# Ankle brachial index for the diagnosis of asymptomatic lower extremity peripheral arterial disease

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## ABSTRACT

Peripheral arterial disease (PAD) is a common vascular problem in which progressive narrowing of the arteries due to atherosclerosis reduces blood flow in the lower extremities. This study aimed to assess the prevalence of asymptomatic PAD in patients admitted to an internal medicine ward as well as the risk factors for the onset of the condition. This study included 98 institutionalized patients without a history of PAD. Based on the value of ankle-brachial index (ABI), PAD was classified as mild (0.7-0.9), moderate (0.5-0.7) or severe (<0.5). A detailed lower extremity doppler ultrasound was performed on patients with an ABI index <0.9 to provide more accurate information on peripheral arterial disease. The prevalence of asymptomatic PAD was 10.2%. The mean age of patients with positive ABI was 74. The main risk factors associated with PAD are smoking, chronic kidney disease, dyslipidemia, obesity, hypertension and type 2 diabetes. ABI is a useful and simple tool for detecting asymptomatic PAD. It is also crucial for early diagnosis, prevention and treatment, which can reduce the risk of cardiovascular adverse events as well as limb complications.

## Introduction

Peripheral arterial disease (PAD) is a common vascular problem in which progressive narrowing of the arteries reduces blood flow in the lower extremities.

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Key words: ankle brachial index, peripheral arterial disease.

Conflict of interest: the author declares no potential conflict of interest.

Ethical approval and consent to participate: the study was approved by the scientific ethics committee of the ASL of Teramo, Italy.

Availability of data and material: data and materials are available by the author.

Received: 2 March 2024.
Accepted: 21 June 2024.

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*Bleeding, Thrombosis and Vascular Biology 2024; 3:128*
*doi:10.4081/btvb.2024.128*



The prevalence of PAD was about 202,000,000 in 2010 and 236,000,000 in 2015;[1] among which two-thirds of the cases were mainly in Bangladesh, Brazil, China, France, Germany, India, Indonesia, Japan, Mexico, Pakistan, Russia, Spain, UK, USA and also Italy,[2] with an increasing trend related to both an increase in life expectancy and the attention paid to this disease, although still underestimated.

Africa is also seeing a notable increase in cases of PAD because of the rise of two important risk factors: smoking and type II diabetes mellitus. More than 70% of the global burden of PAD is concentrated in low-income countries with particularly high prevalence in sub□Saharan Africa, where traditional risk factors are known to be poorly controlled.[3,4]

Unfortunately, in these low- income countries, few therapeutic strategies can be introduced for the treatment of PAD and very often the main therapeutic choice remains amputation with significant consequences on quality of life.

Although it shares with coronary artery disease and cerebral ischemia the terrain predisposing to atherosclerosis, there is growing evidence that PAD represents a peculiar connotation of atherosclerotic disease, characterized by a high risk not only of limb complications (major adverse limb events, MALE), but also of cardiovascular adverse events (major adverse cardiovascular events, MACE).

The patient with PAD is a poly-vasculopathic patient with atherosclerotic complications also in other arterial districts (coronary, carotid, aortic), and therefore when PAD is diagnosed, it is necessary to study the other arterial districts as well. The patient with ischemic heart disease, with severe carotid stenosis (>50%), with PAD or with abdominal aortic aneurysm is a patient at very high cardiovascular risk.

Although revascularization improves symptoms in most patients, it does not prevent many from subsequently developing vascular complications, including acute limb ischemia, which is expected to occur 4 times more frequently than in subjects who have not undergone revascularization.

Patients' awareness of PAD is very low: 1 in 2 knows that diabetes and smoking increase the risk of PAD; 1 in 4 knows that PAD is associated with an increased risk of acute myocardial infarction and stroke; 1 in 7 knows that PAD can lead to amputation.[5]

There is also a lack of awareness of PAD on the part of physicians, and this overall results in underestimation and undertreatment of PAD itself, and thus there has not been much improvement over the decades both in terms of early diagnosis that would identify individuals with very high cardiovascular risk, and in terms of early treat-

ment that would result in a reduction in future atherosclerotic events and cardiovascular mortality.[6]

The symptomatology associated with PAD is termed claudication: lower extremity pain in the thigh or calf that appears during walking and ceases as soon as walking stops. Generally, if the pain is in the thigh, the obstructive pathology is at the aorto-iliac level; if the symptomatology is in the calf, the site of arterial obstruction is likely to be at the femoral or femoral-popliteal level.

PAD has different presentations, categorized according to Fontaine or Rutherford's classifications.

In Fontaine's classification, stage I corresponds to the asymptomatic patient, stage II is subdivided into IIa if claudication is not disabling to the patient, IIb if it is disabling to the patient, stage III corresponds to the presence of pain at rest and stage IV to the presence of acral ulcers or gangrene. The latter two stages (III and IV) correspond to the so-called critical ischemia.

Acute ischemia (ALI) is an acute event, diagnosed clinically with sudden pain, hypothermia, and cyanosis of the affected limb, and is often due to atherosclerotic plaque instability with intravascular or in situ thrombosis formation in cases of obstruction of a stent or graft in revascularized patients.

The stages at which surgical intervention is performed are stages III and IV, which correspond to critical ischemia, and stage IIb where the symptomatology for the patient is disabling.

Between 25% and 70% of PAD patients also have concomitant coronary artery disease, 14% to 19% have significant carotid vasculopathy (>70%), and 10% to 23% have renal artery stenosis.[7] Fifty percent of patients with claudication or silent PAD have coronary artery disease; in more severe phases (Fontaine stage III or IV), up to 90% of patients have both coronary artery disease and 60% cerebrovascular disease.[8]

In these patients, the causes of death are as follows: myocardial infarction (40-60%), non-cardiovascular causes (<30%) and stroke (10/20%).[9]

Patients with PAD have a high risk of MACE and MALE. The risk of MACE increases progressively from single PAD to PAD associated with CAD, up to PAD associated with CAD and a recent acute coronary event.

As for the risk of MALE, it increases progressively from asymptomatic PAD up to recent lower extremity revascularization for acute or critical ischemia.

Asymptomatic patients are more common than symptomatic patients. Let's consider an iceberg that is visible from a ship: what we see is only the tip emerging from the water, while the much more imposing base remains hidden. Asymptomatic patients represent the base and patients at stages III and IV of Fontaine's classification represent the tip of this iceberg. The number of patients is inversely proportional with the advancement of the disease with maximum number in the asymptomatic. If the presence of symptomatology brings the patient to medical attention, asymptomatic PAD is essentially diagnosed occasionally, and its true incidence is unknown and certainly of great significance. Hence the importance of diving into the sea to unearth asymptomatic patients for the purpose of slowing their inexorable progression to the apex of the iceberg.

Asymptomatic patients include patients with masked PAD: patients unable to walk a sufficient distance to trigger pain. These are usually patients with heart failure, joint problems, diabetic neuropathy. They may have severe disease in the absence of symptoms. Before making an estimate of pain while walking, it is therefore necessary to estimate a patient's walking ability.[10]

The aim of this study was to evaluate the prevalence of asymptomatic lower extremity PAD in patients admitted to an internal medicine ward, as well as the factors associated with the disease's development.

An additional purpose was to raise awareness of this disease among physicians, so that they understand the importance of early diagnosis and treatment for reducing the risk of MACE and MALE.

## Materials and Methods

This single center observational cohort study aims to assess the prevalence of asymptomatic peripheral arterial disease of the lower limbs in patients admitted to an Internal Medicine ward.

We included all inpatients who could give written consent who were asymptomatic for PAD.

Patients were provided with detailed information about the procedures. Patients with a positive history of PAD or with symptoms attributable to PAD were excluded.

Ankle-brachial index (ABI) was calculated with the patient at rest for at least 5 minutes, in supine position, by measuring the blood pressure in both upper and lower limbs (measured on the posterior tibial artery or, if absent, on the dorsalis pedis artery), dividing the ankle systolic pressure value by the higher brachial one.

Based on the value of ABI, PAD was classified as mild (0.7-0.9), moderate (0.5- 0.7) or severe (<0.5).

In cases with ABI index <0.9, Rose's questionnaire was performed with the following questions: *When you walk do you experience pain or other discomfort in your leg(s)? does the pain sometimes start when you are standing or sitting? Do you experience this pain in your calf? Do you accuse it when you walk uphill or at a brisk pace? Do you accuse it when walking at a normal pace? Does the pain sometimes go away when you're walking? What do you do if the pain continues while you are walking? do you stop, slow down, or continue? What happens if you stop? Does the pain disappear in 10 minutes or less or does it last longer than 10 minutes?*

Patients identified as symptomatic were excluded from the study, the purpose of which is the prevalence of asymptomatic PAD in patients admitted to our operating unit.

Patients with ABI<0.9 and negative questionnaire were given lower extremity arterial ultrasound, which allows us to have more detailed information.

The ultrasound study was performed with a linear probe at 5-12 MHz, but sometimes lower frequencies were used to evaluate the abdominal vessels in robust patients. The echo color doppler study began proximally from the distal external iliac artery/common femoral artery in both transverse and longitudinal sections. In case of doppler tracing changes indicative of possible proximal disease, the iliac arteries and abdominal aorta were also studied. We continued by evaluating the bifurcation of the femoral artery into deep and superficial femoral artery, the latter followed along its entire length. We then proceeded to study the popliteal artery posterior to the knee by following it distally to its division into the tibioperoneal trunk and the anterior tibial artery. As a landmark for the posterior and anterior tibial arteries, we can place the ultrasound probe immediately behind the medial malleolus and on the lateral margin of the tibia after the vessel passes between the tibia and fibula, respectively.

## Results

The study included 98 patients, admitted to our internal medicine complex operating unit between July and September 2023. The group of patients consisted of 50 women and 48 men, with a mean age of 68 years (range: 17-95).

Of the 98 patients, 10 have an ABI between 0.7 and 0.9. The prevalence of asymptomatic PAD was 10.2%. The mean age of patients with positive ABI was 74 (range 58-93).

Doppler ultrasound findings of PAD were represented by 60% stenosis in a vessel of the femoropopliteal region observed in 2 (20%) patients, 40-50% stenosis in a vessel of the femoropopliteal region in 2 (20%) patients, a disturbance in the distal waveforms with a monophasic flow in at least one lower extremity in 8 (80%) patients.

The risk factors found in these patients are smoking (80%), chronic kidney disease (60%), dyslipidemia (40%), obesity (60%), hypertension (100%), type 2 diabetes (40%) (Table 1).

Patients with asymptomatic PAD had at least two or more risk factors. None of the patients with PAD were risk factor free. Finally, hyperuricemia was also found in 40% of these patients. Moreover, in 80% of these patients, we found a positive history of vasculopathy in other districts, from carotid atheromasia to revascularized ischemic heart disease.

## Discussion

The polyvasculopathic PAD patient has a high risk of MALE and MACE. Because of the aging population and the increased prevalence of cardiovascular risk factors, the overall number of people with PAD is rising sharply on a global scale.[11] Cigarette smoking, hypertension, diabetes, dyslipidemia, chronic renal failure, and obesity are major risk factors. Age and ethnicity are risk variables that cannot be changed.

Upon admission to a medical setting, upper-limb blood pressure is always measured; ABI is rarely measured instead, although the European Society of Cardiology guidelines on the diagnosis and treatment of peripheral arterial disease (in collaboration with the European Society for Vascular Surgery) recommends ABI measurements as screening for PAD of the lower extremities.

An ABI <0.90 has 75% sensitivity and 86% specificity to diagnose PAD.[12] This sensitivity drops in diabetics and terminal chronic kidney disease, because of medial calcification.[13] In case of strong clinical suspicion and negative ABI, post-exercise ABI and ultrasound can be used before excluding the diagnosis of PAD. There are conditions in which the ABI may be distorted by diffuse calcifications of the vessel walls, as we often have in diabetics.

However, there may be patients with advanced disease and asymptomatic due to the inability to walk enough to determine symptoms (heart failure, orthopedic conditions...) or due to reduced pain sensitivity (diabetic neuropathy). These patients identify masked PAD. A careful history and a good objective examination are important for this purpose in order to understand which patients have masked PAD.

Ultrasound gives us much more accurate information than ABI, providing extensive information on arterial anatomy and hemodynamics and allowing us to evaluate the venous side for possible bypass. It has a sensitivity and specificity in identifying stenosis >50% of 85-90% and >95%, respectively.[14]

Our study shows a prevalence of asymptomatic PAD of 10.2%, a percentage that supports the importance of screening for PAD. If we had excluded younger subjects with a very low risk of PAD, the prevalence of asymptomatic cases calculated only in elderly patients would have been even higher.

The preventive strategies and strict control of risk factors include supervised exercise, cigarette smoking cessation, hypolipidemic and antihypertensive therapy, good glycemic control and weight loss in overweight patients.

However, no antiplatelet therapy should be started, because there is no proven benefit for its use in asymptomatic patients.

**Table 1.** Characteristics and risk factors.

| | Tot. patients | Asymptomatic PAD |
|---|---|---|
| Number of patients | 98 | 10 |
| Females | 50 | 6 |
| Males | 48 | 4 |
| Mean age, years | 68 (range 17-95) | 74 (range 58-93) |
| Total smoker, % | 51 | 80 |
| Current smoker, % | 16.3 | 60 |
| Past smoker, % | 34.7 | 20 |
| BMI >30 kg/m$^2$, % | 10.2 | 60 |
| Hypertension, % | 40.8 | 100 |
| CKD, % | 24.5 | 60 |
| Type 2 diabetes, % | 38.8 | 40 |
| Dyslipidemia, % | 30.6 | 40 |

PAD, peripheral arterial disease; BMI, body mass index; CKD, chronic kidney disease.

## Conclusions

The study shows that ABI is an easy-to-apply and noninvasive method to screen asymptomatic PAD. A method still little used today. Doppler ultrasound provides more accurate information and should be used in all patients with pathologic ABI.

Guidelines suggest screening for PAD in elderly subjects, patients already with atherosclerotic disease in other districts (coronary artery disease, carotid vasculopathy, mesenteric artery stenosis, renal artery stenosis).

We can avoid calculating ABI for young people (except for special cases described below) by focusing on high-risk patients, which are:

i. age ≥65;
ii. age 50-64, with atherosclerosis risk factors (*e.g.,* diabetes mellitus, history of smoking, hyperlipidemia, hypertension) or family history of PAD;
iii. age <50, with diabetes mellitus and an additional risk factor for atherosclerosis;
iv. individual with known atherosclerotic disease in another vascular bed (*e.g.*, coronary, carotid, subclavian, renal, mesenteric artery stenosis, or abdominal aortic aneurysm).[15]

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