of CRP would present an increased risk of cardiovascular disease, where this risk is proportional to increased PCR[35,36]. However, studies published[35,36] are still not able to ensure a causal role of CRP in atherosclerosis.

Our data indicated that, with the severity of PAD, there was an increase in the numbers of major cardiovascular risk factors, and individuals with ABI values ≤ 0.70 had the worst cardiometabolic profile. There is a need for early diagnosis and treatment of PAD, since its presence indicates widespread atherosclerotic process, compromising the survival of the individuals. Belch et al[37] considered PAD a distinct atherothrombotic syndrome that is able to predict the occurrence of stroke, AMI and death. In the absence of concomitance with coronary disease, the PAD has been undertreated and poorly controlled[38].

The REACH Registry[39] a multicenter study of patients with established arterial disease (coronary disease, cerebrovascular or peripheral disease), concluded that the profile of risk factors is similar in the regions analyzed, with a high proportion of hypertensive patients (81.8%), diabetic patients (44.3%) and patients with hypercholesterolemia (72.4%). The treatment of these factors is inadequate and there is disparity between the established guidelines and clinical practice in sick individuals or patients at risk for atherothrombotic disease.

Conclusion

Our study shows a high percentage of subclinical atherosclerotic disease that is similar to other populations of adverse cardiometabolic profile. High frequencies of metabolic disorders in this population may explain the independent relationship of PAD only with smoking and hypertension but not with other classical risk factors. The associations with modifiable risk factors (smoking and hypertension) should serve to motivate and guide interventions and thereby reduce the cost to the health system.

Author contributions

Conception and design of the research, Acquisition of data, Writing of the manuscript and Critical revision of the manuscript for intellectual content: Garofolo L, Ferreira SRG; Analysis and interpretation of the data: Garofolo L, Ferreira SRG, Miranda Junior F; Statistical analysis: Garofolo L; Obtaining funding: Ferreira SRG.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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Study Association

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