Original Article

Association between Ankle-Brachial Index and Carotid Atherosclerotic Disease

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Abstract

Background: The association between the ankle brachial index (ABI) and the measurement of intimal medial thickness (IMT) has not been fully studied.

Objective: We aimed to evaluate whether the prevalence of carotid atherosclerosis was higher in patients with ABI ≤ 0.9 than in those with ABI > 0.9.

Methods: From January 2011 to December 2011, 118 patients (48 men and 70 women) were enrolled. ABI and IMT Measurements were performed in all patients. Patients were divided in Group 1 (ABI ≤ 0.9) and Group 2 (ABI > 0.9) according to ABI values. Mann-Whitney, Chi-square and Fischer tests were used for comparison among the groups. Pearson's correlation was used to assess correlation between ABI and IMT.

Results: The prevalence of ABI ≤ 0.9 was 29.7%, whereas carotid atherosclerosis ≥ 1.5 mm was 34.7 %. Clinical characteristics were similar between groups 1 and 2: mean age (64 ± 9 vs. 62 ± 7.2 years, p = 0.1), male gender (40% vs. 41%, p = 0.9), hypertension (74% vs. 59%, p = 0.1), diabetes mellitus (54% vs. 35%, p = 0.051), dyslipidemia (26% vs. 24%, p = 0.8), smoking (57% vs. 65%, p = 0.4). The prevalence of carotid atherosclerosis was higher in group 1 (48.6% vs. 28.9%, p = 0.04). Pearson's correlation between ABI and IMT was -0.235, with a p value = 0.01.

Conclusion: Patients with ABI ≤ 0.9 showed a higher prevalence of carotid atherosclerosis. There was a negative correlation between ABI and IMT (Arq Bras Cardiol. 2013; 100(5):422-428).

Keywords: Ankle Brachial Index; Carotid Artery Diseases; Ultrasonography / methods.

Introduction

Atherosclerosis is a disease that affects the arterial system in a chronic and systemic way, caused by an inflammatory response together with immune reactions[1]. It occurs from the earliest stages of life, resulting from genetic predisposition and exposure to risk factors that cause endothelial dysfunction[2,3].

Peripheral arterial disease (PAD) refers to atherosclerosis-induced alterations in the wall of the aorta and its branches, with the exception of the coronary arteries. The current concept of PAD is established by non-invasive tests, such as the ankle-brachial index (ABI) and the intima-media complex measurement (IMCM), even before the onset of any clinical symptoms[4]. The abnormal ABI indicates obstructive impairment of lower-limb arteries and is associated with risk of cardiovascular events (CVE), especially acute myocardial infarction (AMI) and cerebrovascular accident (CVA), regardless of other risk factors[5-7].

Thickening of the carotid wall, diagnosed by B-mode ultrasound, represents a subclinical vascular alteration, which may progress to atherosclerosis. The numerical value of the IMCM of the carotid arteries is used for risk stratification of CVE[8,9].

The measurements of the ABI and the intima-media complex (IMC) are low-cost, reproducible and have no associated risks. Both are considered as reference for the diagnosis of atherosclerosis. The ABI evaluates the involvement of the lower limbs, whereas the IMCM assesses carotid artery disease. The association between these measures is described, suggesting an inverse relationship and additionally, they can be used as independent markers for CVE[10,11].

The primary objective of this study was to evaluate whether patients with ABI ≤ 0.9 had a higher prevalence of carotid atherosclerosis when compared to those with index > 0.9. Secondary objectives were to analyze the association between ABI and IMC thickening, as well as verify possible correlations between the numerical values of ABI and the IMCM.

Methods

The study followed the ethical principles of the Declaration of Helsinki (WMA, 2000) and decree 196/96 of the National Health Council (CNS, 1996) and was approved by the Ethics Committee on Human Research of the institution, on April 20, 2011 according to protocol #426/2010.

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Study design

Prospective, cross-sectional, analytical study with recruitment period set between May and December 2011.

Inclusion criteria

Patients aged 50 to 69 who were diabetic and/or smokers, or those older than 70 years regardless of risk factors, were included. All patients signed the informed consent form.

Exclusion criteria

Exclusion criteria were: advanced malignancy, percutaneous or surgical revascularization of lower limb arteries or carotid arteries, terminal liver disease, technical impossibility of measuring the ankle-brachial index or carotid intima-media complex, patients submitted to limb amputation and ABI > 1.4.

Study population

A total of 118 patients treated at the outpatient clinic specialized in cardiovascular surgery of a tertiary hospital and who met the inclusion criteria and had no exclusion criteria of the study were enrolled between April and December 2011.

Statistical Analysis

To compare the groups (ABI> 0.9 *vs*. ABI ≤ 0.9) regarding qualitative variables, the Pearson's Chi-square test or Fisher's exact test were applied, when necessary. To compare the quantitative IMCM variables in the common carotid (IMCM-CC), in the internal carotid (IMCM-IC), in the external carotid (IMCM-EC) and overall (IMCM-OV), which was the maximum among all values, the nonparametric Mann-Whitney test was applied due to the non-normality of these variables. When quantitatively comparing ABI values with the measurements of intima-media complex in the carotid artery, a correlation analysis using Pearson's correlation coefficient was performed.

Statistical calculations were performed using SPSS for Windows release 18.0 - Statistical Package for the Social Sciences.

Ankle-brachial index protocol

ABI was measured using Doppler sonar equipment, model DV 610 (Medmega) and a sphygmomanometer with a 12-cm wide cuff, of which length varied from 29 to 40 cm. All measurements were performed with the patient in the supine position after 10 minutes of rest, and the systolic pressure of the posterior tibial artery, of the dorsalis pedis artery and brachial artery were measured bilaterally. We divided the highest pressure in the ankle by the highest systolic pressure found in the brachial artery of the upper limbs, thus obtaining the ABI[12,13].

The normal values for the ABI are between 0.9 and 1.4. Thus, indices > 1.4 represent non-compression of arteries and an index ≤ 0.9 demonstrate the presence of peripheral arterial disease (PAD)[12].

Carotid intima-media complex measurement protocol

The measurement of intima-media complex was performed using ultrasound equipment model Medison X8 with a linear array transducer of 7.5 to 12 MHz. The common carotid artery was assessed bilaterally using automatic software (auto-IMT ™) and the internal and external carotid arteries were also assessed bilaterally through manual measurements.

The field depth was 30-40 mm. There was adjustment of gain with little intraluminal artifact, harmonic signals were not used and the cardiac cycle was monitored through ECG coupled to the image for verification at the end of diastole[14-16].

A double line, representing the three layers of the arterial wall, was observed in the posterior wall of arteries. The first line is the interface between blood and the intima layer (anechoic lumen and echogenic intima), whereas the second line represents the interface between the media and adventitia layers (hypoechoic media and echogenic adventitia)[17].

IMC thickening occurs between ≥ 0.9 mm and < 1.5 mm, but when the measurement is ≥ 1.5 mm, it is considered atherosclerotic plaque[18].

Study flow chart

Patients were divided into 2 groups: group 1 comprised those who had ABI ≤ 0.9 and group 2 had ABI > 0.9. The clinical variables, the IMCM and the prevalence of carotid plaque were compared between the groups. We tested the possibility of a linear correlation between the numerical values of the IMCM and the ABI.

For the purpose of analysis, we considered the IMCM of the common, internal and external carotid arteries. Measures of right and left were collected from each territory, but the highest value was considered for the statistical analysis. Maximum IMCM was defined as the highest value found, regardless of the carotid artery that was assessed.

Results

During the study period, 362 patients were treated at the vascular surgery outpatient clinic. Of these, 118 (32.5%) patients met the inclusion criteria and showed none of the exclusion criteria and were enrolled in the study. The prevalence of ABI ≤ 0.9 was 29.7% (35 patients), whereas ABI > 0.9 was found in 70.3% of them (83 patients). The IMCM ≥ 0.9 occurred in 69.5% of patients and carotid atherosclerotic plaque in 34.7% of them.

Table 1 shows there was no difference in the clinical profile between groups. However, the prevalence of ABI ≤ 0.9 was higher in patients aged ≥ 70 years (Table 2). The comparison between the groups showed that in group 1 (ABI ≤ 0.9) IMCM was higher in the internal carotid [1.4 mm (max: 0.6 mm - min: 3.5 mm) *vs*. 1 mm (max: 0.5 mm - min: 3.8 mm), p = 0.04] and external carotid [0.7 mm (max: 0.5 mm - min: 3.2 mm) *vs*. 0.6 mm (max: 0.4 mm - min: 2.3 mm), p = 0.047]. The highest IMCM was observed in patients with ABI ≤ 0.9 [1.4 mm (max: 0.7 mm - min: 3.5 mm) *vs*. 1 mm (max: 0.6 mm - min: 3.8 mm), p = 0.01) (Table 3).

Table 1 – Comparison of ankle-brachial index groups according to clinical variables

Variables	Total	ABI > 0.9 (n = 83)	ABI ≤ 0.9 (n = 35)	p-value
Sex				
Male	48	34 (70.8%)	14 (29.2%)	0.922
Female	70	49 (70.0%)	21 (30.0%)	
SAH				
No	43	34 (79.1%)	9 (20.9%)	0.116
Yes	75	49 (65.3%)	26 (34.7%)	
DM				
No	70	54 (77.1%)	16 (22.9%)	0.051
Yes	48	29 (60.4%)	19 (39.6%)	
DLP/Cholesterol				
No	89	63 (70.8%)	26 (29.2%)	0.852
Yes	29	20 (69.0%)	9 (31.0%)	
DLP – Trig				
No	88	62 (70.5%)	26 (29.5%)	0.962
Yes	30	21 (70.0%)	9 (30.0%)	
Smoking				
No	44	29 (65.9%)	15 (34.1%)	0.417
Yes	74	54 (73.0%)	20 (27.0%)	
AC				
Normal	39	29 (74.4%)	10 (25.6%)	0.502
Altered	79	54 (68.4%)	25 (31.6%)	
BMI				
Normal	38	29 (76.3%)	9 (23.7%)	0.607
Overweight	48	32 (66.7%)	16 (33.3%)	
Obesity	32	22 (68.8%)	10 (31.3%)	

ABI: Ankle-Brachial Index; SAH: Systemic Arterial Hypertension; DM: Diabetes mellitus; DLP/Cholesterol: Dyslipidemia – Cholesterol; DLP-Trig: Dyslipidemia – triglycerides; AC: Abdominal Circumference; BMI: Body Mass Index.

Table 2 - Prevalence of abnormal ABI according to patient age range

Variables	Total	ABI > 0.9 (n = 83)	ABI ≤ 0.9 (n = 35)	p-value
Age range				
50 – 59 years	41	34 (82.9%)	7 (17.1%)	0.021
60 – 69 years	37	27 (73.0%)	10 (27.0%)	
≥ 70 years	40	22 (55.0%)	18 (45.0%)	

ABI: Ankle-Brachial Index.

The prevalence of atherosclerotic plaque was 48.6% (17 patients) in patients with ABI ≤ 0.9 and 28.9% (24 patients) in those with ABI > 0.9 (p = 0.04). Pearson's correlation between ABI and maximum IMCM was - 0.234, with p value = 0.01 (Chart 1).

Discussion

Our study showed that patients with ABI ≤ 0.9 had higher IMCM of internal and external carotid arteries, as well as the maximum value of the IMCM in the carotid territory. It is also noteworthy that the prevalence of carotid atherosclerosis was higher in patients with abnormal ABI.

Table 3 – Comparison of groups according to ABI measurements of intima-media complex

	ABI	N	Median	Min	Max	p-value
COMMON CA IMCM	> 0,9	83	0.790	0.510	2.600	0.857
	≤ 0,9	35	0.850	0.590	1.110	
	Total	118	0.800	0.510	2.600	
INTERNAL CA IMCM	> 0,9	83	1.000	0.500	3.800	0.045
	≤ 0,9	35	1.400	0.600	3.500	
	Total	118	1.050	0.500	3.800	
EXTERNAL CA IMCM	> 0,9	83	0.600	0.400	2.300	0.047
	≤ 0,9	35	0.700	0.500	3.200	
	Total	118	0.600	0.400	3.200	
MAXIMUM IMCM	> 0,9	83	1.000	0.600	3.800	0.018
	≤ 0,9	35	1.400	0.700	3.500	
	Total	118	1.200	0.600	3.800	

ABI: ankle-brachial index; IMCM: intima-media complex measurement; CA: carotid artery.

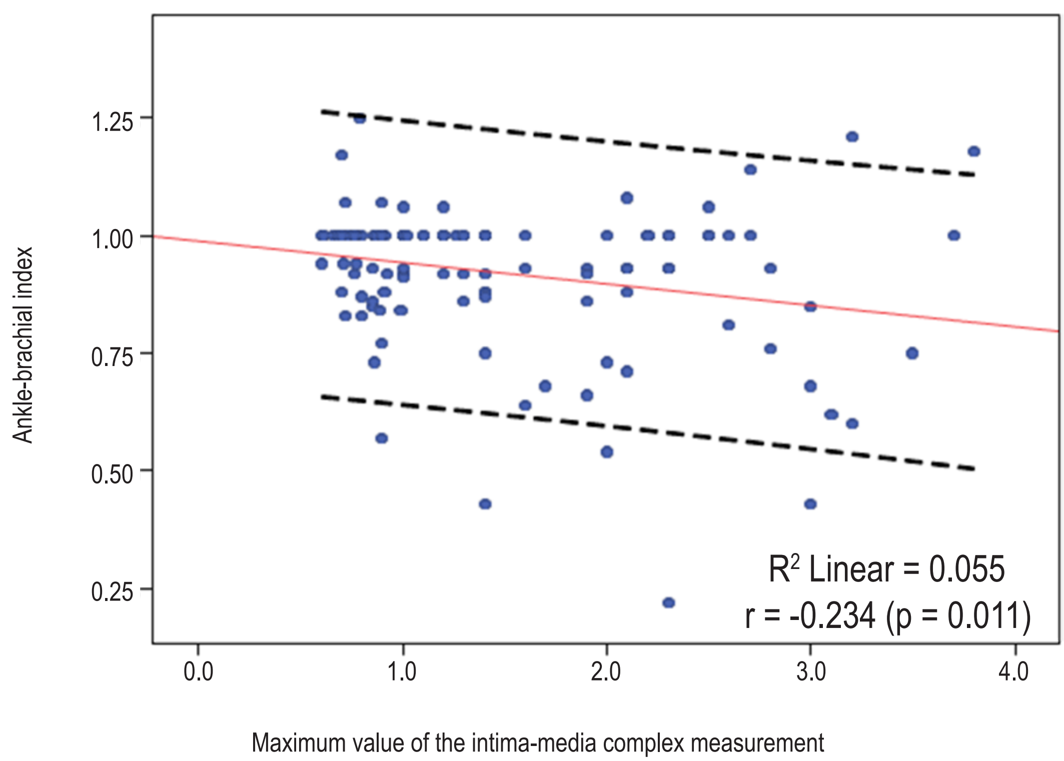

Chart 1 – *Correlation between ankle-brachial index and maximum value of the intima-media complex measurement.*

The ABI is the product of a quantitative reduction in systolic blood pressure in the lower limbs caused by proximal atherosclerotic occlusion[5]. At first, it is thought that it occurs in the advanced stages of atherosclerosis. However, although the atherosclerotic disease is systemic, there are local vascular factors that may perhaps influence atheroma accumulation and vessel obstruction[19]. On the other hand, the thickening of the intima-media complex is considered a marker of premature atherosclerosis and a predictor of cardiovascular disease risk[20-22]. Serial temporal evaluations studies of ABI and IMCM values might explain several aspects of these tests, as well as atherosclerotic disease in peripheral vascular territories.

Researchers have studied the ABI and the IMCM and in this context, Allan et al[23] evaluated 1,106 patients aged 55 to 74 years, included in the Edinburgh Artery Study and searched for associations between ABI and IMCM. They observed that the IMCM was higher in men and that older patients had higher intima-media complex values. There was a negative linear correlation between ABI and IMCM ($r = -0.116$, $p = 0.06$). Patients with ABI ≤ 0.9 had higher IMCM than those with ABI > 0.9 [0.87 mm (0.83 mm - 0.91 mm) *vs*. 0.8 mm (0.79 mm - 0.82 mm) P = 0.01]. In the subgroup of patients with claudication, the numerical values of the IMCM were higher [(0.90 mm (0.85 mm - 0.95 mm)][23].

Two other studies also showed that patients with ABI ≤ 0.9 had higher IMCM when compared to those with ABI > 0.9 [24,25]. Our findings of higher IMCM in patients with ABI ≤ 0.9 are consistent with the studies described above. However, our IMCM values were higher than those of the aforementioned studies and we believe that this fact is justified because we recruited patients with higher-risk clinical profile for advanced peripheral atherosclerotic disease.

It is noteworthy that according to the literature, patients with more advanced PAD, i.e. with claudication, had higher IMCM values than the general population[26]. We believe that patients with significant obstruction of the lower limb arteries have more advanced atherosclerosis and, therefore, have a greater chance of having higher IMCM and a higher prevalence of carotid plaque.

Two decades ago, the Rotterdam Study[10], which included patients from the general population aged > 55 years, showed that the prevalence of ABI < 0.9 was 11.9% and that the increase of 0.1 mm in MCMI was associated with a reduction of 0.026 of the ABI and that patients with claudication had lower ABI values and higher values of IMCM, when compared to individuals without such symptoms.

Our study, in which the prevalence of abnormal ABI was 29.7%, showed a negative linear correlation between the IMCM and the numerical value of ABI. This finding supports the hypothesis suggested over 20 years ago by the researchers of the Rotterdam study.

The study by Parv et al[27] had already found a negative linear correlation between ABI and the IMCM ($r = -0.157$). However, our numerical "r" value of the correlation was higher and we believe that the severity of peripheral arterial disease in our group can be one of the factors that justify such finding.

Based on the concept that the ABI decreases with the progression of lower-limb proximal obstructions and IMCM increases with the progression of carotid atherosclerosis, one would expect to find a negative linear correlation between these two measures. This correlation was found in our study.

The literature shows only a suggestion of a negative linear correlation between ABI and IMCM[23], and thus, it is possible that this is present only in certain subgroups of patients and/or phases of atherosclerosis. Therefore, we infer that such correlation may be present in patients with more advanced atherosclerosis.

When the IMCM value is ≥ 1.5 mm, the atherosclerotic plaque is assumed to be present in the carotid arteries[18]. This finding is associated with an increased chance of myocardial infarction and CVA in these patients[28]. Patients with ABI ≤ 0.9 in our study had a higher prevalence (close to 50%) of atherosclerotic plaque, when compared to those with normal ABI.

The main limitations of our study are: the need to choose a normal IMCM value, as there is no consensus in the literature; the absence of controls from the general population, which would allow the assessment of different stages of atherosclerosis; the lack of serial temporal assessment of ABI and IMCM; no possibility of probabilistic sample calculation, as there is no consensus on the prevalence of carotid atherosclerotic plaque diagnosed by Doppler ultrasound in diabetics and/or smokers with ABI ≤ 0.9. It should be noted that it is possible, based on the prevalence rates of carotid atherosclerosis found in our study, to develop studies with similar sample size calculation.

Conclusions

Our study showed that the prevalence of PAD in the study population is high, which is consistent with the literature. In addition, ABI ≤ 0.9 is related to the higher prevalence of thickening and atherosclerotic plaque in the carotid arteries and there is an inverse association between these two measures.

Author contributions

Conception and design of the research: Brasileiro ACL, Oliveira DC, Victor EG, Oliveira DAGC; Acquisition of data: Brasileiro ACL, Oliveira DC, Oliveira DAGC, Batista LL; Analysis and interpretation of the data: Brasileiro ACL, Oliveira DC, Victor EG; Statistical analysis, Obtaining funding and Writing of the manuscript: Brasileiro ACL, Oliveira DC; Critical revision of the manuscript for intellectual content: Brasileiro ACL, Oliveira DC, Victor EG, Batista LL.

Potential Conflict of Interest

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

Sources of Funding

There were no external funding sources for this study.

Study Association

This article is part of the thesis of master submitted by Augusto Cezar Lacerda Brasileiro, from Universidade Federal de Pernambuco.

Erratum

The version of Association between Ankle-Brachial Index and Carotid Atherosclerotic Disease published as ahead of print by Arquivos Brasileiros de Cardiologia underwent the following modification as required by the Author: replace the name José Laercio Leitão by Laecio Leitão Batista.

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