ABSTRACT

The ankle-brachial index (ABI) is the relationship between the systolic blood pressure taken at the ankle level and the brachial artery. A pathological ABI (<0.90 or >1.40) indicates the presence of peripheral artery disease (PAD). Many studies indicate the great utility of this test in the diagnosis of PAD due to its ease of use, reproducibility, low cost, and high cost-effectiveness. This evaluation can be directly correlated with cardiovascular morbidity and mortality; however, it has recently been confirmed that a low ABI can be a predictor of major cardiovascular events, as it is related to diabetes mellitus, chronic coronary disease, stroke, and more. The objective of this work was to review the current evidence on the importance of ABI in the diagnosis of PAD and its main role as a predictor of cardiovascular morbidity and mortality.

Keywords: Ankle brachial index; Peripheral arterial disease; Cardiovascular risk factor; Morbidity; Mortality (source: MeSH NLM).

RESUMEN

Índice tobillo-brazo: ¿algo más que una prueba diagnóstica?

El índice tobillo-brazo (ITB) es la relación entre la presión arterial sistólica tomada entre el tobillo y la arteria braquial. Un ITB patológico (<0,90 o >1,40) indica la presencia de enfermedad arterial periférica (EAP). Muchos estudios muestran la gran utilidad de esta prueba en el diagnóstico de la EAP debido a su facilidad de uso, reproducibilidad, bajo coste y alta rentabilidad. Esta evaluación puede correlacionarse directamente con la morbimidad y mortalidad cardiovascular; sin embargo, recientemente se ha confirmado que un ITB bajo puede ser un predictor de eventos cardiovasculares mayores, ya que está relacionado con la diabetes mellitus, la enfermedad coronaria crónica y el ictus, entre otros. El objetivo de este trabajo fue revisar la evidencia actual sobre la importancia del ITB en el diagnóstico de la EAP y su papel principal como predictor de morbimidad y mortalidad cardiovascular.

Palabras clave: Índice tobillo braquial; Enfermedad arterial periférica; Factores de riesgo cardiovascular; Morbilidad; Mortalidad (fuente: DeCS BIREME).
**Introduction**

Peripheral Arterial Disease (PAD) is defined as the partial or total obstruction of one or more peripheral arteries due to atherosclerosis [1]. Although the term PAD sometimes encompasses all peripheral arteries, it generally refers to atherosclerotic occlusive disease of the lower extremities [2-4]. PAD is very common and a prevalence of 13% is estimated in patients over 50 years of age [2,2].

The most frequent initial symptom of PAD is muscle pain during exercise, which is relieved with rest, this phenomenon is attributed to reduced blood flow in the lower extremities due to atherosclerosis (a symptom called intermittent claudication) [5,6]. Patients with more severe PAD can develop pain at rest, ulceration, and gangrene (chronic limb-threatening ischemia), and if not treated properly, can lead to amputation of the limb [5,7].

A simple and non-invasive test known as the ankle-brachial index (ABI) or ankle-brachial pressure index (ABPI) could give us indications of PAD, since it allows us to detect subclinical PAD (17,18). Only duplex scanning is more sensitive than ABI in detecting subclinical PAD [17,18].

Classically, the sampling is done using a sphygmomanometer cuff and a 5 or 10 MHz Doppler probe to detect signals within the arteries (Figure 1), the cuffs are placed on both arms above the anterior fossa of the elbow and above of each ankle and inflated sequentially above systolic pressure and then slowly deflated [19]. The Doppler probe monitors pressure when is placed over the brachial artery and the posterior tibial or dorsalis pedis arteries. When deflating the cuff slowly, the reappearance of the Doppler signal indicates the systolic pressure at the cuff position [19]. Currently, oscillometric and photoplethysmographic devices are available which were recently designed to facilitate these measurements more accurately; however, they still do not have the necessary evidence, and the use of handheld Doppler is still recommended [19].

A study included 191 patients over 50 years of age and the diagnostic difference between taking ABI by Doppler and by the palpatory method was assessed, finding 35 cases with PAD with palpatory method (18.8%) and 36 cases by Doppler (19.3%). When analyzing the concordance between both methods, it was found that the Kappa index was 0.8085, the sensitivity of 83.3%, and the specificity of 96.6%, which coincide with those widely described in the literature. Therefore, the determination of ABI by the palpatory method is acceptable as an alternative diagnostic method in the evaluation of PAD [20,21].

Forés R. et al., compared 3 diagnostic methods for peripheral arterial disease: the Doppler, the automatic oscillometric method (Omron), and the automated triple measurement; all these in basal conditions and with the patient in the supine position. He observed a poor correlation between ABI values obtained using the oscillometric and triple-take measurement; all these in basal conditions and with the patient in the supine position. He observed a poor correlation between ABI values obtained using the oscillometric and triple-take method in the evaluation of PAD (20,21).

**Definition and measurement of ABI**

The ABI is a quick, easy, and cost-free diagnostic test obtained by dividing the highest pressure at the ankle level (obtained in the posterior tibial artery, dorsal pedal, and when necessary, the peroneal arteries) by the systolic pressure in the upper arm (brachial artery) [11]. Brachial pressure is used as a surrogate for central aortic pressure, which is not readily available and is generally accurate unless there is an occlusive disease of the vessels supplying the upper extremity. For this reason, pressure is measured in both upper extremities, and the higher of the two is used [12].

This relationship allows a better appreciation of the degree of arterial occlusive disease. Without taking into account the brachial pressure, it would not be possible to know if low pressure in the ankle was caused by systemic hypotension or PAD; conversely, ankle pressure could be normal despite significant disease if the patient was hypertensive [2,13]. The objective is to detect occlusive disease by identifying the pressure drops between the proximal aorta and the ankle arteries [13].

The systolic pressure in the ankle should be at least the same as in the arm; that is, an ABI ≥ 1, as a consequence the proportions of 0.9 to 1.4 are normal for adults, the proportions lower than 0.9 are indicative of arterial stenosis, and the proportions lower than 0.5 are associated with critical ischemia [5-10]. The ABI decreases as the severity and grade of PAD increases and tends to be greater than 0.5 in single-level disease and less than 0.5 with multilevel disease. Most patients with intermittent claudication have an ABI between 0.5 and 0.9, but it can be as high as 1.0 or as low as 0.2; generally, patients with pain at rest have an ABI below 0.5, and those with impeding gangrene have an ABI below 0.3 [7,12,20]. Similarly, values higher than 1.4 are related to arterial calcification, which generates a normal ABI value; however, this finding is present in arteriopathies of diabetic patients, chronic kidney disease, and in the elderly [10].

In general, ABI sensitivity for detection of PAD ranges between 80-95% and the specificity between 95-100%, with positive and negative predictive values greater than 90%. Only duplex scanning is more sensitive than ABI in detecting subclinical PAD [17,18].

A study included 191 patients over 50 years of age and the diagnostic difference between taking ABI by Doppler and by the palpatory method was assessed, finding 35 cases with PAD with palpatory method (18.8%) and 36 cases by Doppler (19.3%). When analyzing the concordance between both methods, it was found that the Kappa index was 0.8085, the sensitivity of 83.3%, and the specificity of 96.6%, which coincide with those widely described in the literature. Therefore, the determination of ABI by the palpatory method is acceptable as an alternative diagnostic method in the evaluation of PAD [20,21].
Ankle-brachial index

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technique about the standard Doppler pattern, concluding that these automated methods are not recommended for PAD screening, especially at the first level of care (22,23). This difference could be explained by the results of many studies that indicate that very severe angiographic lesions are correlated with very low pressures that cannot be detected by automatic devices (13,24). However, to date, there is a controversy regarding the results of agreement between the mentioned methods. Verberk et al., carried out a meta-analysis with more than 4000 people and reported a good correlation between the automated methods despite presenting a relatively low sensitivity (69%) compared to the classic ITB (25).

ABI and Doppler echography

Most vascular laboratories perform lower extremity Doppler ultrasound and use the combination of brightness mode ultrasound (B), color Doppler ultrasound, and velocity analysis using pulsed Doppler, accurately identifying the location and grade of atherosclerotic lesions, in the lower extremities (26).

In a study of 35 patients with PAD and 25 healthy controls, significantly lower tibial velocities and tibial parameters were observed in patients with PAD (38.05 vs. 63.21 cm/s; p<0.001); while the deep femoral artery (DFA) showed significantly higher values (124.2 vs. 79.68 cm/s; p<0.001). Grouping by tertiles according to the ABI, its decrease was found comparably with the decrease in tibial velocities (31.69 cm/s for ITB between 0.4-0.6 and 58.57 cm/s for ITB> 0.6; p<0.001) and the Ankle-Deep Index (IDI), which is nothing more than the division of the peak systolic velocity (PSV) of the posterior tibial artery (PTA) and the DFA (0.285 for ITB between 0.4-0.6 and 0.718 for ITB> 0.6; p<0.001). Therefore, there is a gradual decrease in tibial velocities and their directly proportional relationship with the decrease in ITB and ITP. Therefore, its use is proposed for a more precise diagnosis of the severity of PAD, which may be of special importance in patients with non-compressible ABI (25,27).

ABI and peripheral arterial disease

To date different studies highlight the usefulness of ABI for diagnosis of PAD, granting it high specificity and sensitivity;
furthermore, it is currently considered a useful tool for predicting the risk of amputation and cardiovascular risk, emphasizing its ease of use, as it is a non-invasive test with good acceptability by patients (12,26,28).

Since 1950, low blood pressure in the ankle has been proposed as a test for PAD and this led to the development of a simple measurement, the ABI. An ABI that is too low is indicative of atherosclerosis of the lower extremities, and it has been found to have several optimal characteristics of the diagnostic efficacy curve as a diagnostic test for PAD. Although there is no definitive limit above which disease is always absent or below which disease is always present, an ABI ≤ 0.9 is often used to diagnose PAD in both clinical practice and epidemiological research (14,15,28).

Claudication is highly specific but very insensitive, such as an ABI-based PAD test. For example, in the Rotterdam study, 99.4% of people with ABI ≥ 0.9 did not present claudication and only 6.3% with ABI ≤ 0.9 manifested this symptom (9,30). ABI-based PAD is much more common than claudication in the general population, and many patients without claudication have atypical symptoms or are asymptomatic in the presence of ABI-based PAD. To ratify ABI and the huge burden of previously unrecognized asymptomatic disease that the index implied, early studies compared ABI-based diagnosis with angiography, the latter considered the gold standard for visualizing atherosclerosis in the lower extremities (10,11). From these often-cited studies, they noted a sensitivity and specificity of ABI in the range of 97-100%; However, it would not be correct to perform angiography in patients without suspected PAD (because this also implies a certain risk). These studies made comparisons between patients with PAD confirmed by angiography and healthy young people without suspected PAD (15,29). Therefore, the sensitivities and specificities calculated are based on the ability of the ABI to distinguish between extremes of illness and well-being. If calculated in patients at routine clinical practice or in general population, the specificity of ABI continues to be around 97%, but the sensitivity is somewhat lower (80%), this is because some patients with PAD have peripheral arteries with greater stiffness and with false negatives of ABI (9,31).

Many degrees of recommendation have been established on the usefulness of ABI in PAD. The American Heart Association (AHA) establishes it with a level of evidence B and class I (19); likewise, the European Society for Vascular Surgery (ESVS) in its latest clinical guide on the diagnosis and treatment of PAD (2019) strongly recommends its use (24). Studies such as the one by Recarey et al. carried out a broad bibliographic search on the subject to find the quality of evidence regarding ABI as a reliable means of diagnosis for PAD and its relationship with its associated risk factors (14,35). When analyzing 12 studies, it was found that none met the criteria to be considered of high quality of evidence; however, they concluded of the great utility of ABI for the diagnosis of PAD, especially in patients with diabetes mellitus, reinforcing the recommendation to perform it on an outpatient, systematic and routine basis.

**ABI and physical activity**

During the doctor’s visit, climbing stairs or active plantar flexion of the foot are activities that can cause symptoms and allow detecting a decrease in ankle pressure (and ABI) to confirm the diagnosis of intermittent claudication (12).

The correlation between ABI, functional capacity and symptoms is weak, ABI at rest can be normal in patients with PAD, like in patients with aortoiliac stenosis and with an appropriate collateral arterial system that maintains perfusion pressure (36). In patients with a normal ABI and a strong suspicion of advanced PAD, a stress test can be used in the office. Exercise widens arterial gradients by increasing turbulence through an obstruction that reduces flow and decreases muscular arteriolar resistance until the lower extremity perfusion pressure is significantly reduced (20). Blood pressure in the ankle can reach zero in claudication patients and recover more than 10 min after stopping exercise (28).

In a multicenter, population-based study in Barcelona, 3786 subjects over 49 years of age were selected, and it was evidenced that physical activity in free time (walking, sports, and daily activities) was positively and significantly related to ABI in patients with peripheral arterial disease and in healthy patients. The results adjusted for age, sex, educational level, work, body mass index, smoking, arterial hypertension, hypercholesterolemia, diabetes mellitus, and treatment with antiaggregants or anticoagulants showed a protective effect of walking (OR 0.55, 95% CI 0.35-0.84, p < 0.001) for those who walked more than one hour a day compared to those who walked less than half an hour (17).

**ABI and cardiovascular risk factors**

Many studies support that PAD is considered the most prevalent noncardiac artery disease and is a significant predictor of cardiovascular morbidity and mortality; likewise, it has an independent attributable risk with age, sex, and the presence of cardiovascular risk factors (CRF) (37,38).

Both symptomatic and asymptomatic PAD are associated with a very high risk of mortality from coronary heart disease and cerebrovascular disease (12,14,39). A value equal to or less than 0.9 is diagnosis of PAD and is related to high risk and cardiovascular mortality, a value equal to or greater than 1.4 diagnoses arterial calcification, increasing cardiovascular morbidity and mortality compared to normal values (24,30).
Hypertension and diabetes are the main CRF factors, and they also predict the presence of an altered ABI. In a prospective study, different cardiovascular factors were analyzed in a population with low ABI values, and they observed higher incidences of low ABI in smokers, dyslipidemia, diabetes mellitus, and arterial hypertension. Olivas et al., conducted a case-control study in a matched sample of 122 hypertensive and non-hypertensive patients, finding in the univariate analysis a strong association between pathological ABI (<0.9 or >1.4) with smoking ($p=0.010$), obesity ($p=0.006$), abdominal obesity ($p=0.002$) and presence of moderate CRF ($p=0.029$) measured using REGICOR tables. Likewise, no significant differences were observed in terms of ABI > 1.4, diabetes, and hypercholesterolemia, as for the multivariate analysis, the significant association of hypertension with pathological ABI was highlighted (OR 5.9; 95% CI: 1.2-28.3, $p<0.05$). Similarly, hypertensive patients showed a significantly higher frequency of smoking (OR 2.7; 95% CI: 1.1-6.2, $p<0.05$), abdominal obesity (OR 2.8; 95% CI: 1.3-5.1, $p<0.05$ and elderly. In conclusion, ABI is a tool that allows detecting peripheral arterial disease and highly associated arterial calcification in hypertensive patients and other cardiovascular risk factors.

A pathological ABI is a marker of risk and of subclinical disease in asymptomatic subjects; so, it is essential to investigate which population can benefit from this technique, especially the middle-aged population, which are often labeled with low-moderate cardiovascular risk; however, they can be asymptomatic carriers of target organ lesions, related to multiple comorbidities such as hypertension and diabetes.

Cardiovascular risk can be calculated by assessing the presence of target organ injury (TOI); so much so, that in a large proportion of young hypertensive patients, cardiovascular events were evidenced in those labeled low and moderate risk; however, they had TOI in its asymptomatic phase. That is why the guidelines of the European Society of Hypertension and the European Society of Cardiology maintain the prognostic importance of the various markers of TOI, among which is ABI.

### ABI and ischemic cardiopathy

Recently, there has been great interest in the early identification of peripheral arterial disease, since it has been classified as a marker of atherosclerotic risk in other vascular territories, particularly in the coronary tree and in the brain. The main problem is that PAD is underdiagnosed, taking into account that most patients are asymptomatic.

Núñez et al., studied 1031 patients with a mean age of 67.7 years, 52.6% had multivessel coronary disease and – compared with patients without multivessel involvement – were older (66.6 vs 62.6 years, $p<0.001$), had higher prevalence of hypertension (65.9 vs 56.2%, $p<0.005$), diabetes (40.6 vs 26%, $p<0.001$), hypercholesterolemia (89.1 vs 80.4%, $p<0.001$), history of cardiovascular disease (30.1 vs 13.9%, $p<0.001$) and a pathological ABI (45.4 vs 30.3%, $p<0.001$). In the multivariate analysis, the presence of a pathological ABI was associated with a higher risk of multivessel involvement (OR 1.58; 95% CI 1.16-2.15; $p<0.05$).

Pichin et al., described that 57.1% of the patients suffered from isolated ischemic heart disease and 37.5% of them had a low ABI. These results revealed the association between ischemic heart disease and atherothrombotic stroke as a sign of multisystem involvement of peripheral artery disease, with ABI being a strong risk predictor ($p=0.0002$). Patients with coronary and cerebrovascular disease history, have a high frequency of subclinical PAD diagnosed by ABI; therefore, due to this higher risk, once is detected its necessary to make an optimal treatment, which minimizes the possibility of other vascular complications.

### ABI and diabetes

The diabetic foot is a complex clinical entity formed by three pillars, the neuropathic, the ischemic, and the infectious, these three components coexist in different proportions in the same patient, and clinical evaluation and management must be based on all of them. There is a strong association between diabetes and the risk of amputation, three out of four major amputations are in diabetics, and extremities with severe arterial insufficiency are characterized by a drop in pressure and AB that correlates with clinical evolution.

ABI shows an excellent correlation with the patient’s symptoms and can predict the severity of peripheral arterial disease compared to angiography for the diagnosis of arterial occlusive disease in diabetics. In a study, ABI was determined in 242 patients with a mean evolution of diabetes of 15.8 years for the total population studied, the cumulative percentage of pathological ABI was greater related to the time of evolution of diabetes. In this study, patients who underwent amputation presented ABI >1.4 ($p=0.0001$) more frequently than normal ABI. In the logistic regression analysis, the factors that showed a statistically significant relationship with pathological ABI were: age, presence of vascular calcification, retinopathy, nephropathy, cardiovascular outcomes, claudication, and fasting hyperglycemia, and it was also determined that there is a relationship between pathological ABI and amputation ($p<0.05$).

In a Peruvian study by Vidal et al., the concordance between ABI and the segmental differential pressure (SDP) in patients with diabetic foot amputation was determined. There were 70 amputees and 50 non-amputees, the correlation between ABI and SDP was high ($r = 0.79$ and $p<0.01$), and the area under the ROC curve for ABI and SDP was 0.68, and 0.80
respectively. The optimal cut-off point for ABI and DPS was 0.75 and 10 mmHg, respectively, and the sensitivity and specificity for ABI was 52.9% and 86.0%, and for SPD of 65.7% and 84.0%, respectively. The positive (CP +) and negative (CP-) likelihood ratios for ABI were 3.78 and 0.55; and for the SPD of 4.11 and 0.41 respectively, concluding that the ABI and the SPD have good predictive value to assess the risk of amputation due to diabetic foot [49].

**ABI and chronic kidney disease**

A strong relationship exist between PAD and chronic kidney disease (CKD), the latter in its different stages has been seen in up to 39% of patients with PAD. This is because both share atherosclerosis as a common pathological substrate, but they also share risk factors such as diabetes, high blood pressure, and smoking. Therefore, patients with decreased kidney function will have a higher prevalence and incidence of arterial disease and therefore low ABI [3,5,7,11].

The prognostic role of ABI in CKD is still controversial, a meta-analysis by Chen et al. evaluated whether ABI was an independent predictor of cardiovascular or all-cause mortality in CKD patients with or without hemodialysis. Six studies with 5820 patients were identified and an abnormal ABI was associated with an increased risk of mortality from all causes (HR 2.26; 95% CI 1.60-3.18, p<0.05) and cardiovascular mortality (HR 3.58; CI 95% 2.53-5.06, p<0.05). Likewise, a low ABI was related to an increase in mortality from all causes by 2.45 times and 5.18 times in cardiovascular mortality [52]. Similarly, an abnormally high ABI increased all-cause mortality by 1.94 times and cardiovascular mortality by 4.04 times; likewise, abnormal ABI on all-cause mortality was more pronounced among hemodialysis patients (HR 3.06; 95% CI: 2.30-4.07; p<0.05) but not in CKD patients (HR 1.42; 95% CI: 0.98-2.05, p<0.05) [52].

**ABI, metabolic syndrome and obesity**

Patients with PAD have high prevalence of metabolic syndrome (MS), and in individuals in whom both diseases coexist, a higher prevalence of the main classic cardiovascular risk factors is observed, such as kidney failure, coronary heart disease, and cerebrovascular disease [3,5,7,10,11].

Orio et al. [25] described a prevalence of 48% of MS in patients with PAD, and observed that those individuals who suffered from MS had a higher prevalence of hypertension (87.3 vs. 60.3%; p<0.05), diabetes (69.8 vs. 39.9%; p<0.001), dyslipidemia (77.8 vs. 60.3%; p<0.05) and obesity (25.4 vs. 10.3%; p<0.05) compared to those who did not. Likewise, patients with MS presented more cerebral and cardiac ischemic events (42.9 vs. 19.1%; p<0.05), a higher prevalence of CKD (40.3 vs. 17.9%; p<0.05) and erectile dysfunction (81.3 vs. 54.3%; p<0.02). These results contrast with those reported by Estirado et al. [56], who developed a multicenter study conducted with almost 4,000 patients with PAD without associated ischemic heart or brain disease. In this study, a prevalence of MS of 63% was found in patients with PAD.

ABI as a marker of cardiovascular risk may also be related to abdominal obesity, and in a study visceral obesity was related with the ABI values obtained in patients who came to the outpatient clinic, concluding that a marked abdominal circumference and a altered waist-to-hip ratio index were associated with a low ABI, but not the body mass index (BMI) [23,46].

**ABI and stroke**

Hong et al. [57] developed a meta-analysis considering prospective studies of patients with cerebrovascular accident and transient ischemic attack, in whom ABI was measured at the beginning of the studies, and carried out a 12-month follow-up after the attack. They analyzed 5374 patients and found that a low ABI was associated with an increased risk of recurrent stroke (RR 1.70; 95% CI: 1.10-2.64, p<0.05) and an increased risk of vascular events or vascular death (RR 2.22; 95% CI: 1.67-2.97, p<0.05). This study suggests that a low ABI is an independent risk factor for both stroke recurrence and additional vascular events.

Several studies investigated the relationship between low ABI and stroke risk in cohorts without previous events. Sander et al. [58] analyzed 4 relevant studies (2762 patients) and found that ABI <0.9 was associated with stroke (RR of 2.33, 95% CI: 2.02-2.68, p<0.05). In patients with acute events and low ABI values, the risk of a new vascular event increases significantly (HR 2.1; 95% CI: 1.6-2.8, p<0.05). Fan et al. [59] analyzed 10 studies with a total of 22,355 participants in a meta-analysis where they described that low ABI was associated with a higher risk of stroke (RR 1.43; 95% CI: 1.23-1.5, p<0.05) and ischemic events (RR 1.83; 95% CI: 1.29-2.58, p<0.05). Likewise, a low ABI was also related to a higher risk of recurrent cerebrovascular accidents (RR 3.02; 95% CI: 1.26-7.25, p<0.05); however, a low ABI was not associated with an increased risk of a hemorrhagic brain event (RR 1.55; 95% CI: 0.34-7.08, p<0.05). Therefore, various studies highlight among their findings that a low ABI seems to be an independent predictor of ischemic and recurrent stroke events. Likewise, an altered ABI provides complementary information on subjects who are at increased risk of recurrent cerebral events [33,35].
Conclusions

This review allows us to conclude that ABI is a safe, simple, and reliable tool for the detection of PAD of the lower extremities in patients with or without claudication. Likewise, the association of ABI with the various classic cardiovascular risk factors such as arterial hypertension, diabetes mellitus, chronic kidney disease, metabolic syndrome, dyslipidemia, among others, makes it a good predictor of the severity of atherosclerotic disease, and its associated cardiovascular diseases complications. Finally, ABI is a marker of risk and subclinical disease in asymptomatic subjects, for this reason, its use is becoming increasingly important from the first level of care.

References


