The relation between ankle-brachial index (ABI) and coronary artery disease severity and risk factors: an angiographic study

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### **Abstract**

**BACKGROUND:** The current study aims to determine the relation between ankle-brachial index (ABI) and angiographic findings and major cardiovascular risk factors in patients with suspected coronary artery diseases (CAD) in Isfahan.

**METHODS:** In this cross-sectional descriptive-analytic research, patients with suspected CAD were studied. Characteristics of studied subjects including demographics, familial history, past medical history and atherosclerotic risk factors such as diabetes mellitus, hypertension, hyperlipidemia and smoking were obtained using a standard questionnaire. ABI was measured in all studied patients. ABI  $\leq$  0.9 (ABI+) was considered as peripheral vessel disease and ABI > 0.9 (ABI-) was considered as normal. Then, all studied patients underwent coronary artery angiography. The results of the questionnaire and angiographic findings were compared in ABI+ and ABI-groups. Data were analyzed by SPSS 15 using ANOVA, t-test, Spearman's rank correlation coefficient, and discriminant analysis.

**RESULTS:** In this study, 125 patients were investigated. ABI  $\leq$  0.9 was seen in 25 patients (20%). The prevalence of ABI+ among men and women was 25.9% and 7.5%, respectively (P = 0.01). The prevalence of atherosclerotic risk factors was significantly higher in ABI+ patients than in ABI- ones (P < 0.05). ABI+ patients had more significant stenosis than ABI- ones. The mean of occlusion was significantly higher in ABI+ patients with left main artery (LMA), right coronary artery (RCA), left anterior descending artery (LAD), diagonal artery 1 (D1) and left circumflex artery (LCX) involvements (P < 0.05).

**CONCLUSION:** The findings of this research indicated that ABI could be a useful method in assessing both the atherosclerotic risk factors and the degree of coronary involvements in suspected patients. However, in order to make more accurate decisions for using this method in diagnosing and preventing CAD, we should plan further studies in large sample sizes of general population.

**Keywords:** Ankle–Brachial Index, Angiography, Atherosclerotic Risk Factors.

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## Introduction

Atherosclerosis, the most common cause of mortality and morbidity worldwide, is considered a generalized process which affects coronary, cerebral, and peripheral arteries of the lower extremities.<sup>1</sup>

An important issue in clinical practice is coronary artery involvements of the disease due to their related high rate of complications and mortality.<sup>2</sup>

Evidence indicated the relation between peripheral

arterial disease (PAD) and occurrence of cardiovascular disease and coronary events in patients with or without known coronary artery disease (CAD). Moreover, PAD is associated with an increased incidence of multivessel and obstructive CAD. The mentioned relationship is independent of the presence of other cardiovascular risk factors.<sup>3</sup>

In most cases, PAD is asymptomatic and therefore underdiagnosed. The clinical presentations of PAD in

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minority of patients are intermittent claudication, rest pain and ulcer. Both symptomatic and asymptomatic PAD patients are at risk of cardiovascular disease and related mortality. Therefore, identifying patients with PAD especially those with asymptomatic disease in atherosclerotic disease is of high prognostic importance.<sup>4,5</sup>

The ankle-brachial index (ABI), calculated by dividing the higher systolic blood pressure of each ankle artery by the higher systolic blood pressure of the upper limbs,<sup>6</sup> is a simple and non-invasive tool with high specificity and sensitivity for the diagnosis of PAD.<sup>7</sup> Many studies have also reported its predictive value in CAD in patients suspected of having ischemic heart disease.<sup>8,9</sup>

Previous investigations revealed an inverse relationship between ABI and cardiovascular and cerebrovascular diseases as well as their risk factors. They found ABI  $\leq 0.9$  as an indicator of PAD, cardiovascular disease and other atherosclerotic disease in different vascular areas. It is associated with a two- to three-fold increased risk of the mentioned disease morbidity and mortality.  $^{10,11}$ 

Considering the increasing burden of atherosclerotic disease and its mortality, and also the usefulness of non-invasive, easy and practical methods for identifying atherosclerotic risk factors for prevention or early treatment of atherosclerotic diseases, the aim of current study is to determine the relation between ABI with angiographic stenosis and major cardiovascular risk factors in patients with suspected CAD, in Isfahan.

## Materials and Methods

In this cross-sectional descriptive-analytic study, patients with suspected CAD, who referred to Nour and Ali Asghar hospital for cardiac angiography during September-December 2008, enrolled. From the referred patients, 125 were selected by convenience method.

The study protocol was approved by the Ethics Committee of Isfahan University of Medical Sciences. Written informed consents were obtained from all studied patients.

Characteristics of the studied subjects including demographics, familial history, past medical history and atherosclerotic risk factors such as diabetes mellitus, hypertension, hyperlipidemia and smoking were obtained using a standard questionnaire.

Atherosclerotic risk factors were described as follows:

• Smoking: Regular smoking of a tobacco product one or more times per day or have smoked in the past 30 days prior to admission.<sup>12</sup>

- Hyperlipidemia: Total cholesterol  $\geq 200$  mg/dl, LDL-cholesterol  $\geq 130$  mg/dl, HDL-cholesterol  $\geq 40$  mg/dl in men, and  $\geq 50$  mg/dl in women, and triglyceride  $\geq 200$  mg/dl or using medicationss.<sup>13</sup>
- Hypertension: Systolic blood pressure ≥ 140 mmHg and/or diastolic blood pressure ≥ 90 mmHg and/or receiving antihypertensive treatment.<sup>14</sup>
- Diabetes mellitus: Positive findings from any two of the following tests on different days: symptoms of diabetes mellitus plus casual plasma glucose concentration ≥ 200 mg/dl or fasting blood glucose ≥ 126 mg/dl or 2-hour blood glucose 200 mg/dl and/or use of glucose lowering drugs.<sup>15</sup>

Patients with peripheral vascular disease and deformity in upper and lower limbs, unclear results of ABI and angiography were excluded.

A Madeco Biderectional Smatdop 30 ultrasonography device (Japan) and a pneumatic cuff were used by a cardiologist to measure the brachial artery and ankle pressure waves. ABI was calculated as the ratio of the blood pressure in ankles to the blood pressure in the arms. ABI  $\leq 0.9~(\mathrm{ABI^{+}})$  was considered as peripheral vessel disease and ABI  $>0.9~(\mathrm{ABI^{-}})$  was considered as normal.  $^{16}$ 

Then all studied patients underwent coronary artery angiography.

Then, all patients underwent selective angiography via the femoral approach with a 5F or 6F catheter. Omnipaque 300 (iohexol 647 mg, trometamol 1.2 mg) was the contrast used in all of the cases. Two cardiologists evaluated each coronary angiography. Based on the angiographic findings, the participants were divided into normal group (with no coronary involvement) and CAD groups. CAD was defined as a stenosis of > 50% in the major coronary vessels. Coronary artery stenosis or CAD was evaluated and categorized as non-significant, significant and cut off if there was a stenosis < 75%,  $\ge 75-99\%$  and 100% in diameter, respectively.<sup>17</sup>

Angiographers made a subjective assessment of coronary vessels involvements including the left main artery (LMA), left circumflex coronary artery (LCX), right coronary artery (RCA), diagonal artery 1 (D1), diagonal artery 2 (D2) and large obtuse marginatus (OM).

The results of the questionnaire and angiographic findings were compared in ABI+ and ABI-groups. The data were analyzed by SPSS15 using ANOVA, t-test, Spearman's rank correlation coefficient (to determine the correlation of ABI and degree of coronary involvement), and discriminant analysis (to assess the predictive value of ABI for coronary involvement). A P-value less than 0.05 was considered significant.

#### Results

In this study 125 patients [85 men (68%) and 40 women (32%)] aging 32-80 years, suspected to CAD, were investigated. Mean age of studied patients was  $58.9 \pm 10.0$  years.

Twenty-five patients (20%) of the studied population had ABI < 0.9 (ABI+). The prevalence of ABI+ among men and women was 25.9% and 7.5%, respectively (P = 0.01).

Abnormal angiographic results were seen in 96% (24 persons) of the ABI+ group and 74% (74 persons

of the ABI- group) (P = 0.01). The prevalence of atherosclerotic risk factors in ABI+ and ABI- patients is presented in Table 1.

The non-significant, significant and cut-off occlusion of different vessels according to angiographic findings in ABI+ and ABI- patients are presented in Table 2.

Mean ± SD of occlusion of different vessels according to angiographic findings in ABI<sup>+</sup> and ABI-patients is presented in Table 3.

**Table 1.** The prevalence of atherosclerotic risk factors in ABI<sup>+</sup> and ABI<sup>-</sup> patients.

Atherosclerotic risk factors	ABI <sup>+</sup> patients N = 25	ABI patients N = 100	P-value
Diabetes mellitus	10 (40%)	23 (23%)	0.04
Hypertension	14 (56%)	32 (32%)	0.02
Hyperlipidemia	11 (44%)	19 (19%)	0.005
Smoking	13 (52%)	27 (27%)	0.01

**Table 2.** Non-significant, significant and cut-off occlusion of different vessels according to angiographic findings in ABI<sup>+</sup> and ABI<sup>-</sup> patients

	<b>ABI</b> <sup>+</sup> patients	ABI patients	P-value
LMA <sup>1</sup>			
non-significant	3 (12%)	3 (3%)	
significant	1 (4%)	1 (1%)	0.01
cut-off	0	0	
$RCA^2$			
non-significant	6 (24%)	17 (17%)	
significant	11 (44%)	14 (14%)	0.001
cut-off	2 (8%)	8 (8%)	
$LAD^3$			
non-significant	3 (12%)	28 (28%)	
significant	17 (68%)	25 (25%)	< 0.001
cut-off	2 (8%)	5 (5%)	
$D1^4$			
non-significant	1 (4%)	4 (4%)	
significant	9 (36%)	17 (17%)	0.02
cut-off	0	0	
$D2^5$			
non-significant	2 (8%)	2 (2%)	
significant	0	7 (7%)	0.3
cut-off	0	1 (1%)	
$OM^6$			
non-significant	2 (8%)	12 (12%)	
significant	4 (16%)	13 (13%)	0.3
cut-off	1 (4%)	0	
LCX <sup>7</sup>	, ,		
non-significant	8 (32%)	15 (15%)	
significant	11 (44%)	11 (11%)	< 0.001
cut-off	2 (8%)	2 (2%)	

<sup>1-</sup> Left Main Artery; 2- Right Coronary Artery; 3- Left Anterior Descending Artery; 4- Diagonal Artery 1;

<sup>5-</sup> Diagonal Artery 2; 6- Large Obtuse Marginatus Artery; 7- Left Circumflex Artery.

<b>Table 3.</b> Mean $\pm$ SD of occlusion	of different vessels according to	angiographic findings in ABI+ and
ABI- patients.		

	$\mathbf{ABI}^{\scriptscriptstyle +}$ patients	ABI patients	P-value
LMA <sup>1</sup>	$10 \pm 24.7$	$1.5 \pm 8.75$	0.006
$RCA^2$	$58.8 \pm 37.1$	$28.5 \pm 38.1$	0.001
$LAD^3$	$76.4 \pm 30.6$	$41.1 \pm 38.5$	0.001
$D1^4$	$33.2 \pm 42.2$	$16.2 \pm 32.1$	0.02
$D2^5$	$4.4 \pm 15.2$	$7.8 \pm 24.1$	0.4
$OM^6$	$22.2 \pm 37.1$	$16.9 \pm 30.7$	0.4
$LCX^7$	$36.1 \pm 31.5$	$19.1 \pm 32.4$	0.0001

- <sup>1-</sup> Left Main Artery
- <sup>2-</sup> Right Coronary Artery
- 3- Left Anterior Descending Artery
- Diagonal Artery 1
- 5- Diagonal Artery 2
- 6- Large Obtuse Marginatus Artery
- 7- Left Circumflex Artery

### Discussion

In this study, the relation between angiographic findings and ABI in patients suspected to CAD was evaluated. The results indicated that the prevalence of atherosclerotic risk factors was significantly higher in ABI+ patients than in ABI- ones. Regarding coronary artery involvement, ABI+ patients had more significant stenosis than ABI- ones and the mean occlusion was significantly higher in ABI+ patients with LMA, RCA, LAD, D1 and LCX involvements.

In the present study, 20% of the subjects had ABI ≤ 0.9 which was higher significantly in men than in women. The prevalence of ABI<sup>+</sup> among high risk subjects, identified by general medical practice, has been reported to be 25-30% which is increased by age. <sup>18</sup> The results of the current study regarding the prevalence of ABI<sup>+</sup> was in line with other studies, but the age of ABI<sup>+</sup> and ABI<sup>-</sup> patients was not significantly different. It may be a result of studying a selective group of patients.

There are different results regarding gender difference of ABI+. Our results were in line with the study of Papamicha et al., which similarly studied 165 patients referred for elective coronary angiography.<sup>19</sup> Ramos et al. have reported similar results, whereas in the study of Taylor-Piliae et al. in Arizona, the prevalence of ABI+ was similar in both sexes.20 Considering the high rate of CAD in men, these findings could be explained. However, in the USA, Sadrzadeh Rafie et al. studied the effect of sex differences on the prevalence of peripheral artery disease in patients referred for elective coronary angiography and showed that though the prevalence of CAD and its severity is lower in women, PAD is more prevalent among them. This was not in agreement with traditional cardiovascular disease risk factors or CAD severity.<sup>21</sup> Therefore, it seems that more studies with larger sample size are needed for more conclusive results.

As mentioned, several studies reported that patients with PAD are at a higher risk of adverse cardiovascular events and other atherosclerotic diseases. ABI  $\leq$  0.9 has widely been used as an indicator of PAD and adjunct to the office-based assessment of cardiovascular risk in high-risk population. It is also associated with increased risk of cardiovascular and all-cause death. 11,22,23

In a systematic review, Doobay et al. determined the sensitivity and specificity of ABI in predicting future cardiovascular events. They concluded that though ABI  $\leq 0.9$  is highly specific but not sensitive in this regard, it is considered a useful cardiovascular events risk prediction tool, especially in selected populations due to its simple assessment.<sup>24</sup>

In a study in Taiwan, Chang et al. studied the usefulness of ABI to predict the complex and diffuse coronary lesions in patients undergoing coronary angiography. They indicated that from atherosclerotic risk factors, diabetes, hypertension and smoking were significantly higher in ABI+ patients. Furthermore, compared to the control group, the ABI+ patients had more critical and stenotic lesions which were difficult to manipulate. Accordingly, they recommended to use this simple, inexpensive and well-established index not only for diagnosing PAD, but also for predicting diffuse and complex lesion subtypes which would be useful in treatment procedures during hospitalization and the follow-up period after subsequent interventions.25

Papamicha et al. reported similar findings regarding the use of ABI as the main variables for predicting the extent and severity of coronary disease especially in male patients and those with diabetes and high levels of HDL cholesterol.<sup>19</sup>

In the current study, the prevalence of all studied risk factors was significantly higher in ABI+ patients than ABI- ones. Though we did not study the correlation between ABI and studied variables in men and women separately, Mc Dermott et al. have reported more significant relationships between mentioned variables in men than in women.<sup>26</sup>

There was not any study evaluating the relation between ABI and involvements of different vessels, as we did in the present study, but Sukhija et al. studied the prevalence of left main coronary artery disease, of three- or four-vessel coronary artery disease, and of obstructive coronary artery disease in patients with and without peripheral arterial disease undergoing coronary angiography for suspected coronary artery disease. They indicated that PAD patients had a higher prevalence of left main CAD (18% vs. < 1%), 3- or 4vessel CAD (63% vs. 11%) and obstructive CAD (98% vs. 81%) comparing with those without PAD. Moreover, in agreement with our study, they reported a higher prevalence of smoking, hypertension, diabetes mellitus, and dyslipidemia in patients with PAD than those without PAD.27

In this study, compared with ABI patients, the degree of occlusion in different involved vessels and also the mean of stenosis were significantly higher in ABI+ patients, for all vessels except for D2 and OM, i.e. the most important arteries that are involved in CAD have more significant stenosis in ABI+ patients.

In contrast to our results, in a study in Lohare, Hakeem et al. have reported that from 41 patients only 3 had ABI  $\leq 0.9$  and all 3 had triple vessel disease. They concluded that there was not a direct association between ABI and significant CAD because only 3 patients out of 22 with triple vessel disease had an ABI  $\leq 0.9$ . However, they indicated an approximately log linear relationship between ABI and CAD risk which means that the average CAD risk increased significantly at ABI values  $\leq 1.0$  and declined at values  $\geq 1.0.28$ 

In conclusion, the findings of this research have indicated that ABI could be a useful method in assessing both the atherosclerotic risk factors and the degree of coronary involvement in suspected patients. However, making more accurate decisions for using this method in diagnosing and preventing CAD needs further studies with large sample sizes of general population. It is recommended to evaluate the relation between different levels of ABI, especially ABI > 1.4, which was not investigated properly, and the risk of atherosclerotic risk factors especially novel risk factors such as CRP, homocysteine and LPa.<sup>29,30</sup>

Recent studies have suggested that an ABI of >1.4, as a marker of calcified, non-compressible arteries, could also predict an increased risk of cardiovascular events.<sup>29</sup>

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## **Conflict of Interests**

Authors have no conflict of interests.

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