Novel Assessment (BlueDop) Device for Detection of Lower Limb Arterial Disease

A Prospective Comparative Study

Ali Kordzadeh, MBBS, MSc, MD, VA-BC, Mekhola Hoff, MRCS, PhD, Evripidis Tokidis, MBBS, David H. King, BSc, MSc, Tom Browne, FRCS, Ioannis Prionidis, FRCS, PhD

According to National Institute of Clinical Excellence guidelines, the ankle-brachial pressure index coupled with a full clinical evaluation has been the mainstay of detecting peripheral arterial disease on its suspicion. However, this technique is not free of its own limitations in calcified arteries, ulcerative and diabetic patients. We introduce a new, novel, and effective assessment device (BlueDop) with a minimal learning curve that could overcome such barriers and serve as a valid replacement in perihospital settings.

Key Words—ankle-brachial pressure index BlueDop; BlueDop; duplex sonography; lower limb arterial examination; novel lower limb arterial examination; novel technique; peripheral vascular

Peripheral arterial disease due to atherosclerosis has an estimated incidence (worldwide) of 10%, and this value is expected to double in the next decade.[1] In Europe and North America, 27 million individuals older than 70 years are believed to be affected by peripheral arterial disease. The estimated annual cost to the National Health Service is understood to be in the region of £200 million.[1]

According to National Institute of Clinical Excellence guidelines, on suspicion of peripheral arterial disease, a full cardiovascular examination is coupled with the ankle-brachial pressure index (ABPI) and handheld Doppler sonography.[2] These modalities are not free of limitations, given that they are operator dependent, thus producing false high and/or low index readings due to arterial calcification.[3] This factor, in conjunction with aging demographics, an increased occurrence of atypical lower limb pain, and social awareness has resulted in a substantial rise in referrals from primary care providers and district and tissue viability nurses to vascular outpatient services, which has resulted in a considerable strain on the system, with a substantial demand and reliance on the use of duplex sonography or computed tomographic angiography.[4,5] To clinically filter referrals (false indices [ABPI], nonarterial lower limb pain and suspected arterial disease, and assessment for other specialties) and avoid unnecessary duplex sonography and computed tomographic angiography, we believe that an easy-to-use and accurate assessment device with a minimal learning curve could be a useful alternative in such circumstances.

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David H. King designed the BlueDop Device, available at: http://bluedop.com.

Address correspondence to Ali Kordzadeh, MBBS, MSc, MD, VA-BC, Department of Vascular, Endovascular, and Renal Access, Mid Essex Hospital Services, National Health Service Trust Broomfield Hospital, Court Road, Essex CM1 7ET, England.

E-mail: alikordzadeh@gmail.com

Abbreviations
ABPI, ankle-brachial pressure index; IQR, interquartile range

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Therefore, we evaluated the efficacy of the BlueDop device in comparison to duplex sonography for detection of lower limb arterial disease at our unit.

Materials and Methods

A prospective consecutive comparative and blinded cohort study between January 1, 2015, and December 31, 2015, at Mid Essex Hospital Services National Health Service Trust with an estimated population coverage of 380,000 was conducted. During this period, all patients who had been referred to vascular outpatient services (one-stop clinic) were evaluated by both the BlueDop device and arterial duplex sonography. These evaluations included 276 limbs in 166 patients (99 patients had bilateral limbs scanned; 62 patients had 1 limb scanned; 4 patients had bilateral and unilateral scans; and 1 patient had 2 bilateral scans). The data on patient demographics (age and sex), comorbidities (diabetes status, hypertension, hypercholesterolemia, ischemic heart disease, renal failure, and smoking history) were prospectively collected. This study used noninvasive scanning of humans and was approved through clinical audit CA16-077 and the Service Improvement Project in accordance with the Declaration of Helsinki.

In our unit, we conduct a one-stop vascular clinic, where all patients with suspected lower limb arterial disease undergo duplex sonography (Toshiba Medical Systems, Crawley, England). The duplex disease definition was derived from a full-length examination from iliac to crural vessels with a local increase in the blood velocity of greater than 3, indicating stenosis of greater than 50%.[6] Duplex evaluations were performed by a senior vascular scientist and BlueDop by a combination of physicians and the vascular scientist, who were blind to each other's assessments. As a part of this study, each patient was also assessed simultaneously by the BlueDop device during the same visit. All comorbidities were defined in accordance to definitions provided by the World Health Organization.[7]

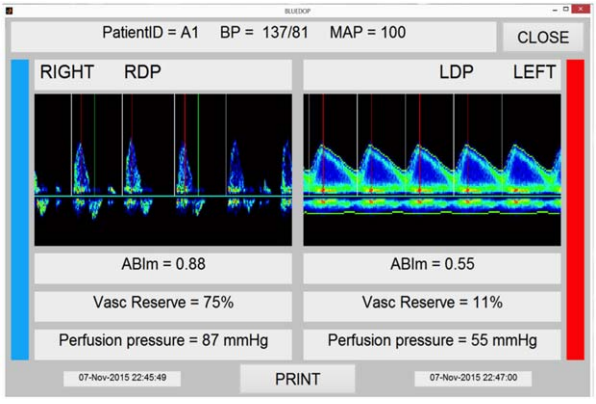
BlueDop Device

The BlueDop device was invented and designed by David H. King (senior vascular scientist) in 2010, with patent number EP2437654. The device comprises an egg-shaped handheld component (Figure 1), which communicates wirelessly (Wi-Fi) with an output monitor device (Figure 2). The device measures the mean arterial blood pressure through an algorithm (pressure from flow). The device extracts mean arterial blood pressure data from raw Doppler-shifted velocity/time spectral waveforms. For this process, a reference pressure is calculated from the arm. A systemic mean arterial pressure is estimated by adding one-third of the pulse pressure to the that of the diastolic pressure. In conclusion, the device provides the user with a cuff-free ABPI. The outcome of the pressure is reported through a range of indices highlighted in Table 1 (Figure 3). The formula for measurement of the indices is as follows: $MBP = MAP/(1 + PFF/VFF)$, where *MBP* indicates mean blood pressure; *MAP*, mean arterial pressure; *PFF*, (systolic – diastolic pressure)/mean arterial pressure; and *VFF*, velocity spectral maximum – minimum/mean.

The pressure from the flow algorithm is based on the ratio between the systolic and diastolic blood pressures divided by the mean arterial pressure (*MAP*). The ratio of the noninvasively obtained blood velocity pulse

Figure 1. Handheld component of the BlueDop device.

Figure 2. Output monitor device (Wi-Fi) connection. LDP indicates left dorsalis pedis artery; and RDP, right dorsalis pedis artery.



is divided by the mean blood velocity (*VFF*). A simple linear relationship was postulated and confirmed experimentally by comparing direct in vivo measurement of the mean blood pressure at the remote site with the algorithm-based remote mean blood pressure (*MBP*). This relationship was estimated from $MAP/(1 + PFF/VFF)$, which was computed in real time heartbeat by heartbeat. *VFF* is independent of transducer/artery angulation; therefore, the velocity measurements need not be calibrated. Thus, it is a simple matter to obtain "real-time" mean blood pressure data from almost anywhere within the arterial system.[8,9] The estimated cost of the device is about £8000, as one unit and can be used by any heath care professional.

Table 1. Index Range for Detection of Lower Limb Arterial Disease Using BlueDop

BlueDop Reading	Severity of Arterial Disease
≥0.8	No substantial stenosis
<0.8	Substantial stenosis
<0.5	Critical limb ischemia

Figure 3. Complete components of the BlueDop device.

Output Monitor Device

Figure 2 shows an arterial assessment conducted on a claudicant with symptoms of calf muscle pain in the left leg at a walking distance of 100 to 200 meters. Doppler spectra recorded from the dorsalis pedis artery bilaterally were analyzed in real time and automatically "accepted" as "physiologic waveforms" by using a proprietary software filter based on waveform repeatability. Apart from the patient identification and arm blood pressure, which was been manually entered by the operator, 8 clinically significant parameters are shown here (4 parameters per limb). The mean ABI is similar but not identical to the conventional ABI and is based on the "cuff-free" mean perfusion pressure (difference between mean arterial pressure and central venous pressure calculated at a pressure of 0) divided[10] by the mean arterial pressure. Normal values range from 1.00 to 0.80; values of 0.79 to 0.50 are associated with substantial arterial disease and less than 0.5 with critical limb ischemia. Maximal exercise stress tests on athletes and claudicants have shown that autoregulation limits perfusion pressure to half of the central mean blood pressure (mean ABI = 0.5) in the immediate postexercise period. At this point, there is no vascular reserve stored in the muscle bed (vascular reserve = 0%) after forced cessation of exercise due to loss of muscle power and pain, followed by a period of rest and recovery. Until the vascular debt is eliminated the mean ABI will remain close to 0.5 before rising toward the resting value as the muscle pain reduces. We calculate the vascular reserve as $200 \times$ (mean ABI – 0.5)%. A negative vascular reserve percentage is therefore consistent with the onset of critical limb ischemia.

The color-coded bars use yet another proprietary software filter to indicate substantial disease. They are based on the appearance of the Doppler spectra of a monotonic blood velocity decay between systole and the following systolic up-rise. This appearance is consistent with substantial arterial disease and is color coded in red. Blue indicates the absence of substantial arterial disease. The spectra show a nonmonotonic decay characteristic,

indicating the presence of reflections, known as the "notch." Absence of the notch has the advantage that it can be used as an independent confirmation of substantial disease. It has accuracy similar to that of the mean ABI and is graphically more obvious to an inexperienced operator. However, it cannot indicate the onset of critical limb ischemia and therefore is an ideal "backup" in the absence of a valid arm blood pressure. An examination of a limb can be performed in about 15 to 20 minutes after a 1-hour lesson.

Statistical Analyses

All of the statistical analyses were performed with SPSS version 20 software (IBM Corporation, Armonk, NY). All continuous variables were reported as medians with their corresponding interquartile ranges (IQRs) and percentages, and comorbidities were presented as their overall numbers and percentages. A receiver operating characteristic curve was created by plotting the true-positive rate (sensitivity) against the false-positive rate (specificity) for the new novel preassessment technique (BlueDop) compared to that of Duplex sonography (reference standard) for detection of arterial disease. In addition, the overall accuracy of the technique was also assessed in combination with the test of probability (P value) at the 95% confidence interval.

Results

The reported median age was 73 years (IQR, 65–81 years), with male predominance (n = 103 [62%] male versus 63 [38%] female). The most common comorbidity was hypertension (n = 111 [67%]), followed by hypercholesterolemia (n = 100 [60%]), active smoking (n = 71 [43%]), ischemic heart disease (n = 54 [33%]), cardiac arrhythmias (n = 37 [22%]), chronic obstructive pulmonary disease (n = 29 [17%]), and renal failure (n = 26 [16%]).

A total of 276 lower limbs were assessed by both BlueDop and duplex sonography at the one-stop clinic. The overall accuracy of the novel assessment technique was 92%, with a true-positive rate (sensitivity) of 95% and a false-positive rate (specificity) of 90% for detection of lower limb arterial disease. The test of probability was significant at $P < .01$ (95% confidence interval, 87.9%–95.4%; Table 2 and Figure 4). A total of 138 limbs were found to have arterial disease of any kind once examined with sonography, whereas this value for BlueDop was 147 limbs. The mean BlueDop Index in this group (n = 10) was 0.72 (IQR, 0.63–0.78). The median index value was 0.73 (Table 3). Therefore, BlueDop overestimated arterial disease in 10 individuals (false-positive) at a median index of 0.73.

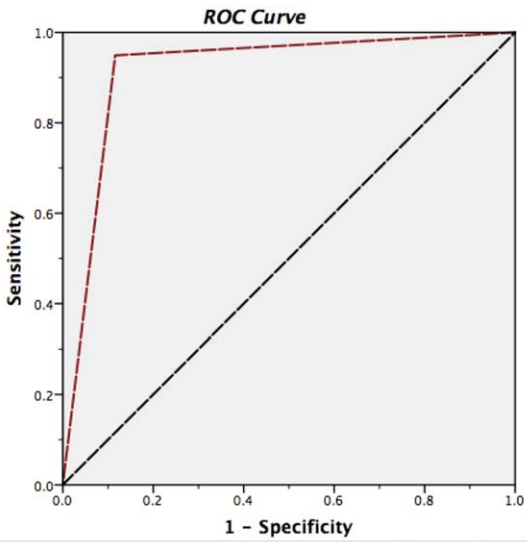
Table 2. Coordinates of the Receiver Operating Characteristic Curve for Sensitivity and 1 –Specificity

Sensitivity	1 – Specificity
0.992	0.199
0.992	0.191
0.985	0.184
0.977	0.184
0.977	0.177
0.962	0.156
0.940	0.149
0.925	0.135
0.917	0.128

Discussion

The outcome of this study demonstrates that BlueDop is an accurate and a sensitive device for detecting lower limb arterial disease. In this study, we only assessed the

Figure 4. Receiver operating characteristic curve analysis: BlueDop device to Duplex sonography for detection of arterial disease along with the accuracy, sensitivity, specificity, and P value at the 95% confidence interval.



Area Under the Curve						
Area	Std. Error	Asymptotic Sig.	95% Confidence Interval		Sensitivity	Specificity
			Lower Bound	Upper Bound		
0.917	*0.019*	*P<0.01*	*0.879*	*0.954*	*95%*	*89%*

presence or lack of arterial disease against the index range (Table 1) and not the anatomic and morphologic status. The diagnostic ability of this device could prove beneficial in the field of vascular surgery and medicine. In recent years, there has been a considerable reliance on diagnostic modalities, early recognition, and detection of arterial disease. Increased social awareness, a rise in the number of primary referrals, and dependence on an accurate diagnostic modality (such as duplex sonography) have markedly increased the burden on service providers, which has resulted in longer waiting lists (referral and assessment), patient anxiety, and reduce cost-effectiveness of health care providers.[11] In addition, the use of duplex sonography is operator dependent and demands hours of training and reporting.[8] The BlueDop device has a minimal learning curve, is easy to use, and is portable. Therefore, it can be used by various primary care providers. This ability permits a reasonable filtration of patients by general practice, tissue viability nurses, and other practitioners, which can subsequently reduce the load of inappropriate referrals to tertiary centers, allowing much more focused and patient-directed care.

Another important aspect of this device is its applicability in tertiary specialized units. The ABPI requires a specialist or well-trained personnel. In addition, it can provide inaccurate results in diabetic and calcified arteries. Furthermore, the presence of wounds and dressing in the lower limbs could be challenging for ABPI calculation.[12] However, BlueDop can be useful in such circumstances, with accurate measurements. This device has also been shown to be accurate in detecting failing arteriovenous fistulas (surveillance) in hemodialysis patients.[8] A future application of this device could be in diagnosing the anatomic levels of lower limb arterial disease, pending future investigations and research.

Table 3. Overestimation of Lower Limb Arterial Disease in 10 Individual at a Median Index of 0.73 (IQR, 0.63–0.78) by BlueDop

BlueDop Index Positive for Arterial Disease	Duplex Sonography for Arterial Disease
0.63	Negative
0.73	Negative
0.78	Negative
0.73	Negative
0.69	Negative
0.74	Negative
0.75	Negative
0.74	Negative
0.72	Negative
0.78	Negative

Strengths and Limitations

This study had adequate (n = 276 limbs) power for a reasonable inference; however, a larger sample size in a randomized setting would have been more optimal. The study benefited from a prospective comparative design and a limited selection bias, as it was consecutive in design. The only setback was related to low specificity (90%); however, sensitivity and specificity are inversely proportional, meaning that when the sensitivity increases, the specificity decreases.[13] In this study, we did not compare the traditional ABPI to that of the BlueDop device, as the main purpose of this study was to evaluate the accuracy of this device (for detection of arterial disease independently), and from the literature, it is evident that the traditional ABPI is not accurate when lower limb arteries are calcified and affected by diabetes mellitus. Therefore, a comparative measurement obtained from the traditional ABPI versus that of the new device would have required another reference point and evaluation.

Conclusions

It appears that BlueDop is an accurate and effective device for detecting lower limb arterial disease and can serve as an important filtering tool in primary care and various other centers where arterial disease or atypical lower limb pain is suspected. In addition, this device, with its portable nature and minimal learning curve, can be used in any office-based setting and is a good alternative to the traditional ABPI and Doppler imaging, that have proven to be ineffective. However, this device cannot be a replacement for duplex sonography without further investigations.

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