Comparing BlueDop Vascular Expert to ankle-brachial index in the identification of peripheral vascular disease in all-comers and diabetic patients

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ABSTRACT

Objective: We compared the screening capabilities of the BlueDop Vascular Expert (BVE) and ankle-brachial index (ABI) in peripheral arterial disease for all-comer patients and those with diagnosed diabetes mellitus (DM).

Methods: Data were collected retrospectively and prospectively at a single center in 104 all-comers from BVE and ABI compared with conventional full leg arterial duplex on the same patient, same limb, and at the same appointment. A final comparison was made between the BVE and ABI using full leg arterial duplex as the diagnostic comparison. 104 all-comers were included, and 35 of those patients had diagnosed DM.

Results: For all-comers, BVE sensitivity was 90%, specificity was 96%, accuracy was 94.5%, and $\kappa = 0.84$. In contrast, ABI sensitivity was 53%, specificity was 95%, accuracy was 86%, and $\kappa = 0.53$. Of the 35 patients with DM, BVE screened 65 limbs and ABI screened 63 limbs. For patients with DM, BVE sensitivity was 90%, specificity was 98%, accuracy was 95.4%, and $\kappa = 0.89$. In contrast, ABI sensitivity was 40%, specificity was 81%, accuracy was 68.3%, and $\kappa = 0.23$.

Conclusions: The need for a device that is easy to use, easy to interpret, portable, and, most important, accurate, is critical in reducing long-term complications of peripheral artery disease. As a cuffless arterial assessment system, the BVE was found to have superior sensitivity, specificity, and accuracy when compared with ABI in all-comers. In patients with DM, BVE also showed greater sensitivity, specificity, and notably an accuracy of 95.4% compared with ABI's accuracy of 68.3%. The data support that BVE is an accurate and easy-to-use lower limb blood flow assessment device, even when assessing the most challenging patients. (JVS-Vascular Insights 2024;■:100144.)

Keywords: Peripheral arterial disease; Ankle-brachial index; Arterial duplex; Doppler waveforms

Peripheral artery disease (PAD) is a progressive disorder that is a common cause of morbidity, mortality, and limb loss in the United States and worldwide. It is estimated that 40 to 45 million Americans and >200 million people worldwide are affected by PAD.[1] PAD is described as the progressive narrowing of peripheral blood vessels, leading to decreased perfusion of the affected areas. The most frequent cause of PAD is atherosclerosis; however, other vascular etiologies such as embolism, vasculitis, and fibromuscular dysplasia also contribute to the pathogenesis of PAD.[2] Leading risk factors for PAD include smoking, diabetes mellitus (DM), and hypertension (HTN), as well as obesity. Owing to the high prevalence of the leading risk factors for PAD in the United States, early detection is paramount in the prevention of long-term complications. However, PAD is often underdiagnosed owing to the lack of awareness of the disease, high prevalence of asymptomatic disease, and inappropriate screening and diagnostic tools.[3] If undiagnosed, patients who have PAD may develop long-term complications such as acute coronary syndrome, stroke, gangrene of the lower extremity, and limb amputation owing to severe ischemia.[1]

Undiagnosed PAD poses a significant financial burden on both the US and global economies, including medical expenses, loss of productivity of patients, and use of health care resources. PAD is also a significant and growing strain on the world health care infrastructure. Empowering primary and tertiary health care providers the ability to accurately rule in and rule out disease will be even more critical as the Baby Boomers age. The annual cost associated with PAD in the United States alone, including hospitalizations, surgical interventions, medications, and long-term care, is estimated to be between \$7 and \$8 billion.[4] Individuals with advanced PAD may require long-term management of the disease,

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The editors and reviewers of this article have no relevant financial relationships to disclose per the Journal policy that requires reviewers to decline review of any manuscript for which they may have a conflict of interest.

2949-9127

https://doi.org/10.1016/j.jvsvi.2024.100144

which contributes to the strain on nursing homes and rehabilitation centers. Furthermore, PAD-related disabilities often lead to decreased workforce participation and increased dependence on social welfare programs.[4]

The ankle-brachial index (ABI) is the current standard of care for the assessment and diagnosis of PAD. The ABI is calculated by determining the ratio of the systolic pressure of the lower extremity to the systolic pressure of the upper extremity and comparing its value with a standard measure of 0.9. An ABI of ≤0.9 is indicative of disease.[5] Although the ABI is regarded as a reliable screening tool for PAD in healthy individuals, its efficacy is compromised in the elderly, as well as patients with comorbidities such as DM, obesity, edema, and other conditions leading to the calcification and stiffening of these vessels. A study on ABI reliability found that almost one-quarter of the population receives an ABI screening with inadequate sensitivity and specificity owing to the variability in vessel compressibility.[6] An ABI assumes that the vessels are compressible, negating variability in the pressure required to compress these vessels while calculating the index. Because these conditions lead to vessels in the ankle (dorsalis pedis and posterior tibial) being more resilient to the compression of the cuff, the index is increased inaccurately.[5]

Inconsistency in ABI measurements has also been attributed to intrinsic characteristics of the test itself. Several variables leading to this inconsistency have been reported, such as cuff size and location, position of the patient, and measurement order, as well as patient ethnicity and race. To negate these inconsistencies, standardized techniques would need to be both determined and put in place.[5] Because many of the standards required for consistency are impractical in a clinical setting, there is a necessity for a new strategy in screening for PAD.

When vascular calcification and hardening is present as in DM, or when an ABI cannot be accurately measured, a toe-brachial index (TBI) is indicated. A TBI may be more accurate when vessel calcification is suspected because the vessels in the toe are less affected by calcification.[7] However, it has been shown that there are limitations regarding the reliability in using the TBI for screening. Additionally, when compared with ABI screening, TBI screening requires greater technical skills, demands additional access to equipment, and lacks adequate literature on standard normative measures. Previous studies have found sensitivities for TBI to range from 45% to 100% and specificity to range from 16% to 100%, indicating the inconsistent reliability of this screening method.[7]

Another tool commonly used in conjunction with ABI is the use of Doppler waveforms. The resulting waveform shape (monophasic, biphasic, or triphasic) through vessels can be interpreted by a trained specialist for the presence of occlusive disease. Lower extremity or full leg arterial duplex (FLAD) is a well-established noninvasive test that can accurately collect data on arterial blood flow and functional impairment for the accurate classification of occlusive and aneurysm disease.[8] Testing can provide information about blood flow (pulsed Doppler spectral analysis) and anatomy (B-mode and color Doppler imaging). For FLAD to be positive for disease, there must be dampening of the waveform upon interpretation. Thus, it is a combination of waveform and duplex assessment. Importantly, FLAD can accurately be used on individuals who have thick and noncompressible vessels who are not candidates for ABI measurement.[9,10]

Although the use of Doppler waveform is an attempt to overcome the shortcomings of ABI, it introduces new challenges. To obtain the waveforms, specialized equipment and trained personnel are required, and the ultrasound session takes approximately 30 to 90 minutes per patient. Once the data are collected, additional interpretations of the waveform shape are sent to vascular disease specialists for interpretation.[10] The need for specialized equipment, technician training, time to gather waveform data, and additional interpretation by specialists all limit its clinical use to the primary care

ARTICLE HIGHLIGHTS

- **Type of Research:** Single-center retrospective and prospective study
- **Key Findings:** In 104 all-comer patients, the BlueDop Vascular Expert demonstrated sensitivity of 90%, specificity of 96%, accuracy of 94.5%, and $\kappa = 0.84$ for peripheral artery disease. In contrast, ankle-brachial index (ABI) sensitivity was 53%, specificity was 95%, accuracy was 86%, and $\kappa = 0.53$. Of the 35 patients with diabetes, the BlueDop Vascular Expert screened 65 limbs and ABI screened 63 limbs. For those all-comers with diabetes, the BlueDop Vascular Expert sensitivity was 90%, specificity was 98%, accuracy was 95.4%, and $\kappa = 0.89$. In contrast, ABI sensitivity was 40%, specificity was 81%, accuracy was 68.3%, and $\kappa = 0.23$.
- **Take Home Message:** The BlueDop Vascular Expert is a cuffless arterial assessment system that overcomes many of the limitations of ABI and other cuff-based systems. It was found to have superior sensitivity, specificity, and accuracy when compared with the ABI in all-comers. In patients with diabetes mellitus, it also showed greater sensitivity, specificity, and notably an accuracy of 95.4% compared with the ABI's accuracy of 68.3%. These data support that BlueDop Vascular Expert is an accurate and easy-to-use lower limb blood flow assessment device, even when assessing the most challenging patients.

providers and the number of patients who can be screened, therefore limiting accurate early detection of PAD.[10] In particular, the rural United States is greatly impacted by these issues; there are few training opportunities, limited access to specialized medicine, and complex disease presentation owing to delayed care.[11]

The BlueDop Vascular Expert (BVE) is intended to address challenges presented by ABI, Doppler waveform analysis, and other PAD screening methods. The BVE is a cuffless, portable probe designed to evaluate vascular health across all patient populations, including those with conditions limiting traditional assessment approaches. The BVE uses two algorithms known as pressure from flow and monotopic Doppler waveform, which analyze Doppler waveform data for signs of disease. The results are presented in a simple color-coded format based on predetermined criteria: green indicates no or mild disease, yellow signifies moderate disease, and red indicates severe disease. This intuitive approach eliminates the need for specialized interpretation by vascular experts, and the entire evaluation can be performed in only 5 minutes. The portability and cuffless design of the BVE enables its use in diverse settings, extending vascular assessment capabilities to all health care providers independent of location. By streamlining interpretation and expanding accessibility, the BVE has the potential to ease the burden on vascular specialists while enhancing patient access to critical vascular care. As PAD prevalence rises in the United State and globally, BVE could become a useful tool in the assessment and diagnosis of PAD and the prevention of long-term complications, as well as decompressing vascular specialist and vascular laboratory schedules from the false-positive studies and identifying the previous false-negative ones.

METHODS

This retrospective and prospective single-center study to compare the accuracy and screening capabilities of BVE and ABI with conventional FLAD was performed at a private clinic in Sioux Falls, South Dakota, with data collected from March 2023 to March 2024. Currently, the BVE carries the European CE Mark but does not yet have Food and Drug Administration approval for use in the United States. This study was undertaken with institutional review board approval. Patients ≥18 years who presented to the center were consented to have BVE, ABI, and FLAD performed.

BVE examination of lower extremity arteries were performed following the instructions for use. As described in Kordzadeh et al,[12] the BVE consists of a handheld component that communicates wirelessly with an output monitor device (Fig 1). The validated pressure from the flow algorithm is based upon the ratio between systolic and diastolic values taken from the incident blood pressure waveform and the resultant blood flow waveform.[13]

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Fig 1. A registered vascular technician is using the handheld device. The extracted data are then wirelessly visualized on the output monitor device.

Mean arterial blood pressure (MAP) data are able to be extracted from raw Doppler-shifted velocity/time spectral waveforms, and the complex and validated pressure from flow algorithm then develops a mean ABI (ABIm) and perfusion pressure (Figs 2 and 3). This is analogous and following much of the physics of measuring the resistance of an electrical circuit and the amplitude of a volt meter (Fig 4). The mABI is similar but not identical to conventional ABI and is based on the mean perfusion pressure (the difference between MAP and central venous pressure calculated at a pressure of 0) divided by MAP. An ABIm reading of 0.8 to 1.0 indicates no significant disease to impact flow, 0.5 to 0.8 indicates moderate level of disease, and <0.5 indicates sufficient disease that requires further investigation.

The color-coded system of green, yellow, and red is based on the appearance of the Doppler spectra of a monotonic blood velocity decay between systole and the following systolic uprise. It has accuracy similar to the ABIm and is graphically more obvious to an inexperienced operator. In this study, BVE results were deemed positive for arterial blockage if the BVE displayed red in both tibial vessels, red in one tibial vessel with yellow in the other, yellow in one vessel and the other undetectable, and red in one vessel and the other undetectable. Results were negative for arterial blockage if BVE displayed green in any tibial vessel or yellow in both. For the ABI, arterial blockage was deemed positive if ≤0.8 the is based on National Health Systems and European standards for notable disease.

BVE, ABI, and FLAD examinations were performed by the same two registered vascular technologists at a

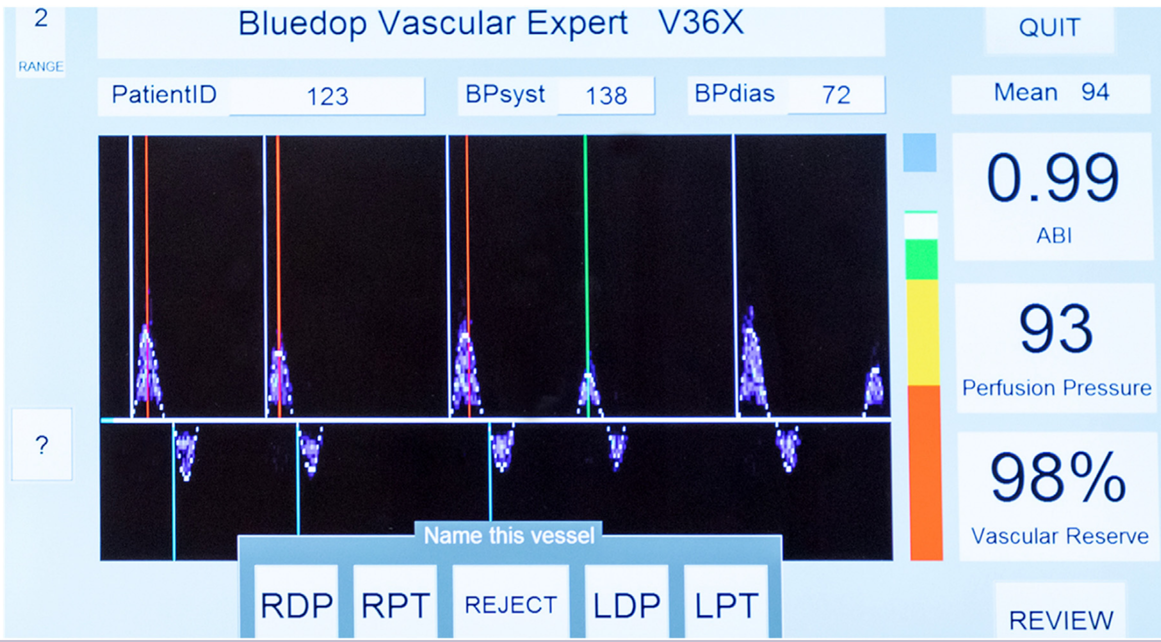

Fig 2. The output monitor device displays real-time results for each limb while scanning.

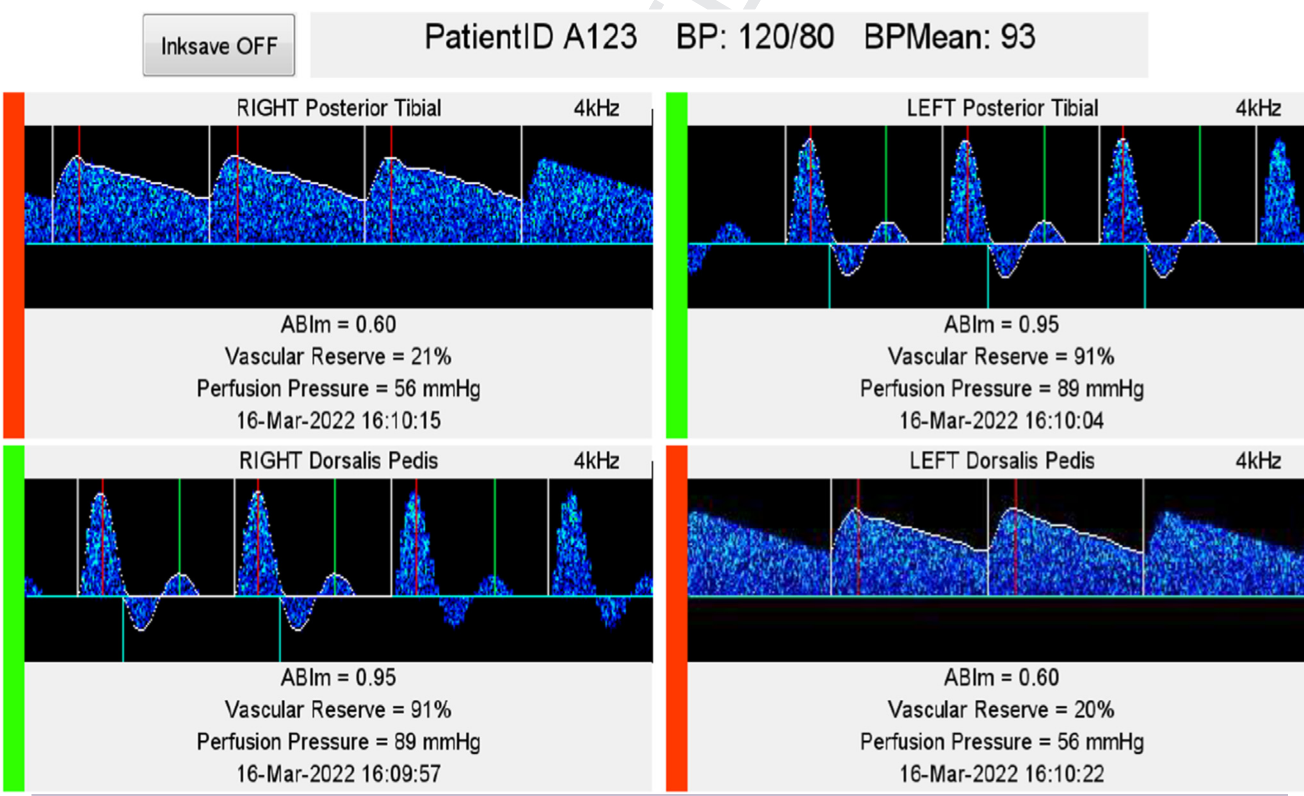

Fig 3. The output monitor is able to calculate full results with quantitative values such as the mean ankle-brachial index (*ABIm*), vascular reserve, and perfusion pressure, as well as the color-coded bars to indicate presence or absence of disease.

single center. All FLAD waveform results were sent to and interpreted by an outside cardiothoracic surgeon who specializes in the treatment of arterial disease to determine the presence or absence of disease. The specialist was masked to the BVE results and was only sent the FLAD ultrasound data to interpret.

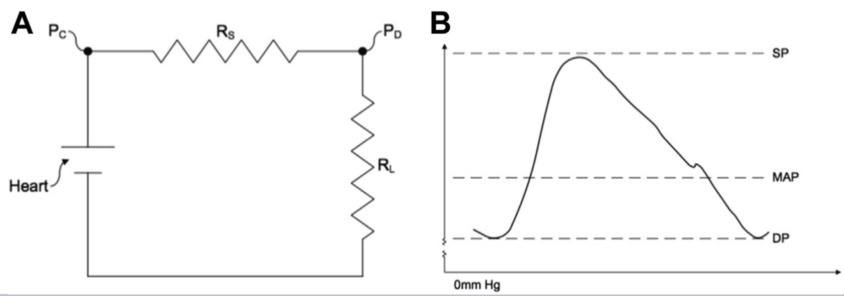

Fig 4. (A) Blood flow through vasculature is analogous to a closed electrical circuit. **(B)** Based on the same physics principles, BlueDop is able to measure the resistance and amplitude and calculate values like mean ankle-brachial index (ABIm) through the validated pressure from flow algorithm.

Patients were excluded if they had incomplete or inadequate data, were known to be pregnant currently, or had contraindications to Doppler ultrasound examination. Assessment accuracy will be evaluated using sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV). Agreement between BVE and FLAD vs ABI and FLAD were assessed using Cohen's kappa coefficient (κ). Data were analyzed for all-comers and those with diagnosed DM.

RESULTS

In 104 all-comer patients, BVE screened 201 limbs and ABI screened 193 limbs (Table I). Of the patients, 65 (62.5%) were male and 39 (37.5%) female. The mean age was 72 with a range of 54 to 84 years. Regarding comorbidities, 35 patients (33.7%) had diagnosed DM, 76 patients (73.1%) identified as current smokers, and 79 patients (76.0%) had diagnosed HTN. For overlapping comorbidities, all patients with DM identified as either a current smoker or having HTN, with 28 (80%) of the patients with DM being both a smoker and having HTN (Table I). Nine patients did not complete either BVE or ABI on the right leg and 6 patients did not complete either BVE or ABI on the left leg. When comparing techniques, four patients who were able to complete BVE were unable to complete ABI on the right leg owing to discomfort from cuff compression, edema, or open wounds. These same four patients were also unable to complete ABI on their left leg owing to discomfort from cuff compression, edema, or open wounds.

For all-comer patients, BVE sensitivity was 90%, specificity was 96%, an accuracy of 94.5% with a PPV of 84.1% and a NPV of 97.5%. In contrast, ABI with Doppler sensitivity was 53%, specificity was 95%, an accuracy of 86%, a PPV of 72.4%, and a NPV of 88.4%. BVE in all-comers had a κ = 0.84, and the ABI in all-comers had κ = 0.53 (Table II).

Results were also analyzed for the 35 patients with diagnosed DM. Of those, BVE screened 65 limbs and ABI screened 63 limbs. For patients with DM, BVE sensitivity was 90%, specificity was 98%, accuracy was 95.4%, PPV was 95%, and NPV was 95.6%. In contrast, the ABI sensitivity was 40%, specificity was 81%, accuracy was 68.3%, PPV was 50%, and NPV was 74.5%. BVE in patients with DM had κ = 0.89, whereas the ABI in patients with DM had κ = 0.23 (Table II).

Table I. Demographics

Demographics	Participants screened with ABI and BVE
Gender	
Male	65 (62.5)
Female	39 (37.5)
Age, years	72 (54-84)
Comorbidities	
DM total	35 (33.7)
DM + smoking	4 (3.9)
DM + HTN	3 (2.9)
DM + smoking + HTN	28 (26.9)
Smoking total	76 (73.1)
HTN total	79 (76.0)

ABI, Ankle-brachial index; *BVE,* BlueDop Vascular Expert; *DM,* diabetes mellitus; *HTN,* hypertension.
Values are number (%) or mean (range).

DISCUSSION

In patients with PAD and related comorbidities such as DM, eventual amputation of the distal extremities is of high concern. When assessing amputations rates worldwide, 50% occur without the patient ever undergoing a lower limb blood flow assessment.[14] It is well-documented that compromised blood flow is a major risk factor for amputation.[1–3] and that nearly 85% of amputations are preventable with early identification of compromised blood flow.[14] Most studies looking at the accuracy of ABI and cuff-based automated systems exclude patients with DM because of the poor accuracy secondary to incompressible ankle vessels. Because of the increased risk of PAD and subsequent amputation in patients with DM, a better method is needed. As a cuffless arterial assessment system, the BVE overcomes many of the limitations of conventional ABI and other cuff-based systems.

Table II. Results of BlueDop Vascular Expert (*BVE*) and ankle-brachial index (*ABI*) testing were compared with full leg arterial duplex (FLAD) in all-comers and patients with diabetes mellitus (*DM*)

	BVE in all-comers	ABI in all-comers	BVE in diabetics	ABI in patients with DM
True positives	37	21	19	8
False positives	7	8	1	8
True negatives	153	145	43	35
False negatives	4	19	2	12
Sensitivity	90%	53%	90%	40%
Specificity	96%	95%	98%	81%
Accuracy	94.5%	86%	95.4%	68.3%
PPV	84.1%	72.4%	95%	50%
NPV	97.5%	88.4%	95.6%	74.5%
Cohen's kappa coefficient (κ)	0.84	0.53	0.89	0.23

NPV, Negative predictive value; *PPV,* positive predictive value.

Current screening methods for PAD include ABI, Doppler waveform, and TBI when vascular abnormalities are suspected. However, all three techniques have their own limitations and disadvantages. The ABI assumes that the vessels being assessed are compressible and not sclerotic. It also contains several variables that skew the results, such as cuff size, cuff placement, position of the patient, and measurement order.[5] A standardized procedure would overcome these variables; however, this goal is not clinically practical. Doppler waveform is another tool commonly used in concert with ABI; however, a vascular specialist is required to read the results, which limits its application and creates a level of subjectivity when determining PAD. Last, a TBI may be performed in patients with suspected vascular abnormalities; however, this technique too requires additional equipment and is limited by many of the same limitations as ABI as and is even more affected by patient medication, body temperature, body position, and previous toe amputation.[7]

The BVE provides a way for health care providers to overcome the present limitations experienced with conventional ABI and other cuff-based systems. The use of this new cuffless technology will simplify lower limb assessments for those with edema, DM, venous stasis changes, open sores, and incompressible vessels. Additionally, the easy-to-interpret and color-coded reading explicitly indicates the level of arterial blockage present. These readings, green (normal), yellow (mild), and red (severe), allow for a mitigated process when triaging at-risk patients.

When comparing the BVE with cuff-based ABI, we found that BVE showed better sensitivity, specificity, and accuracy when compared with ABI in all-comers. In patients with DM, the BVE also showed greater sensitivity, specificity, and notably an accuracy of 95.4% compared with the ABI's accuracy of 68.3%. Even in high-risk patients with DM and sclerotic vessels, the BVE maintained a high level of accuracy. The algorithms of the BVE correctly identified PAD with an accuracy of greater than 94% in all patient groups independent of the patient comorbidities. The κ values of 0.84 and 0.89 for BVE in all-comers and patients with DM, respectively, also strongly supports the reliability of BVE. These results indicate that the BVE is an accurate and easy-to-use lower limb blood flow assessment device, even when assessing the most challenging patients.

These promising results at a single center warrant replication at other facilities. Additionally, future assessments should compare and analyze the BVE's ability to detect PAD with other comorbidities, such as lymphedema and renal insufficiency. Based on the cuffless design, blood flow analysis system of BVE, and the results we found with diabetics, we expect the BVE to be reliable in detecting PAD in other comorbidities notorious for complicating ABI values. Further studies are also warranted to examine the impact of early lower limb blood flow assessment in the management of time to treat for venous and arterial wounds, as well as the impact BVE may have on workflow and cost of care on wound healing and amputation rates.

AUTHOR CONTRIBUTIONS

Conception and design: CT, MO, GA, MQ, PK
Analysis and interpretation: CT, JD, BV, MW, RT, PK
Data collection: CT, GA, PK
Writing the article: CT, JD, BV, MW, RT, PK
Critical revision of the article: CT, JD, BV, MW, RT, MO, GA, MQ, PK
Final approval of the article: CT, JD, BV, MW, RT, MO, GA, MQ, PK
Statistical analysis: CT, JD, BV, MW, RT, MO, GA, MQ, PK
Obtained funding: PK
Overall responsibility: PK Q7

FUNDING

Dakota Vascular provided the materials and staff for the study.

DISCLOSURES

P.K. is an investor and officer in BlueDop Medical, Ltd.

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Submitted Jun 17, 2024; accepted Aug 16, 2024.