

Ankle-brachial index as a predictor of coronary disease events in elderly patients submitted to coronary angiography

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OBJECTIVES: To correlate the importance of the ankle-brachial index in terms of cardiovascular morbimortality and the extent of coronary arterial disease amongst elderly patients without clinical manifestations of lower limb peripheral arterial disease.

METHODS: We analyzed prospective data from 100 patients over 65 years of age with coronary arterial disease, as confirmed by coronary angiography, and with over 70% stenosis of at least one sub-epicardial coronary artery. We measured the ankle-brachial index immediately after coronary angiography, and a value of <0.9 was used to diagnose peripheral arterial disease.

RESULTS: The patients' average age was 77.4 years. The most prevalent risk factor was hypertension (96%), and the median late follow-up appointment was 28.9 months. The ankle-brachial index was <0.9 in 47% of the patients, and a low index was more prevalent in patients with multiarterial coronary disease compared to patients with uniarterial disease in the same group. Using a bivariate analysis, only an ankle-brachial index of <0.9 was a strong predictive factor for cardiovascular events, thereby increasing all-cause deaths and fatal and non-fatal acute myocardial infarctions two- to three-fold.

CONCLUSION: In elderly patients with documented coronary disease, a low ankle-brachial index (<0.9) was associated with the severity and extent of coronary arterial disease, and in late follow-up appointments, a low index was correlated with an increase in the occurrence of major cardiovascular events.

KEYWORDS: Peripheral Artery Disease; Prognosis; Coronary artery Disease; Ankle Brachial Index; Elderly.

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INTRODUCTION

Peripheral Arterial Disease of the lower limbs (PAD) is a prevalent form of atherosclerotic disease. It has been estimated that in both North America and Europe, PAD affects approximately 27 million people, representing 16% of the North American population over 55 years of age (1).

Longevity is a risk factor for the development of PAD

Data from the National Health and Nutrition Examination Survey (NHANES) indicate that PAD prevalence among people over 70 years of age is three times higher compared

to patients 40–70 years of age (14.5% and 4.3%, respectively) (2).

The coexistence of PAD with Coronary Arterial Disease (CAD) and cerebrovascular disease (CVD) is well known. The REACH trial, which involved elderly patients with CAD, CVD and symptomatic or asymptomatic PAD with three or more atherothrombotic risk factors, demonstrated that 70% of patients with PAD have atherosclerotic disease in other vascular beds (3). According to Belch et al. (1), individuals with low ankle-brachial indices (ABIs) have twice the chance of presenting CAD compared to subjects with normal ABIs and have increased risks of fatal and nonfatal myocardial infarctions, stroke and cardiovascular mortality as well as increased overall mortality.

The ABI is a simple, non-invasive method used to diagnose PAD. Compared to lower limb arterial angiography, an ABI <0.9 has been shown to have a sensitivity of 90–97% and a specificity of 98–100% for detecting stenosis that affects the lumen in more than 50% of one or more leg arteries (4). Some studies have shown an association

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between the extent of CAD and PAD detected by ABI, regardless of the presence of symptoms (5), and it is known that the association between PAD and CAD increases all-cause mortality and the cardiovascular risk of these patients two- to three-fold (6). Additionally, in some cases, isolated PAD has been responsible for increased mortality compared to patients with isolated CAD or CVD (3).

Data from patients with suspected CAD who have been referred for coronary angiography indicated that PAD prevalence is high when evaluated by ABI (6,7).

Therefore, although we have examined a high-risk group of patients, elderly patients with documented CAD and no PAD manifestations, this study aims to evaluate the impact of ABI as a marker of cardiovascular events in these patients and to evaluate the relationship between ABI and the extent of CAD as documented by coronary angiography.

■ METHODS

During the study period, 425 coronary angiographies were performed in patients older than 65 years. Of these patients, 109 were evaluated, and 100 patients met the inclusion criteria. Therefore, we conducted a prospective observational cohort study of 100 consecutive patients aged ≥ 65 years who were asymptomatic for peripheral vascular disease and documented CAD by coronary angiography and who, immediately after hemodynamic investigation, were submitted to ABI determination and were followed for a mean period of 28.9 ± 6.6 months by either medical care or telephonic contact. Angiographic inclusion criteria were defined as a stenosis that was $\geq 70\%$ of the epicardial coronary artery in at least one vessel and/or greater than 50% of the left coronary branch. The extent of CAD was evaluated by the number of vessels involved: uniarterial when there was an isolated lesion in one coronary artery and multiarterial when evidence of CAD was present in two or more vessels. Hypertension was defined according to the criteria of the IV Brazilian Guidelines on Hypertension (a systolic blood pressure greater than or equal to 140 mmHg and a diastolic blood pressure greater than or equal to 90 mmHg with an associated cardiovascular risk factor) and/or use of antihypertensive medication (8). Diabetes mellitus was diagnosed using the criteria of the American Diabetes Association: two fasting glucose measurements greater than or equal to 126 mg/dl, an oral glucose tolerance test with a post-load value within the 2 hours that was greater than or equal to 200 mg/dl or a casual plasma glucose greater than or equal to 200 mg/dl (9). Dyslipidemia was defined as having plasma cholesterol levels greater than 240 mg/dl, low-density lipoprotein (LDL) cholesterol levels between 160 and 189 mg/dl and high-density lipoprotein (HDL) cholesterol levels < 40 mg/dl, according to the III Brazilian Guidelines on Dyslipidemia and Atherosclerosis Prevention (10). Smoking was assessed (current smoker or former) regardless of smoking history. We considered the following items as major cardiovascular events (MACE) to be prospectively studied: all-cause mortality, fatal and non-fatal myocardial infarction (MI) and stroke (transient or not).

All patients included in the study were outpatients who were cared for in the Cardiogeriatrics Center at UNIFESP, and the patients who agreed to take part in the study signed an informed consent document. This study was approved by the ethics and research committee of the Universidade

Federal de São Paulo in accordance with the 1975 Helsinki Declaration and was registered as CEP 1254/09.

We excluded elderly patients with a clinical history of intermittent claudication, patients who had no significant coronary atherosclerotic disease after cardiac catheterization angiography, patients with an ABI ≥ 1.3 (non-compressible arteries), patients with decompensated heart failure and/or significant edema in their lower limbs, patients with amputation and patients who refused to participate in the study (11–13). The same physician (EDEP) performed all of the clinical evaluations and ABI measurements; at the inclusion of patients in the study, the physician did not know the specific results of the coronary angiography and the extent of coronary disease in each patient. However, the physician did know that all of the patients would have significant coronary disease.

Ankle-brachial index measurements

The ABI was measured using a portable vascular Doppler scanning MEDPEJ® (São Paulo, Brazil) 10 Mhz DV 2001 model and a BIC® aneroid sphygmomanometer (São Paulo, Brazil) with appropriate cuff inflators for brachial circumference, in accordance with international standards (11).

During physical examination, the right arm circumference was measured at the mid-point between the acromion and the olecranon, and an appropriate cuff was selected. After a least a 5-minute rest, the systolic pressures of the upper (brachial) and lower (tibial posterior and dorsalis pedis) limbs were measured in the supine position, initially taking measures of the right superior member and, in sequence, the left superior member, left inferior member and right inferior member. The ABI of each inferior member was calculated by dividing the highest systolic pressure at the ankles by the highest systolic pressure of the upper arms. The lowest value obtained was validated for analysis, and according to the ABI value, PAD was classified as: severe (≤ 0.5), moderate (0.51–0.7), mild (0.71–0.9), and without PAD (greater than or equal to 0.9). A pathological ABI was considered to be a value < 0.9 (11,12).

Patients with an ABI of 1.3 or more (noncompressible arteries) (13), an acute decompensated heart failure and/or significant lower limb edema and an inferior member amputation as well as those who refused to participate in the study were not analyzed.

Statistical analysis and descriptive statistics

Quantitative data were described as the means and standard deviations (SD). The cutoff for the ABI was < 0.9 for PAD diagnosis, taking into consideration values in the literature as references (11,12). Taking into account the characteristics of our sample, we assumed that we would have a 6% yearly event rate in patients with ABIs < 0.9 and a 1% event rate in patients with normal ABIs.

ABI analysis

We evaluated possible ABI predictors (as a dichotomized variable) with bivariate analysis using the chi-square test or Fisher test.

The continuous variable (age) in relation to ABI was evaluated using Student's t-test for independent samples and the Kolmogorov-Smirnov test when necessary to determine whether the age followed a normal distribution.



The strength of association was measured using the Relative Risk (RR) with a 95% confidence interval (CI).

For the bivariate analysis, we considered a 10% significance level to be significant if more than one isolated tested variable was identified. A Poisson Regression model with an estimated RR was used to evaluate the combined occurrence of highest systolic blood pressure as a continuous variable and multiarterial disease events.

Analysis of clinical events

We evaluated possible clinical event predictors (deaths, acute myocardial infarction [AMI], hospital admissions, MACE) with a bivariate analysis using the chi-square test or the Fisher Test.

The continuous variable (age) was evaluated in relation to the ABI using Student's t-test for independent samples and the Kolmogorov-Smirnov test when necessary.

Time elapsed between the PAD diagnosis and occurrence of MACE, and AMI was estimated calculating the last patient contact date minus the PAD diagnosis date for patients with no events. For patients with events, we determined the time considering the event occurrence date and the PAD diagnosis date. When the event date was uncertain, we considered the last patient contact date as the event date.

We used the time elapsed between the PAD diagnosis and the occurrence of MACE and AMI to obtain event-free survival curves using the Kaplan-Meier method. We compared the survival curves in relation to the ABI risk using the Log-Rank test.

RESULTS

There were no significant hematomas or systemic complications after cardiac catheterization that would have interfered with the ABI measurements. In our sample ($n=100$) there was a predominance of women (57%) and the average age was 77.4 years old (SD 6.7 years), ranging from 65 to 93 years, and the risk factor with the highest prevalence was hypertension (96%). The medium value for the ABI was 0.88 (SD 0.26), and we diagnosed PAD in 47% of the patients. The demographic characteristics of the population studied are presented in Table 1. The mean systolic blood pressure in the PAD group was higher than in the group without PAD ($p<0.001$), and after applying two correlation coefficients, we noted a significant negative correlation between systolic blood pressure and $ABI<0.9$, which is expected because the calculation of ABI is always inversely proportional to the systolic blood pressure. The prevalence of hypertension was high in both groups, among both patients with PAD (100%) and those with a normal ABI (94.3%). The drugs that were used in this study are shown in Table 1. There was a higher proportion of patients without PAD using calcium blockers (32.2% and 13.3%, $p=0.024$); Acetylsalicylic acid was the most frequently prescribed medication in both groups, followed by statins, beta blockers, ACE inhibitors, diuretics, oral hypoglycemics, ARBs, insulin, fibrates and antiplatelet agents, with no difference between groups with PAD and without PAD. Chronic renal failure, defined by a plasma creatinine level greater than 2.0, was not associated with reduced ABI, as shown in Table 1.

The extent of CAD was evaluated according the number of coronary arteries involved and revealed a high prevalence of

multiarterial patients in the PAD group compared to uniaxial patients of the same group. However, there was a high prevalence of uniaxial patients without PAD (Table 1). Thus, we observed that the more severe the CAD, the lower the ABI with higher PAD prevalence. In fact, in multiarterial patients, the ABI medium value was significantly lower compared to uniaxial patients. (0.8 ± 0.2 and 1.0 ± 0.3 , respectively, $p=0.047$).

Data analysis indicated that the presence of multiarterial coronary disease is a risk factor for PAD development, with a two-fold increase (RR=2.19, CI 95%=1.27-3.77).

Over a mean period of 28.9 months (SD 6.6 months), we performed late follow-up assessments on all of the 100 patients who were part of the trial since the trial began. There were 17 major events with 11 deaths (11%), 9 by cardiovascular causes (8 by acute myocardial infarction [AMI], 1 by myocardial revascularization surgery complication), 1 by acute cholecystitis (sepsis) and 1 patient by an undetermined cause. Most deaths occurred in the PAD group. AMI was the main cause of death and was more frequent among patients with PAD, as demonstrated in Table 1.

The average annual event rate was greater than 10%. Mortality in the PAD group was higher for both overall and cardiovascular causes. There was also a higher incidence of stroke in this group (6%) compared to the normal ABI group, where there was no stroke. For non-fatal events, there was no significant difference between patients with or without PAD. However, MACE incidence was higher in PAD patients (Table 1).

An $ABI<0.9$ was the most important factor for all-cause mortality with a three-fold increased risk (RR 3.01; CI 95% 0.91-9.55). Additionally, a low ABI was a strong predictor for AMI and MACE, as shown in Table 2. Even correcting for the statistically significant difference between normal *versus* low ABI and the presence of multivessel coronary disease, the relationship between ABI and MACE remained. Thus, adjusting the analysis for single-vessel or multivessel disease did not significantly modify the RR (original RR 2.71 [95% CI 1.03 to 7.12] and corrected RR 2.90 [95% CI 1.11 to 7.62], as shown in Table 4).

An event-free survival curve analysis (MACE and AMI - Figures 1 and 2, respectively) indicated that the time elapsed between PAD diagnosis and the occurrence of MACE and AMI was shorter in the PAD group, as shown in Table 3.

DISCUSSION

In this study, which involved elderly patients consecutively selected accordingly to coronary cineangiography and with obstructive lesions greater than 70% in at least one epicardial vessel, we found that 47% of these patients had low ABIs. Similarly, a high prevalence of PAD measured by the ABI has been reported in studies focusing on both populations at high risk for PAD and primary care patients. Poredos and Jug (14) correlated 42% of PAD prevalence in elderly patients (with an average age of 63.7 years) with CAD or cerebrovascular disease. In a study regarding acute coronary syndrome, Nuñez et al. (5) reported that approximately 40% of the studied subjects (with an average age of 67.7 years) had an $ABI\leq 0.9$. The high average age of the patients included in our study (77.4 years) was higher than the described series and may partially explain the high prevalence of PAD we detected using the ABI, as this is a



Table 1 - Demographic and angiographic characteristics and the incidence of cardiovascular events in patients with and without PAD.

Variables	PAD (ABI<0.9)	No PAD	p-value
	(n = 47)	(n = 53)	
Age, years (mean ± standard deviation)	77.8 ± 6.6	77.1 ± 8.1	0.524
Blood pressure, mmHg (mean ± standard deviation)			
Systolic blood pressure	158.34 ± 18.75	143.96 ± 20.45	<0.001
Diastolic blood pressure	83.40 ± 7.15	83.00 ± 5.66	0.753
Women, n (%)	29 (61.7%)	28 (52.8%)	0.371
Men, n (%)	18 (38.3%)	25 (47.2%)	
Hypertension, n (%)	47 (100%)	50 (94.3%)	0.245
Diabetes Mellitus, n (%)	20 (37.7%)	19 (40.4%)	0.783
Smoking (current or former) n (%)	15 (31.9%)	15 (28.3%)	0.694
Chronic Renal failure (Creatinine > 2.0)	6 (12.8%)	5 (9.4%)	0.595
CAD extent – uniarterial, n (%)	8 (17%)	23 (43.4%)	0.004
CAD extent – multiarterial, n (%)	39 (83.0%)	30 (56.6%)	
Drugs n (%) Nitrate	17 (32.1%)	16 (34.1%)	0.835
Calcium antagonists	7 (13.3%)	15 (32.2%)	0.024
Statins	44 (83.1%)	44 (93.7%)	0.104
Beta-blockers	44 (83.1%)	35 (74.5%)	0.295
Angiotensin (IECA)	37 (69.9%)	32 (68.1%)	0.852
Diuretics	29 (54.8%)	32 (68.1%)	0.171
Acetylsalicylic acid	49 (92.5%)	44 (93.7%)	1.000
Oral hypoglycemic	11 (20.8%)	11 (23.5%)	0.750
Insulin	4 (7.6%)	6 (12.8%)	0.509
ARBs	8 (15.1%)	11 (23.5%)	0.290
Fibrates	2 (3.8%)	3 (6.4%)	0.664
Antiplatelets	2 (3.8%)	3 (6.4%)	0.664
Death, n (%)	8 (17%)	3 (5.7%)	0.070
Acute myocardial infarction, n (%)	9 (19.1%)	4 (7.5%)	0.085
Stroke, n (%)	3 (6.4%)	0	0.100
MACE n (%)	12 (25.5%)	5 (9.43%)	0.032

Age (mean ± standard deviation) of patients with or without Peripheral Arterial Disease of the lower limbs (PAD). Major cardiovascular events (MACE); Coronary Arterial Disease (CAD). Student's t-test was used for the variable age (years). The chi-square test was used for the variables gender, diabetes mellitus, smoking, CAD extent (uniarterial or multiarterial), death, acute myocardial infarction, stroke and MACE. The Fisher test was used to analyze hypertension. The chi-square test was used to analyze chronic renal failure. Drugs were analyzed by the chi-square test or Fisher's exact test. Student's t-test was used to analyze blood pressure.

Table 2 - Analysis of the incidence of death, fatal and non-fatal acute myocardial infarction and major cardiovascular events related to cardiovascular risk factors and the presence of peripheral arterial disease (PAD) evaluated by the ankle-brachial index.

	RR	CI 95%	p-value
Death			
PAD (ABI<0.9)	3.01	0.91–9.55	0.070
Gender (female)	1.32	0.41–4.22	0.637
Diabetes mellitus	1.30	0.43–3.98	0.642
Smoking	1.33	0.42–4.26	0.625
Fatal and non-fatal AMI			
PAD (ABI<0.9)	2.54	0.87–7.36	0.085
Gender (female)	1.21	0.42–3.44	0.723
Diabetes mellitus	1.34	0.48–3.71	0.571
Smoking	1.46	0.51–4.13	0.475
MACE			
PAD (ABI<0.9)	2.70	1.08–6.77	0.032
Gender (female)	1.38	0.55–3.43	0.481
Diabetes mellitus	1.09	0.45–2.65	0.840
Smoking	1.27	0.51–3.16	0.601

Relative risk values (RR), confidence interval (CI) and p-value. The chi-square test was used for the variables gender, diabetes mellitus and smoking. The presence of Peripheral Arterial Disease (PAD) was considered to have an ankle-brachial index of <0.9. Bivariate analysis was performed using the chi-square test or Fisher's exact test to evaluate possible ABI predictors.

well-known correlation both in the general population and in patients with documented PAD (2,3,5,20).

Major cardiovascular risk factors for CAD are usually the same for PAD. Nonetheless, some authors suggest that there are more specific strong risk factors associated with atherosclerosis in certain vascular beds, such as smoking and PAD, hypertension and cerebrovascular disease as well as dyslipidemia associated with PAD (14). In our study, there was no difference between the prevalence of risk factors in PAD patients and patients with CAD only (Table 1). This observation could be partially explained by the fact that we studied a group of patients with a high risk for cardiovascular events. Additionally, at the time of inclusion, all patients were adequately medicated, and any risk factors, such as smoking, were well controlled. As such, only 20% of the patients were smokers at the beginning of our study.

The evaluation of coronary cineangiography data from this study indicated that patients with a low ABI (<0.9) have a higher prevalence of multiarterial coronary disease compared to uniarterial patients. Additionally, an ABI<0.9 was independently related to the extent of CAD, as measured by the number of coronary arteries with obstructive CAD that were detected in the coronary angiography. Similarly, Sukhija et al. (7,16) analyzed patients with an average age of 71 years who were submitted to coronary angiography for suspicion of CAD and evaluated them for PAD using the ABI. Following their



Table 3 - Time elapsed between the PAD diagnosis and the occurrence of major cardiovascular events (MACE) and acute myocardial infarction (AMI).

	Time (years)	CI 95%	p-value
MACE			
ABI≥0.9	3.05	(2.94–3.16)	0.022
ABI<0.9	2.73	(2.51–2.94)	
AMI			
ABI≥0.9	3.07	(2.97–3.17)	0.082
ABI<0.9	2.83	(2.63–3.03)	

Time (average, years); Major cardiovascular events (MACE); Ankle-brachial index (ABI); Confidence interval (CI); Acute myocardial infarction (AMI). Average time was estimated by the Kaplan-Meier method. The p-value was calculated by the Log-Rank test.

analysis, they reported a high prevalence of multiarterial patients (63%) in the PAD group and 11% of multiarterial patients without PAD ($p<0.001$). Among patients in this same population, it was noted that the lower the ABI measurements, the higher the prevalence of multiarterial and the lower the prevalence of uniarterial patients (84% and 5%, respectively, $p<0.001$).

Papamichael et al. (15), in a study on asymptomatic PAD patients, with an average age of 60 years, evaluated by ABI and submitted to elective coronary angiography demonstrated that a low ABI (≤ 0.9) was related to a greater extension of CAD, evaluated according to the number of coronary arteries with obstructive CAD (variance analysis, $p=0.04$) and to the Gensini score ($p=0.01$).

A late follow-up analysis in our study revealed that only a low ABI (<0.9) was a strong predictor of all-cause death (RR 3.01; CI 95%=0.91–9.95), AMI occurrence (RR 2.54; CI95%=0.87–7.36) and MACE incidence (2.70; CI 95%=1.08–6.77) when evaluated in relation to other risk factors.

In fact, Criqui et al. (17) demonstrated, for the first time, a six-fold increase in CAD mortality in elderly patients (with an average age of 66 years) with reduced ABI compared to patients with normal ABI. Subsequently, Newman et al. (18) also demonstrated an up to three-fold increase in CAD mortality in elderly individuals (with an average age of 77 years) with reduced ABI. Similarly, data from “The Cardiovascular Health Study” (19), which involved 5,888 patients at over 65 years of age, demonstrated that, after a six-year follow up, patients with a low ABI and prevalent cardiovascular disease exhibited a 50% increase in all-cause mortality and up to a 61% increase in fatal and non-fatal AMI when gender and age were adjusted.

Papamichael et al. also evaluated the ABI as a prognostic factor in elderly patients who were submitted to elective coronary angiography and diagnosed with extracoronary

atherosclerosis (carotid and/or femoral) (15); they concluded that an $ABI \leq 0.9$ was the only predictor of major cardiovascular events and revascularization procedures when adjusted for age, LDL and cholesterol levels, intimal-medial thickness and CAD extent.

Diehn et al. (20) concluded that symptomatic or asymptomatic PAD ($ABI \leq 0.9$) has been independently and significantly associated with mortality and major cardiovascular events, with an up to two-fold increase in their occurrences compared to elderly patients without PAD in primary care centers in Germany. Although we studied a group of patients with a high risk for cardiovascular events, that is, elderly patients with documented CAD, our conclusions were similar to those from the patients in primary care centers described in previous studies.

In our study, during late follow-up visits, we detected the presence of stroke in patients with low ABIs (6%); this pathology did not occur in patients with normal ABI. Murabito et al. (21) evaluated patients from the Framingham study, with an average age of 80 years, who were tested for PAD by ABI; most were asymptomatic for the condition (82%). In these patients, the authors also observed a higher prevalence of stroke among persons with PAD compared to patients with normal ABI (13% and 5%, respectively), with a two-fold increased risk of stroke or transitory ischemic stroke compared to patients with normal ABI. In fact, elderly population-based studies revealed a positive correlation between reduced ABI and the presence of carotid atherosclerosis (carotid stenosis or medio-intimal thickness increase) in addition to an increased stiffness of the aorta and the carotid arteries, a common condition in elderly patients with PAD (22).

This study had a few limitations, including the sample size and follow-up time. Although 100 elderly patients with PAD diagnosed by ABI and submitted to coronary angiography could not be regarded as a small casuistic, this sample size was not sufficient for more conclusive associations. In fact, the inclusion of patients after catheterization may have been a limiting factor for the evaluation of patients and may therefore have influenced the results. Furthermore, our follow-up time could have been longer; an increased follow-up time would contribute to an increased number of events and would strengthen our conclusions. However, we have not lost any patients to follow-up since their consecutive inclusion, which strengthens our sample power; additionally, we had more events than initially considered. Finally, the finding of an RR of 3.01 regarding the risk related to a low ABI was similar to findings reported in the literature, even though our starting point for patient selection was considerably different from previous studies.

In elderly patients with asymptomatic PAD and with documented CAD by coronary cineangiography, an $ABI < 0.9$ proved to be a predictor of global and vascular mortality, fatal and non-fatal AMI and stroke, with an up to

Table 4 - MACE analysis adjusting for confounding factors (ABI and multiarterial coronary disease).

Variable	Crude Analysis				Multivariate Analysis			
	RR	CI (95%)		p-value	RR	CI (95%)		p-value
Multiarterial	1.078	0.416	2.797	0.877	0.775	0.302	1.983	0.594
ABI	2.706	1.029	7.115	0.043	2.90	1.11	7.62	0.030

Relative risk values (RR), confidence interval (CI) and p-value. The confounding effect was assessed by regression models considering the Poisson distribution and Robust estimation, considering the RR (relative risk) given the study design. The p-value was estimated using the Poisson regression model.

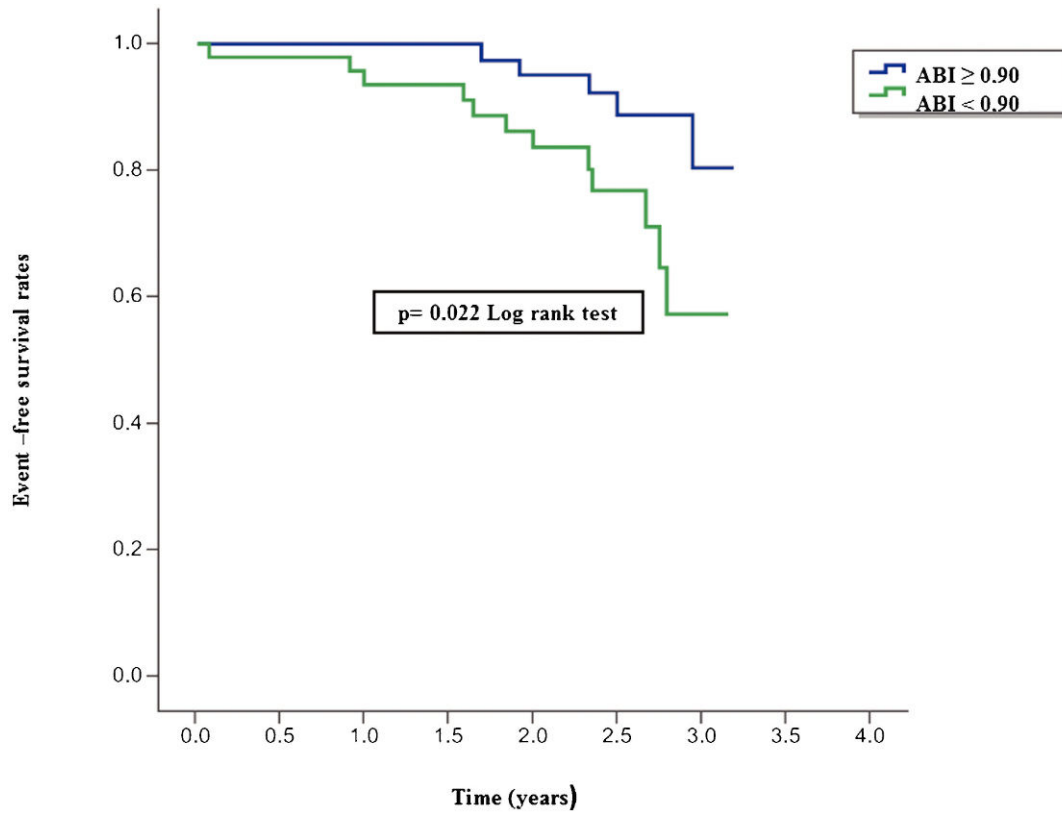


Figure 1 - Event-free survival by ABI categories. Kaplan-Meier estimates showing MACE during the follow-up visit.

three-fold increase compared to individuals without PAD. We also demonstrated that, in this cohort of patients, the lower the ABI value, the more extensive the CAD. Therefore, ABI could be a useful tool not only for early detection of PAD, a condition frequently underdiagnosed

on several levels of elderly care but also for the purpose of risk stratification among CAD patients. Those patients with reduced ABIs should undergo more aggressive cardiovascular management because these patients are part of a high-risk group for cardiovascular events and all-cause mortality.

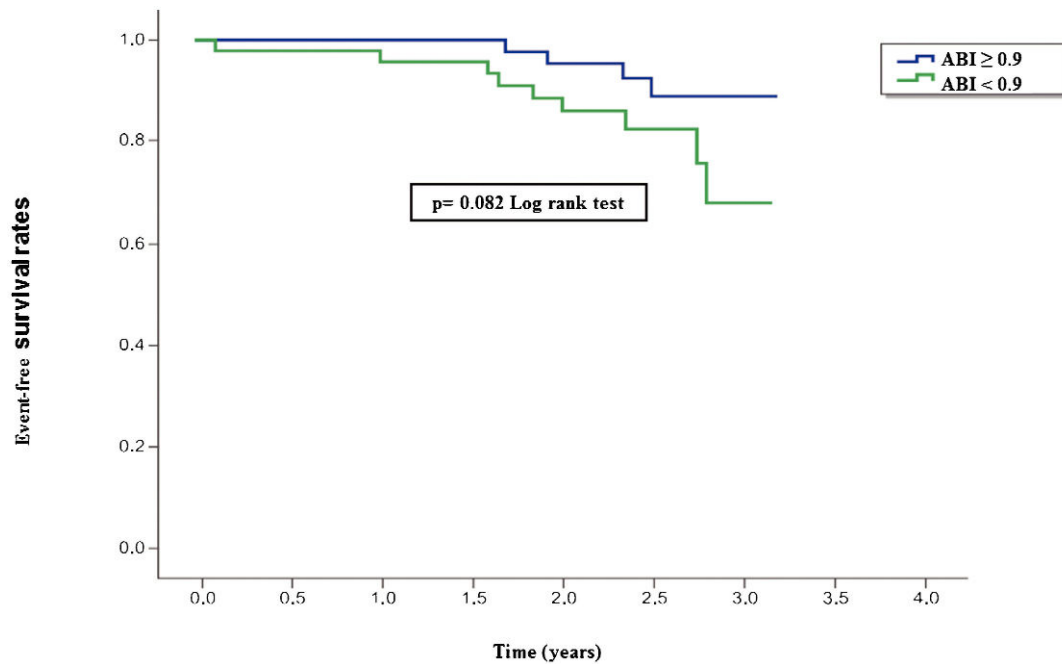


Figure 2 - Event-free survival by ABI categories. Kaplan-Meier estimates showing AMI during the follow-up visit.



AUTHOR CONTRIBUTIONS

Papa EDE conceived and designed the study, acquired data, analyzed and interpreted data and drafted the manuscript. Helber I, Erlichmann MR conceived and designed the study and analyzed data. Alves CM conceived and designed the study, analyzed data and performed coronary cineangiography. Makdisse M analyzed data. Mattos LN analyzed and interpreted data. Borges JL, Stefanini E analyzed data. Lopes RD critically reviewed the manuscript. Carvalho AC conceived and designed the study, analyzed and interpreted data and critically reviewed the manuscript.

REFERENCES

1. Belch JFF, Topol EJ, Agnelli G, Bertrand M, Califf RM, Clement DL, et al. Critical Issues in Peripheral Arterial Disease Detection and Management A call to action. *Arch Intern Med.* 2003;163(8):884-92, <http://dx.doi.org/10.1001/archinte.163.8.884>.
2. Selvin E, Erlinger TP. Prevalence of and risk factors for peripheral arterial disease in the United States: results from the National Health and Nutrition Examination Survey, 1999-2000. *Circulation.* 2004;110(6):738-43, <http://dx.doi.org/10.1161/01.CIR.0000137913.26087.F0>.
3. Eagle KA, Hirsch AT, Califf RM, Alberts MJ, Steg PG, Cannon CP, et al. Cardiovascular ischemic event rates in outpatients with symptomatic atherothrombosis or risk factors in the united states: insights from the REACH Registry. *Crit Pathw Cardiol.* 2009;8(2):91-7.
4. Doobay AV, Anand SS. Sensitivity and specificity of the ankle-brachial index to predict future cardiovascular outcomes: a systematic review. *Arterioscler Thromb Vasc Biol.* 2005;25(7):1463-9, <http://dx.doi.org/10.1161/01.ATV.0000168911.78624.b7>.
5. Núñez D, Morillas P, Quiles J, Cordero A, Guindo J, Soria F, et al. Usefulness of an abnormal ankle-brachial index for detecting multivessel coronary disease in patients with acute coronary syndrome. *Rev Esp Cardiol.* 2010;63(1):54-9, [http://dx.doi.org/10.1016/S0300-8932\(10\)70009-9](http://dx.doi.org/10.1016/S0300-8932(10)70009-9).
6. Moussa ID, Jaff MR, Mehran R, Gray W, Dangas G, Lasic Z, et al. Prevalence and prediction of previously unrecognized peripheral arterial disease in patients with coronary artery disease: the Peripheral Arterial Disease in Interventional Patients Study. *Catheter Cardiovasc Interv.* 2009;73(6):719-24, <http://dx.doi.org/10.1002/ccd.21969>.
7. Sukhija R, Aronow WS, Yalamanchili K, Peterson SJ, Frishman WH, Babu S. Association of ankle-brachial index with severity of angiographic coronary artery disease in patients with peripheral arterial disease and coronary artery disease. *Cardiology.* 2005;103(3):158-60, <http://dx.doi.org/10.1159/000084586>.
8. Brazilian Society of Hypertension. Brazilian Society of Cardiology. Brazilian Society of Nephrology. IV Brazilian Guidelines on Hypertension *Arq Bras Cardiol.* 2004;82(supl 4):1-14.
9. Brazilian Society of Cardiology. III Brazilian Guidelines on Dyslipidemia and Atherosclerosis Prevention Guideline for The Department of Atherosclerosis of Brazilian Society of Cardiology. *Arq Bras Cardiol.* 2001;77(supl 3):1-48, <http://dx.doi.org/10.1590/S0066-782X2001001500001>.
10. Report of the Expert Committee on the Diagnosis and Classification of Diabetes Mellitus. Report of the expert committee on the diagnosis and classification of diabetes mellitus. *Diabetes Care.* 2003;26 Suppl 1:S5-20, <http://dx.doi.org/10.2337/diacare.26.2007.S5>.
11. Hirsch AT, Haskal ZJ, Hertzner NR, Bakal CW, Creager MA, Halperin JL, et al. ACC/AHA 2005 Practice Guidelines for the management of patients with peripheral arterial disease (lower extremity, renal, mesenteric, and abdominal aortic): 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. *Circulation.* 2006;113(11):e463-654.
12. Al-Qaisi M, Nott DM, King DH, Kaddoura S. Ankle brachial pressure index (ABPI): An update for practitioners. *Vasc Health Risk Manag.* 2009;5:833-41, <http://dx.doi.org/10.2147/VHRM.S6759>.
13. Aboyans V, Lacroix P, Postil A, Guilloux J, Rollé F, Cornu E, et al. Subclinical peripheral arterial disease and incompressible ankle arteries are both long-term prognostic factors in patients undergoing coronary artery bypass grafting. *J Am Coll Cardiol.* 2005;46(5):815-20, <http://dx.doi.org/10.1016/j.jacc.2005.05.066>.
14. Poredos P, Jug B. The prevalence of peripheral arterial disease in high risk subjects and coronary or cerebrovascular patients. *Angiology.* 2007;58(3):309-15, <http://dx.doi.org/10.1177/0003319707302494>.
15. Papamichael CM, Lekakis JP, Stamatielopoulou KS, Papaioannou TG, Alevizaki MK, Cimponeriu AT, et al. Ankle-brachial index as a predictor of the extent of coronary atherosclerosis and cardiovascular events in patients with coronary artery disease. *Am J Cardiol.* 2000;86(6):615-8, [http://dx.doi.org/10.1016/S0002-9149\(00\)01038-9](http://dx.doi.org/10.1016/S0002-9149(00)01038-9).
16. Sukhija R, Yalamanchili K, Aronow WS. Prevalence of left main coronary artery disease, of three- or four-vessel coronary artery disease, and of obstructive coronary artery disease in patients with and without peripheral arterial disease undergoing coronary angiography for suspected coronary artery disease. *Am J Cardiol.* 2003;92(3):304-5, [http://dx.doi.org/10.1016/S0002-9149\(03\)00632-5](http://dx.doi.org/10.1016/S0002-9149(03)00632-5).
17. 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.
18. Newman AB, Sutton-Tyrrell K, Vogt MT, Kuller LH. Morbidity and mortality in hypertensive adults with a low ankle/arm blood pressure index. *JAMA.* 1993;270(4):487-9, <http://dx.doi.org/10.1001/jama.1993.03510040091035>.
19. Newman AB, Shemansky L, Manolio TA, Cushman M, Mittelmark M, Polak JF, et al. Ankle-arm index as a predictor of cardiovascular disease and mortality in the Cardiovascular Health Study. The Cardiovascular Health Study Group. *Arterioscler Thromb Vasc Biol.* 1999;19(3):538-45, <http://dx.doi.org/10.1161/01.ATV.19.3.538>.
20. Diehm C, Allenberg JR, Pittrow D, Mahn M, Tepohl G, Haberl RL, et al. Mortality and vascular morbidity in older adults with asymptomatic versus symptomatic peripheral artery disease. *Circulation.* 2009;120(21):2053-61, <http://dx.doi.org/10.1161/CIRCULATIONAHA.109.865600>.
21. Murabito JM, Evans JC, Larson MG, Nieto K, Levy D, Wilson PW, et al. The ankle-brachial index in the elderly and risk of stroke, coronary disease, and death: the Framingham Study. *Arch Intern Med.* 2003;163(16):1939-42, <http://dx.doi.org/10.1001/archinte.163.16.1939>.
22. van Popele NM, Grobbee DE, Bots ML, Asmar R, Topouchian J, Reneman RS, et al. Association between arterial stiffness and atherosclerosis: The Rotterdam Study. *Stroke.* 2001;32(2):454-60, <http://dx.doi.org/10.1161/01.STR.32.2.454>.