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TBI or not TBI: that is the question. Is it better to measure toe pressure than ankle pressure in diabetic patients?

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Abstract

Aims Measurement of ankle blood pressure is a simple method of assessing lower limb arterial blood supply. However, its use in diabetes has been questioned due to the presence of medial artery calcification. Measurement of toe blood pressure has been advocated as an alternative but it is technically more difficult. The aim of this study was to obtain information to guide clinicians as to when pressure measurements should be taken at the toe.

Methods Ankle brachial index (ABI) and toe brachial index (TBI) were measured by Doppler ultrasound, or photoplethysmography on 174 subjects with diabetes and 53 control subjects. The Bland and Altman method, and the Cohen's method of measuring agreement between two tests were used to compare ABI with TBI.

Results The mean differences between ABI and TBI in control and diabetic subjects are 0.40 ± 0.13 and 0.37 ± 0.15, respectively. Nearly all diabetic patients with an ABI < 1.3 have an ABI–TBI gradient falling within the normal range established from the non-diabetic cohort. In contrast, the majority of diabetic subjects with an ABI $\geqslant 1.3$ have ABI–TBI differences outside this range. When patients are categorized according to ABI and TBI, there is also good agreement between the tests when ABI is low or normal (84% and 78% agreement, respectively), but not when ABI is elevated.

Conclusion In the majority of patients with diabetes, assessment of TBI conveys no advantage over ABI in determining perfusion pressure of the lower limbs. Only in those patients with overt calcification, which gives an ABI $\geqslant 1.3$, are toe pressure measurements superior. This guideline should simplify assessment and treatment of diabetic patients with disease of the lower limbs.

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Keywords arteriosclerosis, peripheral vascular disease, Doppler, complications

Abbreviations ABI, ankle brachial index; TBI, toe brachial index; PVD, peripheral vascular disease; PPG, photoplethysmography; VPT, vibration perception threshold; HbA_{1c}, haemoglobin A1c; NCSS, number cruncher statistical system

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Introduction

Macrovascular disease is common in diabetes and is the major cause of morbidity and mortality in this condition. The increase in vascular disease is not restricted to the coronary circulation but also occurs to the cerebrovascular and peripheral vascular systems. It has been estimated that > 30% of patients with diabetes have evidence of peripheral vascular disease (PVD) [1]. Assessment of the circulation in the lower limbs is not only important for patients with symptoms of ischaemia, but also helpful in classifying foot ulcers and predicting the chance of healing. Clinical examination is the first step in this process but in many patients non-invasive vascular tests are required to confirm clinical judgement and to assess more quantitatively the degree of abnormalities. Measurement of the ankle brachial index (ABI) by Doppler ultrasound is a simple and commonly used method for this purpose [2]. However, the applicability of this technique to patients with diabetes is in some doubt because diabetic patients often develop calcification of the lower limb arteries. The presence of calcification may invalidate the ABI as the arterial wall becomes stiffer and resists compression, giving a falsely high ankle systolic pressure [3]. As a result, measurement of great toe artery pressure for calculation of toe brachial index (TBI) is commonly advocated in diabetic patients [3,4]. However, before accepting this approach it should be borne in mind that toe arteries might also be calcified. Moreover, measurement of toe pressure is technically more demanding and requires expensive equipment beyond the scope of most clinicians. It would be worthwhile to have some clinical data to guide clinicians as to when pressure measurements should be taken at the toe rather than at the ankle. Therefore, in this study we compared the measurements of TBI and ABI in 174 diabetic and 53 normal subjects over a wide range of these pressure indices.

Patients and methods

Diabetic subjects

Brachial, ankle and toe arterial pressures were measured by Doppler ultrasound on 174 subjects (M/F: 128/46) with diabetes who attended the Diabetes Centre, Royal Prince Alfred Hospital. Twelve subjects were on dietary treatment alone, 80 subjects were on oral agents, 82 subjects were on insulin or combined insulin/oral agent treatment. Of these patients, nine had Type 1 diabetes. Approximately one-third of patients had symptoms or past history of macrovascular disease (12 stroke, 33 ischaemic heart disease, 41 claudication, 16 impalpable pedal pulses, three rest pain). Sixty-five percent of patients were smokers (36% previous, 29% current). It was estimated that 100 patients would be sufficient to have an 80% power of detecting a correlation coefficient of 0.3 at the 1% significance level.

Control subjects

A total of 53 control subjects (M/F: 28/25) also had brachial and peripheral artery pressures measured. They were either recruited from the general community, or were staff members. All subjects aged ⩾ 40 years had a random blood glucose level checked to exclude the presence of diabetes. Forty-three percent of patients were smokers (32% previous, 11% current).

Measurement of arterial pressures by Doppler ultrasound

The patient was asked to rest supine for 10 min and a 10-cm cuff was wrapped around the upper arm. The brachial pulse was then palpated and the Doppler probe (Parks Medical Electronics, Inc., Aloha, OR, USA) placed at a 45° angle to the skin surface with the probe directed towards the patient's head. Once the best signal was obtained the cuff was inflated until the signal disappeared. The cuff was then slowly deflated, and the point at which the signal returned was taken as the systolic blood pressure. This process was then repeated for the other arm and the higher of the two pressures taken as the brachial artery pressure.

The same cuff was placed around the ankle immediately above the malleoli. The dorsalis pedis pulse was palpated and the pressure reading obtained as described for the brachial pressure. The process was repeated for the posterior tibial artery. The pressure of the artery with the higher reading was taken as the ankle pressure and the ABI was calculated from the ratio of the ankle systolic pressure to brachial systolic pressure. The cuff was not inflated beyond the pressure of 250 mmHg, even if the Doppler signal was not obliterated. In this situation, the ankle systolic pressure was arbitrarily taken as 250 mmHg.

To measure toe pressure a 25-mm digital cuff was placed around the proximal phalanx of the hallux and the Doppler signal was recorded from the distal pad of the great toe. The cuff was inflated to a maximum of 200 mmHg and then slowly deflated. The point at which the arterial waveform reappeared was taken as the toe systolic blood pressure. If an adequate Doppler signal could not be obtained for technical reasons, the pressure was measured using a photoplethysmograph (PPG). This method detects light reflected from blood flow in superficial tissues. It requires specialized equipment and a darkened room. Our controlled studies showed that the Doppler and PPG methods yielded the same toe pressure result.

Calculation of the ABI and TBI

The ABI was calculated as the highest ankle systolic pressure divided by the highest brachial systolic pressure. For the purpose of this study, an ABI < 0.9 was taken as denoting the presence of PVD, those ⩾ 0.9 and < 1.3 as normal, and ⩾ 1.3 as evidence of medial wall calcification. The TBI was calculated as the toe systolic pressure divided by the brachial pressure. Results from both legs were included in the analysis.

Clinical assessment

Vibration perception threshold (VPT) was assessed by biothesiometry (Biomedical, Newbury, OH, USA). HbA_{1c} was measured by HPLC (BioRad, Hercules, CA, USA; normal range 3.5–6.0%).

Statistical analysis

Statistical analysis was performed using the NCSS (Number Cruncher Statistical System, Kaysville, UT, USA) software. Results are expressed as either mean ± SD, or median and interquartile range. A two-sample *t*-test, or Wilcoxon's rank sum test was used to compare diabetic and control subjects in regard to demographic and clinical parameters. The χ^2 test was used to compare the proportion of diabetic subjects vs. controls in regard to sex distribution and smoking history (i.e. ever smoked vs. never smoked). The χ^2 test was also used to compare the proportion of diabetic subjects, stratified by ABI, in regard to type of diabetes, sex distribution and smoking history. Kruskal–Wallis, one-way analysis of variance was used to compare demographic and clinical parameters of diabetic subjects stratified by ABI. When multiple comparisons were performed, adjustment was made using Kruskal–Wallis *Z*-test. The linear relationship between ABI and TBI was examined using Pearson's correlation coefficient. A test for trend was performed for the ABI–TBI differences, demographic and clinical parameters in the diabetic cohort stratified by the three grades of ABI readings. A *P*-value of < 0.05 was considered statistically significant.

The Bland and Altman method is considered to be the best method of measuring agreement of continuous variables between two tests [5] and was adapted to compare the measurements of TBI and ABI. On the ordinate, the difference of ABI and TBI is depicted and plotted against ABI on the abscissa. In addition, Cohen's κ statistic was used to assess the agreement of ABI and TBI in categorizing patients into groups with reduced (ABI < 0.9, TBI ⩽ 0.54), normal (ABI ⩾ 0.9 to < 1.3, TBI > 0.54–0.93) and elevated (ABI ⩾ 1.3, TBI ⩾ 0.94) pressure indices. Landis and Koch classification for the interpretation of κ was used (0.2–0.4 represented fair agreement, whereas 0.4–0.6 represented moderate agreement).

Results

Demographic profiles and clinical parameters for subjects with diabetes ($n = 174$) and controls ($n = 53$) are shown in Table 1. Diabetic subjects were older, more hypertensive and were more likely to have a history of smoking. Clinical parameters of diabetic patients grouped according to their ABI levels are shown in Table 2. The group of patients with obvious calcification of ankle arteries (ABI ⩾ 1.3) had a longer duration of diabetes. In the groups of patients with severe peripheral vascular disease (ABI < 0.9), or obvious calcification (ABI > 1.3), the VPT was elevated (median of 40 and 43, respectively), corresponding to fairly severe sensory loss. Patients with a normal ABI (⩾ 0.9 and < 1.3) had a median VPT of 28, which is near normal for this age group.

The ABI of diabetic subjects ranged from an ischaemic value of 0.3 to a clearly calcified level of 2.4. No control subject had an abnormal ABI (range 0.93–1.28). The relationship between TBI and ABI in diabetic subjects is shown in Fig. 1. There was a progressive rise in TBI with ABI until the latter exceeded 1.3, at which point the TBI actually fell.

The mean difference between ABI and TBI in the control subjects was 0.40 ± 0.13 and for diabetic subjects with normal ABI, the mean difference was similar at 0.37 ± 0.15. There was a significant upward trend for ABI–TBI differences across the three groups of ABI readings ($t = 7.1$; $P = 0.000001$, Fig. 2). The agreement between ABI and TBI in categorizing patients is shown in Table 3. The κ was 0.4 ($t = 6.1$ with 2 d.f.; NS) representing fair overall agreement of the two methods according to the Landis and Koch classification. It could be observed from Fig. 2 that nearly all diabetic patients with an ABI < 1.3 had an ABI–TBI gradient falling within the normal range established from the non-diabetic cohort. In contrast to these patients with normal or low ABI, the majority

Table 1 Demographic and clinical parameters for subjects with diabetes and controls

	Diabetes	Controls	*P**
n	174	53	
Type of diabetes (1/2)	9/165	NA	
Gender (M/F)	128/46	28/25	0.004
Age (years)	60.3 (55.3–65.7)	52.6 (43.3–64.4)	0.002
BMI (kg/m^2)	29.4 (25.8–32.5)	27.2 (23.9–29.3)	0.0005
Smoking: ever/ex/never (%)	(65/36/35)	(43/32/57)	0.005
Duration (years)	11.1 (5.0–17.5)	NA	
HbA_{1c} (%)	7.8 (6.9–8.7)	NA	
Vibration perception (V)	30 (16–45)	NA	
Brachial systolic pressure (mmHg)	142 ± 18	129 ± 17	0.000005

Values are the mean ± SD, the median and interquartile range, or frequency (%).

*By *t*-test or Wilcoxon rank sum test for continuous variables, and χ^2 for categorical variables.

Table 2 Demographic and clinical parameters for subjects with diabetes stratified by ankle brachial index (ABI)

	< 0.9	⩾ 0.9 to < 1.3	⩾ 1.3	*P*
n	25	133	16	
Type of diabetes (1/2)	0/25	8/125	1/15	0.1
Gender (M/F)	20/5	94/39	14/2	0.3
Age (years)	67.5 (58.4–72.2)	59.8 (54.7–64.5)	61.4 (55.4–64.3)†	0.005
Smoking: ever/ex/never (%)	76/42/24	65/36/35	44/24/56†	0.012
Duration of diabetes (years)	10.3 (5.3–17.1)	10.5 (4.3–17.1)	14.8 (12.1–20.4)‡	0.002
HbA_{1c} (%)	8.0 (6.7–9.0)	7.8 (6.9–8.6)	7.8 (7.1–8.9)	0.6
Vibration perception threshold (V)	40 (21–50)	28 (16–40)	43 (35–50)‡	0.0001
Brachial pressure (mmHg)	150 (140–170)	140 (130–150)	140 (135–150)†	0.003
Ankle pressure (mmHg)*	120 (86–135)	145 (135–165)	200 (200–243)§	0.00001
Toe pressure (mmHg)	55 (41–70)	95 (80–110)	90 (65–106)§	0.000002
Ankle brachial index*	0.75 (0.63–0.84)	1.07 (1.0–1.13)	1.47 (1.38–1.58)§	0.000001
Toe brachial index	0.36 (0.30–0.47)	0.71 (0.61–0.80)	0.62 (0.48–0.75)§	0.000001

Values are median and interquartile range, *n* or frequency (%).
†Different from ABI < 0.9.
‡Different from ABI ⩾ 0.9 to < 1.3.
§Different from the other two groups, by ANOVA for continuous variables and χ^2 for categorical variables.
*Significant linear trend, $P < 0.0001$.

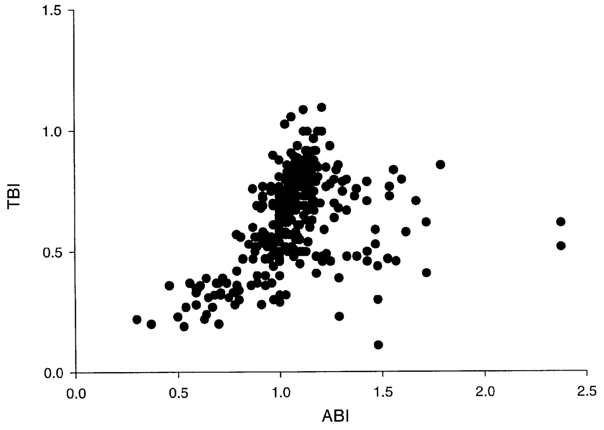

Figure 1 Relationship between ankle brachial index (ABI) and toe brachial index (TBI) for diabetic subjects; $r = 0.38$; $P = 0.00001$.

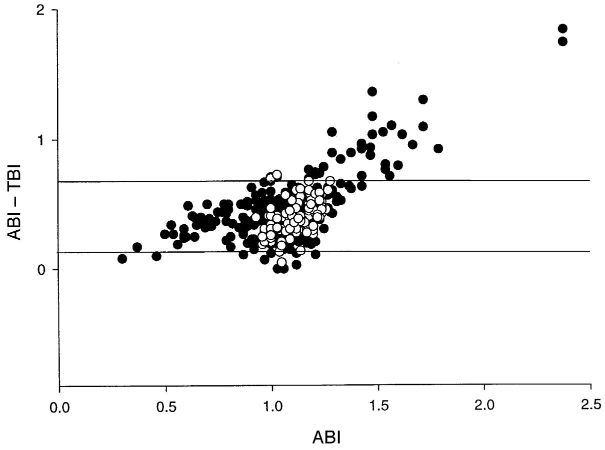

Figure 2 Agreement between ankle brachial index (ABI) and toe brachial index (TBI) for diabetic subjects and control subjects (controls: mean difference 0.40, 2 SD0.14–0.67). ●, Diabetic subjects; ○, control subjects.

of diabetic subjects with an ABI ⩾1.3 had ABI–TBI differences outside this range.

Discussion

Previous research has demonstrated that varying degrees of medial artery calcification are common in diabetic subjects [4]. This has led to the suggestion and common clinical teaching that toe blood pressure is a more reliable indicator than ankle blood pressure for arterial flow to the foot in diabetic subjects. However, toe arteries may also be calcified and consequently have reduced compressibility to some extent. Furthermore, as mentioned previously, measurement of toe pressure is more time-consuming and technically difficult and it requires additional equipment. These considerations suggest that it would be worthwhile testing the relationship between toe and ankle blood pressure and to define more precisely the circumstances in which toe pressure measurement is indeed superior. This is important because ankle or toe blood pressures and their derived indices allow clinicians to judge the vascular status of the lower limbs and to determine whether a foot lesion is well perfused enough to heal.

Table 3 Agreement between ankle brachial index and toe brachial index using Cohen's κ test

	Ankle brachial index		
Toe brachial index	Reduced (< 0.9)	Normal (⩾ 0.9 to < 1.3)	High (⩾ 1.3)
Reduced (⩽ 0.54)	21	27	8
Normal (> 0.54–0.93)	4	102	8
High (⩾ 0.94)	0	4	0

Our findings indicate that assessment of TBI is clearly the method of choice in the presence of overt calcification as defined by an ABI of > 1.3. On the other hand, in the absence of such overt calcification, the differences between ABI and TBI for diabetic subjects were in the same range as control subjects whom we assume have no calcification. There is also a good relationship between ABI and TBI for the diabetic patients who have peripheral vascular disease and an ABI of < 0.9. These results indicate that as long as ABI is normal or low, arterial calcification does not invalidate the ABI any more than TBI as an index of lower limb perfusion pressure. Thus, the traditional teaching that toe pressure is superior to ankle pressure in assessing lower limb perfusion in diabetes is only true for a relatively small number of easily identified patients. There are two possible explanations of our observation. Either that subclinical calcification (i.e. one which does not raise the ABI to > 1.3) does not interfere with the measurement of ABI or TBI, or that it affects them equally. Our study is not designed to answer this question. The findings also do not imply that either ABI or TBI is a sensitive or insensitive method of detecting arterial calcification, or by themselves are adequate tests of arterial perfusion. However, the relevant point is that as long as ABI is not obviously falsely elevated (i.e. ⩾ 1.3), it gives as much information as TBI and can be relied upon to make clinical decisions. This will obviate the necessity of performing too many TBI. It will also avoid the situation of not trusting the ABI and losing useful clinical information. In everyday clinical practice, ABI measurement by simple equipment is readily available whereas TBI measurement is harder to access.

It is true that radiological examination can reveal minor degrees of arterial calcification and is probably the most sensitive test to detect this change. However, it is not quantitative and does not provide information on blood flow. Inadequate perfusion pressure in the presence of arterial calcification can also be suspected by detecting an audibly damped signal, or by monitoring the Doppler signal whilst progressively elevating the leg. However, these tests would only pick up severe cases. In our study, we have found it better to use ABI and TBI rather than the absolute ankle and toe blood pressures. Interpretation of the absolute pressures are more affected by hypertension, a common problem in older patients, especially in a diabetic cohort.

Calcification of the lower limb arteries is an interesting phenomenon in diabetes and recent research has shown that there is increased ossification of the arterial wall due to increased expression of bone morphogenetic protein [6]. Our data confirm that overt arterial calcification is more evident in patients with diabetic neuropathy. This is consistent with the report that it can be induced by sympathetic denervation [7]. Much remains to be studied to understand fully the pathogenesis of this interesting complication of diabetes. Functionally, it does not appear to greatly affect blood flow, but its impact on the clinicians' attitude to non-invasive assessment of vascular supply in the lower limbs of diabetic patients has been profound. If our findings can be confirmed, it will simplify assessment and decision making for diseases of the lower limb in diabetes.

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