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Factors Associated with an Abnormal Ankle-Brachial Index in Patients with Resistant Hypertension

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Abstract – **The ankle-brachial index (ABI) has been used to identify peripheral arterial occlusive disease and is a marker of macrovascular complications in patients with hypertension. The objective of the present study was to investigate factors associated with an abnormal ABI in patients with resistant hypertension. A cross-sectional study with a consecutively selected sample was conducted in a referral cardiology outpatient clinic in Salvador, Bahia, Brazil. Sociodemographic, anthropometric, clinical, laboratory and echocardiographic data were collected. The association between abnormal ABI and possible risk factors was evaluated using odds ratios (OR), with their respective 95% confidence intervals (95%CI). Next, logistic regression analysis was performed, using a hierarchical model. The prevalence of an abnormal ABI was 19.0%. Most patients were female (74.8%), black (57.1%), overweight or obese (85.8%), of 40-65 years of age (60.3%), and with education above primary school level (63.8%). In addition, 44.0% were diabetics; 29.9% had hypercholesterolemia, 21.9% had hypertriglyceridemia and 18.1% had had a cerebrovascular accident. The factors that remained significantly associated with abnormal ABI in the final model were diabetes (OR=4.11; 95%CI: 1.10-15.50), age >65 years (OR=3.30; 95%CI: 1.13-9.69) and hypercholesterolemia (OR=4.18; 95%CI: 1.12-15.58). The prevalence of abnormal ABI, albeit not as high as in groups of patients with specific pathologies, was found to be significantly associated with the risk factors traditionally described in the literature. Therefore, the ABI should be used routinely to evaluate patients with severe hypertension as a method of screening for vascular alterations.**

Index Terms— **ankle-brachial index; resistant hypertension; vascular lesions; peripheral arterial occlusive disease.**

I. Introduction

The ankle-brachial index (ABI) is considered an important marker of peripheral arterial occlusive disease (PAOD) in its asymptomatic phase. This marker has become increasingly important in clinical practice, since it may predict the formation and progression of atherosclerotic plaques, allowing plaque formation to be detected at an early stage, thus improving prognosis and representing a major therapeutic advance [1]. The ABI may be particularly useful when monitoring hypertensive patients, since hypertension constitutes the principal risk factor for cardiovascular disease, the most common cause of death in Brazil and worldwide [2], [3]. Hypertension is currently a public health issue that affects approximately 25% of the adult population worldwide, around 1.2 billion individuals, causing 7 million deaths annually. It is estimated that around 13% of cases may involve resistant hypertension [2].

Although it is impossible to determine the specific arterial blood pressure level at which cardiovascular complications are triggered, studies have shown a direct relationship between sustained high blood pressure levels and cardiovascular complications, and this association constitutes a challenge for the management of patients with resistant hypertension. Resistant hypertension is defined as blood pressure that remains above target levels despite concurrent use of three antihypertensive agents with synergic actions at the maximum recommended and tolerated doses, one of which should be a diuretic, or in cases of hypertension that is controlled with the use of four or more drugs [4].

The physiopathology of resistant hypertension is multifactorial. The vascular alterations may already be present in the early stages of the disease, leading to greater endothelial dysfunction, expressed by a reduction in endothelium-dependent vasodilation and an increase in inflammatory biomarkers [5]. Left ventriclar hypertrophy is the principal cardiac alteration, with a prevalence of approximately 16% in patients with resistant hypertension. The consequences of left ventricular hypertrophy include an increase in the circulation of inflammatory mediators and aldosterone and a reduction in coronary flow reserve, leading to more severe atherosclerosis, arterial stiffness, heart failure and arrhythmia [6]. Atherosclerosis occurs as a result of the interaction between risk factors that damage the endothelial surface and genetic predisposition [7].

The changes in the arterial wall progress slowly and silently, and are characterized by the gradual and progressive thickening of the endothelium [8]. Any of the arteries can be affected; however, the most common repercussions occur in the coronary and carotid arteries, in the arteries of the lower limbs and in the aorta [1]. Epidemiological studies have identified smoking, high serum lipid levels, hypertension, obesity, diabetes mellitus and physical inactivity as risk factors for the development of atherosclerosis [2], [4].

Although the physiopathology of resistant hypertension is multifactorial and its prognosis has been shown to be poorer compared to that of arterial hypertension, few studies have dealt with the presence of abnormal ABI in patients with resistant hypertension. Nevertheless, focusing on this group of patients could help identify diagnostic measures that would permit earlier interventions, representing a major advance in the treatment of heart disease and a better prognosis for patients. Therefore, the objective of the present study was to

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investigate the factors associated with an abnormal ABI in patients with resistant hypertension being followed up at a referral cardiology outpatient clinic.

II. MATERIALS AND METHODS

This was a cross-sectional study developed between September 2015 and December 2016 at the Cardiology Outpatient Clinic of the Professor Edgard Santos Teaching Hospital, Federal University of Bahia. The study included a total of 126 patients with resistant hypertension who were being followed up at the afore mentioned clinic and who were in use of four or more antihypertensive agents at recommended doses, including one diuretic. The patients were consecutively selected during routine consultations and enrolled to the study if they agreed to participate after reading the informed consent form. The internal review board of the Ana Nery Hospital, an institute associated with the Federal University of Bahia, approved the study protocol.

Patients who had previously been diagnosed with severe peripheral arterial disease; stage 3 chronic kidney disease or worse, based on the Cockcroft-Gault equation; those presenting suppurating lesions or patients without a limb; and patients with atrial fibrillation or frequent ventricular extrasystoles were excluded from the study.

Undergraduate students, residents and master's degree students obtained the data from the patients' records. A specially designed form was used to collect the sociodemographic data, data on the patients' lifestyles (alcohol consumption smoking habits), anthropometric, clinical, laboratory and echocardiographic data, as well as data on any comorbidities such as renal insufficiency, diabetes, coronary disease and dyslipidemia.

The patients were evaluated to rule out pseudo-resistance using ambulatory blood pressure monitoring. Their compliance with their medication was evaluated according to the Morisky scale [9]. All the patients were submitted to laboratory blood tests, including full blood count and erythrocyte sedimentation rate, levels of fasting and postprandial glucose, glycosylated hemoglobin, urea, creatinine, sodium, potassium, total cholesterol, high-density lipoprotein (HDL)-cholesterol, low-density lipoprotein (LDL)-cholesterol, triglycerides, uric acid, and high sensitivity C-reactive protein. The tests were performed at the clinical laboratory of the Prof. Edgar Santos Teaching Hospital, Federal University of Bahia.

The dependent variable in this study was the ABI, which was evaluated using a method previously validated by Kawamura [10] in a population of hypertensive Brazilian patients. Blood pressure was measured in all four limbs during routine clinical examination using two blood pressure monitors (Omron HEM-705CP), duly validated by the British Hypertension Society [11]. All the measurements were obtained with the patient in the supine position in a quiet, cool location after five minutes' rest. The arm cuffs were placed comfortably and adjusted at the same height, directed towards the trajectory of the brachial artery on each side. Blood pressure levels in the upper limbs were recorded and the arm in which systolic pressure was higher was selected for comparison with the values recorded in the lower limbs. When the systolic blood pressure values of the upper limbs were identical, the right arm was selected. Blood pressure was then simultaneously determined in the upper arm in which blood pressure was higher and the ankle, first the left ankle, then the right, with the cuff placed above the malleolus and directed towards the trajectory of the posterior tibial artery. If it proved impossible to measure blood pressure in this position, the cuff was then directed towards the trajectory of the dorsalis pedis artery. To calculate the ABI of each limb, the following formula was used: ABI = systolic blood pressure at the ankle divided by the systolic blood pressure in the arm. ABI values considered normal were those between 0.9 and 1.3 [10]. The study population was divided into three groups in accordance with the ABI values: abnormally low ABI (<0.9), normal ABI (0.9 – 1.3) and abnormally high ABI (> 1.3).

The independent variables were the following demographic characteristics: sex (male/female), ethnicity (black/non-black), education level (primary education or less / more than primary education), lifestyle habits (smoker / never-smoker / former smoker), and age (40-65 years / > 65 years). The body mass index (BMI) of the participants was calculated by dividing the person's weight by their height squared. The patients were classified as being: of normal weight (BMI >18.5 to 24.99 kg/m^2), overweight (BMI ≥25 – 29.99 kg/m^2) or obese (BMI ≥30 kg/m^2) (WHO, 2009). The reference values used to define a risk profile were: total cholesterol ≥ 200 mg/dl, LDL-C ≥ 130 mg/dl, HDL-C ≤ 40 mg/dl and triglycerides ≥ 150 mg/dl.

Data entry was performed using a Microsoft Office Excel 2010 spreadsheet and all the statistical analyses were conducted using the SPSS statistical software program, version 20.0. The categorical variables were presented as simple frequencies. The ankle-brachial index values were described as means and standard deviations after testing the normalcy of distribution using the Shapiro Wilk test. Student's t-test for independent samples was used to compare the mean values of the ankle-brachial index as a function of the explanatory variables. The chi-square test and Fisher's exact test were used to compare the prevalence of abnormal ankle-brachial index values as a function of the characteristics of the study population. Significance level was determined as $p \leq 0.05$ throughout the entire analysis. The magnitude of the association between abnormal ankle-brachial index values and the possible determinants was calculated using prevalence ratios and their respective 95% confidence intervals (95%CI). Next, multivariate logistic regression analysis was conducted based on a hierarchical model defined a priori, according to the determination level of the risk factors for an abnormal ankle-brachial index (Figure 1). A forward stepwise procedure was used to insert the sets of variables into the model. The first set consisted of the sociodemographic and lifestyle variables, with the second set consisting of anthropometric status; the third set of the variables on morbidity and the fourth set the variables regarding the use of medicines. The variables that continued to be statistically significant at $p<0.20$ remained in the model.

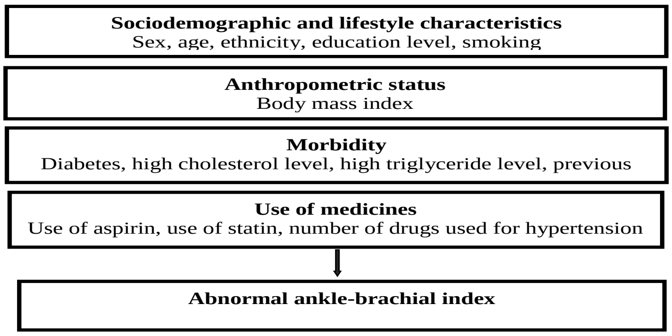

Figure 1. Hierarchical model used to determine the risk factors involved in abnormal ankle-brachial index in patients with resistant hypertension

III. RESULTS

ABI was abnormally low (<0.9) in 19.0% of the patients in the study sample. None of the patients had abnormally high values (>1.3) (Figure 2).

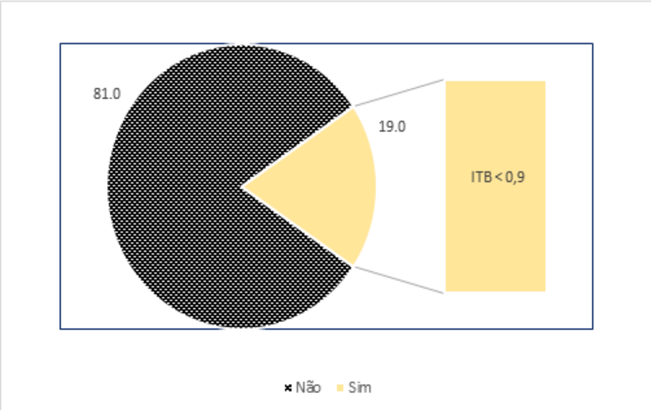

Figure 2: Prevalence of abnormal ankle-brachial index in patients with resistant hypertension receiving care at the Cardiology Outpatient Clinic of the Federal University of Bahia Teaching Hospital. Salvador, Bahia, Brazil.

The majority of the patients were female (74.8%), aged from 40 to 65 years (60.3%), black (57.1%), with more than primary education (63.8%), and overweight or obese (85.8%). In addition, there was a high prevalence of diabetes (44.0%), hypercholesterolemia (29.9%), hypertriglyceridemia (21.3%), and previous cerebrovascular accident (18.9%). The majority of the patients (85%) used up to 5 antihypertensive drugs. In the bivariate analysis, no statistically significant association was found between abnormal ankle-brachial index and any of the sociodemographic or lifestyle characteristics, anthropometric status, morbidity, or the use of medicines. Nevertheless, the greatest differences in the prevalence of abnormal ABI were found as a function of age, with a higher prevalence in the patients over 65 years of age (26.0%) compared to those of 40-65 years of age (14.7%); ethnicity, with a higher prevalence in black patients (23.9%) compared to non-black patients (13.0%); and cholesterol levels, with a greater prevalence in patients with hypercholesterolemia (28.9%) compared to those with normal cholesterol levels (14.3%). A significantly higher mean ABI was found for the male patients (1.04 ± 0.13 [SD]) in relation to the female patients (0.99 ± 0.12) and for patients aged 40-65 years (1.02 ± 0.12) compared to those over 65 years of age (0.97 ± 0.12). No statistically significant difference was found in the mean ankle-brachial index as a function of any of the other explanatory variables evaluated in the present study (i.e. other sociodemographic factors, lifestyle characteristics, anthropometric status, morbidity or the use of medicines) (Table 1).

Table 1. Prevalence of abnormal ankle-brachial index (ABI) and mean ankle-brachial index as a function of sociodemographic and lifestyle characteristics, anthropometric status, morbidity and use of medicines in patients with resistant hypertension.

Characteristics	n	%	ABI Prevalence	P value	Mean ABI		P value
					Mean	SD	
Sex							
Male	31	25.2	15.6		1.04	0.13	
Female	95	74.8	20.2	0.79	0.99	0.12	0.04
Age (years)							
40 - 65	76	60.3	14.7		1.02	0.12	
> 65	50	39.7	26.0	0.16	0.97	0.12	0.03
Ethnicity							
Black	72	57.1	23.9		0.99	0.13	
Non-black	54	42.9	13.0	0.10	1.00	0.11	0.96
Education level							
≤ Primary school	46	36.2	21.7		0.99	0.13	
> Primary school	80	63.8	17.5	0.56	1.00	0.11	0.45
Smoking habit							
Never smoked	78	62.0	14.1		0.97	0.13	
Former smoker	45	36.0	26.7		1.02	0.11	
Current smoker	3	2.0	-	0.08			0.06
Body mass index							
Normal	13	10.2	15.4		1.01	0.11	
Overweight/obese	109	85.8	19.4	0.54	1.00	0.13	0.74
Diabetes							
Yes	55	44.0	22.2		1.00	0.12	
No	70	56.0	15.7	0.36	1.00	0.12	0.92
High cholesterol levels (mg/dl)							
Yes	38	29.9	28.9		1.01	0.11	
No	63	49.6	14.3	0.06	0.98	0.12	0.23
High triglyceride levels (mg/dl)							
Yes	27	21.3	22.2		1.00	0.11	
No	72	56.7	19.4	0.48	1.00	0.12	0.85
Previous cerebrovascular accident							
Yes	23	18.9	17.4		1.00	0.11	
No	99	81.1	17.3	0.99	1.02	0.12	0.78
Use of aspirin							
Yes	40	38.5	20.5		0.97	0.13	
No	64	61.5	15.9	0.60	1.02	0.11	0.06
Use of statins							
Yes	78	68.4	20.8		0.99	0.13	
No	36	31.6	16.7	0.80	1.01	0.10	0.34
Number of antihypertensive drugs							
≤ 5	102	85.0	27.8		1.00	0.12	
> 5	18	15.0	18.0	0.34	0.99	0.12	0.93

ABI= ankle-brachial index

In the first step of the logistic regression analysis, age, ethnicity and smoking were found to meet the previously established criteria for remaining in the model (Table 2).

There was a significant association between age > 65 years and abnormal ankle-brachial index, even after adjustment for sex, education level, ethnicity and smoking (OR=3.30; 95%CI: 1.13 – 9.69). The patients who were former smokers were found to have a 3.1-fold greater likelihood of having an abnormal ankle-brachial index compared to those who had never smoked, an association that was statistically significant. In the second step of the analysis, no statistically significant association was found between the patients' anthropometric status and the ankle-brachial index even following adjustment for age, ethnicity and smoking. The variables related to morbidity were adjusted for the sociodemographic and lifestyle characteristics selected in the previous steps. Diabetes was significantly associated with an abnormal ankle-brachial index (OR = 4.11; 95%CI: 1.10 – 15.50). In the patients with hypercholesterolemia, the likelihood of the ankle-brachial index being abnormal was 4.18 (95%CI: 1.12 – 15.58) times greater than for patients whose cholesterol levels were normal. In relation to the use of medicines, no statistically significant association was found between an abnormal ankle-brachial index and the use of statins or aspirin or the use of more than 5 anti-hypertensive drugs, even following adjustment for the variables selected in the previous steps of the logistic regression (Table 2).

Table 2. Association between abnormal ankle-brachial index and sociodemographic and lifestyle factors, anthropometric status, morbidities and the use of drugs in patients with resistant hypertension.

Characteristics	Crude PR (95%CI)	Adjusted OR (95%CI)	P value
Sociodemographic and lifestyle			
Sex			
Male	1	1.0[a]	
Female	1.29 (0.53 – 3.18)	1.32 (0.39 – 4.38)	0.65
Age (years)			
40 - 65	1	1.0[a]	
> 65	1.77 (0.86 – 3.64)	3.30 (1.13 – 9.69)	0.03
Ethnicity			
Black	1.84 (0.83 – 4.14)	2.55 (0.87 – 7.44)	
Non-black	1	1.0[a]	0.09
Education level			
≤ Primary school	1.24 (0.60 – 2.57)	1.06 (0.38 – 4.38)	0.91
> Primary school	1	1.0[a]	
Smoking habit			
Non-smoker	1	1.0[a]	
Former smoker	1.89 (0.81 – 3.92)	3.01 (1.10 – 8.57)	0.03
Current smoker	Not calculated		
Anthropometric status			
BMI			
< 25	1	1.0[b]	
> 25	1.26 (0.33 – 4.78)	3.01 (0.34 – 26.53)	0.33
Morbidity			
Diabetes			
Yes	1.41 (0.67 – 2.95)	4.11 (1.10 – 15.50)	
No	1	1.0[c]	0.03
High cholesterol levels			
Yes	2.02 (0.92 – 4.43)	4.18 (1.12 – 15.58)	
No	1	1.0[c]	0.03
High triglyceride levels			
Yes	1.14 (0.49 – 2.67)	0.44 (0.09 – 2.08)	0.29
No	1	1.0[c]	
Previous cerebrovascular accident			
Yes	1.00 (0.37 – 2.69)	0.82 (0.18 – 3.68)	
No	1	1.0[c]	0.79
Use of medicines			
Use of aspirin			
Yes	1.29 (0.56 – 2.99)	1.76 (0.40 – 7.70)	
No	1	1.0[d]	0.48
Use of statins			
Yes	1.25 (0.53 – 2.91)	2.57 (0.56 – 11.66)	
No	1	1.0[d]	0.22
Number of antihypertensive drugs			
≤ 5	1	1.0[d]	
> 5	1.54 (0.66 – 3.62)	2.60 (0.64 – 10.57)	0.18

PR: prevalence rate; 95% CI: 95% confidence interval; OR: odds ratio.
a OR adjusted for the variables belonging to the same set: sociodemographic and lifestyle characteristics.
b OR adjusted for age, ethnicity and smoking habits.
c OR adjusted for age, ethnicity and smoking habit and for the variables belonging to the same set: morbidities.
d OR adjusted for age, ethnicity, smoking habit, diabetes, cholesterol and for the variables belonging to the same set: use of medicines.

The data in Table 3 show that the model consisting of the sociodemographic and lifestyle characteristics permitted 10.0% of the patients with an abnormal ankle-brachial index to be identified. This percentage increased slightly to 12.2% following inclusion of the anthropometric status. However, the percentage increased to 24.3% when the set of variables on morbidity was included in the sociodemographic and lifestyle model. The inclusion of the set of morbidities contributed significantly to the model.

Table 3. Contribution of each set of variables to the adjustment of the model.

Set of variables	Deviation function	Degrees of freedom	Chi square	P value	Explanatory power (%)
Sociodemographic and lifestyle	107.65	5	10.95	0.050	10.0
Sociodemographic and lifestyle + anthropometric status	104.297	4	9.22	0.056	12.2
Sociodemographic and lifestyle + Morbidity	73.414	7	15.048	0.035	24.3
Sociodemographic and lifestyle + Morbidity + Use of medicines	54.410	8	11.888	0.156	24.9

IV. DISCUSSION

This study on the prevalence of abnormal ankle-brachial index differs from most reports in the literature, particularly with respect to the study's target population. Hence, the scarcity of more specific data hampers any comparative analysis of the findings. The prevalence of an abnormal ankle-brachial index found in the present study (19.0%) is high compared to epidemiological data from the general population (3-10%) [12]. However, this prevalence is lower than rates found for specific patient populations with a greater likelihood of abnormal ABI. Such population groups include those with hypertension (40.9% [13] and 67.3% [14]), and cardiovascular disease (31.6%) [15], as well as groups of elderly hypertensive individuals (25.5% [16] and 26.8% [17]), and a group of patients attending a specialist outpatient clinic for vascular surgery (29.7%) [18]. Indeed, only one study conducted with hypertensive patients found a prevalence rate of abnormal ABI (17.5%) [19] that was similar to the rate found in the present study; however, it should be emphasized that although that study population consisted of individuals with hypertension, all the participants were asymptomatic patients with no past history of cardiovascular disease, renal disease or diabetes mellitus.

Despite the population differences, the prevalence of abnormal ABI was initially expected to be higher in the present study compared to others, since high rates had been found in patients with atherosclerosis related diseases. Indeed, resistant hypertension would increase the likelihood of a greater number of severe alterations that, taken together, could ultimately predispose these patients to cardiovascular events. In addition, they would have been exposed to a greater number of risk factors such as advanced age, smoking and coronary disease. In this respect, studies have shown that patients with an ABI <0.90 have a 52% greater likelihood of developing hypertension [20]. This finding highlights the importance of providing care to the individual with hypertension, avoiding lesions that could result in the development of arterial disease over a shorter period of time. ABI, as a marker of asymptomatic PAOD, provides important information on subclinical atherosclerosis and represents an important predictor of cardiovascular events.

On the other hand, the prevalence identified in the present study could be partially explained as a result of the therapeutic interventions used, for example the high proportion of patients in use of statins (68.2%). Nevertheless, the percentage of abnormal ABI was higher in the patients who were using aspirin and statins. Since this was an observational study, it is understood that the use of such drugs is associated with individuals with greater cardiovascular risk, prompting the attending team to prescribe these drugs, which are known to reduce cardiovascular events in high-risk patients. In addition, Mönckeberg's medial sclerosis is more prevalent in diabetics and may hamper compression of the arteries of the foot, leading to a falsely high ABI reading [21]. In the present study, 44% of the patients had diabetes.

Few studies in Brazil have investigated the prevalence of abnormal ABI in patients with hypertension. Specifically designed studies could contribute towards explaining causal phenomena, enabling early preventive measures to be developed, since it has already been shown that an abnormal ABI constitutes an independent predictor of future cardiovascular events, with the increase in cardiovascular risk being associated with ABI ≤0.9 or >1.4.[22,23,24,25] A randomized, controlled, double-blind study showed that ABI values ≤0.9 were associated with a 2-3-fold increased risk of cardiovascular mortality and of death from any cause in elderly hypertensive individuals [23]. In addition, after five years of follow-up, a cohort study showed that baseline ABI values ≤0.9 were associated with a 38% increase in the risk of non-fatal myocardial infarction, with a 98% increased risk of a cerebrovascular accident, an 85% increased risk of cardiovascular death and a 58% greater risk of death from any cause, following adjustment for age, sex, the presence of coronary disease and diabetes. In that study, the lower the patients' baseline ABI, the less likely they were to survive (p<0.001) [24]. In the present study, no patients had ABI >1.3. Nevertheless, it is important to emphasize that some studies have shown an association between ABI values >1.3 and the occurrence of cardiovascular events [25].

Age >65 years was associated with an abnormal ABI in this population. These findings agree with other studies that showed a strong association between advanced age and the prevalence of PAOD, as measured by the ABI [20], [26]. The prevalence of PAOD has been shown to increase with age, both in the general population and in patients with chronic kidney disease [20], [26], [27]. Nevertheless, a few studies failed to find any difference insofar as age is concerned. [28] In the present analysis, the risk factors in the study population were present at the time of this evaluation; therefore, it is possible to speculate that the time during which the individuals lived with these comorbidities could represent a relevant factor in the association between PAOD and age.

The association found between smoking and abnormal ABI confirms previous reports [29], [30] The severity of the cardiovascular condition appears to be associated with the number of cigarettes smoked per day [29] The incidence of cardiovascular disease was shown to decrease significantly in individuals who stop smoking [30]. In a study conducted by Woo et al [30]. the number of cigarettes smoked per year was the second most significant independent risk factor associated with the prevalence of PAOD in an elderly Chinese population. In other studies, in which smoking was found to be associated with abnormal ABI, current and former smokers were grouped together in the analysis. Here, the entire study population was evaluated by a multidisciplinary team and encouraged to stop smoking right from the beginning of follow-up. Therefore, in practical terms, the analysis conducted included only former smokers and no current smokers. This association contributed to providing further evidence on the consequences of smoking in adult health even after the individual stops smoking.

In the present study, abnormal ABI was also found to be significantly associated with diabetes, being four times more common in diabetics. These findings are in agreement with previous reports, irrespective of whether the design consisted of a cross-sectional [10], [31] or cohort study [32]. Even in non-diabetic patients, insulin resistance increases the risk of peripheral atherosclerotic disease by around 40-50% [33]. In diabetic patients, PAOD is more aggressive, with early involvement of the distal vessels and distal symmetric neuropathy, which results in an up to 10-fold increase in the risk of amputation [34]. PAOD has certain peculiarities in diabetic patients. The disease tends to affect the distal arteries of the lower limbs such as the popliteal artery, the anterior tibioperoneal trunk and the dorsalis pedis artery, causing an relationship can be established between the risk factors investigated and abnormal ABI values. Furthermore, the sample was a convenience sample, which limits the external validity of the data. This sample may be representative of a high-risk population with a high prevalence of cardiovascular disease and the abnormal ABI values may have been overestimated. On the other hand, this was the first study to systematically evaluate ABI in a population with resistant hypertension.

The prevalence of abnormal ABI, although not as high as that found in a group of patients with specific pathologies, was found to be significantly associated with age over 65 years and with former smokers. Furthermore, taking the risk factors traditionally described in the literature into consideration, an association was found between ABI and high cholesterol levels and between ABI and diabetes in patients with resistant hypertension. This gives strength to the proposal to use this index as a method of screening for the vascular alterations described and suggests that the ABI should be used in the routine evaluation of patients with severe hypertension. In agreement with other authors, the present study failed to find any association between ABI and sex [12], [16], high triglyceride levels [16], poor education level or BMI [16], [30]. Nevertheless, no consensus has yet been reached on the role of these factors, particularly in specific populations. Therefore, epidemiological studies should be conducted in various regions of the world to gather data on the incidence and prevalence of abnormal ABI, both in symptomatic and asymptomatic populations, on the risk factors, progression of the disease and the frequency of coexisting vascular diseases.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

What is known about the topic?

• The ankle-brachial index (ABI) presents 10 to 25% prevalence in the over 55-year-old population, with increased death risk due to cardiovascular disease.

• The ankle-brachial index (ABI) is considered an important marker of peripheral arterial occlusive disease (PAOD) in its asymptomatic phase. This marker has become increasingly important in clinical practice, since it may predict the formation and progression of atherosclerotic plaques, allowing plaque formation to be detected at an early stage.

• There are many factors in the aetiology of abnormal ABI, such as ages, old age, abdominal obesity, diabetes, smoking, hypertension. However, there is still no consensus on the role of these variables, especially in specific populations.

What this study adds?

• This marker has become increasingly important in clinical practice, since it may predict the formation and progression of atherosclerotic plaques, allowing plaque formation to be detected at an early stage, thus improving prognosis and representing a major therapeutic advance

• Although the physiopathology of resistant hypertension is multifactorial and its prognosis has been shown to be poorer compared to that of arterial hypertension, few studies have dealt with the presence of abnormal ABI in patients with resistant hypertension.

• Nevertheless, focusing on factors associated with an abnormal ABI in patients with resistant hypertension could help identify diagnostic measures that would permit earlier interventions, representing a major advance in the treatment of heart disease and a better prognosis for patients.

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