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ORIGINAL ARTICLE

Prevalence of Peripheral Artery Disease and Associated Risk Factors in a Brazilian Rural Population: The Baependi Heart Study

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Abstract

Background: The identification of peripheral artery disease (PAD) can help prevent further progression of the disease and additional complications, considering that this condition is a risk factor for all-cause mortality and cardiovascular death.

Objective: To assess the prevalence of PAD in the Baependi Heart Study and investigate associated risk factors in different age groups.

Methods: A total of 1,627 individuals (of both genders and aged 18 - 102 years) residing in the municipality of Baependi (Minas Gerais, Brazil) were selected for this study. Anthropometric and biochemical parameters were evaluated by standard techniques. Physical activity level was determined by the International Physical Activity Questionnaire - Short Form (IPAQ-SF). The screening of PAD was performed by determination of the ankle-brachial index (ABI). The level of statistical significance was set at 5%.

Results: In the overall sample, the prevalence of PAD was 1.05%, and reached 5.2% after the age of 70 years. The frequency and intensity of smoking were higher in individuals with PAD. A prior history of myocardial infarction and a higher prevalence of hypertension, diabetes, obesity, and sedentary lifestyle were also associated with PAD. In addition, PAD was more frequent in blacks than whites. In multivariable analysis, age, diabetes, smoking, and physical inactivity remained independently associated with PAD.

Conclusion: The prevalence of PAD was low and increased clearly with age in our sample from a Brazilian rural population. Furthermore, the main risk factors for PAD in the investigated sample were smoking, sedentary lifestyle, diabetes mellitus, and age. (Int J Cardiovasc Sci. 2018;31(4)405-413)

Keywords: Peripheral Arterial Disease / prevalence; Risk Factors; Rural Population; Tobacco Use Disorder; Ankle-Brachial Index.

Introduction

Peripheral artery disease (PAD) is classically defined as a condition affecting noncardiac, nonintracranial arteries, majorly due to atherosclerosis, that leads to partial obstruction of the peripheral arteries, reducing perfusion to the tissues irrigated by these arteries.[1,2] Even though PAD is asymptomatic in most patients, the disease may progress with clinical symptoms (like claudication) and eventually lead to tissue necrosis. The identification of PAD can help prevent further progression of the disease itself and additional complications, considering that this condition is a risk factor for all-cause mortality[3-8] and cardiovascular death,[3,4,7,9] including coronary artery disease[3,7] and stroke.[5,7] PAD is also a major cause of quality of life impairment, which in turn, worsen even more with the progression of the disease.[10,11] Therefore, information

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on the prevalence of PAD is important to allow proper planning in public health care. Recommendations on the identification and management of this condition have been published by international medical societies.[12-14]

Epidemiological studies have determined that the prevalence of PAD in the general population range from 4-10%;[15-23] however, there is a clear increase in prevalence with increasing age,[13,17,19,24] with rates as high as 20% over the age of 70 years.[19,20] Data on the prevalence of PAD in the general Brazilian population are scarce. Only one large multicenter study assessed the prevalence of PAD and found a high rate (10.5%) in 1,159 individuals in the general population.[18] Other studies have investigated the prevalence of PAD specifically in Japanese-Brazilians[25,26] and in a small sample of patients with diabetes.[27] Therefore, other large studies are needed to better access the prevalence of PAD and understand the risk factors associated with this condition in the general Brazilian population.

The Baependi Heart Study is an ongoing Brazilian cohort study established in 2005 to investigate cardiovascular risk factors and heritability.[28] The study has now expanded to include other investigations such as nocturnal polygraph, heart rate variability, pulse-wave velocity, 24-hour ambulatory blood pressure monitoring, 24-hour electrocardiography (Holter), and assessment of vascular age by plethysmography. Using data collected from 2010 to 2013 from the above-mentioned research project, the present study aimed to assess the prevalence of PAD and investigate associated risk factors in different age groups.

Methods

Study sample

The Baependi Heart Study is a genetic epidemiological study of cardiovascular disease risk factors with a longitudinal design, whose methodology has been previously described.[28] For the present analysis, we carried out a cross-sectional evaluation of data collected in the second visit of the protocol (between 2010 and 2013). This study invited 2,072 individuals (of both genders and aged 18 - 102 years), distributed across 109 families residing in the municipality of Baependi, a city in a rural area (752 km^2, 18,072 inhabitants) located in Minas Gerais State, Southeast of Brazil. Of these, 1,634 participants underwent screening for PAD. The study protocol was approved by the ethics committee of the *Hospital das Clínicas* (SDC: 3485/10/074), University of São Paulo, Brazil. All procedures involved in this study are in accordance with the Declaration of Helsinki from 1975, updated in 2013. Informed consent was obtained from all participants included in the study.

Anthropometric evaluations

Anthropometric parameters were measured according to a standard protocol.[28] Height was measured in centimeters and weight in kilograms using a calibrated digital balance. Body mass index (BMI) was calculated as body weight (kg) divided by squared height (m^2). Waist circumference was measured at the mean point between the lowest rib margin and the iliac crest with the subject standing and at the maximum point of normal expiration. Obesity was defined as a BMI ≥ 30 kg/m^2.

Blood pressure measurements

Blood pressure was measured with a standard digital sphygmomanometer (OMRON, OMRON Eletrônica do Brasil Ltda., SP, Brazil) on the left arm after 5 minutes of rest, with the subject in the sitting position. Systolic (SBP) and diastolic blood pressures (DBP) were calculated from three readings (mean value of all measurements), with a minimal interval of 3 minutes.[28] Hypertension was defined as a mean SBP ≥ 140 mmHg and/or DBP ≥ 90 mmHg and/or use of antihypertensive drug.[29]

Biochemical measurements

Blood levels of triglycerides, total cholesterol, high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), and fasting glucose were measured by standard techniques in 12-h fasting blood samples.[30] Glycated hemoglobin (HbA1c) levels were determined by high-performance liquid chromatography (National Glycohemoglobin Standardization Program, USA). Diabetes mellitus was diagnosed in the presence of a fasting glucose ≥ 126 mg/dL, HbA1c ≥ 6.5%, or use of antidiabetic drugs. *Hypercholesterolemia was defined* as a total cholesterol level ≥ 240 mg/dL.

Assessment of risk factors and depression

Physical activity level was determined by the International Physical Activity Questionnaire - Short Form (IPAQ-SF). Sedentary lifestyle was identified based on a duration of physical activity lower than 10 minutes/day on the previous week.

Information regarding medical history (angina pectoris, myocardial infarction, stroke, kidney failure, and depression) and environmental risk factors such as smoking and alcohol use were evaluated through a questionnaire completed by each participant. The questionnaire was based on the World Health Organization's Multinational Monitoring Trends and Determinants in Cardiovascular Disease (MONICA)[31] project epidemiological instrument, and was applied and filled out by research assistants specifically trained for this task.

Screening of peripheral artery disease

The screening of PAD was performed with the ankle-brachial index (ABI), which was measured by a single trained examiner using a sphygmomanometer (Heidji, Brazil) with a cuff suitable for the circumference of the limbs and a 10 MHz portable Doppler device (DV 610B, MEDMEGA, SP, Brazil).

The ABI was determined for each leg by the ratio between the highest SBP obtained at the ankle (posterior tibial and dorsalis pedis arteries) and highest SBP obtained in the arms (brachial artery).[12-14] The methodology of the test and the ABI classification were based on recommendations of the American College of Cardiology / American Heart Association (ACC/AHA).[12,13] ABI values between 0.91 and 1.39 were considered normal. Values ≤ 0.90 were considered compatible with PAD and values ≥ 1.40 were considered inconclusive for PAD and were excluded from the analysis.

Statistical analysis

Categorical variables were compared using the chi-square test and are presented as percentage, while continuous variables are presented as mean ± standard deviation. The normality of the data was confirmed with the Kolmogorov-Smirnov test. Unpaired Student *t* test was performed to analyze demographic, hemodynamic, and biochemical data according to PAD status. Since the cutoff value for PAD diagnosis based on ABI is well-established in the literature, we carried out univariate and multivariate logistic regression analyses to determine the association between PAD (ABI < 0.9) as the dependent variable and age, hypertension, diabetes, myocardial infarction, smoking, and sedentary lifestyle as predictor variables. Statistical analyses were carried out using SPSS (version 19) software (Chicago, IL, USA), with the level of significance set at 5%.

Results

A total of 1,634 individuals were screened for PAD. Seven individuals presented an ABI above 1.4 and were excluded from the analysis. Therefore, 1,627 volunteers were included in the study. The age of the participants ranged from 18 to 102 years (mean 44.9 ± 16.4 years). Table 1 shows the demographic, anthropometric, biochemical, and hemodynamic characteristics of the individuals with and without PAD, defined as an ABI equal to or lower than 0.9. Age, BMI, HbA1c, and SBP were higher in volunteers with PAD. The presence of PAD was also more frequent in elderly compared with younger individuals, and in blacks compared with whites.

Figure 1 presents the data related to the prevalence of PAD using the ABI in different age groups. Overall, the prevalence was very low (1.05%). Only one case of PAD was observed below the age of 30 years, and the prevalence of PAD increased after the fifth decade, peaking at the age of 70 years, when it reached 5.2%. The frequency of PAD by decade is presented in the Table 2.

Table 3 presents the data related to the lifestyle characteristics of the volunteers. The frequency and amount of smoking were higher in individuals with PAD. There was also a higher frequency of physically inactive volunteers in the PAD group.

Table 4 presents a comparison of clinical characteristics in individuals with and without PAD. A higher prevalence of hypertension, diabetes, and obesity was observed in individuals with a diagnosis of PAD. The presence of hypercholesterolemia was not different between groups. Also, a prior history of myocardial infarction was more frequent in the PAD group.

Table 5 presents univariate and multivariate logistic regression models for PAD. In multivariate analysis, age, diabetes, smoking, and physical inactivity were significantly and independently associated with PAD.

Discussion

In terms of the number of individuals included, the present study is the largest investigation of the prevalence of PAD in a Brazilian population. The Baependi Heart Study is a Brazilian cohort study investigating cardiovascular risk factors and heritability in residents of

Table 1 - Demographic, anthropometric, biochemical, and hemodynamic characteristics of individuals with and without peripheral artery disease

Variables	Total	PAD present	PAD absent	P value
n	1,627	17	1,610	***
Age (years)	44.9 ± 16.4	66 ± 15	45 ± 16	< 0.001
Gender				
Men (%)	41.5	41.2	41.5	0.59
Women (%)	58.5	58.8	58.5	
Ethnicity				
White (%)	76.7	70.6	76.8	0.001
Black (%)	5.5	29.4	5.2	
Mulatto (%)	17.5	0	17.7	
Others (%)	0.3	0	0.4	
ABI (ratio)	1.11 ± 0.1	0.78 ± 0.11	1.12 ± 0.7	< 0.001
BMI (kg/m²)	25.8 ± 5.1	28.7 ± 5.3	25.7 ± 5.1	0.02
WC (cm)	91 ±12	100 ± 10	91 ± 12	0.003
TC (mg/dL)	197.8 ± 40.7	195.6 ± 59.9	197.9 ± 40.5	0.83
LDL-c (mg/dL)	124.5 ± 35.4	122.2 ± 56.3	124.6 ± 35.2	0.79
HDL-c (mg/dL)	47.2 ± 11.7	45.2 ± 13.1	47.2 ± 11.8	0.49
Triglycerides (mg/dL)	130.3 ± 68.1	141.1 ± 60.0	130.2 ± 68.2	0.52
Fasting glucose (mg/dL)	92.6 ± 19.0	114.6 ± 43.2	92.3 ± 18.5	0.06
HbA1c (%)	5.7 ± 0.7	6.5 ± 1.2	5.7 ± 0.8	0.02
SBP (mmHg)	125.4 ± 16.3	133.5 ± 19.2	125.4 ± 16.2	0.04
DBP (mmHg)	76.2 ± 10.3	75.3 ± 9.2	76.2 ± 10.4	0.72

Categorical variables were compared using the chi-square test, and continuous variables were compared using Student t test. PAD: peripheral artery disease; n: sample size; ABI: ankle-brachial index; BMI: body mass index; WC: waist circumference; TC: total cholesterol; HDL-C: high-density lipoprotein; LDL-C: low-density lipoprotein; HbA1c: glycated hemoglobin; SBP: systolic blood pressure; DBP: diastolic blood pressure.

the rural city of Baependi, located in Southeastern Brazil. In the study sample, which included 1,627 volunteers, the overall prevalence of PAD was 1.05%. The prevalence clearly increased with age, peaking at 5.2% above the age of 70 years. Individuals with PAD were older, heavier, more often smokers, and less physically active. Identified risk factors for PAD in the study sample were age (odds ratio [OR] = 1.08), smoking (OR = 4.01), sedentary lifestyle (OR = 3.75), and diabetes mellitus (OR = 3.07).

The occurrence of PAD in the general population has been assessed in different countries.[15-17,19,20,22,23,32] In Brazil, Makdisse et al.[18] reported in 2008 a high prevalence of PAD (10.5%) in a population with a mean age of 43.8 ± 14.7 years. The study involved volunteers in large cities (over 100 thousand inhabitants) from different Brazilian regions. Another study specifically assessed the Japanese-Brazilian population and determined a prevalence of PAD of 21.1%;[26] however, the mean age of the participants in this study was higher (about 56.5 years). The present study assessed volunteers from a city with an estimated population of 18,072 inhabitants at the time of the study. The prevalence found (around 1%) is considerably low.

Most studies assessing the prevalence of PAD have included samples of individuals older than 40 years (sometimes above the ages of 55 or 65 years). If we consider only the prevalence of PAD in individuals

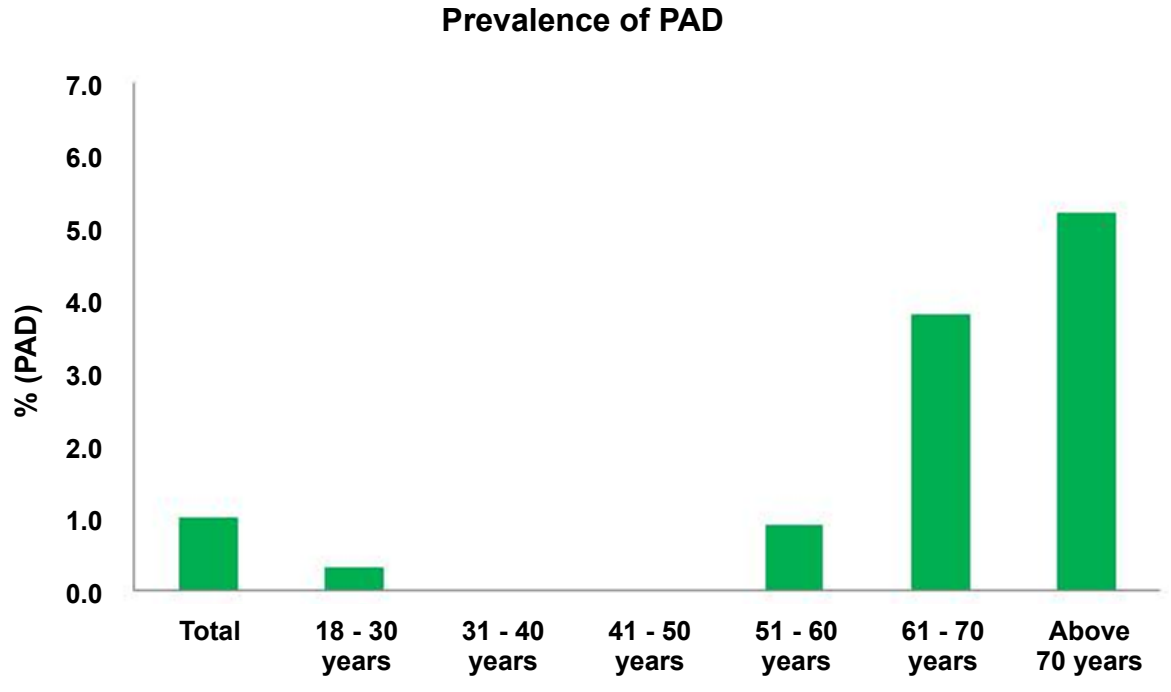

Figure 1 - Prevalence of peripheral artery disease (PAD) in the overall population and stratified by age group.

Table 2 - PAD prevalence by decade in men and women

Age (n)	PAD overall prevalence n cases (%)	PAD prevalence men n cases (%)	PAD prevalence women n cases (%)
Below 30 (397)	1 (0.3)	1 (0.6)	0 (0)
31 - 40 (279)	0 (0)	0 (0)	0 (0)
41 - 50 (335)	0 (0)	0 (0)	0 (0)
51 - 60 (316)	3 (0.9)	1 (0.8)	2 (1.1)
61 - 70 (184)	7 (3.8)	2 (2.5)	5 (4.8)
Above 70 (116)	6 (5.2)	3 (5.4)	3 (5.0)

PAD: peripheral artery disease.

older than 40 years in the present study (1.7%), the data are lower but in agreement to those of other studies such as the ones performed in Sri Lanka by Weragoda et al.[32] in 2015 (3.6%, n = 2,912) and in the US by Razzouk et al.[22] in 2015 (the Life Line Screening®, 4.1%, n = 3.67 million), and Eraso et al.[16] in 2015 (4.6%, n = 7,058), which identified prevalence rates below 5% in the general population. In a study published in 2016, Alzamora et al.[15] described a prevalence of new PDA of 4.3% (n = 2,256) in a study with a follow-up of 5 years conducted in a Spanish population aged more than 55 years and described as having low-risk factors for cardiovascular disease.

In the present study, the prevalence of PAD above the age of 50 years was 2.6%. As expected, age was independently associated with a diagnosis of PAD, as identified by the present and previous studies. Therefore, the low prevalence of PAD in the present study is partially due to the low mean age of the participants, the inclusion of volunteers with age starting at 18 years, and the fact that most volunteers (62.1%) were below the age of 50 years. Additionally, our sample had only about 7% (n = 116) of the volunteers above the age of 70 years, a group in which a higher prevalence of PAD is expected.[15-17,19,20,32]

Volunteers with PAD in the present study were older and had higher BMI, HbA1c, and SBP levels compared

Table 3 - Lifestyle characteristics of individuals with and without peripheral artery disease

Lifestyle characteristics	Total (1,627)	PAD present (n = 17)	PAD absent (n = 1,610)	p value
Smoking				
Have you ever smoked cigarettes?				
Yes, and still smoke	11.0%	5.9%	11.1%	
Yes, in the past	23.3%	58.8%	22.9%	0.02
No	65.7%	35.3%	66.0%	
Nº of cigarettes/day	13.3 ± 12.3	23.2 ± 14.3	13.1 ± 12.2	0.007
Alcohol consumption				
Daily	0.9%	0%	0.9%	
1-3 days/week	10.0%	0%	10.1%	
4-6 days/week	0.9%	0%	0.9%	
1-3 days/month	11.0%	5.9%	11.1%	0.70
Less than 1 day/month	6.0%	11.8%	6.0%	
Gets drunk at least once a month	0.7%	0%	0.7%	
None	70.4%	82.3%	70.3%	
Physical activity				
Very active	3.4%	0%	3.5%	
Active	30.1%	5.9%	30.4%	0.05
Irregularly active	25.2 %	17.6%	25.3%	
Sedentary	41.2%	76.5%	40.8%	

Alcohol consumption (mean frequency of alcohol intake in the last 12 months); physical activity (activities carried out in the last week - International Physical Activity Questionnaire - Short Form [IPAQ-SF]). All variables are categorical and were compared using chi-square test. PAD: peripheral artery disease.

with volunteers with normal ABI. Furthermore, a higher prevalence of physical inactivity, obesity and smoking frequency and intensity (cigarettes/day) was found in volunteers with PAD. These variables are frequently associated with PAD in other studies.[15-17,19,20,22,23,32] The present study also identified a higher frequency of PAD in blacks compared with whites. This finding is aligned with recent data published by Eraso et al.,[16] who assessed data from the National Health and Nutrition Examination Survey (NHANES), including 7,058 subjects above the age of 40 years. Another potential explanation for the low prevalence of PAD in the assessed population is the fact that the study was conducted in a small town where overall habits (e.g., nutritional) and exposure to risk factor (e.g., mental stress), other than the investigated here, are different from those observed in large cities. Comparing our population with the one included in the study by Makdisse et al.[18] (conducted in large Brazilian cities), our results showed a lower percentage of smokers (34.3% versus 46.7%) and physically inactive individuals (41.18% versus 64.8%). Also, the study by Makdisse et al.[18] had a larger number of individuals with chronic kidney disease (2.46% versus 6.12%), which is a well-known risk factor for PAD.[16,33]

Upon applying a multivariable logistic regression model, we determined the independent predictors associated with PAD. Only age, diabetes mellitus, smoking, and sedentary lifestyle emerged as significant

Table 4 - Comparison of clinical characteristics among individuals with and without peripheral artery disease

Clinical characteristics	Total (1,627)	PAD present (n = 17)	PAD absent (n = 1,610)	p value
Hypertension (%)				
Yes	40.0	82.4	39.6	< 0.001
No	60.0	17.6	60.4	
Diabetes (%)				
Yes	7.7	41.2	7.4	< 0.001
No	92.3	58.8	92.6	
Obesity (%)				
Yes	19.1	41.2	18.9	0.03
No	80.9	58.8	81.1	
Hypercholesterolemia (%)				
Yes	15.9	12.5	15.9	0.52
No	84.1	87.5	84.1	
Angina pectoris (%)				
Yes	3.0	5.9	2.9	0.40
No	97.0	94.1	97.1	
Myocardial infarction (%)				
Yes	2.2	11.8	2.1	0.05
No	97.8	88.2	97.9	
Stroke (%)				
Yes	0.6	5.9	0.5	0.09
No	99.4	94.1	99.5	
Kidney failure (%)				
Yes	2.5	5.9	2.4	0.35
No	97.5	94.1	97.6	
Depression (%)				
Yes	19.2	29.4	19.1	0.21
No	80.8	70.6	80.9	

All variables are categorical and were compared using the chi-square test. PAD: peripheral artery disease.

Table 5 - Univariate and multivariate logistic regression analysis of peripheral artery disease (defined as an ankle-brachial index < 0.90) in a Brazilian population

Variables	PAD	
	OR (95%CI), p value	
	Univariate	Multivariate
Age	1.08 (1.05 to 1.13), < 0.001	1.08 (1.03 to 1.13), 0.001
Hypertension	7.12 (2.04 to 24.90), < 0.001	1.53 (0.39 to 5.98), 0.54
Diabetes	8.77 (3.28 to 23.46), < 0.001	3.07 (1.07 to 8.85), 0.04
Obesity	3.01 (1.14 to 7.96), 0.03	2.89 (0.97 to 8.66), 0.06
Myocardial infarction	6.18 (1.36 to 28.07), 0.02	2.19 (0.44 to 11.02), 0.34
Smoking	3.56 (1.31 to 9.68), 0.01	4.01 (1.34 to 11.97), 0.01
Sedentary lifestyle	4.70 (1.53 to 14.48), 0.007	3.75 (1.16 to 12.03), 0.03

Multivariate model: age, hypertension, diabetes, obesity, myocardial infarction, smoking, and sedentary lifestyle. PAD: peripheral artery disease; OR: odds ratio; 95%CI: 95% confidence interval.

risk factors in the study sample. This finding is aligned with that of several other studies.[16,17,19,32,34] Even though PAD is majorly caused by atherosclerotic disease, hypercholesterolemia was not found as a significant risk factor. Other studies have also found a weak association between PAD and hypercholesterolemia when comparing risk factors[16] or no association whatsoever.[35]

Our study has some limitations. First, as a cross-sectional analysis, a causal relationship between several cardiovascular risk factors and PAD could not be established. Second, the diagnosis of PAD in the present study was established only by ABI. Despite being a simple and inexpensive method, studies have shown that ABI has a high sensitivity (90 - 97%) and specificity (98 - 100%) for detection of arterial stenosis greater than 50%.[36]

Conclusion

In summary, in a sample from the Brazilian population, aged 18 years and above and residing in a small rural town, PAD had a low prevalence, clearly increased with age, and was more frequent in blacks than whites. Additionally, risk factors for PAD in the investigated population were smoking, sedentary lifestyle, diabetes mellitus, and age,

which are similar to those in other epidemiological studies including different ethnic groups.

Author contributions

Conception and design of the research and writing of the manuscript: Alvim RO, Dias FAL, Krieger JE, Pereira AC; Acquisition of data abd analysis and interpretation of the data: Alvim RO, Dias FAL, Oliveira CM, Horimoto ARVR, Ulbrich AZ; Statistical analysis: Alvim RO; Obtaining financing: Krieger JE; Critical revision of the manuscript for intellectual content: Oliveira CM, Horimoto ARVR, Ulbrich AZ, Pereira AC.

Potential Conflict of Interest

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

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Study Association

This study is not associated with any thesis or dissertation work.

Ethics approval and consent to participate

This study was approved by the Ethics Committee of the Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo under the protocol number SDC: 3485/10/074. All the procedures in this study were in accordance with the 1975 Helsinki Declaration, updated in 2013. Informed consent was obtained from all participants included in the study.

References

1. Kullo IJ, Rooke TW. Clinical Practice. Peripheral artery disease. N Engl J Med. 2016;374(9):861-71.
2. Olin JW, White CJ, Armstrong EJ, Kadian-Dodov D, Hiatt WR. Peripheral artery disease: evolving role of exercise, medical therapy, and endovascular options. J Am Coll Cardiol. 2016;67(11):1338-57.
3. Criqui MH, Langer RD, Fronek A, Feigelson HS, Klauber MR, McCann TJ, et al. Mortality over a period of 10 years in patients with peripheral arterial disease. N Engl J Med. 1992;326(6):381-6.
4. Criqui MH, Ninomiya JK, Wingard DL, Ji M, Fronek A. Progression of peripheral arterial disease predicts cardiovascular disease morbidity and mortality. J Am Coll Cardiol. 2008;52(21):1736-42.
5. Dormandy JA, Betteridge DJ, Schernthaner G, Pirags V, Norgren L; PROactive investigators. Impact of peripheral arterial disease in patients with diabetes--results from PROactive (PROactive 11). Atherosclerosis. 2009;202(1):272-81.
6. Jager A, Kostense PJ, Ruhe HG, Heine RJ, Nijpels G, Dekker JM, et al. Microalbuminuria and peripheral arterial disease are independent predictors of cardiovascular and all-cause mortality, especially among hypertensive subjects: five-year follow-up of the Hoorn Study. Arterioscler Thromb Vasc Biol. 1999;19(3):617-24.
7. Kornitzer M, Dramaix M, Sobolski J, Degre S, De Backer G. Ankle/arm pressure index in asymptomatic middle-aged males: an independent predictor of ten-year coronary heart disease mortality. Angiology. 1995;46(3):211-9.
8. Resnick HE, Lindsay RS, McDermott MM, Devereux RB, Jones KL, Fabsitz RR, et al. Relationship of high and low ankle brachial index to all-cause and cardiovascular disease mortality: the Strong Heart Study. Circulation. 2004;109(6):733-9.
9. Criqui MH, Langer RD, Fronek A, Feigelson HS. Coronary disease and stroke in patients with large-vessel peripheral arterial disease. Drugs. 1991;42 Suppl 5:16-21.
10. Breek JC, Hamming JF, De Vries J, van Berge Henegouwen DP, van Heck GL. The impact of walking impairment, cardiovascular risk factors, and comorbidity on quality of life in patients with intermittent claudication. J Vasc Surg. 2002;36(1):94-9.
11. Long J, Modrall JG, Parker BJ, Swann A, Welborn MB 3rd, Anthony T. Correlation between ankle-brachial index, symptoms, and health-related quality of life in patients with peripheral vascular disease. J Vasc Surg. 2004;39(4):723-7.
12. Hirsch AT, Haskal ZJ, Hertzer NR, Bakal CW, Creager MA, Halperin JL, et al; American Association for Vascular Surgery; Society for Vascular Surgery; Society for Cardiovascular Angiography and Interventions; Society for Vascular Medicine and Biology; Society of Interventional Radiology; ACC/AHA Task Force on Practice Guidelines; American Association of Cardiovascular and Pulmonary Rehabilitation; National Heart, Lung, and Blood Institute; Society for Vascular Nursing; TransAtlantic Inter-Society Consensus; Vascular Disease Foundation. ACC/AHA 2005 guidelines for the management of patients with peripheral arterial disease (lower extremity, renal, mesenteric, and abdominal aortic): executive summary a collaborative report from the American Association for Vascular Surgery/Society for Vascular Surgery, Society for Cardiovascular Angiography and Interventions, Society for Vascular Medicine and Biology, Society of Interventional Radiology, and the ACC/AHA Task Force on Practice Guidelines (Writing Committee to Develop Guidelines for the Management of Patients With Peripheral Arterial Disease) endorsed by the American Association of Cardiovascular and Pulmonary Rehabilitation; National Heart, Lung, and Blood Institute; Society for Vascular Nursing; TransAtlantic Inter-Society Consensus; and Vascular Disease Foundation. J Am Coll Cardiol. 2006;47(6):1239-312.
13. Norgren L, Hiatt WR, Dormandy JA, Nehler MR, Harris KA, Fowkes FG, et al; TASC II Working Group. Inter-society consensus for the management of peripheral arterial disease (TASC II). J Vasc Surg. 2007;45 Suppl S:S5-67.
14. Rooke TW, Hirsch AT, Misra S, Sidawy AN, Beckman JA, Findeiss LK, et al; American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines; Society for Cardiovascular Angiography and Interventions; Society of Interventional Radiology; Society for Vascular Medicine; Society for Vascular Surgery. 2011 ACCF/AHA focused update of the guideline for the management of patients with peripheral artery disease (updating the 2005 guideline): a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines: developed in collaboration with the Society for Cardiovascular Angiography and Interventions, Society of

Interventional Radiology, Society for Vascular Medicine, and Society for Vascular Surgery. J Vasc Surg. 2011;54(5):e32-58.

15. Alzamora MT, Fores R, Pera G, Baena-Diez JM, Heras A, Sorribes M, et al. Incidence of peripheral arterial disease in the ARTPER population cohort after 5 years of follow-up. BMC Cardiovasc Disord. 2016;16:8.

16. Eraso LH, Fukaya E, Mohler ER 3rd, Xie D, Sha D, Berger JS. Peripheral arterial disease, prevalence and cumulative risk factor profile analysis. Eur J Prev Cardiol. 2014;21(6):704-11.

17. Fowkes FG, Housley E, Cawood EH, Macintyre CC, Ruckley CV, Prescott RJ. Edinburgh Artery Study: prevalence of asymptomatic and symptomatic peripheral arterial disease in the general population. Int J Epidemiol. 1991;20(2):384-92.

18. Makdisse M, Pereira Ada C, Brasil Dde P, Borges JL, Machado-Coelho GL, Krieger JE, et al; Hearts of Brazil Study and Peripheral Arterial Disease Committee of the Brazilian Society of Cardiology/Funcor. Prevalence and risk factors associated with peripheral arterial disease in the Hearts of Brazil Project. Arq Bras Cardiol. 2008;91(6):370-82.

19. Meijer WT, Hoes AW, Rutgers D, Bots ML, Hofman A, Grobbee DE. Peripheral arterial disease in the elderly: The Rotterdam Study. Arterioscler Thromb Vasc Biol. 1998;18(2):185-92.

20. Newman AB, Siscovick DS, Manolio TA, Polak J, Fried LP, Borhani NO, et al. Ankle-arm index as a marker of atherosclerosis in the Cardiovascular Health Study. Cardiovascular Heart Study (CHS) Collaborative Research Group. Circulation. 1993;88(3):837-45.

21. Norgren L, Hiatt WR, Dormandy JA, Nehler MR, Harris KA, Fowkes FG, et al. Inter-Society Consensus for the Management of Peripheral Arterial Disease (TASC II). Eur J Vasc Endovasc Surg. 2007;33 Suppl 1:S1-75.

22. Razzouk L, Rockman CB, Patel MR, Guo Y, Adelman MA, Riles TS, et al. Co-existence of vascular disease in different arterial beds: Peripheral artery disease and carotid artery stenosis--Data from Life Line Screening(®). Atherosclerosis. 2015;241(2):687-91.

23. Velescu A, Clara A, Penafiel J, Grau M, Degano IR, Marti R, et al. Peripheral Arterial Disease Incidence and Associated Risk Factors in a Mediterranean Population-based Cohort. The REGICOR Study. Eur J Vasc Endovasc Surg. 2016;51(5):696-705.

24. Hirsch AT, Criqui MH, Treat-Jacobson D, Regensteiner JG, Creager MA, Olin JW, et al. Peripheral arterial disease detection, awareness, and treatment in primary care. JAMA. 2001;286(11):1317-24.

25. Garofolo L, Barros N Jr, Miranda F Jr, D'Almeida V, Cardien LC, Ferreira SR. Association of increased levels of homocysteine and peripheral arterial disease in a Japanese-Brazilian population. Eur J Vasc Endovasc Surg. 2007;34(1):23-8.

26. Garofolo L, Ferreira SR, Miranda Junior F. Study of risk factors associated with peripheral arteriopathy in Japanese-Brazilians from Bauru (SP). Arq Bras Cardiol. 2014;102(2):143-50.

27. Sales AT, Fregonezi GA, Silva AG, Ribeiro CT, Dourado-Junior ME, Sousa AG, et al. Identification of peripheral arterial disease in diabetic patients and its association with quality of life, physical activity and body composition. J Vasc Bras. 2015;14(1):46-54.

28. Egan KJ, von Schantz M, Negrao AB, Santos HC, Horimoto AR, Duarte NE, et al. Cohort profile: the Baependi Heart Study-a family-based, highly admixed cohort study in a rural Brazilian town. BMJ Open. 2016;6(10):e011598.

29. Whitworth JA; World Health Organization, International Society of Hypertension Writing Group. 2003 World Health Organization (WHO)/International Society of Hypertension (ISH) statement on management of hypertension. J Hypertens. 2003;21(11):1983-92.

30. Pereira AC, Sposito AC, Mota GF, Cunha RS, Herkenhoff FL, Mill JG, et al. Endothelial nitric oxide synthase gene variant modulates the relationship between serum cholesterol levels and blood pressure in the general population: new evidence for a direct effect of lipids in arterial blood pressure. Atherosclerosis. 2006;184(1):193-200.

31. Tunstall-Pedoe H, Kuulasmaa K, Amouyel P, Arveiler D, Rajakangas AM, Pajak A. Myocardial infarction and coronary deaths in the World Health Organization MONICA Project. Registration procedures, event rates, and case-fatality rates in 38 populations from 21 countries in four continents. Circulation. 1994;90(1):583-612.

32. Weragoda J, Seneviratne R, Weerasinghe MC, Wijeyaratne M, Samaranayaka A. A cross-sectional study on peripheral arterial disease in a district of Sri Lanka: prevalence and associated factors. BMC Public Health. 2015 Aug 28;15:829.

33. Wattanakit K, Folsom AR, Selvin E, Coresh J, Hirsch AT, Weatherley BD. Kidney function and risk of peripheral arterial disease: results from the Atherosclerosis Risk in Communities (ARIC) Study. J Am Soc Nephrol. 2007;18(2):629-36.

34. Bennett PC, Silverman S, Gill PS, Lip GY. Ethnicity and peripheral artery disease. QJM. 2009;102(1):3-16.

35. Diehm C, Lange S, Trampisch HJ, Haberl R, Darius H, von Stritzky B, et al; GetABI Study Group. Relationship between lipid parameters and the presence of peripheral arterial disease in elderly patients. Curr Med Res Opin. 2004;20(12):1873-5.

36. Lamina C, Meisinger C, Heid IM, Rantner B, Döring A, Löwel H, et al. Ankle-brachial index and peripheral arterial disease. Gesundheitswesen. 2005;67 Suppl 1:S57-61.