Toe-Brachial Index in the Second Toe: Substitutability to Toe-Brachial Index in the Great Toe and Ankle-Brachial Index

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Objectives: Toe-brachial index (TBI) is usually measured in the great toe (TBI-1). However, this is not always possible. To determine the usefulness of TBI measurement in the second toe (TBI-2), we examined the relation between systolic pressure in the second toe (toe pressure [TP-2]) and that in the great toe (TP-1) and evaluated the association between TBI and ankle-brachial index (ABI).

Materials and Methods: We retrospectively analyzed patients who underwent a series of measurements of TBI-2, TBI-1, and ABI using an automatic oscillometric device at Kawasaki Medical School Hospital, Japan in 2012.

Results: We evaluated 114 feet without severe ischemia symptoms in 57 patients (median age: 73 years). TP-2 was similar to TP-1 (correlation coefficient [r] = 0.769, 95% confidence interval [CI]: 0.681–0.836, p < 0.001). ABI showed a mild correlation with TBI-2 (r = 0.463, 95% CI: 0.303–0.598, p < 0.001) and a moderate correlation with TBI-1 (r = 0.586, 95% CI: 0.450–0.696, p < 0.001). The TBIs of 0.65 and 0.5 corresponded to the ABIs of about 1.0 and 0.9, respectively, in both toes.

Conclusion: TBI-2 measurement can be considered as an acceptable substitute to TBI-1 or ABI measurement to assess the patients in whom ABI and TBI-1 cannot be measured.

Keywords: toe-brachial index, ankle-brachial index, second toe pressure, great toe pressure, oscillometric pressure measurement

Introduction

For the primary assessment of peripheral artery disease (PAD), ankle-brachial index (ABI) measurement is the most common, relevant, and non-invasive approach for detecting the disease, grading the severity, and predicting the cardiovascular risk. However, the number of patients with non-compressible ankle arteries caused by severe medial calcification, known as Mönckeberg’s sclerosis, has been increasing recently, particularly among patients with long-standing diabetes, with chronic kidney disease, or who are receiving hemodialysis.1–3 These patients often show false elevated ankle systolic pressures despite having the highest risk of PAD. For such patients, toe pressure (TP) and toe-brachial index (TBI) measurements have been recommended as more reliable markers than ABI4–8 because pedal arteries are very slowly affected by calcification than ankle arteries.

TP and TBI are usually measured in the great toe, as mostly shown in previous studies.9–12 However, in PAD patients, occasional problems involving the great toe have been encountered such as inflammatory lesions, pain, or ulcerations, or absence of the great toe from amputation. As a substitute, several guidelines and textbooks have stated that TBI may be measured in the second toe.4,5,13,14 However, there are apparently no sufficient major references showing the interchangeability of the systolic pressure in the second toe (TP-2) with the systolic pressure in the great toe (TP-1). Thus far, only a few studies have provided clinical information about TP-2.8,15–17 Although TBI has been recommended as a substitute for the assessment of patients with possible false ABI values, the corresponding relationship between ABI and TBI has not yet been sufficiently clarified.10 At this point, only the estimated values for detecting PAD are known, which are 0.9 for ABI and about 0.6 or 0.7 for TBI. The TBI value is based on relations to the presence of clinical symptoms or angiographic PAD findings, not on the measurement results to assess the equivalent for an ABI of 0.9.12,18
To clarify the clinical significance and usefulness of second toe TBI (TBI-2) measurement, we examined the relationship between TP-2 and TP-1, and the association between ABI and TBI.

Materials and Methods

Patients
We retrospectively analyzed the patients who had routinely undergone a series of measurements consisting of TBI-2, great toe TBI (TBI-1), and ABI in both lower extremities at the Vascular Laboratory of Kawasaki Medical School Hospital in 2012. The study protocol was approved by the Research Ethics Committee of Kawasaki Medical School and Hospital.

Measurements
All measurements were performed at room temperature (25°C) using a fully automated oscillometric ABI/TBI measuring device, BP-203RPEIII form (Omron Colin Co., Tokyo, Japan). The measurement principals of this device are identical to those of the old model, as previously described.19–21) Each patient was examined in the supine position with the pressure cuffs wrapped on the bilateral brachia and toes when measuring TBI. In all the patients, 2.5 cm wide cuffs were used for the great toes and 1.9 cm wide cuffs for the second toes. When measuring ABI, middle size ankle cuffs were connected to the device in place of the toe cuffs and were wrapped on the bilateral ankles. Pressure measurements were performed simultaneously in the bilateral brachia and lower limbs. The higher value of either the left or right brachial systolic pressure in every measurement was used for the automatic TBI and ABI calculation. Measurements were performed in the order of TBI-2, TBI-1, and ABI.

Statistical analysis
Body sizes were presented as medians, quartiles 1–3, and ranges according to a non-normal distribution. Relationships between two variables (TP-2 vs TP-1, TBI-2 vs ABI, and TBI-1 vs ABI) were examined using scatterplots and Pearson’s correlation coefficient (r). We assumed that all pressure measurements had included equal error variances. Therefore, we conducted analyses of the linear relationship in two variables using orthogonal least-squares line regression. When the systolic pressure was undetectable, it was plotted as zero in the scatterplots and excluded from the correlation analysis. Statistical significance was defined as p < 0.05. Statistical analyses were performed using JMP statistical software (version 12.2.0; SAS Institute, Cary, NC, USA).

Results
We identified 57 patients who underwent the series of measurements in their bilateral lower extremities (Table 1). Their median age was 73 years, and their body sizes ranged within those of the general Japanese adults. There was no patient with severe pain, infection, or ulceration in his or her feet. In one patient with a known PAD, ankle systolic pressure was undetectable in both legs, whereas TP-2 was undetectable in one foot. TP-2 was also undetectable in one foot of another patient with cerebral vascular disease, in which both ABI and TBI-1 showed low values.

Table 1 Characteristics of patients

| Characteristics                     | Number of patients | Male:female | Age, years, median (quartiles 1–3) | Height, cm, median (quartiles 1–3) | Weight, kg, median (quartiles 1–3) | Brachial systolic pressure, mmHg, median (quartiles 1–3) |
|-------------------------------------|--------------------|-------------|-------------------------------------|-------------------------------------|------------------------------------|----------------------------------------------------------|
|                                    |                    |             |                                     |                                     |                                    |                                                          |
| Number of patients                  | 57                 |             |                                     |                                     |                                    |                                                          |
| Male:female                         | 38:19              |             |                                     |                                     |                                    |                                                          |
| Age, years, median (quartiles 1–3) | 73 (63–83)         |             |                                     |                                     |                                    |                                                          |
| Range                               | 32–90              |             |                                     |                                     |                                    |                                                          |
| Height, cm, median (quartiles 1–3) | 160 (153–167)      |             |                                     |                                     |                                    |                                                          |
| Range                               | 136–176            |             |                                     |                                     |                                    |                                                          |
| Weight, kg, median (quartiles 1–3) | 59.0 (49.6–64.6)   |             |                                     |                                     |                                    |                                                          |
| Range                               | 35.0–81.5          |             |                                     |                                     |                                    |                                                          |
| Brachial systolic pressure, mmHg,  | 132 (121–146)      |             |                                     |                                     |                                    |                                                          |
| median (quartiles 1–3)              | 87–182             |             |                                     |                                     |                                    |                                                          |

Arteriosclerosis obliterans except for one patient with Buerger’s disease. n: number of patients; PAD: peripheral artery disease
Relationship between TP-2 and TP-1

The TP-2 and TP-1 scatterplots are shown in Fig. 1a. After excluding 2 of 114 feet with undetectable TP-2, TP-2 and TP-1 showed a good positive correlation ($r = 0.769$, 95% confidence interval [CI]: 0.681–0.836, $p < 0.001$). We obtained a linear regression model (Model A) as follows:

Model A: $TP-1 = 13.7 + 0.84 \times TP-2$ (95% CI for slope: 0.71–0.98).

The residuals of TP-1 with a normal distribution and the plot of residuals versus fitted values with a random pattern of the residuals near the horizontal axis (Fig. 1b) supported Model A. There was no outlier due to height or weight of the patient.

Relationship between TBI and ABI

The TBI-2 and ABI scatterplots are shown in Fig. 2. There was no specific tendency in the patients with diabetes or receiving hemodialysis compared with the other patients although the ABI in one lower extremity of each of the two patients receiving hemodialysis was relatively high. After excluding 3 of 114 lower extremities with undetectable TBI-2 or ABI, TBI-2 and ABI showed a mild correlation ($r = 0.463$, 95% CI: 0.303–0.598, $p < 0.001$). We obtained a linear regression model (Model B) as follows:

Model B: $ABI = 0.56 + 0.69 \times TBI-2$ (95% CI for slope: 0.48–0.94).

TBI-1 and ABI showed a moderate correlation (Fig. 3; $r = 0.586$, 95% CI: 0.450–0.696, $p < 0.001$) and produced a linear model (Model C) after excluding 2 of 114 lower extremities with undetectable ABI as follows:

Model C: $ABI = 0.40 + 0.91 \times TBI-1$ (95% CI for slope: 0.68–1.19).
Most TBI-2 and TBI-1 values ranged from 0.4 to 1.1. By assigning TBI values in this range, we calculated ABI using the regression Models B and C (Table 2). Both TBI-2 and TBI-1 of 0.65 derived an ABI of about 1.0 and those of 0.5 derived an ABI of about 0.9. The ABI values calculated using Model B were slightly higher than those using Model C in the range of TBI < 0.5 and slightly lower in the range of >0.9.

**Discussion**

It has been clearly stated that TP or TBI measurement is performed on the great or second toe.\(^4,5,13,14\) However, the specific characteristics of TP-2 have not yet been fully clarified.\(^8,15–17\) In this study, we showed the similarity between TP-2 and TP-1 using an oscillometric measurement device. The present results also indicate that a TBI of 0.65 is likely comparable to an ABI of about 1.0 and that a TBI of 0.5 is likely comparable to an ABI of about 0.9, whether TBI is measured in the great toe or in the second toe.

**Similarity between TP-2 and TP-1**

Thus far, only limited studies have provided information regarding TP-2, particularly the relationship between TP-2 and TP-1, using different measurement tools. Carter et al. measured TP-2 alone using an early method in 1971. They determined the systolic pressure with the resumption of arterial flow which was detected either by the skin color change of the digit or by the increase in the digital volume recorded by mercury-in-rubber strain-gauge plethysmography.\(^8\) The TP-2 was 100 mmHg in 16 young normal volunteers and 120 mmHg in 12 elder normal volunteers; the TBI-2s could be calculated from the whole data as 0.86 and 0.91, respectively. However, they did not measure TP-1. In 2001, de Graaff et al.\(^15\) measured TP-1 and TP-2 in 107 feet of 54 patients at various PAD stages by photoplethysmography. TP-2 appeared similar to TP-1; however, their study aimed to examine only the reproducibility of measurement in each toe but not the relationship between TP-2 and TP-1.

Kröger et al. demonstrated the similarity between TP-1 and TP-2 using the Doppler method in only 24 of 51 patients owing to the detection failure. They detected a strong correlation only on the right feet but not on the left feet.\(^17\) This may have been caused by the difficulties in performing the Doppler technique and the blood pressure variations owing to time intervals between the bilateral feet. In recent days, TP and TBI measurements have become more simplified to enable their performance as part of the general examination in many hospitals and institutions.\(^22–25\) Bhamidipaty et al.\(^16\) used an automated TP measuring system with a systole photoplethysmograph sensor on the bilateral feet of 100 participants with diabetes mellitus. They also showed the similarity of TP-2 to TP-1 as demonstrated in our results. The strong correlation between the photoplethysmography procedure and the oscillometric method has already been demonstrated in TP-1 measurement.\(^24\) As an additional advantage, the automated device used in our study can perform simultaneous measurements of TBI from the four limbs in a short time and thus avoiding the time difference.

### Table 2

| TBI   | Calculated ABI (Using Model B of TBI-2) | Calculated ABI (Using Model C of TBI-1) |
|-------|--------------------------------------|---------------------------------------|
| 0.4   | 0.836                                | 0.764                                 |
| 0.5   | 0.905                                | 0.855                                 |
| 0.6   | 0.974                                | 0.946                                 |
| 0.7   | 1.043                                | 1.037                                 |
| 0.8   | 1.112                                | 1.128                                 |
| 0.9   | 1.181                                | 1.219                                 |
| 1.0   | 1.250                                | 1.310                                 |
| 1.1   | 1.319                                | 1.401                                 |

ABI: ankle-brachial index; TBI: toe-brachial index; TBI-2: second toe TBI; TBI-1: great toe TBI
Relationship between TBI and ABI

To date, the corresponding relationship between TBI and ABI has not yet been well clarified. Moreover, the TBI cutoff value for detecting PAD has been estimated without consensus. The various and cumbersome techniques for TP measurement not only hindered research to a few and small studies lacking evidence, but also made it difficult to determine the association between TBI and ABI values. Brooks et al. measured ABI by the Doppler method and TBI by either the Doppler method or the photoplethysmography procedure in 174 feet from patients with diabetes; the difference between ABI and TBI was 0.4. When calculating from the results of the study by de Graaff et al., the difference between the ABI measured using the Doppler method and the TBI using photoplethysmography ranged from about 0.3 to 0.35 in any limbs at various levels of ischemia. Stoekenbroek et al. also reported an ABI-TBI difference that ranged from 0.35 to 0.45 using Doppler and photoplethysmography devices. Our present results well corroborated these previous findings: the TBIs of 0.65 and 0.5, respectively, corresponded to the ABIs of about 1.0 and 0.9 in either toe.

The accuracy and reproducibility of TP-2 measurement are also important subjects, including problems of the measurement methods. Only two studies previously assessed the reproducibility of TP-2 using photoplethysmography procedures. In 2001, de Graaff et al. worked on a classic method and pointed out that TP-2 showed less reproducibility than TP-1 because the interclass correlation coefficients (ICCs) were 0.85–0.99 in TP-1 and 0.68–0.98 in TP-2, whereas the reproducibility of TP-1 was comparable to that of ABI measurement using the Doppler method (ICC: 0.87–0.98). However, their results were possibly affected by the different sizes of the cuffs selected by the different examiners, particularly for the second toes, and the ICCs of TP-2 were still substantial. In 2015, the study of Bhamidipaty et al. using an automated system with a fixed size of the cuff demonstrated an excellent repeatability of TP-2; the coefficient of repeatability of TP-2 was only 0.5% larger than that of TP-1. We also used a fixed size of the cuffs as follows: a 2.5 cm wide cuff provided for the toes with a circumference ranging from 6 to 9 cm (a diameter ranging from 1.9 to 2.8 cm) and a 1.9 cm wide cuff provided for the toes with a circumference ranging from 4.5 to 6 cm (a diameter ranging from 1.4 to 1.9 cm). Each cuff should be of an appropriate size for the respective great and second toes in Japanese adults. Additionally, fully automated oscillometric devices can be used without any special skills, and thus they hardly cause interobserver variations. Moreover, other researchers used an old model device and obtained a quite similar relationship between TBI-1 and ABI. This suggests that the measurement method using such oscillometric devices has a high reproducibility and accuracy for TBI-1 and ABI. A similar reliability may be expected in TBI-2. As a supplementary examination, we also measured TBI in 10 healthy students using BP-203RPEIII form with a fixed size of the cuffs in the present study. The series measurements including ABI, TBI-2, and TBI-1 were repeated three times with 15 minutes of rest for each subject. The mean values of TBI-1 (0.768) and TBI-2 (0.779) were not significantly different (p = 0.57). The mean differences from their respective mean values of the three-time measurements in each person were small: only 0.055 in TBI-1 and 0.061 in TBI-2. However, in the present study, the TBI-2 values were more widely varied than the TBI-1 values, as Model B was less fitted than Model C owing to the relatively high TBI-2 of some feet. Additionally, a foot with an undetectable TP-2 despite an ABI near 1.0 was present. The mild slope of the Model B regression line may also indicate the less diagnostic ability or accuracy of TBI-2. Nonetheless, Models B and C produced approximate ABI values within the clinical range. From this good similarity between TP-1 and TP-2, TBI-2 is expected to be an applicable index for patients who cannot undergo great toe measurement.

Study limitations

Our study has some limitations. First, the angiographic statuses of the subjects were not confirmed because of the retrospective design of the study. When substituting TBI-2 to TBI-1 as well as TBI to ABI, it is a premise that the subjects have no significant arterial lesions in their feet. However, all the patients had no symptoms of severe ischemia in their feet. Most of the patients showed a small difference between TP-1 and TP-2. Second, we included some patients with diabetes or those who were receiving hemodialysis, and their disease severity and duration were not considered; they potentially might have shown a falsely elevated ABI. Nevertheless, the measurement values of these patients showed no difference from those of other patients and likely affected the correlation analyses between TBI and ABI slightly. Finally, TP-2 can differ from TP-1, and ABI can differ from ABI among patients with severe ischemic damage in their great toe. Additionally, the oscillometric device may have a disadvantage of detecting signals in the low-pressure range, as some TBIs and ABIs were undetectable. However, this simple TBI measurement method can be sufficiently acceptable to many patients, particularly patients with diabetic foot, in finding out whether their condition is PAD and in estimating the severity of their PAD before it reaches an advanced stage.
Conclusion

TP-2 was found to be similar to TP-1 in patients without severe limb ischemia. TBI-2 measurement may therefore be considered as an acceptable substitute for assessing patients in whom ABI and TBI-1 measurements are not appropriate. The TBIs of 0.65 and 0.5 likely correspond to the ABIs of about 1.0 and 0.9, respectively, either from the second or great toe, when measured using an oscillometric device. As the number of patients having non-compressible ankle arteries caused by long-standing diabetes or chronic kidney disease has been increasing, the corresponding number of patients who need to be evaluated by TBI measurement but who present with problems in their great toe is likewise increasing. The present clarification of the clinical roles of TBI-2 potentially ushers in an alternative method of providing the much needed assistance to patients in whom TBI-1 measurement is not possible.

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Disclosure Statement

The authors have no conflicts of interest.

Author Contributions

Study conception: YW, KK, HM, and KT Data collection: KK and YW Analysis: YW Investigation: YW Writing: YW Funding acquisition: none Critical review and revisions: all authors Final approval of the article: all authors

Accountability for all aspects of the work: all authors

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