

Ankle-Brachial Index as a Prognostic Factor and Screening Tool in Coronary Artery Disease: Does it Work?

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Abstract

Background: Given the lack of consistency in the literature regarding the reliability of the ankle-brachial index (ABI) as a valid screening tool and an independent risk indicator of cardiovascular events and mortality, we compared it with angiography as a reference standard test.

Methods: This case-control study, conducted between 2010 and 2011 in Tehran Heart Center, recruited 362 angiographically confirmed cases of coronary artery disease (CAD) and 337 controls. A standard protocol was used to measure the ABI and different CAD risk factors.

Results: A low ABI had specificity of 99.7%, positive predictive value of 95.8%, negative predictive value of 49.8%, sensitivity of 64%, likelihood ratio of 24.07, and odds ratio (OR) of 22.79 (95%CI: 3.06-69.76). The role of the associated risk factors was evaluated with OR (95%CI), with the variables including gender 3.15 (2.30-4.30), cigarette smoking 2.72 (1.86-3.99), family history 1.72 (1.17-2.51), diabetes 1.66 (1.15-2.4), and dyslipidemia 1.38 (1.02-1.88). In a multivariate model, the following variables remained statistically significantly correlated with CAD [OR (95%CI)]: ABI 13.86 (1.78-17.62); gender 3.69 (2.43-5.58); family history of CAD 2.18 (1.41-3.37); smoking 1.69 (1.08-2.64); age 1.04 (1.02-1.06).

Conclusions: A low ABI had specificity of 99.7%; however, because of its low sensitivity (64%), we should consider CAD risk factors associated with a low ABI in order to use it as a first-line screening test.

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Introduction

A low ankle-brachial index (ABI) is deemed a feasible,

valid, and noninvasive indicator of atherosclerosis.^{1, 2} A low ABI suggests the development and severity of lower-limb peripheral arterial disease² and can play a crucial role

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as an independent risk indicator of cardiovascular events and mortality.¹ A reclassification of the cardiovascular risk assessment model to include the ABI led to the modification of the management of cardiovascular diseases in women (almost 36%) and in men (19%).¹ The early detection and prevention of cardiovascular and cerebrovascular events require a precise identification of individual risks through the use of accurate indicators.

A low ABI (≤ 0.90) has been demonstrated to correlate with a twofold increase in cardiovascular mortality, ten-year mortality, and coronary events rate.¹ A low ABI is considered a potential factor in the detection of symptomatic and asymptomatic patients afflicted with peripheral arterial disease and could, as such, be an accurate and effective screening test for peripheral arterial disease² and coronary artery disease (CAD).³ The ABI might also provide more information regarding the prognosis of the long-term survival of patients with peripheral arterial disease.⁴

The ABI, alongside type-D personality, has been shown to predict the quality of life and depressive symptoms in patients with peripheral arterial disease.⁵ Both resting and post-exercise measures of the ABI were strong independent predictors of mortality⁶ in a cohort study of 3209 patients⁴ and increased risk of stroke or transient ischemic attack in the elderly in another study.⁷ There has been other evidence for a significant decline in the ABI after modifying the risk factors of CAD among a cohort of 5888 participants over 6 years of follow-up.⁸

Nonetheless, the reported evidence regarding the accuracy of the ABI suffers from a lack of consistency. This prospective investigation was, therefore, performed to evaluate whether the ABI could provide evidence for the prediction of CAD, and if so, to determine the accuracy of this indicator compared with coronary angiography.

Methods

A population of 699 was recruited in this case-control study with incidence cases (362) and controls (337) between 2010 and 2011 in Tehran Heart Center. The CAD cases were confirmed by angiographic findings, and the controls comprised patients with normal angiographic findings. The definition of obstructive CAD was decided as stenosis of 50% or more of the diameter of any coronary artery.⁹

For the measurement of risk factors, such well-known risk factors as age, gender, hypertension, diabetes, dyslipidemia, cigarette smoking, physical activity, body mass index, family history of CAD, and ABI were assessed via standardized methods.

The ABI measurements were done using a standard sphygmomanometer and a Doppler device, after 30 minutes of rest in a supine position. The detection of both upper- and lower- limb blood pressures was done by placing the blood

pressure cuffs over the brachial arteries and malleoluses. For each right and left brachial artery and right and left dorsalis pedis artery, the cuff was inflated to 20 mmHg over the detectable systolic blood pressure and deflated appropriately. The ABI was calculated in accordance with the American Heart Association definition¹ as the ratio of the higher systolic blood pressure of each ankle-brachial artery. The ABI was considered attenuated if the quotient was < 0.9 . All the ABI measurements were performed by 2 well trained physicians. In this study, the ABI was treated as a categorical variable of an ABI ≤ 0.9 and an ABI > 0.9 .

Univariate analysis was performed by applying the Pearson chi-squared test and the independent sample T-test as well as the estimation of the odds ratio and 95% confidence interval (95%CI) and measures of accuracy. The odds ratio, 95%CI, and likelihood ratio were calculated for different endpoints of CAD. Bivariate analysis was carried out by performing age- and sex-adjusted Mantel-Haenszel odds ratio and 95%CI. Multivariate analysis was conducted via the logistic regression model to evaluate multivariate adjusted relationships between CAD and independent variables and for adjusting potential confounders. Statistical comparisons were considered significant at a p value < 0.05 . Measure of validity was done to assess the accuracy of the ABI (≤ 0.90) compared to angiographic results through the calculation of the sensitivity, specificity, and predictive values.

Results

This research was performed on 362 cases and 337 controls. Table 1 compares the different risk factors and systolic blood pressures of both extremities between the two groups of cases and controls.

The calculated measures of accuracy for the ABI (≤ 0.9) compared to the results of coronary angiography revealed sensitivity of 64%, specificity of 99.7%, positive predictive value of 95.8%, and negative predictive value of 49.8%.

The crude OR and 95%CI of the relationship between the studied risk factors and CAD associated with the likelihood ratio are presented in Table 2. Based on the likelihood ratio, we could strongly predict angiographically confirmed CAD with the presence of gender differences, cigarette smoking, age, and low ABI.

Crude and adjusted Mantel-Haenszel odds ratio and 95%CI [OR (95% CI)] for age- and sex-matched comparisons were as: for age under 60 years to age above 60 years, the comparison crude estimate was 0.07 (0.01-0.45) and the common adjusted parameter estimate was 2.65 (0.97-4.86).

The sex-matched estimate of the parameters demonstrated that the crude odds ratio for the male-to-female comparison was 3.15 (2.32-4.30) and that the common adjusted odds ratio was 3.69 (2.43-5.58).

A low ABI did not significantly predict the unstable angina

pectoris in terms of an odds ratio and 95%CI of 2.94 (0.29-29.23) and a likelihood ratio of 0.97 (p value = 0.32).

Acute myocardial infarction could not be predicted by a low ABI with an odds ratio and 95%CI of 1.11 (0.97-1.28) and a likelihood ratio of 0.19 (p value = 0.65).

Non-ST-segment elevation myocardial infarction was of a prognostic value of 1.42 (1.05-1.96) and a likelihood ratio of 1.30 (p value = 0.25) with a low ABI.

A low ABI predicted stable angina pectoris with an odds ratio and 95%CI of 2.43 (2.17-2.70) and a likelihood ratio of 20.65 (p value = 0.001).

Table 3 shows the adjusted odds ratios and 95%CIs for the different variables derived from a logistic regression model that controlled the potential confounders, when the ABI was

treated as a categorical variable and was considered abnormal at ≤ 0.9 . According to the above multivariate results, an $ABI \leq 0.9$ had a strong and significant prognostic value for predicting CAD (odds ratio= 13.86).

Discussion

The results of our investigation demonstrated that the measures of the accuracy of a low ABI (≤ 0.90) had very high specificity (99.7%) and a positive predictive value of 95.8% but low sensitivity (64%) and a low negative predictive value of 49.8%. Furthermore, the ABI provided strongly signifi-

Table 1. Characteristics of the patients*

	Cases (n = 362)	Controls (n = 337)	P value
Age (y)	60.01±0.01	55.48±10.69	< 0.001
Gender			< 0.001
Female	106 (29.3)	191 (56.7)	
Male	256 (70.7)	146 (43.3)	
Diabetes mellitus	93 (25.7)	58 (17.2)	0.006
Hypertension	134 (37.0)	117 (34.7)	0.521
Dyslipidemia	111 (30.7)	119 (35.5)	0.034
Cigarette smoking	156 (43.1)	47 (13.9)	< 0.001
Family history of CAD	88 (24.3)	53 (15.7)	0.005
Physically active	25 (6.9)	37 (11.0)	0.058
Triglyceride (mg/dl)	175.62±26.40	151.24±66.36	0.002
LDL-C (mg/dl)	111.42±47.45	108.35±40.58	0.368
HDL-C (mg/dl)	43.81±10.90	49.58±27.53	< 0.001
Total cholesterol (mg/dl)	186.48±46.44	178.79±62.03	0.062
Fasting blood glucose (mg/dl)	115.18±62.51	104.04±30.78	0.003
ABI	1.06±0.12	1.09±0.08	< 0.001
Body mass index (kg/m ²)	27.36±3.90	28.29±5.08	0.007
Right-hand SBP (mmHg)	126.83±19.35	126.80±17.44	0.985
Left-hand SBP (mmHg)	126.46±19.02	125.94±16.71	0.706
Right-leg SBP (mmHg)	134.2±20.96	137.91±17.89	0.013
Left-leg SBP (mmHg)	134.59±21.35	138.5±18.17	0.011

*Data are presented as mean±SD or n (%).

CAD, Coronary artery disease; LDL-C, Low-density lipoprotein; HDL-C, High-density lipoprotein; ABI, Ankle brachial index; SBP, Systolic blood pressure

Table 2. Comparison between case and controls based on predictive factors

	OR	95% CI	Likelihood Ratios	P value
Gender				
Male	3.15	2.32-4.30	54.26	< 0.001
Female	0.31	0.23-0.43	54.26	< 0.001
Age	1.04	1.02-1.06	26.17	< 0.001
Dyslipidemia	1.38	1.02-1.88	4.43	0.021
Cigarette smoking	2.72	1.86-3.99	28.60	< 0.001
Family history of CAD	1.72	1.17-2.51	8.06	0.003
ABI(≤ 0.90)	19.31	3.06-69.76	24.07	< 0.001
FBS (≤ 126 mg/dl)	1.66	1.15-2.40	8.84	0.003
HDL-C (≤ 40 mg/dl)	0.79	0.68-0.92	9.15	0.002

CAD, Coronary artery disease; ABI, Ankle brachial index; OR, Odds ratio; CI, Confidence interval, FBS, Fasting blood sugar, HDL-C, High-density lipoprotein



Table 3. Adjusted OR and 95% CI for the relationship between different factors with CAD when ABI is categorical

	OR	95% CI	P value (Wald test)
Gender			
Male	3.69	2.43-5.58	< 0.001
Female	0.27	0.17-0.41	< 0.001
Age	1.04	1.02-1.06	< 0.001
Family history of CAD	2.18	1.41-3.37	< 0.001
Cigarette smoking	1.69	1.08-2.64	0.021
ABI (≤ 0.9)	13.86	1.78-17.62	0.012
ABI (> 0.9)	0.07	0.05-0.56	0.012

CAD, Coronary artery disease; ABI, Ankle-brachial index; OR, Odds ratio; CI, Confidence interval

cant information on the prediction of CAD [OR (95%CI): 13.86 (1.78-17.62)] after multivariate adjustment for the potential confounding variables.

There is no doubt that a low ABI (≤ 0.90) increases the risk of overall mortality, proportional cardiovascular mortality, and coronary events by about twofold.¹ Cardiovascular risk assessment based on traditional CAD risk factors is deemed difficult, and the introduction of new noninvasive, feasible, and valid prognostic factors seems to be necessary. Therefore, in accordance with the guidelines published by the American Heart Association/ American College of Cardiology, the present study showed that the ABI had the potential to be implemented for the risk assessment of CAD.^{1, 10} Future cardiovascular events in people with traditional and novel risk factors, as well as in individuals with asymptomatic atherosclerosis, may be easily predicted by the ABI, which is feasible, noninvasive, and accurate. The ABI has been traditionally applied for the screening of peripheral arterial disease, Nowadays given that a resting attenuated ABI of ≤ 0.90 is associated with an increased risk of overall mortality of about 2-7 fold and cardiovascular mortality of 2-4 fold,⁶ it can be considered as a feasible, noninvasive, and accurate tool for the screening of cardiovascular events for generalized atherosclerosis. There is also reported evidence that supports the role of a low ABI in increasing the risk of cerebrovascular events, especially in the elderly.^{7, 11, 12} Our results revealed that a resting attenuated ABI had low sensitivity (64%) but enormous specificity (99.7%) and positive predictive value (95.8%). This measure of high specificity implies that a low ABI, as a valid and trustworthy sensitive screening tool, might rule out the presence of CAD. Sensitivity of 64% demonstrates that a low ABI at rest, when considering the higher systolic blood pressure of the limbs, should improve. Considering other major CAD risk factors combined with a low ABI is suggested to have the potential to improve the sensitivity of this index. The second definition and calculation of the ABI based on the measurement of the lower systolic blood pressures of both dorsalis pedis and brachial arteries may also augment the ability of a low ABI to predict the existence of CAD.

The difference between our findings and those of a study previously published in 2008 could be explained by the

discrepancy in the applied gold standard test for comparison. In our research, we considered angiographic findings as a gold standard in comparison with the ABI, whereas the older study³ compared the results of the ABI with single-photon emission computed tomography and electrocardiography.³

A low ABI has been found to be associated with other CAD risk factors, and it seems that the modification of modifiable CAD risk factors and declining ABI may cause a statistically significant decrease in the lower extremity arterial diseases.⁸ In order to evaluate the risk factors of a declining ABI, the Cardiovascular Health Study Cohort was conducted. The frequency of a decrease in the ABI over a follow-up period of 6.5 years was estimated at 9.5%. Predictive factors for a declining ABI included age, cigarette smoking, hypertension, diabetes, and high density lipoprotein cholesterol (HDL-C) level. We found out more features of prognostic factors. In the present study beyond the result of the previous research,⁸ we showed that gender, age, cigarette smoking, family history of CAD, and ABI ≤ 0.9 , played a statistically significant role in the prediction of future CAD.

A low ABI accurately predicts the presence of peripheral arterial disease in both symptomatic and asymptomatic individuals and is also associated with the severity^{13, 14} and progression¹⁵ of peripheral arterial disease. These findings demonstrate that ABI has the potential to detect the peripheral arterial disease at an early stage.

Since a low ABI shows a strong positive correlation with peripheral arterial disease, it can predict cardiovascular and cerebrovascular mortality.¹⁶⁻¹⁹ Also, in concord with our findings, a low ABI could be considered as a predictive factor for such events. It also can be pivotal in the risk assessment for afflicted or healthy individuals. A valid and reliable model of risk factor assessment guides the management strategies, in both primary and secondary prevention.²⁰

Conclusion

A low ABI has almost perfect specificity (99.7%) and positive predictive value of 95.8% but low sensitivity (64%). Therefore, in order for a low ABI to be considered a first-line screening test for the early detection of CAD, we need

to factor in other CAD risk factors associated with the ABI. Our multivariate adjusted relationships provided strongly accurate information regarding the prediction of CAD with an odds ratio of 13.86 with a low ABI (≤ 0.90).

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