The ankle brachial index (ABI) is the most commonly used noninvasive method of diagnosing peripheral artery disease (PAD). An ABI <0.9 identifies PAD with high sensitivity and specificity. However, arterial stiffness and calcification may result in noncompressible results (defined as ABI >1.4), and this reduces the accuracy of ABI testing. Indeed, up to 8% of patients undergoing ABI testing have abnormally elevated ABI because of noncompressible vessels, and although unclear, the prevalence may be as high as 20% in patients with critical limb ischemia (CLI). Further, noncompressible ABI results are especially prevalent in patients with diabetes mellitus (DM) or end-stage renal disease (ESRD), common comorbidities in CLI. As such, the presence of noncompressible arteries represents a clinical challenge in determining foot perfusion in patients with CLI.

The ankle brachial index (ABI) is the most commonly used noninvasive method of diagnosing peripheral artery disease (PAD). An ABI <0.9 identifies PAD with high sensitivity and specificity. However, arterial stiffness and calcification may result in noncompressible results (defined as ABI >1.4), and this reduces the accuracy of ABI testing. Indeed, up to 8% of patients undergoing ABI testing have abnormally elevated ABI because of noncompressible vessels, and although unclear, the prevalence may be as high as 20% in patients with critical limb ischemia (CLI). Further, noncompressible ABI results are especially prevalent in patients with diabetes mellitus (DM) or end-stage renal disease (ESRD), common comorbidities in CLI. As such, the presence of noncompressible arteries represents a clinical challenge in determining foot perfusion in patients with CLI.

Previous studies of the association between noncompressible ABI and occlusive PAD have been limited because of small sample size and unavailability of tibial artery and pedal arch cine angiography. We, therefore, performed a study to identify the prevalence of angiographic patency of the tibial arteries and pedal arch in patients with CLI and noncompressible ABI.

Methods

Study Population

In this retrospective, observational study, we identified individuals with clinical evidence of CLI (Rutherford class IV–VI) and noncompressible ABI between January 1, 2012, and December 31, 2015. A total of 125 lower extremities with noncompressible ABI (ABI>1.4) were included (from 89 individual patients). In every case, angiography was performed within 1 year after ABI testing. In addition, 133 limbs from 133 unique patients with clinical CLI but with compressible
WHAT IS KNOWN

- A significant proportion of patients with CLI have noncompressible vessels by ABI testing, which represents a clinical challenge in determining tibial artery patency.
- Few studies have evaluated AT and PT artery patency in patients with CLI and noncompressible ABI.

WHAT THE STUDY ADDS

- This study shows that patients with CLI and noncompressible ABI are at high risk of AT, PT, and pedal arch occlusion or severe stenosis.
- A TBI <0.70 is highly sensitive for the identification of AT and PT occlusion in patients with noncompressible ABI, whereas PVR waveform dampening was not sensitive.
- It may be reasonable to consider angiography in patients with CLI and noncompressible ABI, especially if TBI <0.70, regardless of PVR waveform.

ABI (ABI<1.4) were also identified as a comparison group. These patients were selected as a comparison group because these were all of the patients with CLI who had compressible ABI and angiography at our institution within the study time period. Demographic and medical history of each patient were recorded in standard fashion by reviewing electronic medical records. Institutional review board approval was obtained before data collection.

Definitions and Study Variables

ABI was recorded for each limb in every patient. Where available, TBI and PVR waveform measurements were also obtained. The ABI and TBI were measured with the patient at rest and in the supine position and using continuous wave Doppler ultrasound and appropriately sized cuffs to measure blood pressure at ankles and arms. Digit pressure measurements were made with an appropriate sized digit cuff and a photoplethysmographic sensor. The highest of the brachial pressures was chosen for the ABI and TBI ratio. All studies were performed at the accredited institutional noninvasive vascular laboratory by registered vascular technologists. Noncompressible ABI was defined as an ABI $\geq$1.4 or if the pulse was still audible and had a measurable pulse volume waveform even when cuff pressure exceeded 255 mmHg at the level of the ankle. ESRD was defined as a creatinine clearance $\leq$ 15 mL/min.

PVR Waveforms

PVR waveforms were recorded using air the plethysmography method at the level of the ankles. A standardized protocol was used for cuff size and inflation and calibration of equipment. The PVR waveform was qualitatively assessed and classified as normal, mild, moderate, or severe dampening as endorsed by the consensus document.11

Severity of Arterial Disease

The severity of PAD was categorized using the Rutherford/Baker classification.12 Only patients with Rutherford class IV to VI (CLI) were included.12 Individual lower extremity angiograms were reviewed blindly (without the knowledge of ABI, TBI, and PVR) by the interventional and vascular physicians.

Anterior tibial (AT) and posterior tibial (PT) artery disease were classified as complete occlusion, significant stenosis (250%), or patent (<50% stenosis). The pedal arch was classified as complete if the anastomosis between the main pedal arteries and dorsalis pedis artery or one of the lateral or medial plantar arteries was present through an arcuate artery or its perforators. The absence of an actual anastomosis but the presence of at least one of the main pedal arteries was categorized as an incomplete arch, and the pedal arch was categorized as absent if both of the main pedal arteries were absent.13

Classification of Wounds According to Angiosome

In patients with lower extremity wounds (Rutherford class V and VI), the location of each wound was described based on its angiosome.14,15 Broadly, angiosomes were classified into 4 categories: the AT angiosome included the dorsum of the foot and medial malleolus, the PT angiosome included the plantar surface of the foot, the shared/combined AT and PT angiosome included the toes and heel, and the peroneal angiosome included the lateral malleoli.

Statistical Methods

Continuous data were described using mean and SD if normally distributed or median and interquartile range if non-normally distributed. Categorical measures and prevalence were summarized as percentages. Direct comparisons of the demographic variables, medical history, and angiographic variables between patients with noncompressible and compressible ABI were performed using Student t test or $\chi^2$ testing, where appropriate. The sensitivity of ABI, TBI, and TBI for diagnosing occlusive and significantly stenotic tibial arterial disease was also determined.

Results

Patient Characteristics

Demographic and baseline features of the study population with noncompressible ABI are shown in the Table. The mean age of the study group was 70.8±11 years. The median time from ABI to angiography was 19 days, mean, 49 days. In total, 97 of 125 (77.6%) limbs were from men. An overwhelming number of limbs were from individuals with hypertension, DM, hyperlipidemia, and coronary artery disease. Further, 91 of 125 (72.8%) limbs were from patients who had chronic kidney disease (CKD), including ESRD. The majority of limbs were Rutherford class V or VI as 217 of 256 (84.1%) had wounds. In addition, we compared the demographic variables and medical profile of these patients with those with CLI and compressible ABI (Table). The prevalence of DM, coronary artery disease, and ESRD were slightly more frequent in patients with noncompressible ABI compared with compressible ABI; however, in general, patient characteristics were relatively similar. Patients with compressible ABI were more likely to have wounds (Rutherford Class V or VI) than patients with noncompressible ABI (94% versus 75.3%; P=0.003).

Angiographic Features of Patients With CLI and Noncompressible or Compressible ABI

Among the 125 limbs with CLI and noncompressible vessels by ABI, 72 of 125 (57.6%) AT and 80 of 125 (64%) PT arteries were occluded by angiography (Figure 1). In addition, another 23 of 125 (18.4%) AT and 13 of 125 (10.4%) PT arteries were $\geq$50% stenosed (Figure 1). In total, 95 of 125 (76%) limbs with noncompressible ABI had completely occluded or severely stenosed AT. This was similar to the comparison group of patients with compressible ABI (Figure 2), in which 111 of 133 (83.4%) had a completely occluded or
severely stenosed AT ($P=0.136$). In those with noncompressible ABI, 93 of 125 (74.4%) limbs had completely occluded or significantly stenosed PT, which was also similar to the 105 of 133 (78.9%) with compressible ABI ($P=0.388$). Pedal arch angiography was performed for 103 (82.4%) limbs in the noncompressible group and 96 (72.2%) limbs in the compressible group. In the noncompressible group, 86 of 103 (83.5%) had either an absent or incomplete pedal arch, not significantly different to the compressible group 83 of 96 (86.5%; $P=0.559$; Figures 1 and 2).

**Utility of PVR Waveforms and TBI in CLI With Noncompressible ABI**

PVR waveform at the level of ankles was moderate to severely dampened in 54 of 119 (45.4%) limbs. In patients with occluded AT arteries, PVR was moderate to severely dampened in only 30 of 71 (42.3%) limbs. Similarly, in patients with occluded PT arteries, PVR was moderately to severely dampened in only 35 of 80 (43.8%) limbs.

TBI data were available for 83 of 125 (66.4%) limbs with noncompressible ABI. Of these, 75 of 83 (90.4%) had TBI <0.7. On further analysis of the data in patients with TBI <0.7, 62 of 75 (82.7%) had at least one of the AT or PT arteries occluded. When combining with significantly stenosed (>50%) arteries, 70 of 75 (93.3%) patients were found to have either occluded or significantly diseased tibial arteries with TBI <0.7. Therefore, PVR (moderate to severe dampening) was 43.6% sensitive in diagnosing occluded and severely stenotic tibial artery disease, whereas TBI <0.7 was 89.7% sensitive for diagnosing the same.

**Wound and Angiosome**

Wound location data were available for 91 of the 92 patients in the noncompressible ABI group that had wounds (98.9%). Most wounds (77 of 91 [84.6%]) originated at toes or heels, within a shared angiosome between the AT and PT. Of these, 5 of 91 (5.5%) and 5 of 91 (5.5%) wounds originated from the angiosome of the AT or PT alone, respectively (Figure 3).

---

**Table.** Comparison of Demographics and Medical Comorbidities in Patients With Clinical Critical Limb Ischemia and Compressible or NC Arteries (ABI ≥1.4)

<table>
<thead>
<tr>
<th>Patient Characteristics</th>
<th>Compressible ABI</th>
<th>NC ABI</th>
<th>$P$ Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of limbs</td>
<td>133</td>
<td>125</td>
<td>—</td>
</tr>
<tr>
<td>No. of unique patients</td>
<td>133</td>
<td>89</td>
<td>—</td>
</tr>
<tr>
<td>Age, y, mean±SD</td>
<td>70.1±12.7</td>
<td>70.9±11.4</td>
<td>0.632</td>
</tr>
<tr>
<td>Male</td>
<td>82 (61.7)</td>
<td>68 (76.4)</td>
<td>0.028</td>
</tr>
<tr>
<td>BMI, mean±SD</td>
<td>28.1±5.8</td>
<td>27.4±4.4</td>
<td>0.335</td>
</tr>
<tr>
<td>HTN</td>
<td>118 (88.7)</td>
<td>82 (92.1)</td>
<td>0.249</td>
</tr>
<tr>
<td>HLD</td>
<td>108 (81.2)</td>
<td>77 (86.5)</td>
<td>0.360</td>
</tr>
<tr>
<td>CAD</td>
<td>78 (58.7)</td>
<td>71 (79.8)</td>
<td>0.001</td>
</tr>
<tr>
<td>DM</td>
<td>95 (71.4)</td>
<td>78 (87.6)</td>
<td>0.005</td>
</tr>
<tr>
<td>ESRD</td>
<td>9 (6.8)</td>
<td>23 (25.8)</td>
<td>0.007</td>
</tr>
<tr>
<td>History of smoking</td>
<td>82 (61.7)</td>
<td>60 (67.4)</td>
<td>0.396</td>
</tr>
<tr>
<td>Rutherford class V or VI</td>
<td>125 (94)</td>
<td>67 (75.3)</td>
<td>0.003</td>
</tr>
</tbody>
</table>

Data presented as n (%) unless otherwise stated. ABI indicates ankle brachial index; BMI, body mass index; CAD, coronary artery disease; CVA, cerebrovascular accident; DM, diabetes mellitus; ESRD, end-stage renal disease; HLD, hyperlipidemia; HTN, hypertension; and NC, noncompressible.
The peroneal artery was occluded or severely stenotic in 79 of 125 (63.2%) limbs with noncompressible ABI, and 82 of 133 (61.7%) limbs with compressible ABI (P non-significant between groups). Only 3 (3.3%) patients in the noncompressible ABI group had a wound involving the peroneal artery angiosome alone. On further analysis, 80 of 87 (91%) wounds were found to have occluded or >50% stenosis in tibial arteries in their respective angiosomes (Figure 3). The remainder of patients had isolated above the knee (ie, supratibial) disease.

Figure 2. Prevalence of below the knee arterial disease in patients with critical limb ischemia (CLI) and compressible anterior brachial index (ABI). In a comparison group of patients with CLI and compressible ABI, 83% of patients had either occluded or severely stenosed anterior tibial (AT) arteries, 79% had occluded or severely stenosed AT arteries, and 86% had either an incomplete or occluded pedal arch. ABI indicates ankle brachial index; AT, anterior tibial; and NC, noncompressible. *For pedal arch, the severe category indicates an incomplete arch.

Figure 3. Number of patients with wounds and occluded or significantly stenosed arteries in the respective angiosome. Most wounds were located in the shared anterior tibial (AT) and posterior tibial (PT) angiosome (88.5%), and the majority of patients had either a completely occluded or significantly stenosed vessel within the distribution of the respective angiosome (92%). AT indicates anterior tibial; and PT, posterior tibial.
Discussion

In this study, we demonstrate that patients with CLI and noncompressible ABI are at high risk of complete tibial and pedal arch occlusion or significant stenosis. In general, individuals with CLI and noncompressible ABI have similar angiographic characteristics to patients with CLI and compressible ABI, and the majority of patients with noncompressible ABI had a completely occluded AT or PT. However, only approximately half of patients with noncompressible ABI had moderately or severely dampened PVR waveform despite a high rate of arterial occlusion in these patients. In comparison, a TBI <0.7 was highly sensitive for the identification of AT and PT occlusion in patients with CLI and noncompressible ABI. Given this high prevalence of complete or severe arterial occlusion, it may be reasonable to consider angiography in patients with CLI and noncompressible ABI, especially among those with TBI <0.7, regardless of the appearance of the PVR waveform.

To the best of our knowledge, ours is the first study to quantify the prevalence of AT, PT, and pedal arch occlusion in patients with noncompressible ABI using angiography or to compare this to patients with compressible ABI. Although it is established that patients with CLI often have below knee disease as the cause, ABI has been shown to be an inaccurate and insensitive means of diagnosing infrapopliteal disease, especially among patients with DM and even in patients with compressible ABI. In addition, a large number of patients with CLI have DM and chronic kidney disease, both of which are associated with arterial calcification, medial calcinosis, and concomitant noncompressible ABI. As such, hemodynamic assessment may be particularly challenging in these subsets of patients with CLI, and additional techniques for assessment of arterial perfusion beyond ABI may be needed in certain patients.

Given the shortcomings of ABI, other tools may be useful in identifying patients with CLI. In our study, we show that PVR waveform morphology was relatively insensitive for the diagnosis of CLI. These results agree with those of Eslahpazir et al. and as such, we cannot endorse the view of some authors who have suggested using PVR to complement ABI in diagnosing PAD in setting of noncompressible ABI. Similar to our study, Eslahpazir et al demonstrated that the PVR does not add to the combined accuracy of segmental pressure and Doppler waveform velocimetry in diagnosing CLI, in part, because of considerable interobserver variance in reading PVR. Further, our results are reinforced by the study of Faglia et al., which showed that occlusion was more common than stenosis in patients with CLI and reduced foot perfusion.

Further, we found that a TBI <0.7 is highly sensitive for the diagnosis of CLI in patients with noncompressible ABI; results that are supported by other recent studies. Another option may be ABI with the addition of arterial duplex ultrasound; however, ultrasound has several limitations, including calcific shadowing and the challenges in determining the patency of very small distal arteries including the pedal arch. In addition, although TcPO2 and skin perfusion pressure may be useful adjuncts, these methods can be time consuming and are not available at all centers. Given the high prevalence of arterial occlusion in patients with clinical CLI and noncompressible ABI, it may be reasonable to perform angiography in these patients because this remains the gold standard to assess AT, PT, and pedal arch patency.

One strategy recently used in clinical practice is angiosome-based (or direct) revascularization. In this approach, priority is given to restoring flow to the artery that supplies the territory of the wound. In a recent meta-analysis, the angiosome approach improved wound healing compared with indirect (nonangiosome) revascularization (odds ratio, 0.40; 95% confidence interval, 0.29–0.54) and 1-year amputation (limb salvage) rates (odds ratio, 0.24; 95% confidence interval, 0.13–0.45). As angiosome-based revascularization becomes more common, understanding AT and PT patency in patients with noncompressible ABI is all the more relevant. In our study, most wounds were located in the shared AT and PT angiosome (88.5%), and the majority of patients had either a completely occluded or significantly stenosed vessel within the distribution of the respective angiosome (92%), highlighting the importance of this concept.

In addition, this is the first study to evaluate the angiosgraphic patency of the pedal arch in patients with CLI and noncompressible ABI. We demonstrate that the vast majority of patients with noncompressible ABI have an absent or incomplete pedal arch, which is similar to a previous study by Rashid et al that evaluated all patients with CLI (regardless of arterial compressibility). This finding is important because pedal arch patency has been associated with wound healing in patients with CLI. This may even be more relevant among patients with CLI and noncompressible ABI because majority are patients with DM and ESRD and have high prevalence microvascular disease and poor distal foot perfusion.

Our study has certain limitations. It was a retrospective study, and by design only included patients with clinical CLI who had angiography and noninvasive vascular laboratory testing in our tertiary care center. Thus, our findings may have been affected by selection bias and cannot be generalized to all patients with PAD or CLI. In addition, a time lag of up to 1 year was permitted between ABI and angiography in our study. Although arterial disease may have progressed during this time, the median time from ABI to angiography was 19 days and the vast majority had angiography within 4 months of ABI, suggestive that this effect was likely small.

Conclusions

The prevalence of significant stenosis or complete occlusion of the AT, PT, or pedal arch is high in patients with clinical CLI and noncompressible ABI, and comparable to patients with CLI and compressible ABI. ABI and ankle PVR waveform morphology are nonreliable modalities for confirmation of perfusion in patients with lower extremity ulcers and noncompressible ABI. A TBI <0.7 is more sensitive in diagnosing occluded and severely stenotic tibial artery disease compared with PVR in these patients. However, given the importance of revascularization for CLI and the inaccuracy of ABI in diagnosing tibial and pedal arch patency, it may be reasonable to pursue a strategy of angiography in these patients.
Disclosures
Dr Gornik is named in a patent by Summit Doppler Systems related to ankle brachial index testing. The other authors report no conflicts.

References
Prevalence of Tibial Artery and Pedal Arch Patency by Angiography in Patients With Critical Limb Ischemia and Noncompressible Ankle Brachial Index
Mandeep Singh Randhawa, Grant W. Reed, Kevin Grafmiller, Heather L. Gornik and Mehdi H. Shishehbor

Circ Cardiovasc Interv. 2017;10:
doi: 10.1161/CIRCINTERVENTIONS.116.004605
Circulation: Cardiovascular Interventions is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2017 American Heart Association, Inc. All rights reserved.
Print ISSN: 1941-7640. Online ISSN: 1941-7632

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circinterventions.ahajournals.org/content/10/5/e004605

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation: Cardiovascular Interventions can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation: Cardiovascular Interventions is online at:
http://circinterventions.ahajournals.org//subscriptions/