Sensitivity and Specificity of the Toe-Brachial Index for Detecting Peripheral Arterial Disease

Initial Findings

Peta Tehan, B Health Sc (Pod) G Cert Wound Care, Alan Bray, MBBS, FRACS (Vascular Surgery), MD, DDU, Ruth Keech, Grad Dip Ultrasonography, DMU (Vascular), Richard Rounseley, Dip Health Sc (Pathology), B Med Sc, DMU (Vascular), Angela Carruthers, B Health Sc, RN, Vivienne Helaine Chuter, B Pod (Hons), PhD

Objectives—The toe-brachial index (TBI) is an alternative to the ankle-brachial index (ABI) in screening for peripheral arterial disease (PAD); however, there is limited evidence comparing their diagnostic accuracy. This study compared the diagnostic accuracy of the ABI and TBI in a population at risk of PAD.

Methods—The sensitivity and specificity of the ABI and TBI were determined by color duplex sonography. Receiver operating characteristic (ROC) analysis was performed.

Results—A total of 119 participants were recruited (75 male and 44 female). The sensitivity for PAD was highest for the TBI (71%; ABI, 45%), and the specificity was highest for the ABI (93%; TBI, 78%). Receiver operating characteristic analysis indicated that the TBI (ROC area, 0.77; \(P = .0001\)) had greater clinical efficacy for diagnosis of PAD than the ABI (ROC area, 0.65; \(P = .005\)).

Conclusions—In specific populations, the TBI may have greater clinical efficacy than the ABI for diagnosis of PAD.

Key Words—ankle-brachial index; peripheral arterial disease; sensitivity; specificity; toe-brachial index; vascular ultrasound

Peripheral arterial disease (PAD) involves progressive stenosis and, potentially, occlusion of arterial beds supplying the lower extremity through the development of atherosclerosis. The risk of PAD increases with age, affecting 21% of those older than 65 years, and in the presence of risk factors such as smoking, diabetes, dyslipidemia, and hypertension.1,2 As many people with PAD are asymptomatic, the condition is highly under-recognized3 and if untreated can ultimately lead to the development of wounds, gangrene, and amputation.4 The presence of PAD is also an indicator of systemic arterial disease and is associated with an increased risk of a cardiovascular event5 and associated mortality.6

Traditionally, the ankle-brachial index (ABI) has been used as a noninvasive method for assessing peripheral vascular status in patients at risk of PAD. An ABI is calculated by taking the higher of the systolic pressure of the dorsalis pedis or posterior tibial artery and dividing it by the highest systolic brachial pressure.7 An ABI of greater than 1.0 is considered normal,7 with a ratio of less than 0.90 considered diagnostic for PAD.8
The ABI is a highly sensitive and specific screening tool for PAD. The relative simplicity of application and low cost make the ABI an easily accessible assessment tool for many clinicians. However, recent research suggests that the diagnostic accuracy of the ABI is reduced in specific populations. Decreased sensitivity and specificity of the ABI for the presence of PAD have been demonstrated in the elderly and in the presence of renal disease or diabetes. It is widely recognized that higher rates of medial arterial calcification in these populations leads to stiffening of the arterial wall, preventing full compression of the lower extremity arteries, inflating the ABI value, and reducing the clinical efficacy of the test. An elevated ABI (>1.4), is generally accepted to be indicative of medial arterial calcification. However, further complicating lower extremity vascular testing in these patients, the presence of medial arterial calcification is also associated with substantial lower extremity atherosclerosis. The combination of these two conditions may result in a normal ABI in the presence of substantial PAD due to partial loss of compressibility of the artery, leading to undiagnosed PAD. Additionally, more distal anatomic distribution of atherosclerotic lesions occurring in both people with diabetes and those of advanced age further affects the ABI, with an inability to detect stenosis of arteries at the level of, or distal to, the ankle by ankle pressure measurements.

Alternative methods of noninvasive vascular assessment may be performed using small vessel–testing methods such as the toe-brachial index (TBI). The TBI is a ratio of the systolic toe pressure divided by the highest systolic brachial pressure. Normal values for the TBI are less than those for the ABI, with 0.7 and greater considered normal. The TBI has been shown to be an accurate indicator of PAD in specific populations who are prone to medial calcification, including those with diabetes-related PAD, sensorimotor neuropathy, and patients undergoing hemodialysis for end-stage renal failure. The TBI is by no means a new assessment method; however, its use remains limited, particularly in the vascular laboratory.

Despite the potentially wide applicability of the TBI as a test for PAD, evidence evaluating its diagnostic accuracy is limited. There is also a lack of comparative data assessing the relative diagnostic accuracy of the TBI and ABI for the presence of PAD using diagnostic imaging as the reference standard. The aim of this study was to examine the sensitivity and specificity of the TBI and the comparative diagnostic accuracy of the TBI versus the ABI for detecting PAD in a population of patients at risk of PAD.

Materials and Methods

This study was undertaken at a private vascular clinic in Lake Macquarie, New South Wales, Australia. Ethical approval was obtained from the University of Newcastle Human Research Ethics Committee. All participants provided written informed consent before participation.

Over 28 months (August 2011–December 2013), participants were recruited on a volunteer basis from a private vascular clinic and a podiatry service in Newcastle. Inclusion criteria were set in accordance with current guidelines for lower extremity vascular screening: participants older than 65 years or older than 50 years with a history of diabetes, current smoking, exertional leg pain, or nonhealing wounds. Exclusion criteria were contraindications to ankle, toe, and brachial pressure measurements, including active hallux or leg ulceration preventing cuff placement, history of deep venous thrombosis, lymphedema, and previous bilateral mastectomy or vasospastic disorders.

All participants attended a single testing session at the vascular clinic with 1 of 3 sonographers. During the testing session, ABI and TBI measurements, color duplex sonography, and neurologic testing were performed on the right leg. Color duplex sonography was chosen, as it has been demonstrated to be a valid imaging technique for noninvasive vascular diagnostic testing. The right limb only was used to comply with the assumption of independence of data in statistical testing. The medical history was obtained from each participant. Participants were asked to avoid alcohol, smoking, exercise, and caffeine 1 hour before the testing session to avoid influencing pressure measurements. Participants were placed in a supine position and rested for at least 10 minutes before pressure measurements. A subset of 10 participants randomly selected returned within 1 week of the initial testing session. At the second testing session, all tests (vascular and neurologic) were repeated by a different clinician blinded to the results of the initial test to establish intertester reliability.

Color duplex sonography was performed with either a CX-50 ultrasound system (Philips Healthcare, Best, the Netherlands) or a LOGIQ I system (GE Healthcare, Little Chalfont, England). All ankle and brachial pressures and continuous wave Doppler tracings of pedal arteries were taken with a Parks 1050c Vascular MiniLab (Parks Medical Electronics, Inc, Aloha, OR) equipped with 8.2-MHz continuous wave Doppler, a Parks standard 10-cm inflatable cuff, and an ERKA switch blood pressure gauge (ERKA Kallmeyer Medizintechnik GmbH & Co. KG, Bad Tölz, Germany). Toe pressures were obtained with...
a photoplethysmograph probe, a Hokanson toe pressure cuff (1.6, 1.9, or 2.5 cm; D. E. Hokanson, Inc, Bellvue, WA), and an ERKA switch blood pressure gauge. The size of the cuff used was in accordance with current guidelines for cuff size.7

Room temperature was monitored with a thermometer and was maintained between 23°C and 25°C.22 Bilateral brachial systolic pressures were obtained in all participants with a Parks continuous wave Doppler system and a hand-held sphygmomanometer. Ankle systolic pressures of the right leg only were taken by placing the brachial pressure cuff around the lower leg, proximal to the medial and lateral malleoli. Both dorsalis pedis and posterior tibial artery pressures were recorded, with the higher of the two being used for calculation of the ABI. Toe systolic pressures were obtained by placing a photoplethysmograph probe directly on the distal pulp of the right great toe, affixed with adhesive tape. Once a clear signal was obtained, a toe cuff was placed immediately proximal to the photoplethysmograph probe. If the great toe was too large for the toe cuff, the second toe was used. The cuff was then inflated to 20 mm Hg above the last visual photoplethysmograph signal. The cuff was then slowly deflated, and the pressure reading was recorded when a consistent waveform returned. The TBI was calculated by dividing the toe pressure by the highest brachial pressure.

Color duplex sonography was performed after pressure measurements, from the abdominal aorta to the distal ankle on the right side as the reference standard. For calculations relating to diagnostic accuracy, the presence of PAD was defined as 1 or more arteries with greater than 50% stenosis.23,24 Distal disease was defined as disease distal to and including the proximal popliteal artery, and proximal disease was defined as disease from the common iliac artery to the distal superficial femoral artery. The sensitivity, specificity, diagnostic accuracy, and positive predictive value of the ABI and TBI for the presence of PAD were calculated by using the standard cutoff scores for an abnormal ABI of 0.90 or less and greater than 1.4, consistent with current screening guidelines,7 and the suggested cutoff score for the TBI of less than 0.70.9,25 Ankle pressures exceeding 200 mm Hg were considered incompressible.7

Receiver operating characteristic (ROC) analysis was performed for the ABI and TBI and was calculated with SPSS version 19 statistical software (IBM Corporation, Armonk, NY). Standard deviations were derived for all means, sensitivities, specificities, and positive and negative predictive values. Calculations of diagnostic accuracy were performed with Microsoft Excel (Microsoft Corporation, Redmond, WA).

INTERTESTER RELIABILITY

Interobserver reliability of color duplex sonography was calculated by using the presence or absence of PAD as a dichotomous variable and an unweighted Cohen κ statistic. Intraclass correlation coefficients (ICCs) with 95% confidence intervals (CIs) were calculated to determine the level of agreement between test and retest for the ABI and TBI. All ICC values for intertester reliability were interpreted according to cutoffs suggested by Fleiss.26 Interpretation of the Cohen κ statistic was performed by the method proposed by Landis and Koch.27 All reliability analyses were conducted with SPSS version 19 software.

Results

A total of 120 participants were recruited. One participant was excluded, as the color duplex sonographic scan was performed on a different day from the remainder of the vascular examination. Participant characteristics are included in Table 1.

The mean ABI was 1.13 (SD, 0.23). The mean fell within the normal range for an ABI measurement. The ABI results ranged from 0.34 to 2.0, which indicated that the participants’ peripheral arterial status included both those with substantial PAD and substantial medial arterial calcification. The ABI was more likely to fail to diagnose the presence of PAD. Receiver operating characteristic analysis showed that the ROC area for an ABI set at less than 0.9 or greater than 1.4 for detecting PAD was only 0.65 (95% CI, 0.54–0.77; Figure 1). This result indicates that the ABI was a poor test in this population.28 The sensitivity and negative predictive value of 45% and 69%, respectively, for the ABI reflect an increased risk of failure to diagnose existing disease (Table 2). However, the specificity (93%) and

Table 1. Participant Characteristics

| Characteristic                  | Value     |
|--------------------------------|-----------|
| Total participants, n          | 119       |
| Male, n (%)                   | 75 (63.02)|
| Female, n (%)                 | 44 (36.97)|
| Age range, y                  | 53–92     |
| Diabetes, n (%)               | 73 (61.34)|
| Mean age (SD), y              | 73.1 (7.2)|
| Incompressible ankle pressure, n (%) | 16 (13.44) |
| Distal PAD, n (%)             | 37 (31.09)|
| Proximal PAD, n (%)           | 7 (5.88)  |
| Distal and proximal PAD, n (%) | 7 (5.88)  |
| PAD, n (%)                    | 51 (42.85)|
| Proximal occlusions, n (%)    | 1 (8.4)   |
| Distal occlusions, n (%)      | 40 (33.3) |
positive predictive value (82%) were high, indicating that the ABI is relatively unlikely to falsely diagnose PAD.

The mean TBI was 0.71 (SD, 0.21) which was within the normal range. The ROC area was 0.77 (95% CI, 0.69–0.87), indicating that the TBI was a fair test in this population (Figure 1). The sensitivity of the TBI for detecting PAD was 71%, indicating that the TBI was quite likely to accurately detect PAD in this population (Table 2). The specificity was 79%, which, whereas lower than the ABI result, suggests that the TBI is relatively unlikely to falsely detect PAD.

The intertester reliability of the color duplex sono-
graphic scans between the 3 sonographers was high ($\kappa = 0.78; P < .01$).27 The ICCs showed good test-retest reliability of the toe pressures (ICC, 0.80; 95% CI, 0.39–0.95) and moderate reliability of the brachial pressures (ICC, 0.66, 95% CI, 0.09–0.90) and ankle pressures (ICC, 0.62; 95% CI, 0.03–0.89).29

### Discussion

The results of this study indicate that overall the TBI has much higher sensitivity (71%) for the presence of PAD than the ABI (45%). However, the ABI had slightly higher specificity (93%) than the TBI (79%). The negative predictive value of the ABI (69%) together with poor ROC analysis (0.65) has significant clinical implications, leaving approximately one-third of participants falsely undiagnosed.

Previous research studies have reported a range of results regarding the sensitivity of the ABI, depending on the cohort of participants studied. In healthy individuals, the ABI has been shown to be highly sensitive (95%);30–33 however, in patients with diabetes or renal disease, the sensitivity of the ABI has been shown to be considerably lower (29.9%–53%).10,11 The population in this study met current criteria for lower extremity vascular screening and consisted of an older group with a large number of people with diabetes. The findings of our study suggest that there may be a high prevalence of concurrent medial arterial calcification and PAD within the general population, requiring peripheral vascular screening. This prevalence is expected, as this population is older and at higher risk of comorbidities such as diabetes, which are both associated with the development of medial arterial calcification. Although medial arterial calcification is known to affect the accuracy of the ABI in people with diabetes, renal disease, and older age, the prevalence of clinical and subclinical medial arterial calcification within the general population remains controversial.

Medial arterial calcification has been estimated to affect approximately 13.3% of men and 6.9% of women in a population at risk of PAD.34 However, cutoff points for diagnosis of medial arterial calcification by the ABI have been questioned. Further complicating matters, the presence of subclinical medial arterial calcification has been proposed, which goes undetected by the ABI.4 It is therefore difficult to determine the extent to which the accuracy of the ABI may be affected and the efficacy of using the measurement as a screening tool. Current recommendations suggest that a toe pressure be used only in the presence of an ABI elevated to greater than 1.40; however, these recommendations do not address the presence of PAD coexisting with medial arterial calcification, which may reduce the ABI to within a normal range.12,35–37

This study supports previous findings indicating that the ABI has decreasing levels of sensitivity in a population at risk of PAD and concurrent medial arterial calcification. Conversely, the specificity of the ABI (93%) in this study was higher than that of the TBI (79%). Previous studies in different populations have shown that the ABI had differ-

| Characteristic                  | ABI | TBI |
|--------------------------------|-----|-----|
| Mean (SD)                      | 1.13 (0.23) | 0.71 (0.21) |
| Sensitivity (95% CI), %        | 45 (32–59) | 71 (57–81) |
| Specificity (95% CI), %        | 93 (84–97) | 79 (67–87) |
| Positive predictive value (95% CI), % | 82 (63–93) | 72 (57–83) |
| Negative predictive value (95% CI), % | 69 (58–78) | 77 (65–86) |
| ROC area (P)                   | 0.65 (.005) | 0.77 (.0001) |
ing specificity rates (88%–100%). However, this study included a mixed population with a larger sample size, and participants rested for 10 minutes, which has been shown to be the ideal rest time for ankle pressures. This factor may have resulted in higher specificity rates.

Previous research in small cohorts of people with diabetes has shown that the TBI had superior sensitivity for the presence of PAD compared to the ABI. In this study, the TBI also had superior sensitivity and ROC results compared to the ABI. Although the specificity of the TBI was lower than that of the ABI, the TBI still fared better overall, showing a more significant result with ROC analysis. This finding suggests that the TBI has a wider applicability to a broader population at risk of PAD than previously believed.

In this study, 61% of the participants had diabetes, and the average age was older than previously reported. As both advanced age and diabetes are associated with more distally distributed atherosclerotic lesions, these participants had higher rates of distally located stenoses. Our finding of increased sensitivity of the TBI for PAD in our sample is congruent with previous suggestions that the TBI has high sensitivity for more distally distributed disease and should therefore be a test of choice in populations at risk of such disease patterns. However it is important to note that in this study, a photoplythsmograph probe was used to measure the TBI. There are other methods of obtaining toe pressures, including strain gauge plethysmography, oscillometric plethysmography, and laser Doppler imaging; therefore, our study applies only to the photoplethysmograph method.

In addition to being highly sensitive, our results also suggest that the TBI had higher specificity (79%) than previously reported in small groups of people with diabetes (61%–65%). However, this difference may be due to the effect of diabetes on microcirculation and impairment of vasodilatory capacity, which would remain undetected by large vessel–screening methods such as the ABI and color duplex sonography. The presence of microvascular disease that drops the TBI without coexistent PAD would reduce the specificity of the test for PAD. Conversely, in studies examining people with chronic renal failure, the specificity of both the TBI and the ABI has been shown to be up to 100%, potentially due to the high rates of medial arterial calcification in this population without the presence of peripheral microvascular disease.

To our knowledge, a study assessing the sensitivity and specificity of the TBI across a mixed population at risk of PAD has not been reported previously. However, the findings of this study need to be considered carefully because of some potential limitations. Although a valid form of noninvasive vascular assessment, color duplex sonography is heavily dependent on operator skill, and whereas an intertester reliability study was performed and shown to be adequate, the results are nevertheless subjective and dependant on clinician skill and experience. The intertester reliability testing for color duplex sonography was limited to 10 participants due to financial restraints and may not have been statistically robust; however, it had a similar participant number as another study of diagnostic accuracy using color duplex sonography as a reference standard.

Our convenience sample consisted of a large proportion of people with diabetes and an older mean age; however, this factor reflects the sample population, who were attending a podiatry and vascular clinic and were at risk of PAD. People older than 75 have a higher prevalence of PAD. People with diabetes are at increased risk of PAD, with disease occurring earlier and more aggressively, with a more distal distribution frequently reported. The results of this study therefore reflect a population at substantial risk of PAD with more distally located stenoses.

In conclusion, this study demonstrated that the TBI had greater sensitivity than the ABI in participants at risk of PAD. The specificity of the TBI was lower than that of the ABI but higher than previously reported. These results suggest that the TBI may be a more clinically effective form of vascular assessment in this population. Further research in larger cohorts is required to further elucidate the sensitivity and specificity of the TBI in broad populations at risk of PAD.

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