Diagnostic accuracy of ankle-brachial index measurement in peripheral arterial disease in Turkish adults: A comparison with angiography

Tolga Doğan1*, İlker Taşçı1, Uğur Bozlar2, Birol Yıldız1, Cengizhan Açikel3, Selim Sayın1, Celalettin Günay4, Erol Arslan1, Kenan Sağlam1

1 Department of Internal Medicine, Gülhane School of Medicine, Ankara, TR
2 Department of Radiology, Gülhane School of Medicine, Ankara, TR
3 Department of Public Health, Gülhane School of Medicine, Ankara, TR
4 Department of Cardiovascular Surgery, Gülhane School of Medicine, Ankara, TR

* Corresponding Author: Tolga Doğan E-mail: doktortolga@gmail.com

ABSTRACT

Objective: This study aims to assess the sensitivity and specificity of ankle-brachial index (ABI) measurements in diagnosing peripheral artery disease (PAD) among a cohort of Turkish subjects, with angiography serving as the reference standard.

Material and Methods: In this single-center, cross-sectional and observational study, subjects who had an aorta and lower extremity arterial imaging by angiography subsequently underwent an ABI measurement. Anthropometric measurements, cardiovascular risk factors, and blood biochemistry data were recorded. Sensitivity and specificity analyses were performed for a low ankle-brachial index (ABI ≤ 0.9), with angiography as the reference standard.

Results: A total of 57 patients (age: 59.1 ± 15.9, male/female: 47/10) were included. Diabetes mellitus, coronary artery disease and cerebrovascular disease were present in 40.4%, 42.1% and 15.8% of the participants, respectively. Three or more cardiovascular risk factors were present in 54.4%. The angiographic diagnostic method was computed tomography angiography in 57.9%, digital subtraction angiography in 38.6%, and magnetic resonance angiography in 3.5% of the subjects. The presence of PAD on angiography was documented in 55 of 57 participants. The calculated mean ABI value was 0.6 ± 0.2 in the overall group, and a low ABI (≤ 0.9) was found by 82.5% (n = 47). Compared to angiography, the low ankle-brachial index (ABI) test demonstrated a sensitivity of 83.6% and a specificity of 50%. The positive predictive value of 97.9% was calculated. When an ABI ≤ 0.95 was used as the diagnostic threshold, the sensitivity of the ABI test increased to 90.9%.

Conclusion: Our study confirms the reliability of ABI measurements as a diagnostic method for lower extremity peripheral artery disease (PAD) when compared to angiographic techniques, the gold standard. Establishing a higher cut-off value (≤ 0.95) may enhance the diagnostic performance of the test in Turkish patients.

Keywords: Ankle-brachial index, peripheral arterial disease, sensitivity, specificity, angiography

INTRODUCTION

Peripheral arterial disease (PAD) is a chronic and progressive deterioration of lower extremity arterial blood circulation due to systemic atherosclerosis. Initially, it was narrowly defined as occlusion of the distal portion of the stenosis. While it was considered a condition requiring intervention as a result of related complications, coronary artery disease (coronary artery disease) is now included in the classification of cardiovascular disease (CVD). Heart disease, cerebrovascular disease and aortic atherosclerosis/aneurysm.

Peripheral artery disease (PAD) is associated with an increased risk of morbidity and mortality (1). The prevalence of PAD in the lower limbs was reported to be 20% in a multicenter survey of Turkish adults aged 50 years or older having moderate to high cardiovascular risk (2). However, a recent study from our clinic showed that the incidence of PAD was around 5% among outpatients in internal medicine (3). However, it is crucial to emphasize the importance of awareness, detection, treatment, and prevention for a vascular disease with a prevalence ranging from 5% to 20%.
While angiographic techniques serve as the gold standard for PAD diagnosis, Doppler ultrasound can provide an alternative diagnostic method. Surgical interventions are considered for confirmed cases, and Doppler ultrasound plays a role in preoperative assessments.

The Edinburgh Claudication Questionnaire exhibits low sensitivity, and its application without guidance in our country does not yield optimal results. Although a definitive diagnosis of PAD can only be made using angiographic techniques, the ankle-brachial index (ABI) measurement has emerged as a powerful, non-invasive diagnostic test option in identifying the disease (4,5).

Currently, available data on the sensitivity and specificity of ABI measurement are mostly from the USA, and ethnic variations in ABI are largely unknown. Moreover, worldwide frequency of ABI-detected PAD varies markedly across countries and regions, suggesting that diagnostic accuracy of ABI measurement may also differ. Therefore, the main objective of this research project was to evaluate the sensitivity and specificity of a low ABI value based on angiographic findings in subjects with suspected lower extremity arterial stenosis.

MATERIAL and METHODS

Study population

This was a single-center, cross-sectional and observational study conducted at the GATA Cardiovascular Surgery, Geriatrics and Internal Medicine Clinics between March 2012 and May 2013. Participants were selected from outpatients and inpatients referred to the institution's cardiovascular surgery clinic. They were routinely ordered for angiography based on clinical judgement or suspected arterial stenosis on ultrasound, regardless of the presence or absence of symptoms. Due to the observational study design, the decision of angiography was made before enrollment. Finally, the main inclusion criteria were 1) having angiography for aorta and lower extremity arterial system shortly before enrollment and 2) no extremity amputation; the presence of cancer or any other terminal illness and any condition that prevented giving a signed, informed consent were the exclusion criteria.

Data collection

As the main procedure of this study, all enrolled subjects underwent an ABI measurement after angiography. Demographic and anthropometric data including age, height, body mass index, waist circumference and hip circumference measurements were recorded on a standard chart. Smoking status, presence of hypertension, diabetes mellitus, dyslipidemia, coronary artery disease (CAD), cerebrovascular disease or stroke, and current medications were also recorded. Blood test results obtained in the past two months, including complete blood count, glucose, renal and liver function tests and lipid profile, were recorded from the hospital or patients’ self-records. The total number of major cardiovascular risk factors including diabetes mellitus, dyslipidemia, hypertension, obesity, age and cigarette smoking were determined for each patient under four categories: none, one risk factor, two risk factors and ≥3 risk factors.

Ankle-brachial index

ABI measurements were conducted using a hand-held Doppler (Hadeco, Japan) and four standard, fully calibrated sphygmomanometers with Velcro cuffs (size 12 cm, ERKA, D-83646, Germany). After a resting period of at least 5 minutes in the supine position, systolic blood pressure measurements were bilaterally taken from the brachial arteries, anterior tibial arteries, and posterior tibial arteries. The first flow sound heard during cuff deflation was recorded as the target value. Two cycles of measurements were performed, starting from the right arm and followed by the right leg, left leg, and left arm. The mean of the two readings for each pulse was used to calculate the ABI. Previously developed improved standardization facilities were used for all measurements (6). ABI was measured by an observer blinded to the outcome of angiography.

ABI was calculated according to The Trans-Atlantic Inter-Society Consensus Document on Management of Peripheral Arterial Disease (TASC II) recommendations (4). First, the ABI was calculated separately for the right and left limbs. The highest value in either the anterior or posterior tibial artery in each lower extremity was divided by the highest value in the brachial artery (right or left). The lower one of the right and left ABI values was considered as the final ABI result.

Categorical definitions of ABI

Subjects with an ABI value of ≤ 0.90 were considered to have PAD (4). In addition, participants were also classified into four other ABI categories: 0.91 to 1: borderline, 1.0 to 1.1: low normal, 1.10 to 1.4: normal, and >1.4: high (7,8).

Angiographic assessments and radiological classification

Computed tomography angiography (CTA), digital subtraction angiography (DSA) and magnetic resonance arteriography (MRA) were the angiographic techniques used to identify PAD. An experienced radiologist performed anatomical classification through re-examination of imaging records of patients who were diagnosed with PAD by angiography. The locations of the stenoses were classified into three main groups: aortoiliac, femoropopliteal, and tibioperoneal (9). Aortic stenoses in the aortoiliac group were separately indicated. The degree of any stenosis was divided into two categories: between 0 to 49%, indicating the absence of PAD, and 50% and above, indicating the presence of PAD.

Statistical analyses: Commercial software SPSS (version 15.0, SPSS Inc, Chicago, Illinois) was used for the statistical analyses. Descriptive data were presented as percentages for categorical variables and mean ± standard deviation for continuous data. The Chi-square test or Fischer’s exact test was used to compare categorical variables. Normal distribution was assessed using the One-Sample Kolmogorov-Smirnov test. Comparisons between groups were made using Mann Whitney U test. Correlations were tested using Pearson or Spearman tests where appropriate. P <0.05 values were considered statistically significant. Two different ABI cut-off values were tested separately, as ≤ 0.90 and ≤ 0.95. The ratio of the detection of PAD as sensitivity and the ratio of the detection of non-PAD as specificity were finally calculated.
RESULTS

Demographics, clinical characteristics and laboratory findings: Initially, 60 patients were enrolled, and 57 of them (mean age: 59.1 ± 15.9 years, male: 82.5%) were included in the analyses. Three patients were excluded due to incomplete angiographic images. The basic characteristics of the study population are presented in Table 1.

Hypertension was present in 27 (47.4%) patients, diabetes mellitus in 23 (40.4%), obesity in 6 (10.5%; BMI≥30), dyslipidemia in 33 (57.9%), CAD in 24 (42.1%), and cerebrovascular disease in 9 (15.8%) patients. Smoking was reported in 26 (45%) patients, rising to 47 (82.5%) subjects when ex-smokers were included. A total of 45 patients (80.4%) were under treatment with cardiovascular drugs, 20 patients (35.7%) were on antidiabetic drugs, 41 patients (73.2%) were taking antithrombotics or warfarin, and 6 patients (10.7%) were on psychiatric medications.

Risk factors for cardiovascular disease: The total number of male patients aged > 45 and female patients aged > 55 years was 43 (75.4%). Nine patients (15.8%) had no or one risk factor, 17 (29.8%) had two risk factors, and 31 (54.4%) had three or more risk factors.

ABI vs. angiographic diagnosis of PAD: The mean ABI value was 0.6 ± 0.2 in the entire study group, with no gender difference (ABI: 0.6 ± 0.2 in men vs. 0.6 ± 0.3 in women). According to the predefined ABI classification (see Methods), 82.5% of the patients had PAD, 12.3% had a borderline value, 1.8% had a low normal ABI, and 3.5% had a normal ABI (Table 2).

Sensitivity and specificity of ABI in the diagnosis of PAD with respect to angiography (Table 3): A low ABI value was found in 46 (83.6%) of 55 patients who had angiographically detected PAD. One of the two patients with no PAD, according to angiography, had a low ABI value (false positive). Finally, the sensitivity of the ABI test to detect angiographically proven PAD was 83.6%, but specificity was 50%. A strong positive predictive value of 97.9% was calculated for a low ABI to identify angiographically proven PAD. When the same analysis was applied to an ABI ≤ 0.95 threshold for PAD diagnosis, 50 (90.9%) of the 55 patients with angiographically detected PAD were classified as having PAD. In this case, both the sensitivity and positive predictive value improved (90.9% and 98%, respectively) (Table 3). However, the specificity remained unchanged (50%) due to an insufficient number of participants with non-diagnostic angiography for PAD.

Table 1. Demographic characteristics and laboratory findings

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mean ± SD(min-max)</th>
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<tbody>
<tr>
<td>Age (years)</td>
<td>59.1 ± (15.9; 20-82)</td>
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<tr>
<td>Gender, male, n (%)</td>
<td>47 ± 82.5</td>
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<tr>
<td>Anthropometrics</td>
<td>Mean ± SD (min-max)</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>169.6 ± 9.1 (153-185)</td>
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<tr>
<td>Body weight (kg)</td>
<td>74.0 ± 11.4 (52-100)</td>
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<tr>
<td>Body mass index (kg/m²)</td>
<td>25.9 ± 4.3 (16.7-37.5)</td>
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<tr>
<td>Waist circumference (cm)</td>
<td>93.8 ± 12.6 (65-137)</td>
</tr>
<tr>
<td>Hip circumference (cm)</td>
<td>98.0 ± 10.6 (78-147)</td>
</tr>
<tr>
<td>Waist to hip ratio</td>
<td>1.0 ± 0.8 (0.8-1.2)</td>
</tr>
<tr>
<td>Blood tests</td>
<td></td>
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<tr>
<td>Hemoglobin (g/dL)</td>
<td>13.9 ± 4.9 (8.0-17.1)</td>
</tr>
<tr>
<td>Leukocyte (x10³/microL)</td>
<td>7.5 ± 2.2 (3.2-12.8)</td>
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<tr>
<td>MCV (fL)</td>
<td>84.7 ± 12.1 (56-104)</td>
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<tr>
<td>Platelets (x10³/microL)</td>
<td>273.8 ± 96.1 (69-523)</td>
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<tr>
<td>Sedimentation (mm/hour)</td>
<td>28.0 ± 29.3 (2-131)</td>
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<tr>
<td>Glucose (mg/dL)</td>
<td>126.1 ± 67.8 (59-340)</td>
</tr>
<tr>
<td>Urea (mg/dL)</td>
<td>47.4 ± 32.3 (12-172)</td>
</tr>
<tr>
<td>Creatinine (mg/dL)</td>
<td>1.3 ± 1.2 (0.6-8.8)</td>
</tr>
<tr>
<td>AST (U/L)</td>
<td>20.1 ± 6.2 (11-46)</td>
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<tr>
<td>ALT (U/L)</td>
<td>17.4 ± 8.2 (7-53)</td>
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<tr>
<td>GGTP (U/L)</td>
<td>37.4 ± 36.5 (7-192)</td>
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<tr>
<td>Total cholesterol (mg/dL)</td>
<td>180.5 ± 48.3 (67-277)</td>
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<tr>
<td>Triglyceride (mg/dL)</td>
<td>149.2 ± 120.5 (40-471)</td>
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<tr>
<td>HDL-cholesterol (mg/dL)</td>
<td>47.0 ± 25.3 (20-67)</td>
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<tr>
<td>LDL-cholesterol (mg/dL)</td>
<td>113.8 ± 37.6 (36-182)</td>
</tr>
<tr>
<td>Albumin (g/dL)</td>
<td>4.1 ± 0.4 (2.9-4.9)</td>
</tr>
<tr>
<td>Total protein (mg/dL)</td>
<td>7.0 ± 0.4 (6.0-7.9)</td>
</tr>
<tr>
<td>Sodium (mEq/L)</td>
<td>140.0 ± 2.4 (135-146)</td>
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<tr>
<td>Potassium (mEq/L)</td>
<td>4.3 ± 0.4 (3.2-5.4)</td>
</tr>
<tr>
<td>Calcium (mg/dL)</td>
<td>9.6 ± 0.5 (8.5-10.4)</td>
</tr>
<tr>
<td>LDH (IU/L)</td>
<td>354.1 ± 103.3 (172-667)</td>
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AST: Aspartate aminotransferase; ALT: Alanine aminotransferase; GGTP: Gamma glutamyl transferase; HDL: High density lipoprotein; LDH: Lactate dehydrogenase; LDL: Low density lipoprotein; MCV: Mean corpuscular volume
DISCUSSION

This study on a group of Turkish people demonstrated that ABI measurement is a reliable test in diagnosing PAD based on angiographically proven disease. To the best of our knowledge, this is the first report from Turkey to provide evidence of the utility of non-invasive ABI measurement in detecting lower extremity PAD.

Smoking, older age, diabetes mellitus, hyperlipidemia and hypertension have been associated with an increased incidence of PAD, with the presence of at least one cardiovascular disease risk factor up to 95% of individuals with PAD (1). Given the identification of at least one cardiovascular risk factor in 84% and ≥3 risk factors in 54.4% among our participants, with co-existing hypertension, diabetes mellitus or CAD by more than 40%, the present study population was quite similar to those that different authors previously studied. However, the enrollment of the small number of subjects with normal or non-diagnostic angiography for PAD appeared as a drawback of our study. While ordering angiography for study purposes only in asymptomatic subjects with a normal ABI was not possible for ethical considerations, it is also not recommended for most cases with a low ABI value (4).

ABI has been a sensitive, reliable and cost-effective method in diagnosing PAD (4,10). It has also been demonstrated to be useful in detecting generalized atherosclerosis (11). The presence of a low ABI or subclinical atherosclerosis in elderly patients without a history of CAD was shown to be a significant predictor of all-cause mortality and cardiovascular morbidity (12).

Therefore, effective routine use of ABI measurement can improve patient management in any population.

Compared to DSA, CTA had 96.4% sensitivity and 98.4% specificity for the detection of peripheral arterial stenosis (13), while the sensitivity and specificity of MRA were reported to be almost 100% (14). Less invasive CTA and MRA have increasingly been preferred to more invasive DSA due to patient comfort and low risk of complications. Accordingly, despite being considered as a gold-standard imaging method, DSA could only be performed in less than one third of our patients.

Based on a threshold value of ≤ 0.9, ABI was reported to have 79-95% sensitivity and 85-100% specificity concerning angiographic methods in diagnosing PAD (15). In our study, the sensitivity of ABI using this threshold was found to be 83.6%, which seems acceptable and in line with the literature. Although the main objective of our study was to determine the sensitivity, the specificity of ABI could be evaluated in only two cases that had <50% stenosis on angiography. Due to the small sample size, the specificity value of 50% for a low ABI in our study population lacks adequate accuracy.

The sensitivity and specificity of ABI measurement for lower extremity PAD diagnosis revealed inconsistent findings in several studies, depending on various factors including observer, equipment and methods (16). In a study by Khusrow et al. conducted on 107 patients based on DSA and ABI in the diagnosis of PAD, the sensitivity and specificity of ABI using higher or lower ankle pressures were reported as 69-84% and 83-64%, respectively (17).
Calculating ABI using a lower ankle pressure was associated with improved sensitivity and decreased specificity values in other studies (18,19). However, the American Heart Association and TASC2 guidelines continue to recommend using higher ankle pressures to calculate ABI which was also the chosen method in the present investigation. In a recent study conducted by Nam et al., 79 patients with intermittent claudication underwent serial CTA, DSA, and ABI assessments. The authors reported relatively lower levels of sensitivity and specificity of ABI as 61% and 87%, respectively (19). The performance of the ABI test was also evaluated according to the observer, which generally showed a high reproducibility of the method (10, 20, 21). ABI measurement was performed meticulously under improved conditions for each patient in the present study. The same trained and experienced observer performed all measurements using the same 8 Hz. Doppler and four Velerco cuff (12 cm wide and 29-40 cm long) sphygmomanometers wrapped on four extremities simultaneously. The environment was also specially arranged with a comfortable stretcher and two metal armrests placed at 30 degrees to ensure the comfort of the upper extremities. Measurements were taken twice in each vessel in two rounds and the mean value was used for each vessel readings. Therefore, unfavorable factors that could affect the result of ABI measurement were minimized.

Given the decrease in the sensitivity of ABI measurement in diabetics and elderly populations who frequently have calcified vessels, ABI has been considered less reliable in calcified and incompressible arteries, leading to falsely higher values (15). For example, the sensitivity of > 90% in patients with PAD was reported to decrease to 50% in a group with diabetic neuropathy, and to 30% in asymptomatic subjects (22,23). Although a high ABI is common among diabetics and/or the elderly population, these patients are considered to have the same risk as those having a low ABI value, even when they have no symptoms. Although the average age of our participants was 59, diabetes mellitus was recorded by 40% in the whole study group but we detected no high ABI value in these participants who had angiographically proven PAD. A high ABI was also less common in our previous studies on Turkish subjects compared to other populations (3); however, whether ethnic differences in the rate of vessel calcnosis exist has not been clearly reported to date.

While an ABI value below ≤ 0.90 is commonly accepted as diagnostic for PAD, some studies (24,25) suggest that using a threshold index value of ≤ 0.95 may enhance diagnostic performance. Accordingly, in our study population, the sensitivity of the ABI test increased from 83.6% to 90.9% when the diagnostic cut-off was set at ≤ 0.95. Whether some higher ABI threshold values provide better diagnostic performance in Turkish subjects with PAD needs to be further tested.

CONCLUSION

The sensitivity of the ABI test in our study is 83.6%. This study on Turkish subjects showed that the sensitivity of a low ABI value to detect angiographically proven PAD was in the acceptable range, with an impressive positive predictive value. Moreover, using the value of ABI ≤ 0.95 as the diagnostic threshold markedly improved the sensitivity ratio, it increases to 90.9%. Nevertheless, clearer specificity values could not be obtained due to the low number of participants without PAD as confirmed by angiography. Turkey carries a significant burden of PAD, emphasizing the critical need for identifying patients with a non-invasive, cost-effective, and efficient method to prevent morbidity. Our study supports the use of ABI in the Turkish population.

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Author Contributions: TA, İT, UB, BY, CA, SS, CG, EA, KS: Designed and directed the study. Literature search, Data collection, analysis and interpretation of results TA: Article writing, Final revisions. All authors reviewed the results and approved the final version of the manuscript.

Ethical approval: The present study was conducted in strict accordance with the principles outlined in the Declaration of Helsinki. Ethical approval for the study was obtained from the appropriate ethics committee, and all participants provided informed consent before participating in the study.

REFERENCES


