IJKD KIDNEY DISEASES

Correlation Between Ankle-Brachial Index and Microalbuminuria in Type 2 Diabetes Mellitus

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Keywords. diabetes mellitus, ankle-brachial index, diabetic nephropathies, atherosclerosis

Introduction. Microalbuminuria is a reliable marker of diabetic nephropathy. Establishment of peripheral vascular complications leads to early diagnosis, prevention, and treatment of renal and cardiovascular complications. This study investigated the value of ankle-brachial index (ABI) for prediction of microalbuminuria in type 2 diabetic patients.

Materials and Methods. Measurement of ABI with color Doppler ultrasonography was carried out for 206 patients with type 2 diabetes mellitus. An ABI Index less than 0.9 was defined as a predictive marker for atherosclerosis. Microalbuminuria and risk factors of atherosclerosis were compared between the patients categorized based on the ABI values.

Results. The mean ABI was 1.1 ± 0.2 (range, 0.052 to 1.6), and 41 (20%) had an abnormal ABI (< 0.9). The correlations were significant between abnormal ABI and duration of disease (P = .04), cardiovascular event and cardiac care unit admission (P = .001), hypertension (P = .01), and dyslipidemia (P = .01). There was a significant correlation between ABI and microalbuminuria (odds ratio, 0.05; 95% confidence interval, 0.038 to 0.630; P < .001). A cutoff point of an ABI less than or equal to 1.04 had a sensitivity of 71.6% and a specificity of 64.2% for prediction of microalbuminuria.

Conclusions. The ABI is a noninvasive and reliable assay for detection of peripheral and cardiovascular complications, and also early stage of nephropathy in diabetic patients. In patients with an abnormal ABI, long-term follow-up for earlier detection and prevention of complications is helpful.

IJKD 2013;7:204-9
www.ijkd.org

Original Paper

INTRODUCTION

Diabetes mellitus (DM) is a metabolic disorder that can be affected by genetic factors, environment, and life style. The incidence of DM, especially type 2, is increasing due to the growing obesity and immobility in the world.[1,2] Considering the secondary pathophysiologic changes in many organs caused by DM, this disorder puts the health system to a lot of expense.[3]

Diabetes mellitus is the most common cause of end-stage renal disease, blindness, and nontraumatic lower extremity amputation in adults, all caused by progressive atherosclerosis.[3] Acceleration in atherosclerosis with a nonenzymatic glycosilation mechanism involves coronary, cerebral, visceral, and peripheral vessels, which leads to increase in cerebrovascular accidents by 2-fold and cardiovascular accident by 3-fold in these patients. High rates of hypertension, lipid metabolism disturbance, and obesity accompanies this metabolic

syndrome and causes aggravated complications.[4]

Use of ankle-brachial index (ABI) is an easy and noninvasive method for screening atherosclerosis. Association between ABI and coronary, cerebral, and peripheral vessels involvement has been shown in different studies.[5,6] Progression of atherosclerosis occurs even in the state of impaired glucose tolerance test.[7] The normal range of ABI is between 0.9 and 1.4. Values below 0.9 show peripheral vessel disease and an occlusion more than 50% in one or more important body vessels, with a sensitivity of 95% and specificity of 100%. More severe coronary vessel involvement is considered as the value of the index decreases, and the value below 0.4 shows advanced ischemia. An ABI more than 1.4 is characteristic of calcified and nonsqueezable vessels.[8] In these cases toe-brachial index could be used for definite establishment of peripheral vessel involvement.[9,10]

We aimed to investigate the value of ABI for prediction of microalbuminuria (an early marker of renal involvement) in type 2 diabetic patients. Regarding the importance of early diagnosis of coronary disease in diabetic patients and the predictive value of ABI in identifying cardiovascular complications, this study could inform the screening approach for vessel involvement in patients with type 2 DM to prevent serious complication of DM relevant with other risk factors.

MATERIALS AND METHODS

This cross-sectional study was performed on 206 type 2 diabetic patients, all of whom were members of the Society of Diabetes (West Azarbayjan branch). The inclusion criterion was type 2 DM with relatively good glycemic control (HbA1c between 6.9 and 7.8). Intermittent claudication was assigned as an exclusion criterion. Recruitment was done through a convenient sampling method after obtaining informed consent. Data on age, sex, duration of DM, history of smoking, history of cardiovascular or cerebral accidents (including history of admission to intensive unit care), hypertension (blood pressure equal to or more than 125/75 mm Hg), dyslipidemia (low-density lipoprotein level > 100 mg/dL), microalbuminuria (urine albumin between 30 mg and 300 mg per 24 hours), and body mass index were obtained from medical charts and interview of the patients.

In all patients, blood pressure was measured, cardiovascular examination was done, and brachial, radial, ulnar, femoral, pobliteal, dorsalis pedis, and posterior tibialis pulses were measured by one same examiner. Then the highest systolic pressure in the lower and upper extremities was measured by one radiologist by means of a Doppler ultrasonography device (Toshiba Nemio-30, Osaka, Japan) using an AT probe. Systolic blood pressure was measured by wrapping sphygmomanometer cuff around each of the two ankles and wrists, respectively, after a 10-minute rest and the ABI was calculated as the highest ankle systolic pressure divided by highest brachial systolic pressure in each patient.

Of 149 patients who participated in the urine albumin assay, 5 were excluded because of macroalbuminuria (urine albumin > 300 mg/24 h). Albumin in the urine was measured with turbidometry method through a Minineph Nephlometry machine (Binding Site Ltd, Birmingham, UK) that was specified for quantitative assay. Only one sample was obtained from each patient for measurement of albumin and this was one of the limitations in this study.

The patients were categorized into 3 groups based on their ABI (< 0.9, 0.9 to 1.4, and > 1.4). The three groups were compared using the chi-square test and the 1-way analysis of variance, where appropriate. The SPSS software (Statistical Package for the Social Sciences, version 16.0, SPSS Inc, Chicago, Ill, USA) was used for analyses. A *P* value less than .05 was considered significant.

RESULTS

This study was performed on 206 patients with type 2 DM, including 84 men (40.8%) and 122 women (59.2%). The mean age was 54.08 ± 9.20 years. The mean duration of DM was 124.27 months with the shortest duration of 3 months and the longest duration of 432 months. Body mass index was greater than 25 in 152 participants (74%) and less than 25 in 54 participants (26%). Thirty-one patients (15%) were smoker. The average of cigarette use was 22.71 pack.years (with the least of 4 and the most of 90 pack.years). A history of dyslipidemia was present in 139 patients (67.5%), high blood pressure in 106 patients (51.5%), cardiovascular events and admission to cardiac care unit in 13 (6.3%), cerebrovascular events in 2 (1%), and diabetic foot ulcer in 35 (17%; Table 1).

The mean ABI measured by Doppler

Table 1. Demographic Data

Characteristic	Number (%)
Sex	
Male	84 (40.8)
Female	122 (59.2)
Body mass index	
> 25	152 (74.0)
≤ 25	54 (26.0)
Hypertension	106 (51.5)
Dyslipidemia	139 (67.5)
Microalbuminuria	42 (29.16)
Smoking	31 (15.0)
Mean diabetes duration, mo	124.27
Cardiovascular disease	13 (6.3)
Foot Ulcer	35 (17.0)
No dorsalis pedis pulse	19 (9.2)
No tibialis posterior pulse	22 (10.7)

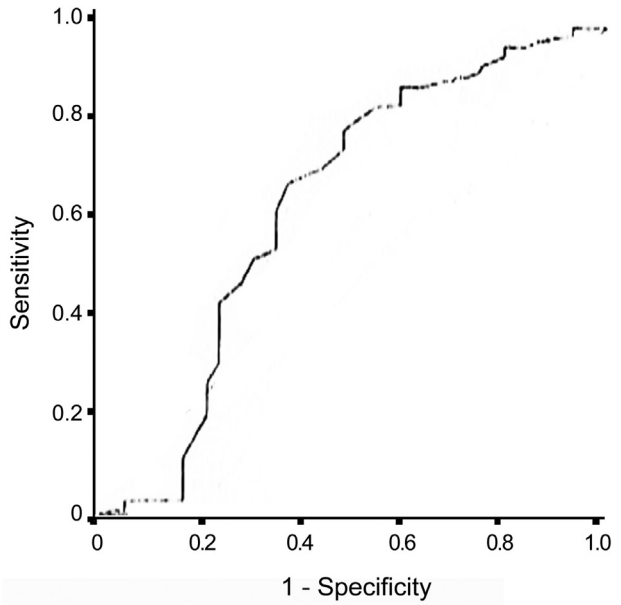
ultrasonography was 1.1 ± 0.2 (range, 0.052 to 1.6). The patients were stratified into 3 groups: the first group were 54 men (36.2%) and 95 women (63.8%) with an ABI between 0.9 and 1.4 (mean, 1.14 ± 0.12); the second group were 17 men (41.5%) and 24 women (58.5%) with an ABI between 0.52 and 0.89 (mean, 0.79 ± 0.09); and the third group were 13 men (81.3%) and 3 women (18.8%) with an ABI between 1.41 and 1.6 (mean of 1.4 ± 0.04). There was no significant relationship between sex and ABI groups (P = .50). The mean age was 53.4 ± 9.3 years in the first group, 55.5 ± 8.5 years in the second group, and 56.2 ± 9.5 years in the third group (P = .20). The mean duration of DM was higher in those with high ABIs (P = .04; Table 2). A history of cardiovascular events was higher in the first group. In addition, there was a significant correlation between high blood pressure and an ABI less than 0.9 (odds ratio, 0.34; 95% confidence interval, 0.18 to 0.81; P = .01; Table 2). There was also a significant correlation between dyslipidemia and an ABI less than 0.9 (odds ratio, 0.34; 95% confidence interval, 0.14 to 0.82; P = .01; Table 2).

Of all the participants 35 (17%) had a history of diabetic foot ulcer, of whom 16 patients (39%) had an ABI less than 0.9 (the second group). In addition, 19 patient (9.2%) had no pulse in the dorsalis pedis, of whom 8 patients (19.5%) were in the group with abnormal ABI. Twenty-two patients (10.7%) had no tibialis posterior pulsation, of whom 10 patients (24.4%) were in the group with abnormal ABI.

Of 144 patients who participated in the urine microalbuminuria assay, 105 patients were in the first group, 28 in the second group, and 11 in the third group. Microalbuminuria was found 18 patients (17.1%) of the first group, in 16 patients (57.1%) of the second group, and in 8 patients (72.8%) of the third group. There was a significant correlation between an ABI less than 0.9 and microalbuminuria (odds ratio, 0.05; 95% confidence interval, 0.038 to 0.630; P < .001). A cutoff point of an ABI less than or equal to 1.04 had a sensitivity of 71.6%, a specificity of 64.2%, a positive predictive value of 63.0%, and a negative predictive value

Table 2. Correlation Between Atherosclerosis Risk Factors and Ankle-Brachial Index

Characteristic	Ankle-Brachial Index			*P*
	< 0.9	0.9 to 1.4	> 1.4	
Mean age, y	53.4	55.5	56.2	.20
Sex				
Male	17 (41.5)	54 (36.2)	13 (81.2)	.50
Female	24 (58.5)	95 (63.8)	3 (18.8)	.50
Body mass index				
> 25	27 (65.9)	112 (75.5)	13 (81.2)	.20
≤ 25	14 (34.1)	37 (24.5)	3 (18.8)	.20
Hypertension	28 (68.3)	68 (45.6)	10 (62.5)	.01
Dyslipidemia	34 (82.9)	93 (62.4)	12 (75)	.01
Microalbuminuria	16 (57.1)	18 (17.1)	8 (72.8)	< .001
Smoking	9 (30.0)	18 (12.1)	4 (25.0)	.70
Mean smoking, pack.year	21.22	24.06	20	.70
Mean diabetes duration, mo	144.29	113.74	171.06	.04
Cardiovascular disease	8 (19.5)	4 (2.7)	1 (6.2)	.001
Foot Ulcer	16 (39)	15 (10.1)	4 (25)	…
No dorsalis pedis pulse	8 (19.5)	9 (6)	2 (12.5)	…
No tibialis posterior pulse	10 (24.4)	9 (6)	3 (18.8)	…



The receiver operation characteristic curve for the predictive value of the ankle-brachial index for microalbuminuria.

of 75.0% for prediction of microalbuminuria (the area under the curve, 0.6; Figure)

DISCUSSION

Diabetes mellitus is an extending metabolic disorder in the world with microvascular and macrovascular complications that if not being diagnosed and properly treated leads to debility, increased mortality, and morbidity. Diabetes mellitus leads to acceleration of atherosclerotic changes in vessels and thus involvement of different organs. In this study, we evaluated identifying and screening of atherosclerosis in diabetic patients by the use of the ABI and found that 72.3% of the diabetic patients had normal ABI (between 0.9 and 1.4), while 19.9% had an ABI less than 0.9, and 16 (7.8%) had an ABI greater than 1.4. This indicator was associated with microalbuminuria and with a cutoff point of 1.04 it could predict microalbuminuria with acceptable diagnostic accuracy.

Resnick and colleagues reported an ABI less than 0.9 in 4.9% of their patients,[16] and Li and coworkers reported it in 32.2 % of their participants.[9] The lower average of patients' age in this study compared with the higher average of age in the similar studies, due to selecting participants from the patients admitted to the hospital, is the main reason for discrepancies in these studies. In the current study, the average number of patient in all three groups of ABI was approximately the same and with incidental adjustment, the biasing variant of age was omitted. Therefore, the rate of abnormal ABI calculated in this study has a better predictive value.

In this study, there was no correlation between sex and an ABI less than 0.9. This was in accordance with the results of the study conducted by Tseng and colleagues,[15] and also with the study carried out by Polenova and colleagues in Russia.[17] However, Li and associates[9] found a significant correlation between an ABI less than 0.9 and female sex.

There was no significant relationship between obesity and an ABI less than 0.9 in the current study, which was in line with the some other studies.[9,15] This implies that obesity may not be a risk factor for atherosclerosis. There was no correlation between cigarette smoking on the basis of pack.year and ABI in our study, either. In the studies conducted by Khammash and colleagues[6] and some other studies[9,17] the comparison was between being smoker or not, without regarding the amount of pack.year use, which showed significant correlation with abnormal ABI.

The rate of dyslipidemia was 67.5% in this study. It was more (82.9%) in the group with an ABI less than 0.9 and there was a significant correlation between dyslipidemia and an ABI less than 0.9. This was in accordance with similar studies.[5,9] This shows the effect of dyslipidemia in progression of atherosclerosis. In the study conducted by Jabbari and coworkers[18] the prevalence of peripheral arterial disease in the patients with chronic kidney disease was 10% and ABI was correlated with several classical risk factors for atherosclerosis, including elevated low-density lipoprotein cholesterol and total cholesterol levels. Similarly, high blood pressure, found in 68.3% of the patients with abnormal ABI, was a significant correlate. This result was similar to many other reports on ABI in diabetic patients, as well,[6,9,15,16] which suggests the effect of hypertension in acceleration of atherosclerosis. Another predictor of an abnormal range for ABI was the duration of DM, which has been shown by others too.[5,11,15]

Microalbuminuria was found in 29.16% of our patients and in 57.1% of those with an ABI less than 0.9. There was a significant correlation between an ABI less than 0.9 and microalbuminuria ($P < .001$).

Tseng and colleagues[15] also demonstrated that albumin-creatinine ratio significantly correlated with abnormal ABI (less than 0.9) and peripheral arterial disease, but the mean age of patients was 65 years old, and thus, coexistence of peripheral arterial disease and abnormal ABI may be due to physiologic atherosclerotic changes in this range of age. In our study, the cutoff point equal to or less than 1.04 was calculated for ABI as a prediction of microalbuminuria in type 2 DM, with a sensitivity of 71.6% and a specificity of 64.2%.

In our study, cardiovascular events were more frequent in the patients with abnormal ABI and a significant relationship was found between an ABI less than 0.9 and cardiovascular events; there was a strong correlation even after omitting the bias-inducing variants. In the Rafii and colleagues' study,[12] a significant correlation was found between abnormal ABI and positive exercise test. Nematipoor and colleagues[13] measured ABI and performed coronary angiography and showed that all the patients with an ABI less than 0.9 had coronary vessel disease and ABI decreased with increasing number of vessels involved.

CONCLUSIONS

Considering cardiovascular complications as the most important factor in the mortality of diabetic patients, the use of simple, easily available, noninvasive, and reliable methods as screening test for these complications is recommended. The use of the criterion of an ABI less than 0.9 in diabetic patients declines the necessity of monitoring cardiovascular complications and related risk factors. The abnormality of this index also warrants evaluating the other asymptomatic vascular complications such as carotid artery and coronary vessels involvement in order to prevent severe vascular complications in organs such as the heart and brain. However, impossibility of a fully evaluation of cardiac complications was the limitation of the current study.

ACKNOWLEDGMENTS

We are grateful to the board of managers of Iran Diabetes Society, branch of West Azarbayejan, especially Dr Hamid Asgharzadeh, Chief of Diabetes Society. We also wish to thank Mrs Rabie, secretary of the Society and all the diabetic patients for their assistance in all the processes of this research.

CONFLICT OF INTEREST

None declared.

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Received May 2012
Revised November 2012
Accepted December 2012