

## Case series of macroalbuminuria and toe-brachial index in type 2 diabetes mellitus

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### ABSTRACT

Diabetes mellitus is a growing health problem with a significant global disease burden. The complications and mortality rate associated with diabetes are increasing. Albuminuria is one of its complications and evidence of established nephropathy. Low toe-brachial index (TBI) is more strongly associated with albuminuria and may be a suitable tool for evaluating peripheral arterial disease in patients with type 2 diabetes mellitus. Our study evaluated the association between macro albuminuria and low toe brachial index in type 2 diabetic patients to identify those who need specialized foot care and adequate renal protection.

**Keywords:** Ankle brachial index, Toe-brachial index, Medial arterial calcification, Type 2 diabetes mellitus, Peripheral arterial disease

### INTRODUCTION

Type 2 diabetes mellitus is a chronic metabolic disease that affects the body's metabolism and is characterized by elevated blood glucose levels. Overtime, this condition causes the body to produce advance glycation products, which can seriously harm the heart, blood vessels, eyes, kidneys and nerves. More than 84% of people with pre diabetes are unaware of their condition.<sup>1</sup>

A higher risk of cardiovascular mortality has been linked to an elevated albumin excretion rate, a helpful indicator of diabetic nephropathy. Patients with macro albuminuria appear to have more pronounced arterial stiffness and carotid atherosclerosis. Therefore, the presence of macro albuminuria might represent an independent risk factor for vascular disease and the presence of toe brachial index could be a useful tool to detect and prevent cardiovascular events.<sup>2</sup>

An easy and effective way to evaluate peripheral arterial disease is the ankle-brachial index (ABI) and toe-brachial index (TBI). Additionally, it has been noted that a risk factor for CVD events is an ABI value <0.9. However, since medial arterial calcification artificially inflates the ABI value, its use in diabetic patients is regarded as dubious. Since medial arterial calcification is less common in the toe than the ankle, TBI is recommended for diabetic patients.<sup>2</sup>

TBI (the ratio between systolic blood pressures in the first toe and in the arm) is generally not affected by MAC since collateral vessels of the toe are less prone to suffer from calcification. This discovery makes TBI a viable peripheral arterial disease (PAD) diagnostic test particularly for MAC level afflicted patients.<sup>3,4</sup>

In cases of diminished ankle brachial index efficacy, which most frequently occurs in diabetes, the toe-brachial index (TBI) is advised for identification of lower extremity

arterial disease (LEAD). In this case, TBI is predicted to produce more precise outcomes.<sup>4</sup>

**Table 1: Range of toe brachial index.**

Severity	Values
Low risk	>0.6
Moderate risk	0.4-0.6
High risk	0.2-0.4
Severe risk	<0.2

Foot wound development is frequently multifaceted and may be a consequence of microvascular dysfunction or ischemia because of PAD. Up to one-third of lower limb wounds are ulcers or wounds caused by PAD which causes severe discomfort, morbidity and lower quality of life. In addition, they impose a significant economic burden and particularly in people with diabetes, are a leading cause of non-traumatic lower limb amputation. Early identification of wound aetiology and routine vascular examination are required to implement timely and appropriate treatment, limit morbidity and prevent recurrence. Current PAD screening methods are intended to detect extensive atherosclerotic lesions of the large arteries of the lower limb; however, stenosis or occlusion of the small arteries can reduce blood flow and impair healing. The American College of Cardiologists/American Heart Association (ACC/AHA) recommends that a TBI of <0.70 be considered diagnostic of PAD. However, low toe blood pressures (used to calculate the TBI ratio) have been found to predict impaired healing of chronic foot wounds and progression to amputation. While the TBI is a measure of peripheral vascular status, particularly the health of the small arteries, there has been little research investigating the relationship between the TBI and risk of foot complications, including ulceration and amputation in diabetic patients.<sup>5</sup>

**CASE SERIES**

Our 6-month retrospective study involved 62 type 2 diabetic patients who were receiving outpatient care in a tertiary care hospital in Kerala and had substantial TBI values. 62 patients with type 2 diabetes had their bilateral lower limb evaluated. A vascular doppler method was used to calculate TBI. TBI <0.7 is used as cut-off point to assess the validity parameters. Vasocheck+ is a complete non-invasive unidirectional vascular Doppler recorder designed to measure the TBI, ABI and the velocity waveform with a connection to a Windows 7/8/10 operated computer for storage of data and patient generation. Interpretation as per TASC II guidelines.

**DISCUSSION**

This study aims to demonstrate the association between macro albuminuria and low toe brachial index in patients with type 2 diabetes mellitus. Out of 62 type 2 diabetic patients, the association between macro albuminuria and

toe brachial index were found to be significant among 35 study subjects.

As depicted in Tables 2 and 3, among 62 diabetic patients with substantial TBI values, 35 patients had macro albuminuria and 27 patients had micro albuminuria. 29 patients had normal TBI and 33 patients had low TBI.

**Table 2: No. of patients with and without macroalbuminuria.**

No. of patients with macroalbuminuria	No. of patients without macroalbuminuria
35	27

**Table 3: No. of patients with normal TBI and low TBI.**

No. of patients with low TBI	No. of patients with normal TBI
33	29

**Statistical data analysis**

Approximately 27% of the patients were seen to have urine micro albumin creatinine ratio above 500 mg/g and most of the patients (43.54%) were seen to have urine micro albumin creatinine ratio below 300 mg/g.

When we classify patients according to the range of TBI, 13% of the patients were at high risk and 53% of the patients were at low risk.

**Table 4: Frequency table.**

Variables	Frequency (%)
<b>Urine micro albumin creatinine ratio</b>	
<300	27 (43.54))
300-400	11 (17.74)
400-500	7 (11.29)
Above 500	17 (27.41)
<b>Toe brachial index (TBI)</b>	
Low risk	33 (53.22)
Moderate risk	21 (33.87)
High risk	8 (12.90)

Urine micro albumin-creatinine ratio and left toe brachial index shows strong negative correlation (correlation coefficient,  $\rho=-0.7722327$ ) which indicates that as urine micro albumin-creatinine ratio increases left toe brachial index decreases. Also, this correlation is statistically significant and linear since the p value is less than 0.05. Urine micro albumin-creatinine ratio and right toe brachial index shows strong negative correlation (correlation coefficient,  $\rho=-0.7894361$ ) which indicates that as urine micro albumin- creatinine ratio increases right toe brachial index decreases. Also, this correlation is statistically significant and linear since the p value is less than 0.05. Urine micro albumin- creatinine ratio and toe brachial index shows strong negative correlation (correlation

coefficient,  $\rho=-0.7815604$ ) which indicates that as urine micro albumin- creatinine ratio increases toe brachial index decreases. Also, this correlation is statistically significant and linear since the p value is less than 0.05. Since medial arterial calcification is less frequent in toe than in ankle, TBI is advocated for diabetic patients. TBI

is more strongly associated with albuminuria or eGFR than ABI, hence a more suitable tool for evaluating the association between PAD and diabetic nephropathy than ABI, and TBI is recommended to be substituted for ABI for evaluating PAD in patients with type 2 diabetes.<sup>2,3</sup>

**Table 5: Correlation.**

Relation between urine micro albumin- creatinine ratio and left toe brachial index		Relation between urine micro albumin- creatinine ratio and right toe brachial index		Relation between urine micro albumin- creatinine ratio and toe brachial index	
Spearman correlation coefficient	P value	Spearman correlation coefficient	P value	Spearman correlation coefficient	P value
-0.7722327	<0.001*	-0.7894361	<0.001*	-0.7815604	<0.001*

**CONCLUSION**

According to the interim results of this work, type 2 diabetes mellitus patients with increased macro albuminuria have decreased TBI. Type 2 diabetes mellitus with elevated urine macro albumin creatinine ratio results in a decreased TBI according to our study. Since TBI is strongly correlated with urine macro albuminuria, the urine micro albumin creatinine ratio test is a more easily verifiable method to determine whether a diabetic patient will develop foot complications.

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