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Correlation between the ankle–brachial index and microalbuminuria with certain risk factors in type 2 diabetes patients

Van Tuan Nguyen[a], Ha Linh Phan[b], Thi Minh Hoang[c], Thị Phuong Lan Dam[c], Thi Hang Ho[c] and Quang Thuan Huynh[c]

Background **The ankle–brachial index (ABI) is a fast, simple, noninvasive method that provides accurate results in the early diagnosis of peripheral artery disease. Microalbuminuria is considered a predictor of renal and cardiovascular complications in patients with diabetes. This study was conducted to determine the correlation between ABI and microalbuminuria with certain risk factors in patients with type 2 diabetes.**

Subjects and research methods **A cross-sectional descriptive study was performed on 62 inpatients with type 2 diabetes. All patients were measured for ABI as well as microalbuminuria, HbA1c, glucose and lipidemia in the blood.**

Results **The study results showed that in patients with dyslipidemia, the risk of having microalbuminuria (+) increased 5.7 times and ABI ≤0.90 increased 8.6 times ($P = 0.004$ and 0.021, respectively). Fasting blood glucose >7.2 mmol/L had 5.7 times higher microalbuminuria (+) risk and 8.6 times higher ABI ≤0.90 ($P = 0.004$ and 0.021, respectively). Patients with HbA1c ≥7% were 2.9 times more likely to have microalbuminuria (+) and ABI ≤0.90 ($P = 0.043$ and 0.048, respectively).**

Conclusions **Peripheral vascular disease risk factors such as hypertension, dyslipidemia and waist circumference and the effectiveness of fasting blood glucose and HbA1c control increased the risk of high microalbuminuria and ABI in patients with type 2 diabetes.** ***Cardiovasc Endocrinol Metab*** **10: 210–214**

Cardiovascular Endocrinology & Metabolism 2021, **10**:210–214

Keywords: ankle–brachial index, microalbuminuria, peripheral artery disease, type 2 diabetes mellitus

[a]Internal Medicine Department, [b]Biochemistry and Hematology Department, Vinh Medical University, Nghe An and [c]Biochemistry Department, [d]Military Hospital 103, Vietnam Military Medical University (VMMU), Hanoi, Vietnam

Correspondence to Huynh Quang Thuan, Biochemistry Department, 103 Military Hospital, Vietnam Military Medical University, No. 160, Phung Hung Street, Phuc La Ward, Ha Dong District, Hanoi City, Vietnam
E-mail: huynhquangthuan2002@yahoo.com

Received 11 January 2021 **Accepted** 25 March 2021

Introduction

Diabetes is a chronic medical condition that greatly affects the socioeconomic life of countries worldwide [1]. The disease causes many serious complications such as coronary artery disease, cerebrovascular accident and blindness, in which peripheral artery disease (PAD) and diabetic kidney disease are common complications [2]. Not only does it affect the health and quality of life of the patient, but the treatment of these complications in the late stage of the disease is also complicated and expensive. Therefore, early detection of atherosclerotic lesions to plan treatment and prevention is essential.

Currently, there is a fast, simple and noninvasive method that provides an accurate early diagnosis of PAD – the ankle–brachial index (ABI). This index not only is effective in screening for PAD but also helps predict future cardiovascular events [3]. ABI is established by dividing the higher lateral ankle systolic blood pressure by the higher lateral arm blood pressure [4]. The normal limit value for ABI generally accepted by most studies and cardiovascular practice guidelines is between 0.9 and 1.4. ABI values <0.9 show a strong association between other cardiovascular risk factors and the presence of PAD [3].

Since 1982, the term 'microalbuminuria' is officially used in clinical practice. It has become a medical interest, especially in the areas of cardiovascular disease and metabolic endocrine disorders. Microalbuminuria is considered a predictor of renal and cardiovascular complications in patients with diabetes. Microalbuminuria is defined as albuminuria excretion of 30–300 mg/day or 20–200 μg/min and is an early sign of vascular damage [5].

Currently, worldwide as well as in Vietnam, studies on increased urinary albumin excretion – a risk factor for PAD – especially the relationship between microalbuminuria and ABI in type 2 diabetes patients, are still limited. Therefore, this study was conducted to investigate the association between microalbuminuria and ABI with certain risk factors in patients with type 2 diabetes.

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Subjects and methods

Subjects and study design

A descriptive cross-sectional study was performed on 62 patients with type 2 diabetes treated at the Department of Endocrinology–Diabetes of Huu Nghi Hospital in Nghe An from 1 January to 30 April 2018.

All patients were diagnosed with type 2 diabetes and assessed for blood sugar control based on the guidelines of the American Diabetes Association [6]. The study excluded patients with consciousness disorders; with severe and acute complications such as ketoacidosis coma, hyperosmolar coma and acute infections; with kidney disease such as urinary infection, microscopic or macroscopic hematuria and urinary kidney stones; with type 2 diabetes with gross proteinuria and kidney failure; women patients who were menstruating or pregnant; with malignant hypertension; who were currently feverish or dehydrated; with amputation or deep vein thrombosis; infected with swelling of the arms or legs; with diffuse scleroderma or calcified vessels; and who refused to participate in the study.

Clinical examination and testing

All patients were asked about their medical history, such as the time of diagnosis, hypertension and drug use history. Clinical examination was performed to detect associated diseases, and height, weight, BMIs, waist circumference, pulse and blood pressure were measured on the same day.

Blood pressure was measured in the right arm with a mercury sphygmomanometer after 20 min of rest with the patient in a sitting position. BMI was calculated as the ratio of body weight (kg)/height squared (meters).

The total cholesterol, triglyceride, LDL-C and HDL-C levels were quantified in serum based on the colorimetric method, and fasting blood glucose level was determined based on the hexokinase method on an AU680 analyzer (Beckman Coulter, California, USA). HbA1c level was quantified on EDTA blood by HPLC using Premier Hb9210 (Trinity Biotech, Kansas City, USA). Spot urine samples were collected in the morning. microalbuminuria was quantified based on the turbinal method using an AU680 analyzer (Beckman Coulter).

Ankle–brachial index measurement

The ABI was measured using a VP-1000 plus analyzer (Omron Healthy, Kyoto, Japan) based on the oscillometric method, following the standardized produce. Systolic pressure was measured in the arms and ankles on both sides. Patients were asked not to smoke or drink alcohol or coffee 30 min before measurement. They should rest on their backs in bed for at least 15 min prior to the measurement.

ABI = (highest left and right ankle systolic blood pressure)/(highest left and right arm systolic blood pressure).

PDA severity	ABI
Normal	0.9–1.3
Severe	< 0.4
Moderate	0.4–0.7
Mild	<0.9 and >0.7
Abnormal, suggestive of noncompressible vessels	>1.3

PDA was diagnosed based on ABI, and the severity was classified into five levels, as shown in the following table:

Statistics

All data were analyzed with SPSS version 26 (64-bit version) for Windows (SPSS Inc., Chicago, Illinois, USA). Data are expressed as mean ± SD or percentage, and statistical significance was set at $P < 0.05$. The relationship between microalbuminuria, ABI and risk factors was indicated by the odds ratio (OR) and 95% CI.

Results

Characteristics of the subjects

The average age of the study subjects was 59.24 (11.7) years. Among them, 15 patients (24.2%) were diagnosed with PAD, while 30 patients (48.4%) had positive microalbuminuria (Table 1).

Prevalence of PAD based on ankle–brachial index

The rate of ABI ≤0.90 in type 2 diabetic patients without microalbuminuria was 24.2%. The percentages of mild, moderate and severe PAD based on ABI were 21, 3.2 and 0%, respectively. The percentages of ABI >1.3 and normal ABI were 2 and 45%, respectively (Table 2).

Relationship between ankle–brachial index and microalbuminuria with some cardiovascular risk factors

Microalbuminuria and ABI were associated with a history of hypertension, dyslipidemia and waist circumference. In patients with a history of hypertension, the risk of having microalbuminuria (+) increased by 5.1 times and

Table 1 Characteristics of research subjects

Characteristics	Value	
Age (years)	Mean ± SD 59.24 ± 11.7	
Sex	Men *n* (%) 37 (59.7)	Women *n* (%) 25 (40.3)
Time to detect disease	≤5 years *n* (%) 26 (42)	>5 years *n* (%) 36 (58)
Overweight	Yes *n* (%) 20 (32.3)	No *n* (%) 42 (67.7)
Hypertension	37 (59.7)	25 (40.3)
Central obesity	27 (43.5)	35 (56.5)
PAD	15 (24.2)	47 (75.8)
Microalbuminuria	30 (48.4)	32 (51.6)

PAD, peripheral artery disease.

an ABI ≤0.90 was 3.7 times higher than that in patients without hypertension (P = 0.002 and 0.038, respectively). The risk of having microalbuminuria (+) increased by 5.7 times and an ABI ≤0.90 increased by 8.6 times compared to that in patients without the disorder (P = 0.004 and 0.021, respectively). In patients with central obesity (waist circumference >90 cm in men and >80 cm in women), the risk of microalbuminuria (+) was 3.3 times higher and ABI ≤0.90 was 5.8 times higher than that in noncentral obese cases (P = 0.023 and 0.005, respectively; P < 0.05). MAUs are related to blood pressure, while ABIs are not. Patients with hypertension were at risk of having microalbuminuria (+) 3.3 times higher than those with normal blood pressure (P = 0.023; P < 0.05). There was no relationship between microalbuminuria and ABI and BMI (Table 3).

Relationshipbetween ankle–brachial index and microalbuminuria and blood glucose control

The risk of positive microalbuminuria in the group with FBG level >7.2 mmol/L was 5.7 times higher than that in the group with FBG level ≤7.2 mmol/L (P = 0.004). The group with FBG level >7.2 mmol/L had 8.6 times higher risk of PAD than that in the group with FBG level ≤7.2 mmol/L (P = 0.021). Patients with HbA1c level ≥7% had 2.9 times higher risk of microalbuminuria (+) and ABI ≤0.90 than those with HbA1c level <7% (P = 0.043 and 0.048, respectively; P < 0.05) (Table 4).

Discussion

Vascular complications associated with diabetes are a global dilemma. In particular, kidney complications or peripheral vascular disease are among the most serious complications of diabetes. This is not only the leading cause of end-stage chronic kidney disease but is also related to mortality rate as well as early cardiovascular events.

Our research was conducted on 62 patients with type 2 diabetes who were treated at the Department of Endocrinology–Diabetes, Huu Nghi Hospital, in Nghe An. This study aimed to show the relationship between certain risk factors and the risk of vascular diseases (PAD and renal nephrology) in patients with T2DM.

We found that the incidence of PAD was 24.2% (n = 15), of which mild PAD (ABI 0.70–0.90) accounted for 21.0% and mean PAD (ABI 0.40–0.69) 3.2%, and there was no severe PAD (ABI <0.40). A normal ABI rate of 0.91–1.30 accounted for 73.8%. An ABI rate >1.30 accounted for 3.2% (Table 2). These results were similar to those of Makhdoomi *et al*., which included 206 patients with type 2 diabetes and 144 patients with microalbuminuria, of which 105 patients had an ABI at 0.90–1.40, 28 patients with an ABI at 0.61–0.89, and 11 patients with an ABI at 1.41–1.60. The number of patients with PAD accounted for 19.4% [7]. In the study by Li *et al*. on 1647 subjects, 32.2% had an ABI <0.9 [8].

Table 2 Prevalence of PAD based on ABI

Variable		*n* (%)
ABI	0.91–1.30	45 (73.8 %)
	ABI 0.70–0.90	13 (21.0%)
	ABI 0.40–0.69	2 (3.2%)
	ABI <0.40	0 (0%)
	>1.30	2 (3.2%)
Total		62 (100%)

ABI, ankle–brachial index; PAD, peripheral artery disease.

Regarding microalbuminuria quantitative results, the rate of microalbuminuria (+) detection in 62 patients with type 2 diabetes who were microalbuminuria (–) was 48.4% (n = 30). Thus, although in the subjects studied using quantitative methods, proteinuria was not observed. When testing for microalbuminuria, nearly half of them began to display glomerular membrane damage. The frequency of microalbuminuria (+) found in our research group was higher than that reported by some authors, such as Mogensen [9]. This difference might be due to the patient selection and the evaluation method being qualitative, semiquantitative or quantitative. In addition, this difference was influenced by the uneven management of blood glucose and blood pressure among different treatment facilities.

The results of our study (Table 3) show that microalbuminuria and ABI were related to a history of hypertension. For those with a history of hypertension, the risk of microalbuminuria (+) was 5.1 times higher (P = 0.002; P < 0.05) and the risk of ABI ≤0.90 was 3.7 times higher (P = 0.038; P < 0.05) than those without a history of hypertension. Subjects with uncontrolled blood pressure had a 3.3 times higher risk of microalbuminuria (+) than those with controlled blood pressure (P = 0.023; P < 0.05). This result was similar to that of many other reports on ABI in diabetic patients [7,8,10]. This shows the effect of hypertension on accelerating atherosclerosis. Systolic hypertension is an important factor in the progression of microalbuminuria. Hypertension and diabetic nephropathy aggravated each other, contributing to a spiral of hypertension progression, kidney disease and cardiovascular disease. According to Stults, in patients with type 2 diabetes, the rate of hypertension is 50% at the time of diagnosis, up to 80% with urinary microalbuminuria, and up to >90% with urinary macroalbuminuria [11]. Thus, it could be observed that hypertension plays an important role in the development of vascular complications in diabetes. The control of blood pressure in diabetic patients plays an important role in reducing renal and peripheral vascular disease complications.

There was no significant relationship between BMI and microalbuminuria and ABI in our study. This result is also consistent with those of other studies [7,8,10]. This implies that obesity may not be a risk factor for atherosclerosis. However, subjects with type

Table 3 **Relationship between ABI and microalbuminuria with some cardiovascular risk factors**

Variable		Microalbuminuria (–)	Microalbuminuria (+)	ABI ≤0.90	ABI >0.90
Blood pressure	<130/80 mmHg	21	11	7	25
	≥130/80 mmHg	11	19	8	22
OR, 95% CI, *P*		*P* = 0.023 OR = 3.3		*P* = 0.660	
History of hypertension	With hypertension	10	21	11	20
	Without hypertension	22	9	4	27
OR, 95% CI, *P*		*P* = 0.002 OR = 5.1		*P* = 0.038 OR = 3.7	
Blood lipid level	No disturbances	25	9	5	29
	With disturbances	7	21	10	18
OR, 95% CI, *P*		*P* = 0.004 OR = 5.7		*P* = 0.021 OR = 8.6	
Waist circumference	No center fat	23	13	4	32
	Fatty central part	9	17	11	15
OR, 95% CI, *P*		*P* = 0.023 OR = 3.3		*P* = 0.005 OR = 5.8	
BMI	Not overweight	24	18	34	8
	Overweight	8	12	13	7
P value		*P* = .207		*P* = 0.170	

ABI, ankle–brachial index; CI, confidence interval; OR, odds ratio.

Table 4 **Relationship between ABI and microalbuminuria and blood glucose control**

Variable		Microalbuminuria (–)	Microalbuminuria (+)	ABI ≤0.90	ABI >0.90
Fasting blood glucose level	≤7.2 mmol/L	15	4	1	17
	>7.2 mmol/L	17	26	14	29
OR, 95% CI, *P*		*P* = 0.004 OR = 5.7		*P* = 0.021 OR = 8.6	
HbA1c level	<7 %	21	12	5	28
	≥7 %	11	18	10	19
OR, 95% CI, *P*		*P* = 0.043 OR = 2.8		*P* = 0.048 OR = 2.9	

ABI, ankle–brachial index; CI, confidence interval; OR, odds ratio.

2 diabetes with central obesity had a significant relationship with microalbuminuria and ABI. For those with central obesity, the risk of microalbuminuria (+) was 3.3 times higher (P = 0.023; P < 0.05) and the risk of ABI ≤0.90 was 5.8 times higher (P = 0.005; P < 0.05) than those with noncentral obesity. Therefore, we propose that the management of overweight and obesity in type 2 diabetic patients to reduce vascular complications and prevent major cardiovascular events should be considered in the treatment strategy.

We found that microalbuminuria (+) and ABI ≤0.90 were associated with dyslipidemia, those with dyslipidemia had 8.3 times higher risk of microalbuminuria (+) than those without disorders (P = 0.0001; P < 0.05). Patients with dyslipidemia and ABI ≤0.90 had 3.2 times higher risk than those without dyslipidemia (P = 0.045; P < 0.05), indicating the effect of dyslipidemia on the progression of atherosclerosis. In a study conducted by Jabbari *et al.*, the incidence of PAD in patients with chronic kidney disease was 10%, and ABI was correlated with some classic risk factors for fibrosis and atherosclerosis, including increased LDL-C and total cholesterol levels [12].

Diabetes is a chronic disorder of carbohydrate metabolism that progressively leads to many complications. Recent studies have shown a relatively clear correlation between blood glucose levels and major vascular and microvascular complications in patients with type 2 diabetes [13,14]. Our results showed that microalbuminuria and ABI were related to fasting blood glucose and HbA1c level control. The group with fasting blood glucose level >7.2 mmol/L had 5.7 times higher microalbuminuria (+) risk and 8.6 times higher ABI ≤0.90 compared to that in the group with blood glucose level ≤7.2 mmol/L (P = 0.004 and 0.021, respectively; P < 0.05) (Table 4). Patients with HbA1c level ≥7% were 2.9 times more likely to have microalbuminuria (+) and ABI ≤0.90 than those with HbA1c level <7% (P = 0.043 and 0.048, respectively; P < 0.05). Thus, it could be seen that the blood glucose level in T2D patients with microalbuminuria (+) and microalbuminuria (–) with or without PAD was not properly controlled. Therefore, these patients might not pay much attention to their disease status, which is also the general situation of diabetic patients in Vietnam. The main cause might remain due to the gaps between

treatment guidelines and clinical practice, as well as good management strategies to help patients achieve their blood glucose control targets.

This study had some limitations. The first was the small number of participants. Second, this was a cross-sectional study, so it lacked information on the progression of vascular complications of T2D over time. The third was the absence of some patient information such as their medications, eGFR level, etc.

Conclusion

Peripheral vascular disease risk factors such as hypertension, dyslipidemia and waist circumference and the effectiveness of fasting blood glucose and HbA1c control increased the risk of high microalbuminuria and ABI in patients with type 2 diabetes.

Acknowledgements

This study was approved by the Ethical Committee of Vinh Medical University, Vietnam. All the participants were given informed consent before enrollment. All authors did not receive any private or governmental funding. Van Tuan Nguyen and Quang Thuan Huynh conceptualized, designed and critically revised the article. Thuy Linh Phan accquired data. Thi Minh Hoang, Thị Phuong Lan Dam and Thi Hang Ho analyzed, interpreted and drafted the article. All authors finally approved the article.

Conflicts of interest

There are no conflicts of interest.

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