

Usefulness of an Abnormal Ankle-Brachial Index for Detecting Multivessel Coronary Disease in Patients With Acute Coronary Syndrome

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Introduction and objectives. The presence of peripheral arterial disease in patients with coronary artery disease is associated with a poor cardiovascular outcome. However, the majority of affected patients are asymptomatic and the condition is underdiagnosed. The ankle-brachial index (ABI) provides a simple method of diagnosis. The aim of this study was to assess the usefulness of an abnormal ABI for identifying multivessel coronary artery disease in patients with acute coronary syndrome (ACS).

Methods. We analyzed data on all ACS patients included in the PAMISCA multicenter study (with 94 participating hospitals) who underwent catheterization during admission. Patients were diagnosed with multivessel coronary disease if two or more major epicardial vessels or the left main coronary artery, or both, were affected. An ABI ≤ 0.9 or > 1.4 was considered abnormal.

Results. The study included 1031 patients with a mean age of 67.7 years. Of these, 542 had multivessel disease (52.6%). Compared with those without multivessel disease, these patients were older (66.6 years vs 62.6 years; $P < .001$), had higher prevalences of hypertension (65.9% vs 56.2%; $P < .005$), diabetes mellitus (40.6% vs 26.0%; $P < .001$) and hypercholesterolemia (89.1% vs 80.4%; $P < .001$), and were more likely to have a history of cardiovascular disease (30.1% vs 13.9%; $P < .001$) or an abnormal ABI (45.4% vs 30.3%; $P < .001$). Multivariate analysis showed that the presence of an abnormal ABI was associated with an increased risk of multivessel disease (odds ratio = 1.58; 95% confidence interval, 1.162-1.15; $P < .05$).

Conclusions. In patients with ACS, an abnormal ABI was independently associated with the risk of multivessel coronary artery disease.

Key words: Myocardial infarction. Peripheral vascular disease. Coronary angiography.

Utilidad de un índice tobillo-brazo patológico en la identificación de la enfermedad coronaria multivaso en pacientes con síndrome coronario agudo

Introducción y objetivos. La presencia de enfermedad arterial periférica se asocia con un peor pronóstico cardiovascular en el paciente coronario; sin embargo, la mayor parte de ellos están asintomáticos e infradiagnosticados. El índice tobillo-brazo (ITB) es un método sencillo para el diagnóstico de esta entidad. El objetivo del presente estudio es determinar el papel de un ITB patológico en la identificación de enfermedad coronaria multivaso en pacientes con síndrome coronario agudo (SCA).

Métodos. Se analizaron todos los pacientes con SCA del registro multicéntrico PAMISCA (94 centros participantes) a los que se les había realizado un cateterismo durante su ingreso. Se consideró enfermedad coronaria multivaso la afectación de dos o más vasos mayores epicárdicos y/o enfermedad de tronco coronario izquierdo. Se consideró patológico un ITB $> 1,4$ o $\leq 0,9$.

Resultados. Se incluyeron 1.031 pacientes, con una edad media de 67,7 años. De ellos, 542 pacientes presentaron afectación multivaso (52,6%). Respecto a los pacientes sin afectación multivaso, este grupo presentaba una mayor edad (66,6 frente a 62,6; $p < 0,001$) y una mayor prevalencia de hipertensión arterial (el 65,9 frente al 56,2%; $p < 0,005$), diabetes mellitus (el 40,6 frente al 26%; $p < 0,001$), hipercolesterolemia (el 89,1 frente al 80,4%; $p < 0,001$), antecedentes de enfermedad cardiovascular (el 30,1 frente al 13,9%; $p < 0,001$) y un ITB patológico (el 45,4 frente al 30,3%; $p < 0,001$). En el análisis multivariante la presencia de un ITB patológico se asoció con un mayor riesgo de afectación multivaso (*odds ra-*

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$tio=1,58$; intervalo de confianza del 95%, 1,16-2,15; $p < 0,05$).

Conclusiones. En el paciente con SCA, un ITB patológico se asocia de manera independiente con la probabilidad de padecer enfermedad coronaria multivascular.

Palabras clave: Infarto de miocardio. Enfermedad vascular periférica. Coronariografía.

ABBREVIATIONS

ABI: ankle-brachial index
 ACS: Acute coronary syndrome
 CI: confidence interval
 OR: odds ratio
 PAD: Peripheral arterial disease

INTRODUCTION

Earlier studies have shown an association between peripheral arterial disease (PAD) and a high risk of cardiovascular events and death in patients with or without known coronary artery disease, independent of the presence of other cardiovascular risk factors.¹⁻³ Clinically, the main symptom of PAD is intermittent claudication, but this disease is asymptomatic in most patients and therefore underdiagnosed.⁴

The ankle-brachial index (ABI), a simple, non-invasive measurement, shows high sensitivity and specificity in the diagnosis of PAD when its value is ≤ 0.9 . It is also a powerful indicator of atherosclerotic disease in other vascular areas and of increased cardiovascular morbidity/mortality.^{5,6} Previous studies have shown that the ABI has a high specificity and good negative predictive power with respect to coronary artery disease in patients suspected of having ischemic heart disease^{7,8} or more severe coronary involvement.⁹ However, to date, its usefulness as an indicator of multivessel disease in patients with acute coronary syndrome (ACS) has not been examined. The aim of the present work was to determine the role of a pathological ABI value in the identification of multivessel coronary disease patients admitted for ACS.

METHODS

PAMISCA (*Prevalencia de Afectación de Miembros Inferiores en el paciente con Síndrome Coronario Agudo*; Prevalence of the Involvement of the Lower Limbs in Acute Coronary Syndrome) study is an observational, prospective, multicenter study

promoted by the *Sección de Hipertensión Arterial* (High Blood Pressure Section) of the *Sociedad Española de Cardiología* (Spanish Society of Cardiology). Its aim is to determine the prevalence of PAD in patients admitted to Spanish hospitals for ACS. The baseline study involved 1410 patients consecutively admitted to 94 participating hospitals between September and November 2005. The inclusion criteria for the PAMISCA registry were reported in an earlier paper.¹⁰ Briefly, the patients included were ≥ 40 years of age and had been admitted for ACS defined as: a) typical chest pain; b) electrocardiographic changes showing ischemia or myocardial lesion; and/or c) an increased level of myocardial damage markers. The present subanalysis involved patients who, on the decision of the attending physician, were subjected to a coronary angiographic study during their stay in hospital. Stenosis of $\geq 50\%$ in the main epicardial vessels or the left main coronary artery were deemed to reflect significant coronary artery disease. Multivessel coronary artery disease was defined as the involvement of at least two main vessels and/or the left main coronary artery.

All patients gave their written consent to be included in the study, which was performed in accordance with the principles of the Helsinki Declaration (Edinburgh Amendment, 2000). The study was approved by the *CECI de Galicia* (Santiago de Compostela) ethics committee.

Determination of the Ankle-Brachial Index

On day 3-7 following the ischemic episode the ABI was determined for both sides of the body using a pocket Doppler BIDOP ES-100V3[®] device and a blood pressure cuff following established recommendations.⁵ Systolic blood pressure was measured in both arms and both ankles (posterior tibial artery) with the patient in the supine position. The ABI for each leg was calculated by dividing the systolic pressure at the right and left ankles by the highest systolic pressure recorded in either arm. The lowest ABI value for each patient was then examined; a pathological ABI was considered to be a value of either > 1.4 or ≤ 0.9 . Each center was equipped with an identical Doppler device and specific training in the measurement of the ABI was given to all researchers to guarantee the coherence of the results.

Statistical Analysis

Quantitative values were described in terms of means and standard deviation; these were compared by the Student *t* test. Qualitative variables were described in terms of relative frequencies and compared using the χ^2 test.

TABLE 1. Baseline Characteristics of the Patient Population

Variable	Total (n=1031)	Patients With Multivessel Disease (n=542)	Patients With 0 or 1 Diseased Vessel (n=489)	P
Age, mean (SD), y	64.7 (11.4)	66.6 (10.8)	62.6 (11.7)	<.001
Sex (male) (%)	777 (76.1)	397 (74.1)	380 (78.4)	0.11
HBP (%)	632 (61.3)	357 (65.9)	275 (56.2)	<.005
Smokers (%)	348 (33.8)	162 (29.9)	186 (38)	<.01
Hypercholesterolemia (%)	876 (85)	483 (89.1)	393 (80.4)	<.001
Diabetes mellitus (%)	347 (33.7)	220 (40.6)	127 (26)	<.001
Prior MI (%)	231 (22.4)	163 (30.1)	68 (13.9)	<.001
Prior coronary revascularization (%)	188 (18.2)	130 (24.1)	58 (11.9)	<.001
Prior CVA (%)	70 (6.8)	51 (9.4)	19 (3.9)	<.001
STEACS (%)	436 (43.9)	221 (42.7)	215 (45.2)	<.05
LVEF <40% (%)	130 (14.2)	78 (16.2)	52 (12)	.07
Glomerular filtrate, mean (SD), mg/dL/min	81.3 (33.8)	77.9 (35.2)	84.6 (32.1)	<.005
ABI	0.92 (0.2)	0.89 (0.2)	0.95 (0.2)	<.001
Pathological ABI (%)	394 (38.2)	246 (45.4)	148 (30.3)	<.001

ABI indicates ankle-brachial index; HBP, high blood pressure; CVA, cerebrovascular accident; LVEF, left ventricular ejection fraction; MI, myocardial infarction; STEACS, ST elevation acute coronary syndrome.

A binary logistic regression model was used to determine the relationship between pathological ABI and the severity of coronary artery disease. The model included the variables which, in bivariate analysis, were associated with multivessel coronary disease ($P<.20$). Significance was set at $P<.05$. All calculations were performed using SPSS v.15.0 software for Windows.

RESULTS

Of the 1410 patients included in the PAMISCA registry, 1031 (73%) were initially selected, all of whom had undergone coronary angiography during their hospital stay. The mean age of the study subjects was 67.7 (11.4) years. Some 85% showed hypercholesterolemia, 61.3% had high blood pressure, 33.8% were active smokers, and 33.7% had diabetes mellitus (Table 1). No significant differences were seen between these patients and those that were not subjected to catheterization, with the exception of the number of active smokers (33.8% vs 23.2%; $P<.05$) and history of prior revascularization (18.2% vs 8.2%; $P<.001$). Of the 436 patients (43.9%) admitted for ST segment elevation ACS, catheterization showed 1 affected vessel in 33.9%, 2 in 24.6%, and 3 in 26.5% of cases. No significant lesion was seen in 13.5%, and 63 patients (6.1%) had a significant lesion in the leftmain coronary artery. The 542 subjects with multivessel disease (52.6%) were older, more had a history of cardiovascular disease (infarction or cerebrovascular accident), and risk factors were more prevalent among these patients (Table 1).

After determining the ABI, 394 patients (38.2%) were found to have pathological values. Such values were more prevalent among the patients

with multivessel disease (45.4% vs 30.3%; $P<.001$). Multivariate analysis showed a pathological ABI to be significantly associated with a greater risk of multivessel disease (odds ratio [OR] = 1.58; 95% confidence interval [CI], 1.16-2.15; $P<.05$) both among patients with ST segment elevation (OR=1.60; 95% CI, 1.05-2.43; $P<.05$) and those without (OR=1.61; 95% CI, 1.06-2.44; $P<.05$). The sensitivity of ABI for the diagnosis of multivessel disease was 44.7% (95% CI, 40.5-48.9), its specificity was 70.1% (95% CI, 66.1-74.1), the positive predictive power 62.4% (95% CI, 57.6-67.2), and the negative predictive power 53.3% (95% CI, 49.5-57.1). Other factors associated with multivessel disease included age, diabetes mellitus, hypercholesterolemia, and a history of myocardial infarction and cerebrovascular accident (Table 2).

DISCUSSION

This work is one of the first large scale studies to analyze the value of the ABI to actively and systematically search for PAD as an indicator of multivessel coronary disease in patients who have suffered an ACS. The present results show that a pathological ABI can be useful in raising suspicion of multivessel disease in such patients. Pathological ABI values should therefore be taken into account when contemplating cardiac catheterization in the context of ACS.

The present findings showed a high prevalence (nearly 40%) of PAD among our patients with ACS, though this was largely subclinical. This figure is higher than that reported by other authors.¹¹ For example, Froelich et al¹² reported a prevalence of just 9.7% in a subanalysis of the GRACE (Global Registry of Acute Coronary Events) study, which

TABLE 2. Multivariate Analysis of the Factors Associated With Multivessel Coronary Disease

Variable	OR (95% CI)	P
Pathological ABI	1.58 (1.16-2.15)	<.005
Age	1.02 (1.00-1.03)	< 0.05
Hypercholesterolemia	1.70 (1.12-2.56)	<.05
Diabetes mellitus	1.49 (1.09-2.05)	<.05
Prior infarction	2.14 (1.48-3.10)	<.001
Prior CVA	2.24 (1.21-4.17)	<.05
Sex	1.05 (0.74-1.50)	.76
HBP	1.07 (0.80-1.45)	.68
Smoker	1.13 (0.80-1.69)	.49
LVEF <40%	0.97 (0.82-1.15)	.75
Glomerular filtrate, mg/dL/min	0.99 (0.80-1.23)	.95
Prior coronary revascularization	1.40 (0.89-2.20)	.14

ABI indicates ankle-brachial index; CVA, cerebrovascular accident; HBP, high blood pressure; LVEF, left ventricular ejection fraction.

The independent variables introduced into the model were sex, age, high blood pressure, smoking, hypercholesterolemia, diabetes mellitus, prior myocardial infarction, prior cerebrovascular accident, prior coronary revascularization (aortocoronary bypass and/or percutaneous angioplasty), type of acute coronary syndrome (with or without ST segment elevation), glomerular filtrate, left ventricular function <40%, and the ABI value.

included 41 108 patients admitted for ACS. It is likely that PAD is underdiagnosed in these studies because the group of PAD patients included only those in whom a diagnosis had already been made; no vascular tests were undertaken to detect patients with subclinical disease. It is well known that a large proportion of patients with atherosclerotic disease of the lower limbs have no signs of intermittent claudication,⁵ therefore limiting the sensitivity of the clinical history to raise suspicions regarding such a diagnosis. Measuring the ABI involves a simple, cheap and non-invasive procedure that allows one to estimate with high sensitivity and specificity the degree of atherosclerotic involvement of the lower limbs. In Spain, only one other, relatively small, study has analyzed the presence of PAD via measurement of the ABI in the setting of ACS.¹³ This study identified PAD in 26% of its 141 patients, a much lower figure than that recorded in the present work. This difference is probably due to the age of the patients analyzed, who were 35-70 years of age, whereas in the present study there was no upper age limit. The close relationship between the prevalence of PAD and age is well known, both in the general population¹ and in patients with established coronary artery disease.¹⁴

Several studies report that an ABI of ≤ 0.9 is highly predictive of cardiovascular morbidity/mortality, both in the general population and in patients with known coronary artery disease.^{5,6} In fact, it is estimated that an ABI of < 0.9 increases the risk of cardiovascular death and all-cause death by

factors of 3 to 8 and 2 to 5, respectively, compared to an ABI of > 0.9 .¹⁵ However, few studies have analyzed its role in the prognosis of patients with ACS. Recently, the PAMISCA registry found an association between an ABI of ≤ 0.9 and a greater risk of cardiovascular death in patients admitted for ACS, and a greater incidence of complications (angina, heart failure and atrial fibrillation).¹⁰ In a 1 year follow-up of 1003 patients with ACS, Agnelli et al¹⁶ showed that an ABI of < 0.9 increased the risk of non-fatal myocardial infarction and all-cause death (*hazard ratio* [HR] = 1.96; 95% CI, 1.36-2.81), especially among those with the lowest indices. Similarly, the present results show that the patients with a pathological ABI had more extensive coronary disease, with a greater prevalence of multivessel disease.

Similar results have been reported in other contexts of coronary artery disease. In 165 patients referred for elective coronary angiography, Papamichael et al¹⁷ showed the ABI to be inversely correlated to the extent and severity of coronary disease, and to be one of the main variables for predicting the extent of disease, along with advanced age, diabetes mellitus, male sex, plasma high density lipoprotein cholesterol (HDL-C), the intimomedial thickness of the common femoral artery and the waist/hip ratio. In 485 stable patients suspected of having coronary artery disease, Chang et al⁹ showed the usefulness of ABI for predicting complex and diffuse coronary lesions, reporting a greater proportion of lesions at the ostial level and in proximal segments in patients with an ABI of < 0.9 than in those with an ABI of ≥ 0.9 . In addition, the percentage of diffuse, irregular, calcified lesions affecting bifurcations was higher. However, unlike the present study, Chang et al excluded patients with myocardial infarction or unstable angina, and an ABI of > 1.4 was not considered pathological. In fact, several studies have reported that an ABI of > 1.4 (a marker of calcified, non-compressible arteries) also predicts an increased risk of cardiovascular events.¹⁸ In the Strong Heart Study, Native Americans with an ABI of > 1.4 were shown to be at greater risk of cardiovascular and all-cause death than those with an ABI between 0.9 and 1.4. This suggests a U-shaped curve relating ABI and mortality.³

These studies, plus the present work, provide scientific evidence of the progression of atherosclerotic disease in different artery beds, and show that a simple method—the determination of the ABI—can be useful in assessing the risk faced by patients with ischemia. The main limitation of the present work is the inclusion of patients at 48 h after admission; patients who died before this time were therefore not included. Other limitations are the exclusion of patients aged < 40 (with a low

probability of suffering PAD) and the fact that not all patients admitted and included in the registry were subjected to coronary angiography. The latter reflects possible changes in coronary angiography criteria during the study period.

CONCLUSIONS

A pathological ABI value is related to a greater extent of coronary artery disease in patients aged ≥ 40 with a diagnosis of ACS. Although a normal ABI does not rule out the presence of severe coronary artery disease, a high ABI should raise the suspicion of advanced disease, alerting to the need for more aggressive diagnostic and therapeutic strategies.

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