

Pressures, indexes and peripheral arterial disease: Time to rethink our approach?

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Most patients with peripheral arterial disease (PAD) are asymptomatic. Despite the absence of symptoms, these patients have a significantly increased risk of death and adverse vascular events.¹ Early detection of individuals with asymptomatic PAD facilitates prompt introduction of secondary prevention (lifestyle modification, smoking cessation, anti-platelet medications and lipid management). Ankle-brachial pressure index (ABPI) is generally considered the default screening test for PAD. It is relatively simple and non-invasive, with an ABPI less than 0.9 considered diagnostic for PAD. The prevalence of ABPI less than 0.9 among people under 50 years of age with no cardiovascular risk factors is less than 1% and routine PAD screening with ABPI is not recommended.² PAD screening with ABPI is reasonable in asymptomatic individuals with at least one atherosclerotic risk factor.¹

ABPI is an attractive point-of-care option to screen for PAD. However, varying degrees of arterial stiffness may modify or abrogate the ABPI values obtained. This results in false-negative ABPI values that appear in the normal range, but in fact simply reflect vessel calcification in the presence of PAD. Recent interest has focused on the use of toe pressure measurements as an alternative as the hallux digital arteries are thought to be relatively spared from calcification and therefore less prone to false-negative results. However, it is important to point out that toe pressure have not been a useful predictor of limb salvage in patients with critical limb treating ischaemia. Either the absolute systolic toe pressure (ASTP) or the toe-brachial index (TBI) can be used.

In this issue of the *Annals*, Ng et al. reported data from a large Singapore diabetic cohort in which the diagnostic performance of ASTP and TBI were evaluated.³ Both ASTP and TBI had area under the receiver operating characteristic (ROC) curve values of 0.89 and 0.94, respectively, which are in the range indicating excellent test performance. An ASTP threshold of 95.5mmHg yielded a sensitivity of 0.84 and a specificity of 0.86 for

ABPI less than 0.9. Taking approximate values from the data illustrated in Fig. 2 (Ng et al.), 275 of 1,454 screened individuals (19%) had an ASTP less than 95.5mmHg. Based on these data, 190 out of 1,000 diabetics will have PAD. Of these 1,000 diabetics, ASTP less than 95.5mmHg will correctly detect PAD in 160 patients. It will miss PAD in 30 patients who actually have the condition. It will correctly detect the absence of PAD in 697 patients but will incorrectly label 113 patients as having PAD when they are, in fact, PAD-free. With 11% of the hypothetical cohort being false-positive, there may be an argument that an ASTP-positive should be confirmed on another test, such as duplex ultrasound, computed tomography (CT) or magnetic resonance angiography (MRA), before initiating pharmacological interventions with the associated side effects.

Underlying all these calculations is the widely held assumption that an ABPI value less than 0.9 indicates the presence of PAD. However, when ABPI is compared to imaging modalities for the detection of arterial stenosis $\leq 50\%$, the results may not support this belief. A recent meta-analysis that pooled results from studies comparing ABPI to an imaging reference standard (duplex ultrasound, CT, MRA or digital subtraction angiography) reported a pooled sensitivity of 61% and a specificity of 92%. If we apply these figures to the hypothetical Singapore diabetic cohort of 1,000 patients, how does ABPI perform? Only 114 patients will be correctly labelled as PAD, the condition will be missed in 76 patients, while another 65 patients will have a false-positive result. TBI was evaluated in the same review. It performed somewhat better in terms of sensitivity (81%) but was less specific (77%).⁴

Clearly, it is unrealistic to suggest that all diabetic patients should be screened regularly for occult PAD with an imaging modality. The current imaging modalities are restricted to symptomatic patients given the use of ionising radiation (CT and invasive angiography),

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contrast-related renal injury (CT, invasive angiography and MRA) and operator-dependency (duplex ultrasound). There is a need for a simple bedside screening test. Novel technologies are beginning to focus more on toe perfusion pressures over the traditional indices, adding another dimension for PAD screening in these patients. The full value of these remains to be seen. As the situation stands, the diagnostic performance of the available bedside tests (ABPI, TBI and ASTP) could use improvement compared to the imaging modalities.

Where to go from here? Perhaps the debate is not whether ASTP is equivalent to ABPI or TBI. Perhaps it is time to utilise all the available data rather than just consider the component parts. Would a combination of ASTP, TBI and ABPI perform better than any component alone? Could they be integrated with other measures such as pulse waveform or velocity acceleration time? Utilising all the available resources is theoretically the most ideal format for providing quantitative evidence of disease. Bedside technology is improving with more

data now easily acquired in the clinic. An integrated approach could yield significant improvements in how PAD is investigated and diagnosed, but first the dogma that ABPI less than 0.9 always indicates PAD should be revised.

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