

# Diagnostic Value of Ankle Brachial Index for Myocardial Ischemia in Asymptomatic Diabetic Patients and Comparison with Myocardial Perfusion Imaging

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## Abstract

**Objective:** The ankle-brachial index (ABI) as a simple test which can detect peripheral arterial disease (PAD). Therefore in this study we try to evaluate the diagnostic value of ABI for silent myocardial ischemia in diabetic patients and compare the results with myocardial perfusion imaging (MPI) results.

**Materials and Methods:** All 149 diabetic patients in this study were categorized according to different parameters including sex, smoking, cholesterol, familial history, and high blood pressure, level of ischemia, myocardial infarction (MI), left ventricle (LV) volume, ejection fraction (EF), and wall motion. Then the relationship of ABI index and these parameters were investigated.

**Results:** According to the calculated ABI the data was investigated based on ABI lower and higher than 0.9. The frequency of  $ABI > 0.9$  was 16 (11%) and  $< 0.9$  was 133 (89%). There was no significant relationship between all the mentioned parameters and ABI index ( $P$ -value: 0.05).

**Conclusion:** This study suggests the ABI sensitivity and specificity for diagnose of silent ischemia in asymptomatic diabetic patients is very low and in this case ABI cannot replace MPI by any means.

**Keywords:** Ankle-brachial index, Diabetes, Myocardial perfusion imaging, Coronary artery disease

## Introduction

The ankle-brachial index (ABI) as a simple test can detect peripheral arterial disease (PAD) especially in the lower extremities (1). ABI is equal to the ratio of the ankle systolic pressure to the brachial systolic pressure. In a normal person the ankle pressure

is slightly more or close to the brachial pressure; hence ABI is around 1-1.4 (1-3). In PAD patients, the ankle pressure lowers due to the upstream hemodynamic lesions which results in a lower ABI ( $ABI < 1$ ) (4,5). The ABI depends on qualitative and quantitative aspects

of other diseases such as atherosclerotic disease. In atherosclerotic disease the serially located lesions additively contribute to decrease distal pressure which enables the ABI to measure the severity and number of atherosclerotic lesions located in the lower extremity (6,7).

On the contrary, the ABI is particularly unreliable in diabetes disease, which is attributed to the stiffness of arterial vessel walls. These rigid arteries cause a false positive read by the sphygmomanometer (8,9). Diabetic patients are susceptible to a wide range of other disease including retinopathy (10), obesity (11), resistance to insulin (12), infections (13,14), antonym disorders and most importantly coronary artery disease (CAD) and PAD (15-17). The incidence of silent myocardial ischemia (SMI) and stroke in diabetic patients is 2-7 times higher than non-diabetic patients. Therefore continuous monitoring of diabetic patients could prevent the SMI (18,19).

Myocardial perfusion imaging (MPI) as the gold standard for prognosis and diagnosis of CAD. However, due to ionizing radiation of MPI method encourages finding different and safer methods. In this study we are trying to evaluate the diagnostic value of ABI for SMI in diabetic patients and compare the results with MPI results.

## Materials and Methods

### Settings and Patients

This study was organized in Fatemeh Zahra Hospital of Sari located in the north of Iran. The subjects of this study were 149 type 2 diabetes who referred to the hospital for MPI. These patients were selected by convenient method during 2015-2016. All the patients were 30-70 years old. We excluded patients who had heart disease from this study. All the demographic information including smoking, type and duration of diabetes, sex, age, blood pressure and etc. were registered for the selected patients.

### MPI test

First, a standard dose of  $^{99m}$ Tc-MIBI was injected to the patient and the rest phase image was acquired by a gamma camera (Zemence Company, dual headed gamma camera, Germany 2011). The following day the stress phase image was acquired.

### ABI measurement

Before any measurement, the patient should be in the supine position for 5 min. then, the systolic blood pressure of one arm and one ankle were measured. The ABI value was calculated using the following equation:

$$ABI = \frac{\text{systolic blood pressure of the ankle}}{\text{brachial arterial systolic pressure}}$$

### Statistical Analysis

*P*-value <0.05 is considered as a significant difference. In addition, SPSS version 14 software was used for data analysis. Negative predictive value (NPV), positive predictive value (PPV) and overall accuracy (OA) were also calculated.

### Ethical considerations

The subjects in this study agreed to contribute in this study and their health were not endanger in this study by any means. All the patients' information will stay confidential. This study was approved by Mazandaran University of Medical Sciences ethical committee. The ethical code for this study is IR.MAZUMS.REC.94-1843.

## Results

### Descriptive statistics

All 149 patients in this study were statistically analyzes and categorized according to different parameters (table 1). The mean ( $\pm SD$ ) age of patients was 61.06 ( $\pm 9.18$ ) years old.

The mean ( $\pm SD$ ) Systolic blood pressure of right brachial was 135.22 (25.35) and right ankle was 156.89 (28.58) for all the 149 patients.

Based on the systolic blood pressure of right brachial and right ankle, ABI was calculated.

**Table 1. Descriptive statistics for patients**

Parameter	Frequency (%)
<b>Sex</b>	43 (28.86)
Male	106 (71.14)
Female	
<b>Diabetic</b>	111 (74)
Treatment with peals	29 (19)
Treatment with insulin	9 (6)
Treatment with life style	
<b>Smoking</b>	6 (4)
Yes	143 (96)
No	
<b>High cholesterol</b>	116 (78)
Yes	33 (22)
No	
<b>High blood pressure</b>	110 (74)
Yes	39 (26)
No	
<b>Familial history</b>	33 (22)
Yes	116 (78)
No	
<b>Level of ischemia</b>	77 (52)
No	40 (27)
Mild	18 (12)
Moderate	14 (9)
Sever	
<b>Level of ischemia (bi-level)</b>	77 (52)
Yes	72 (48)
No	
<b>MI</b>	12 (8)
Yes	137 (92)
No	
<b>Mixed</b>	18 (12)
Yes	131 (88)
No	
<b>LV volume</b>	136 (91)
Normal	13 (9)
Dilated	
<b>EF</b>	130 (87)
Normal	19 (13)
Decreased	
<b>Wall motion</b>	115 (77)
Normal	33 (23)
Decreased	

According to the calculated ABI the data was investigated based on ABI lower and higher than 0.9. The frequency of  $ABI > 0.9$  was 16 (11%) and  $ABI < 0.9$  was 133 (89%).

In order to evaluate the relationship of ABI with ischemia, MI, LV volume, EF and wall motion first we categorized the patients based on ABI values (above 0.9 and under 0.9) for each parameter. Then, we performed Chi-square test to determine whether there is a significant relationship between or not. Based on the data present in table 3 there is no significant relationship between ABI and other parameters (table2).

### A receiver operating characteristic (ROC) curve

ROC curve can determine the diagnostic value of ABI. By using this curve different parameter including the area under curve (AUC), p-value and 95% percent confidence interval are provided in table 6. Moreover, diagnostic indicators including sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), true negative rate (TNR) and true positive rate (TPR) are calculated (Table 3). This data indicate the low diagnostic value of ABI for prediction of silent ischemia in diabetic patients in comparison with MPI.

### Discussion

Most of the patients (71.14%) in this study are

**Table 2. Statistical investigation for relationship of ABI and different parameters in diabetic patients**

Parameter	Sub-parameter	ABI < 0.9 Number (%)	ABI > 0.9 Number (%)	P-value from Chi-square test
<b>Level of ischemia</b>	No	6 (38)	71 (53)	> 0.05
	Mild	5 (31)	35 (26)	
	Moderate	3 (19)	15 (11)	
	Sever	2 (13)	12 (9)	
<b>Level of ischemia (bi-level)</b>	Yes	10 (63)	62 (47)	> 0.05
	No	6 (38)	71 (53)	
<b>MI</b>	Yes	2 (13)	10 (8)	> 0.05
	No	14 (88)	123 (92)	
<b>Mixed</b>	Yes	3 (19)	15 (11)	> 0.05
	No	13 (81)	118 (89)	
<b>LV volume</b>	Normal	16 (1)	120 (90)	> 0.05
	Dilated	0	13 (10)	
<b>EF</b>	Normal	15 (94)	115 (86)	> 0.05
	Decreased	1 (6)	18 (14)	
<b>Wall motion</b>	Normal	11 (69)	104 (78)	> 0.05
	Decreased	5 (31)	29 (22)	

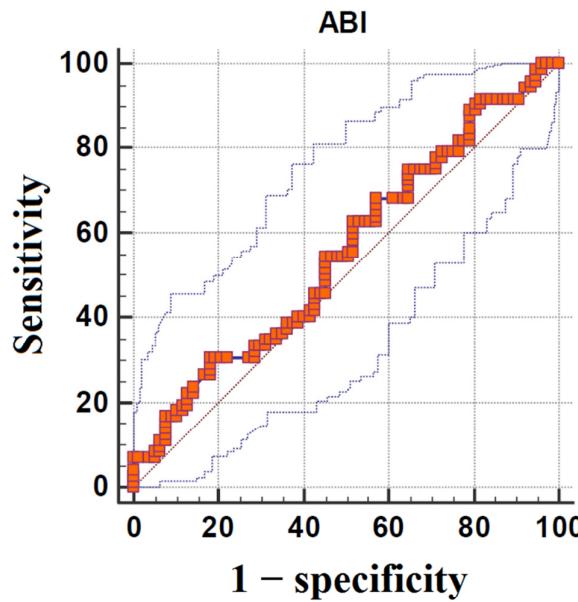


Figure 1. ROC curve for ABI diagnostic value

female. The administration of insulin is the most common treatment for these patients, and most of them possess high level of cholesterol which is very common for diabetic patients. The calculation of ABI for this population indicates a normal distribution for the most part. However, different studies suggest that diabetic patients have low ABI and they are very susceptible to CAD and PAD (20-24). The relationship between ABI and different level of ischemia was also investigated. Even though the findings suggested that mild, moderate and sever ischemic diabetic patients ABI are lower than normal ABI, but these difference were not statistically significant. It is noteworthy that the increment in the population of patients may change the results. Likewise the relationship of ABI and MI was

also not statistically significant which agrees with other studies (22). However some studies suggested that patients with low ABI are 2-3 times more susceptible to heart stroke (25). Diabetic patients with low ABI are highly at risk of CAD in previous studies (26-28). This contradictory can be due to the small patient population of our study.

For good measures we also investigated the relationship between heart function (EF, wall motion and LV function) and ABI. The data indicates that there was no significant relationship between ABI and neither EF nor wall motion and LV function which is in parallel with other studies (29).

Finally, ROC curve displayed a very low diagnostic value for ABI in ischemic diabetic patients in comparison with MPI. According

Table 3. the ROC extracted data for diagnostic value of ABI

Diagnostic test	Value
AUC	0.552
Standard error	0.0474
95% percent confidence interval	0.468 and 0.633
Z-score	1.094
p-value	0.274
Sensitivity (at 95% percent confidence interval)	68.06 (56.0, 78.6)
Specificity (at 95% percent confidence interval)	42.86 (31.6, 54.6)
TPR (at 95% percent confidence interval)	1.19 (0.9, 1.5)
TNR (at 95% percent confidence interval)	0.75 (0.5, 1.1)
PPV (at 95% percent confidence interval)	52.7 (42.1, 62.1)
NPV (at 95% percent confidence interval)	58.9 (45.0, 71.9)

our findings ABI cannot replace MPI by any means in the case of ischemia in diabetic patients. On the contrary, Chang et al. suggested that sensitivity, specificity, PPV and NPV for ABI in diabetic and non-diabetic patients is significantly different and diabetic patients with vessel calcification and ischemia possess significantly lower ABI. They also expressed that the ABI is a useful and noninvasive method to evaluate the CAD even in diabetic patients which does not correlate with our study (30).

Dachun et al. performed a systematic review on sensitivity and specificity of ABI in PAD. They implied that for  $ABI \leq 0.9$  the precision and specificity are 89.2-92.1% and 83.3-99%, respectively. However, the sensitivity of ABI in this study was very variant (15-79%) and more interestingly sensitivity and specificity of

ABI for elderly diabetic patients was lower (29).

## Conclusions

This study suggests the ABI sensitivity and specificity for diagnose of silent ischemia in asymptomatic diabetic patients is very low and in this case ABI cannot replace MPI by any means. However it is noteworthy that more profound studies with a larger patient population (especially above 55 years old) is needed to shed light upon this topic.

## Funding

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## Conflict of Interest

The authors declared no conflict of interest.

## References

1. Abouhamda A, Alturkstani M, Jan Y. Lower sensitivity of ankle-brachial index measurements among people suffering with diabetes-associated vascular disorders: A systematic review. *SAGE Open Med.* 2019;7:2050312119835038.
2. Casey S, Lanting S, Oldmeadow C, Chuter V. The reliability of the ankle brachial index: a systematic review. *Journal Foot Ankle Res.* 2019;12:39.
3. McClary KN, Massey P. Ankle, Brachial Index (ABI). InStatPearls [Internet] 2019 Jun 26. StatPearls Publishing.
4. Herráiz-Adillo Á, Cavero-Redondo I, Álvarez-Bueno C, Martínez-Vizcaíno V, Pozuelo-Carrascosa DP, Notario-Pacheco B. The accuracy of an oscillometric ankle-brachial index in the diagnosis of lower limb peripheral arterial disease: A systematic review and meta-analysis. *International journal of clinical practice.* 2017;71(9):12994.
5. Guirguis-Blake JM, Evans CV, Redmond N, Lin JS. Screening for peripheral artery disease using the ankle-brachial index: updated evidence report and systematic review for the US Preventive Services Task Force. *Jama.* 2018;320(2):184-96.
6. Prasada S, Shah SJ, Michos ED, Polak JF, Greenland P. Ankle-brachial index and incident heart failure with reduced versus preserved ejection fraction: The Multi-Ethnic Study of Atherosclerosis. *Vascular Medicine.* 2019;24(6):501-10.
7. Garcia AB, Dardin LP, Minali PA, Czapkowsky A, Ajzen SA, Trevisani VF. Asymptomatic atherosclerosis in primary Sjögren syndrome: correlation between low ankle brachial index and autoantibodies positivity. *JCR: Journal of Clinical Rheumatology.* 2016;22(6):295-8.
8. Aerden D, Massaad D, von Kemp K, van Tussenbroek F, Debing E, Keymeulen B, et al. The ankle-brachial index and the diabetic foot: a troublesome marriage. *Annals of vascular surgery.* 2011;25(6):770-7.
9. Asbeutah AM, AlMajran AA, Asfar SK. Diastolic versus systolic ankle-brachial pressure index using ultrasound imaging & automated oscillometric measurement in diabetic patients with calcified and non-calcified lower limb arteries. *BMC Cardiovascular Disorders.* 2016;16(1):202.
10. Wong TY, Cheung CM, Larsen M, Sharma S, Simo R. Diabetic retinopathy. *Nature Reviews Disease Primers.* 2016;2:16012.
11. Gonzalez N, Moreno-Villegas Z, Gonzalez-Bris A, Egido J, Lorenzo O. Regulation of visceral and epicardial adipose tissue for preventing cardiovascular injuries associated to obesity and diabetes. *Cardiovasc Diabetol.* 2017;16(1):44.
12. Ahmad K. Insulin sources and types: a review of insulin in terms of its mode on diabetes mellitus. *Journal of Traditional Chinese Medicine.* 2014;34(2):234-7.
13. Johargy AK. Antimicrobial susceptibility of bacterial and fungal infections among infected diabetic patients. *Depression.* 2016;8:9.

14. Sathasivam P. Head and Neck Infections in Diabetic Patients. *Journal Assoc Physicians India*. 2018;66(9):84-8.
15. Papanas N, Tziakas D, Hatzinikolaou E, Chalikias G, Maltezos E, Louridas G, et al. Revisiting the frequency of peripheral arterial disease in patients with coronary artery disease: is there a difference between diabetic and non-diabetic patients? *Vasa*. 2006;35(4):227-31.
16. Parhofer KG, Zeymer U, Stark RG, Binz C, Schwertfeger M, Bhatt DL, et al. In Germany diabetic patients with coronary artery disease are treated more intensively than diabetic patients with other manifestations of atherothrombosis--results from the REACH registry. *Experimental and clinical endocrinology & diabetes*. 2010;118(1):51-6.
17. Sandhiya S, Dkhar SA, Pillai AA, George M, Jayaraman B, Chandrasekaran A. Comparison of ranolazine and trimetazidine on glycemic status in diabetic patients with coronary artery disease - a randomized controlled trial. *Journal of clinical and diagnostic research: JCDR*. 2015;9(1):Oc01-5.
18. Mitevska IP, Baneva N, Bosevski M, Kostovska ES. Prevalence of risk factors and asymptomatic carotid atherosclerosis in diabetic patients screened for silent myocardial ischemia by SPECT myocardial imaging. *Nuclear Medicine Review*. 2017;20(1):3-9.
19. Bosone D, Fogari R, Ramusino MC, Ghiotto N, Guaschino E, Zoppi A, et al. Ambulatory 24-h ECG monitoring and cardiovascular autonomic assessment for the screening of silent myocardial ischemia in elderly type 2 diabetic hypertensive patients. *Heart Vessels*. 2017;32(5):507-13.
20. Candler T, Mahmoud O, Edge J, Hamilton-Shield J. Hypercholesterolaemia screening in Type 1 diabetes: a difference of opinion. *Diabetic Medicine*. 2017;34(7):983-6.
21. Hua S, Loehr LR, Tanaka H, Heiss G, Coresh J, Selvin E, et al. Ankle-brachial index and incident diabetes mellitus: the atherosclerosis risk in communities (ARIC) study. *Cardiovascular diabetology*. 2016;15(1):163.
22. Suominen V, Uurto I, Saarinen J, Venermo M, Salenius J. PAD as a risk factor for mortality among patients with elevated ABI--a clinical study. *European Journal of Vascular and Endovascular Surgery*. 2010;39(3):316-22.
23. Potier L, Roussel R, Labreuche J, Marre M, Cacoub P, Rother J, et al. Interaction between diabetes and a high ankle-brachial index on mortality risk. *European journal of preventive cardiology*. 2015;22(5):615-21.
24. Chevtchouk L, Silva M, Nascimento O. Ankle-brachial index and diabetic neuropathy: study of 225 patients. *Arquivos de neuro-psiquiatria*. 2017;75(8):533-8.
25. Busch MA, Lutz K, Röhl JE, Neuner B, Masuhr F. Low ankle-brachial index predicts cardiovascular risk after acute ischemic stroke or transient ischemic attack. *Stroke*. 2009;40(12):3700-5.
26. Li J, Luo Y, Xu Y, Yang J, Zheng L, Hasimu B, et al. Risk factors of peripheral arterial disease and relationship between low ankle - brachial index and mortality from all-cause and cardiovascular disease in Chinese patients with type 2 diabetes. *Circulation Journal*. 2007;71(3):377-81.
27. Resnick HE, Lindsay RS, McDermott MM, Devereux RB, Jones KL, Fabsitz RR, et al. Relationship of high and low ankle brachial index to all-cause and cardiovascular disease mortality: the Strong Heart Study. *Circulation*. 2004;109(6):733-9.
28. Igarashi Y, Chikamori T, Hida S, Tanaka H, Shiba C, Usui Y, et al. Importance of the ankle-brachial pressure index in the diagnosis of coronary artery disease in women with diabetes without anginal pain. *Circulation Journal*. 2011;75(9):2206-12.
29. Xu D, Li J, Zou L, Xu Y, Hu D, Pagoto SL, et al. Sensitivity and specificity of the ankle—brachial index to diagnose peripheral artery disease: a structured review. *Vascular Medicine*. 2010;15(5):361-9.
30. Chang ST, Chu CM, Hsu JT, Pan KL, Lin PG, Chung CM. Role of ankle-brachial pressure index as a predictor of coronary artery disease severity in patients with diabetes mellitus. *Canadian Journal of Cardiology*. 2009;25(9):S301-5.