Clinical Value of the Ankle-Brachial Index in Patients at Risk of Cardiovascular Disease but Without Known Atherothrombotic Disease: VITAMIN Study

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Introduction and objectives. Detecting peripheral arterial disease by measuring the ankle-brachial index can help identify asymptomatic patients with established disease. We investigated the prevalence of peripheral arterial disease (i.e., an ankle-brachial index <0.9) and its potential clinical and therapeutic impact in patients with no known arterial disease who were seen at internal medicine departments.

Methods. This multicenter, cross-sectional, observational study included patients at risk of cardiovascular disease who were selected on the basis of age, gender and the presence of conventional risk factors. No patient was known to have arterial disease who were seen at internal medicine departments.

Results. The study included 493 patients, 174 (35%) of whom had diabetes, while 321 (65%) did not. Only 16% were in a low-risk category according to their Framingham score. An ankle-brachial index <0.9 was observed in 27.4%, comprising 37.9% of those with diabetes and 21.3% of those without. Multiple logistic regression analysis showed that the risk factors associated with an ankle-brachial index <0.9 were age, diabetes, and hypercholesterolemia.

Conclusions. Asymptomatic peripheral arterial disease was detected in a high proportion of patients with an intermediate or high cardiovascular disease risk. The ankle-brachial index should be measured routinely in patients at risk of cardiovascular disease who are seen at internal medicine departments.


Valor de la determinación del índice tobillo-brazo en pacientes de riesgo vascular sin enfermedad aterotrombótica conocida: estudio VITAMIN

Introduction y objetivos. La detección de la enfermedad arterial periférica, mediante el índice tobillo-brazo, permite identificar a los pacientes asintomáticos con una lesión establecida. Investigamos la prevalencia de enfermedad arterial periférica (índice tobillo-brazo < 0.9) en sujetos sin enfermedad arterial conocida atendidos en el ámbito de medicina interna y su potencial impacto clínico-terapéutico.
INTRODUCTION

The cardiovascular complications of arteriosclerosis are the main cause of morbidity and mortality in the Western world. This histopathological lesion is characterized by its slow progression and systemic nature, which is manifested by various vascular syndromes that often appear simultaneously and depend on the vascular territory affected (ischemic heart disease, ischemic cerebrovascular disease and peripheral arterial disease). The natural history of arteriosclerosis includes an asymptomatic first phase of lengthy duration, followed by a clinical phase that is often sudden and fatal as a consequence of vascular stenosis or acute thrombosis associated with the atheroma plaque. Treatment of this condition is mainly based on prevention, or, at least, control of progression before the development of severe cardiovascular complications.

To provide adequate multifactorial therapeutic interventions, scales assessing vascular risk, such as the Framingham cardiovascular risk equation, have been established to allow overall evaluation of specific patients. A complementary approach is noninvasive direct assessment of the arteriosclerotic lesion in the target organ, which allows identification of patients at a high risk for future development of a cardiovascular complication.

Along this line, there is growing interest in the detection of peripheral arterial disease (PAD) of the lower limbs using a simple noninvasive technique, known as the ankle-brachial index (ABI). This is calculated by dividing the systolic blood pressure in the ankle by the systolic pressure in the arm to determine the arterial pressure (AP) ratio. As compared to angiography, an ABI value of <0.9 has a sensitivity of 95% and a specificity >95% for detecting stenosis of at least 50% of the arterial lumen. Moreover, it is an inexpensive, accurate, reproducible procedure that does not require specialized personnel. Because of its diagnostic precision and widespread availability, the ABI is the method of choice for diagnosing PAD, which in most patients is not manifested by symptoms, and should be routinely used when assessing patients at a risk of developing atherothrombotic disease. In addition to its use in the diagnosis of symptomatic PAD, the greatest value of ABI lies in its function as an independent predictive marker of cardiovascular death in patients with asymptomatic PAD. The main clinical impact of this technique is obvious: it allows the detection of high-risk patients in the primary care setting who would benefit from a more intensive multifactorial therapeutic approach. To date, numerous studies have been published on the prevalence of PAD and the prognostic value of the ABI in the general population. Nevertheless, there is little data on the prevalence of low ABI values in selected, at-risk patients with no known atherothrombotic event, who may be the population that could most benefit from the application of this index. Based on these considerations, we measured the ABI in a population of at-risk patients with no known arterial disease, seen in an internal medicine department. The aims of this study were the following: a) determine the prevalence of PAD (ABI<0.9), b) identify the clinical and biological profile of patients with ABI<0.9 in this clinical setting, and c) assess the potential therapeutic impact of using the ABI in the population studied.

Métodos. Estudio multicéntrico, transversal, observacional en el que se incluyó a pacientes con potencial riesgo cardiovascular, seleccionados en función de la edad, el sexo y la presencia de factores de riesgo convencionales, pero sin enfermedad arterial conocida.

Resultados. Se evaluaron 493 casos, de los que 174 eran diabéticos (35%) y 321, no diabéticos (65%). Sólo un 16% presentó un riesgo bajo según la ecuación de Framingham. Del total de la muestra, el índice tobillo-brazo fue < 0,9 en el 27,4% (el 37,9% de los diabéticos y el 21,3%, de los no diabéticos). En el análisis multivariable, los parámetros que se asociaron con un índice tobillo-brazo < 0,9 fueron la edad, la diabetes mellitus y la hipercolesterolemia. Se objetivó una relación significativa entre las categorías de riesgo de Framingham y el índice tobillo-brazo. Al considerar a los pacientes con un índice tobillo-brazo < 0,9, sólo el 21% recibía tratamiento antiagregante, el 20% presentaba valores de colesterol unido a lipoproteínas de baja densidad (LDL) < 100 mg/dl (el 52% con LDL < 130 mg/dl) y el 42% tenía unos valores de presión arterial < 140/90 mmHg.

Conclusiones. En una proporción elevada de pacientes con riesgo cardiovascular intermedio o alto se detecta enfermedad arterial periférica asintomática. El índice tobillo-brazo debería medirse sistemáticamente en enfermos con riesgo vascular, evaluados en el ámbito de la medicina interna.


ABREVIATIONS

DM: diabetes mellitus.
PAD: peripheral arterial disease.
HT: hypertension.
ABI: ankle-brachial index.
AP: arterial pressure.
VITAMIN: Valor del Índice Tobillo-Brazo en Medicina Interna (Value of the Ankle-Brachial Index in Internal Medicine).
Manzano L et al. Value of Ankle-Brachial Index in Patients Without Known Arterial Disease

METHODS
Design and Patients
This is a cross-sectional, descriptive, observational study involving no therapeutic interventions, performed in outpatients and hospitalized patients, and carried out during the period of October 2003 to June 2004 in 12 internal medicine services in the communities of Madrid, Castilla y León, and Castilla-La Mancha, Spain. Participating patients were selected on the basis of age, sex, and the presence of conventional cardiovascular risk factors: smoking, hypertension (HT), diabetes mellitus, hypercholesterolemia, low concentrations of high-density lipoprotein cholesterol (HDL-C), and a family history of early coronary disease. Specifically, the criteria for inclusion were the following: a) men aged >65 years, >55 years with at least one conventional risk factor, or >45 years with two or more risk factors; b) women aged >65 years with at least 1 risk factor or >55 years with 2 or more risk factors; and c) patients with non-insulin-dependent diabetes mellitus (DM) or a family history of hypercholesterolemia, regardless of sex or age. The sample was comprised of outpatients consulting to monitor their risk factors and patients hospitalized for acute processes or exacerbations of nonvascular medical conditions. Patients were excluded if they had prior evidence of an atherosclerotic lesion (coronary, cerebrovascular, peripheral, or aortic), hyperthyroidism, uncontrolled neoplastic disease, cognitive deterioration greater than stage 4 on the Global Deterioration Scale (GDS), or a grade of dependence for the activities of daily living >3, as measured by the Katz Index.

Clinical and Biological Variables
All patients underwent a complete anamnesis and physical examination, as well as the following basic analyses: glucose, total cholesterol, low-density lipoprotein cholesterol fraction (LDL-C), high-density lipoprotein cholesterol fraction (HDL-C), triglycerides, and HbA1c in diabetic patients. Analytic values obtained within 2 months of the assessment were considered valid. In hospitalized patients, the analyses used were those performed in the 2 months before hospitalization or following discharge. All patients gave their informed consent to participate and the study was approved by the Ethics Committee for Clinical Research of the Hospital Príncipe de Asturias of Madrid. Cardiovascular risk at 10 years was estimated with the Framingham formula.11 Intermittent vascular claudication was defined according to the Edinburgh questionnaire, modified into 3 categories: absent, atypical, and defined (Figure 1).11

Determination of the Ankle-Brachial Index
The ABI was measured with an automatic device that incorporates a sphygmomanometer and 2-way Doppler with an 8-MHz probe (Smartdop® 30, Hayashi Denki Co., Ltd.), strictly following the procedure currently considered to be the method of choice.6 Briefly, after resting for 5 min in the supine decubitus position, systolic arterial pressure (SAP) was measured in both arms and the highest value was selected for calculation of the ABI (denominator). The SAP of the posterior tibial artery and pedal artery was then measured in each leg, and the highest value (whether tibial or pedal) was taken as reference for calculating the individual ABI of each leg (numerator). The ABI of both the left and right legs was recorded, and the lower of the 2 values was used to assess the patient’s overall cardiovascular risk. The ABI was considered low at a value of <0.9. Based on the fact that an elevated ABI (>1.4) might be related with a rigid, incompressible wall in an artery affected by arteriosclerosis, which has been associated with a poorer prognosis, ABI values >1.4 were also considered abnormal. Therefore, the following ABI categories were established: a) low, <0.9, b) normal, 0.9-1.4, c) high, >1.4, and d) pathologic, <0.9 or >1.4.

Statistical Analysis
The sample size was calculated considering that the primary endpoint was estimation of the prevalence of ABI<0.9. With a total of 500 participants in the study and assuming a worst possible prevalence of 50%, the maximum error in estimating the prevalence would be <5% at the usual 95% confidence interval. Categorical variables are expressed as absolute frequency and relative frequency (percentage) and continuous variables as the mean ± standard deviation. Proportions were compared with Pearson’s χ² test or Fisher’s exact test, where appropriate. When the distribution of proportions was compared with respect to ordinal categories, the χ² test for linear trends was used. Correlations between the ABI and quantitative variables were performed with Spearman’s correlation coefficient.

The magnitude of the association between the presence or not of a pathological ABI and the characteristics of the patients was quantified with the odds ratio (OR) and the 95% confidence interval (CI). Lastly, multiple logistic regression analysis was used to determine the subset of independent variables predictive of a pathological ABI. To construct the models, all the major factors known to cause cardiovascular risk were introduced in the models as independent variables, regardless of their statistical significance in the univariate analyses. A backward step-wise selection approach was used to eliminate variables. Probability levels of .05 and .10 were used to determine whether an
independent variable was retained in, or eliminated from the model, respectively. All statistical analyses were done with SPSS version 12. Significance was set at a level of 5% for all the analyses.

RESULTS

Demographic and Clinical Characteristics of the Patient Sample

The study included a total of 493 patients, with a mean age of 67.9 years and 61.3% men. The number of patients selected per center ranged from 20 to 68, with a median of 50. Among the total sample, 262 cases (53.1%) were outpatients and the remaining hospitalized patients. The demographic characteristics and proportions of patients with the main cardiovascular risk factors are shown in Table 1. Table 2 summarizes the patients’ AP values, body mass index, and analytical results.

According to the Adult Treatment Panel III (ATP III) criteria, 16% of the patients were classified as low risk, 37% as intermediate risk, and the remaining 47% as high risk because of an estimation >20% or the fact of having DM.

Prevalence and Clinical Expression of Peripheral Arterial Disease

Low ABI values (<0.9) were detected in 135 patients, indicating a prevalence of 27.4% (21.3% of the nondiabetic and 37.9% of the diabetic patients). The ABI was >1.4 in 37 other patients (7.3%), which, when grouped together with the abnormally low values, gave a total of 172 patients (34.7%) with a pathological ABI (28.2% of the nondiabetic and 46.6% of the diabetic patients).

Only 13 patients (2.6%) showed define claudication and 23 (4.7%) had an atypical presentation. Analysis of the predictive capacity of intermittent vascular
TABLE 1. Demographic Characteristics and Risk Factors in the Sample of Patients, According to the Criteria of the ATP III Report (n=493)*

<table>
<thead>
<tr>
<th>Factor</th>
<th>Mean±SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years, mean ± SD</td>
<td>67.9±10.9</td>
</tr>
<tr>
<td>Men, n (%)</td>
<td>302 (61.3)</td>
</tr>
<tr>
<td>Active smoker, n (%)</td>
<td>92 (18.7)</td>
</tr>
<tr>
<td>Ex-smoker, n (%)</td>
<td>116 (23.5)</td>
</tr>
<tr>
<td>Hypertension (≥140/90 mm Hg), n (%)</td>
<td>377 (76.5)</td>
</tr>
<tr>
<td>Diabetes mellitus, n (%)</td>
<td>174 (35.3)</td>
</tr>
<tr>
<td>Hypercholesterolemia (TC&gt;200 mg/dL), n (%)</td>
<td>312 (63.3)</td>
</tr>
<tr>
<td>Low HDL-C (&lt;40 mg/dL), n (%)</td>
<td>107 (21.7)</td>
</tr>
<tr>
<td>Obesity (BMI&gt;30), n (%)</td>
<td>136 (27.6)</td>
</tr>
<tr>
<td>Central obesity (waist men &gt;102 cm, women &gt;88 cm), n (%)</td>
<td>229 (44.6)</td>
</tr>
<tr>
<td>Metabolic syndrome, n (%)</td>
<td>259 (52.5)</td>
</tr>
<tr>
<td>Family history ECD, n (%)</td>
<td>80 (16.2)</td>
</tr>
</tbody>
</table>

*BMI indicates body mass index; HDL-C, high-density lipoprotein cholesterol; ECD, early coronary disease; SD, standard deviation TC, total cholesterol.

The prevalence of pathological ABI (<0.9 or >1.4) among the participating centers presented a median of 31.4%, with no statistically significant differences. A slightly higher percentage of pathological ABI (37.7%) was found among hospitalized patients with respect to outpatients (32.1%); nevertheless, this difference did not reach statistical significance (OR=1.28; 95% CI, 0.88-1.86; P=.19).

Factors Related to the Ankle-Brachial Index

The correlations between ABI values and the various quantitative parameters studied are shown in Table 3. The prevalence of a low ABI (<0.9) or pathological ABI (≥0.9 or ≥1.4) according to the presence of risk factors, as well as the associations between them are shown in Table 4. The associations with HT, DM, and the presence of intermittent vascular claudication (whether atypical or defined) are noteworthy. It is paradoxical, however, that a negative association was found with the remaining variables and the finding of a low or pathological ABI were alternative dependent variables, age (ORs adjusted for yearly increase, 1.06 and 1.05, respectively), DM (adjusted ORs, 2.64 and 2.21), and hypercholesterolemia (adjusted ORs, 1.86 and 1.76) were the only characteristics selected with an independent association (Table 5).

Specific analysis of the 37 patients with a high ABI (≥1.4) yielded a significant association between this factor and age (>75 years (OR=2.70; 95% CI, 1.28-5.72), female sex (OR=2.21; 95% CI, 1.06-4.64), and a family history of early vascular disease (OR=2.20; 95% CI, 1.02-4.72). In addition, there was trend approaching statistical significance toward an association with DM (OR=1.68; 95% CI, 0.83-3.38) and HT (OR=1.71; 95% CI, 0.73-4.04). No associations were found with the remaining variables.

Ankle-Brachial Index and Overall Coronary Risk

In light of the relationship found between the ABI and coronary risk estimated with the Framingham
equation (Table 6), we tested whether there was a progressive linear increase in the prevalence of a low 
ABI (<0.9) in the successive risk categories. No 
association was observed, however, between a high 
ABI (>1.4) and the risk estimation according to the 
Framingham equation.

### TABLE 4. Prevalence of Low (<0.9) and Pathological (<0.9 or >1.4) Ankle-Brachial Index Values in the Various 
Subgroups

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>ABI Value</th>
<th>n (%)</th>
<th>P‡</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men (n=302/286)</td>
<td>&lt;0.9 or &gt;1.4</td>
<td>100 (33.1)</td>
<td>.35</td>
<td>0.84 (0.57-1.22)</td>
</tr>
<tr>
<td></td>
<td>&lt;0.9</td>
<td>84 (29.4)</td>
<td>.99</td>
<td>0.99 (0.66-1.51)</td>
</tr>
<tr>
<td>Active smoker (n=92/87)</td>
<td>&lt;0.9 or &gt;1.4</td>
<td>23 (25.0)</td>
<td>.03</td>
<td>0.57 (0.34-0.96)</td>
</tr>
<tr>
<td></td>
<td>&lt;0.9</td>
<td>18 (20.7)</td>
<td>.05</td>
<td>0.59 (0.32-1.00)</td>
</tr>
<tr>
<td>Active or prior smoker (n=208/197)</td>
<td>&lt;0.9 or &gt;1.4</td>
<td>70 (33.7)</td>
<td>.72</td>
<td>0.93 (0.64-1.36)</td>
</tr>
<tr>
<td></td>
<td>&lt;0.9</td>
<td>59 (29.9)</td>
<td>.81</td>
<td>1.05 (0.70-1.58)</td>
</tr>
<tr>
<td>Hypertension (n=377/347)</td>
<td>&lt;0.9 or &gt;1.4</td>
<td>147 (39.0)</td>
<td>&lt;.001</td>
<td>2.45 (1.49-4.02)</td>
</tr>
<tr>
<td></td>
<td>&lt;0.9</td>
<td>117 (33.7)</td>
<td>&lt;.001</td>
<td>2.75 (1.57-4.83)</td>
</tr>
<tr>
<td>Diabetes mellitus (n=174/159)</td>
<td>&lt;0.9 or &gt;1.4</td>
<td>81 (46.6)</td>
<td>&lt;.001</td>
<td>2.22 (1.51-3.26)</td>
</tr>
<tr>
<td></td>
<td>&lt;0.9</td>
<td>66 (41.5)</td>
<td>&lt;.001</td>
<td>2.39 (1.50-3.62)</td>
</tr>
<tr>
<td>Hypercholesterolemia (n=312/289)</td>
<td>&lt;0.9 or &gt;1.4</td>
<td>115 (36.9)</td>
<td>.20</td>
<td>1.29 (0.88-1.91)</td>
</tr>
<tr>
<td></td>
<td>&lt;0.9</td>
<td>92 (31.8)</td>
<td>.14</td>
<td>1.38 (0.90-2.02)</td>
</tr>
<tr>
<td>Low HDL-C (n=107/97)</td>
<td>&lt;0.9 or &gt;1.4</td>
<td>34 (31.8)</td>
<td>.59</td>
<td>0.88 (0.56-1.30)</td>
</tr>
<tr>
<td></td>
<td>&lt;0.9</td>
<td>24 (24.7)</td>
<td>.32</td>
<td>0.77 (0.46-1.32)</td>
</tr>
<tr>
<td>Obesity (BMI=30) (n=136/127)</td>
<td>&lt;0.9 or &gt;1.4</td>
<td>52 (38.2)</td>
<td>.31</td>
<td>1.24 (0.82-1.87)</td>
</tr>
<tr>
<td></td>
<td>&lt;0.9</td>
<td>43 (33.9)</td>
<td>.19</td>
<td>1.34 (0.86-2.09)</td>
</tr>
<tr>
<td>Central obesity (n=220/198)</td>
<td>&lt;0.9 or &gt;1.4</td>
<td>83 (37.7)</td>
<td>.20</td>
<td>1.27 (0.88-1.85)</td>
</tr>
<tr>
<td></td>
<td>&lt;0.9</td>
<td>61 (30.8)</td>
<td>.56</td>
<td>1.13 (0.75-1.69)</td>
</tr>
<tr>
<td>Intermittent vascular claudication§ (n=36/34)</td>
<td>&lt;0.9 or &gt;1.4</td>
<td>24 (66.7)</td>
<td>&lt;.001</td>
<td>4.26 (2.07-8.76)</td>
</tr>
<tr>
<td></td>
<td>&lt;0.9</td>
<td>22 (64.7)</td>
<td>&lt;.001</td>
<td>5.15 (2.47-10.8)</td>
</tr>
</tbody>
</table>

*ABI indicates ankle-brachial index; BMI, body mass index; HDL-C, high-density lipoprotein cholesterol; CI, confidence interval; OR, odds ratio.
†The first number under n corresponds to the total sample and is used as the denominator for the proportion of patients with an ABI value <0.9 or >1.4; the second 
number under n excludes the 37 patients with ABI>1.4, and is used as the denominator for the proportion of patients with an ABI value <0.9.
‡Statistical significance of the proportion as compared to the absence of the characteristic, as a reference group. 
§Includes defined and atypical.

### Control of Vascular Risk Factors in Patients With a Low (<0.9) and Pathological (<0.9 or >1.4) Ankle-Brachial Index

It should be pointed out that only one of every 5 
patients with a low ABI received antiplatelet therapy, a 
similar proportion had an optimal LDL-C
concentration (<100 mg/dL), and around 25% presented AP values ≤130/85 mm Hg, all of which seem optimal in patients with established vascular disease. In any case, if other cut-off points were used for LDL-C (<130 mg/dL) and AP (<140/90 mm Hg), the percentage of cases with satisfactory control would be around 50% (Figure 2). Only 4.1% of patients with a pathological ABI maintained adequate overall treatment with respect to antiplatelet therapy and optimal control of LDL-C and HT.

DISCUSSION

In this study, application of the ankle-brachial index for the detection of peripheral arterial disease in outpatients and hospitalized internal medicine patients had a pronounced clinical impact. Specifically, in the sample of risk patients selected, 27.4% (21.3% of non-diabetic patients and 37.9% of diabetic patients) had an ABI<0.9 and consequently presented PAD. It is important to point out that the sample selected was representative of the population seen in daily internal medicine practice; moreover, none of the patients had a history of atherothrombotic disease and the treatment they received was for primary prevention.

When the presence of PAD was demonstrated in these patients and the therapeutic goals of secondary prevention were applied, we found that only 4% complied with all the recommendations, 20% received antiplatelet therapy, and approximately 20%-50% reached the goals for LDL-C or HT, depending on the criteria used.

There is a great deal of information on the ABI in epidemiological population studies performed in the primary care setting. Apart from age, the other factors that explain the differences in the reported prevalence in the published studies include ethnic group and the percentage of patients with a cardiovascular event, DM, or other associated risk factors. In the PARTNER study, which included patients at moderate-to-high risk (>70 years, or 50-69 years and additionally smoker or diabetic), low ABI values were found in 29%. The available figures specifically for diabetic patients are sparse, although a prevalence of 20%-30% is estimated, with the rate mainly depending on the age of the patient and the time of evolution of DM.5,18,19

The present study provides some additional information to the population studies mentioned above, since it specifically assesses selected patients.
within the internal medicine setting with vascular risk and no known arterial disease. This population is likely to be the one in which ABI determination may have the greatest clinical interest, since detection of a low ABI in these patients implies a substantial change in therapy from an underestimated previous situation of primary prevention to a real situation of secondary prevention. To our knowledge, there is only one other similar study in the literature, although patients with coronary disease (12%) and cerebrovascular disease (13%) were not excluded from the study population; the prevalence of ABI <0.9 was 36%.23

One fact that should be highlighted about the present study is the reliability of the results, which is supported by the rigorous method used and the similarity of the data obtained among the various participating investigators. In other studies, the interpretation of the ABI and the procedure used to measure the index may not have been entirely appropriate. Some authors,11 for example, establish the cut-off for low ABI at 0.95, others determine the ABI only on one side (right or left)19 and others measure SAP only in the posterior tibial artery and not in the pedal artery. Moreover, in some studies SAP measurement in the leg is performed with less reliable methods, e.g., with a conventional stethoscope or by palpating the pulses.6 It is generally considered that detection of a high ABI (>1.4) indicates that the artery under study has a rigid incompressible wall, presumably due to an arteriosclerotic process. The clinical significance of this finding is still uncertain and almost all the studies exclude these cases from the statistical analysis. Nevertheless, a recent article reported that an ABI value >1.4 is nearly as important a prognostic marker of morbidity and mortality as a low ABI.22 On this basis, and establishing the criteria of pathological ABI supported by the rigorous method used and the similarity of the data obtained among the various participating investigators, in other studies, the interpretation of the ABI and the procedure used to measure the index may not have been entirely appropriate. Some authors,11 for example, establish the cut-off for low ABI at 0.95, others determine the ABI only on one side (right or left) and others measure SAP only in the posterior tibial artery and not in the pedal artery. Moreover, in some studies SAP measurement in the leg is performed with less reliable methods, e.g., with a conventional stethoscope or by palpating the pulses.6 It is generally considered that detection of a high ABI (>1.4) indicates that the artery under study has a rigid incompressible wall, presumably due to an arteriosclerotic process. The clinical significance of this finding is still uncertain and almost all the studies exclude these cases from the statistical analysis. Nevertheless, a recent article reported that an ABI value >1.4 is nearly as important a prognostic marker of morbidity and mortality as a low ABI.22 On this basis, and establishing the criteria of pathological ABI as a value less than 0.9 or greater than 1.4, the overall percentage of cases in our sample with a pathological ABI reached 34.7% (28.2% of the nondiabetic patients and 46.6% of diabetic patients), thereby highlighting the clinical impact of this finding even more. With the information available to date, however, it cannot be unquestionably assured that detection of a high ABI reflects the presence of PAD in the same manner as a low ABI.

One of the most important limitations of the present study is its inability to precisely determine the risk factors associated with detection of a low or pathological ABI. In effect, even though a close relationship was found with age, DM and, to a lesser extent, hypercholesterolemia, other highly consolidated predisposing factors, such as smoking and HT were not associated with the presence of a low or pathological ABI in the multivariate analysis. For an adequate interpretation of these data it should be remembered that our sample does not represent the general population, but instead a group of patients at risk of vascular disease, with no prior atherothrombotic events, and assessed in the framework of the internal medicine setting. Thus, it is a selected sample, in which the majority of cases were diabetic patients or patients with moderate-to-high vascular risk, regardless of the factors contributing to this status. Thus, for example, the analysis of the group of young, actively smoking patients together with elderly non-smoking women who had other associated risk factors yielded results that paradoxically might attribute a protective effect to smoking, since detection of a low or pathological ABI was less frequent in the younger population. In addition, the fact that patients with a prior cardiovascular event were excluded may have altered the association between risk factors and peripheral arterial disease. The paradox of the negative association of active smoking with a low ABI could be explained, moreover, by the bias of reverse causality inherent to cross-sectional studies such as ours. This would imply that patients with a greater accumulation of risk factors might have quit smoking more frequently because they were more motivated or had received a more intense health intervention for this purpose. The loss of the effect of HT in the adjusted analysis may be justified to a great degree by its relationship with age.

In any case, it was not the objective of this study to determine the risk factors associated with the presence of a low ABI, which have been defined in prior population cohort studies,23,24 but instead to identify the profile of the patients encountered in internal medicine practice that would benefit from this test. Along this line, we consider that the inclusion criteria in our sample can be a guide to the characteristics of the patients who would most benefit from the ABI examination. The only exception would be patients <50-55 years old in whom the prevalence of a low ABI is so small that performing the test for therapeutic purposes might not be justified, regardless of the associated risk factors. The Framingham score was also an excellent predictor of a low ABI (<0.9) in our population, such that the prevalence virtually doubled with the progression from low risk (12.8%), to intermediate risk (20.6%), and to high risk or DM (36.7%). To our knowledge, the relationship between the probability of presenting a pathological ABI (<0.9 or >1.4) and the Framingham score has been examined in only one previous study, which also reported that the score is a good predictor of a pathological ABI.24 With respect to the group in whom a high ABI (>1.4) was detected, the number of patients was too small to allow a consistent statistical analysis. Nevertheless, there were no differences in the frequency of ABI>1.4 among the low and moderate risk categories on the Framingham scale, which might
indicate that these patients are at lower risk than those with a low ABI. In any case, the clinical significance of a high ABI is now uncertain; more studies are needed to confirm the usefulness of this parameter as a predictor of PAD and to determine the risk factors associated with its presence.

Another limitation of our study is its cross-sectional nature, which makes into investigation the prognostic value of ABI detection impossible. This, however, was not an objective of the study, since the prognostic relevance of the ABI has been firmly established in previous several longitudinal studies. In addition, the selection of hospitalized patients might be considered inappropriate, because certain biological parameters (e.g. lipid values) and clinical factors (e.g., blood pressure) can be modified in these circumstances. In this regard, it should be pointed out that the analytic determinations performed during the patient’s hospitalization were not included in the study. Furthermore, although the SAP may be decreased at hospital admittance, the ABI value would not change since it is not an absolute value, but instead the ratio of the SAP between the leg and the arm.

**CONCLUSIONS**

Our study shows that there is an elevated prevalence of asymptomatic PAD detected by the ABI in patients consulting in an internal medicine department who could benefit from more intense preventive measures. The ABI should be part of the routine assessment of most patients at vascular risk attended in the internal medicine setting, particularly diabetic patients and those at moderate-to-high risk according to the Framingham score.

**REFERENCES**