



Non-invasive vascular screening test to diagnose peripheral vascular disease

Lawrence A. Lavery, Peter Andrew Crisologo

Department of Plastic Surgery, University of Texas Southwestern Medical Center, Dallas, Texas, USA

Correspondence to: Lawrence A. Lavery, DPM, MPH. Department of Plastic Surgery, University of Texas Southwestern Medical Center, 5323 Harry Hines Blvd, Dallas, Texas, USA. Email: larry.lavery@utsouthwestern.edu.

Provenance: This is an invited Editorial commissioned by the Section Editor Kaiping Zhang (AME College, AME Group, China).

Comment on: Vriens B, D'Abate F, Ozdemir BA, *et al.* Clinical examination and non-invasive screening tests in the diagnosis of peripheral artery disease in people with diabetes-related foot ulceration. *Diabet Med* 2018;35:895-902.

Submitted Nov 20, 2018. Accepted for publication Nov 22, 2018.

doi: 10.21037/atm.2018.11.54

View this article at: <http://dx.doi.org/10.21037/atm.2018.11.54>

One of the biggest unmet needs in diabetic limb salvage is an effective tool to identify peripheral arterial disease (PAD) in diabetic foot ulcers to predict wound healing and amputation level survival. PAD in diabetes is characterized by multiple segmental occlusions below the trifurcation and microvascular disease. Many methods have been used to assess PAD but there is not a consensus (1,2) regarding the best method. For example, many use whether pedal pulses are palpable or not but this is not to be reliable in neuropathic diabetics where waveform analysis and toe brachial indices are more reliable (3). The aim of this editorial was to evaluate the study by Vriens and colleagues (4) who used seven tests to evaluate PAD that are widely available [ankle systolic pressure, ankle brachial pressure index (ABPI), toe pressure, toe brachial index, pole test, transcutaneous oxygen and digital waveforms] and eight clinical exam findings (foot pulse, hair loss, atrophy, dependent rubor, cool skin, blue/purple skin, capillary refill, and venous filling).

The authors used likelihood ratios as the main focus of their analysis. In addition, they provided positive and negative predictive values and sensitivity and specificity data. When the positive likelihood ratio (PLR) is >10 , this indicates the test confirms the presence of the disease. Two tests had a PLR >10 (pole test LHR 10.29 and toe pressure >50 mmHg LHR 17.55). Negative likelihood ratio (NLR) values <0.1 are indicative that the test can exclude the disease. The NLR was poor for all of the tests evaluated and ranged from 0.15 to 1.0.

There are mythological issues in the criteria for the reference standard and how the tests were “scored”

or interpreted that are concerning. When evaluating the efficacy of a test to identify a disease process, the reference standard used to define the disease is critical. In this study, the “gold standard” for PAD was based on duplex ultrasound of lower extremity arteries (femoral, popliteal, posterior tibial and anterior tibial arteries) that demonstrated $>50\%$ stenosis, or monophasic waveforms of the popliteal artery at mid-calf, posterior tibial artery at the level of the medial malleolus and the dorsalis pedis on the dorsum of the foot. At face value, duplex ultrasound that shows $>50\%$ stenosis of a lower extremity artery seems arbitrary and not specifically related to disease that would require intervention or disease severity associated with poor clinical outcomes.

The other part of the authors' assessment that is concerning, is that they did not evaluate the systolic ankle pressure, ABPI, or pole tests specifically in the diseased artery or arteries that were identified by duplex ultrasound as abnormal. Instead, the best artery was selected with the best test result to include in the analysis. For instance, if the posterior tibial artery had $>70\%$ stenosis while the peroneal and anterior tibial arteries did not demonstrate stenosis, the ankle systolic pressure, ABPI, and pole test should focus on the diseased artery to evaluate PAD and the other two arteries to demonstrate lack of disease. Instead only the best pressure, the best ABPI, and best pole test would have been used in the analysis to identify PAD. It would be more logical to determine if the diseased artery was identified by the seven tests in the corresponding artery. The author's approach introduces a fatal flaw in the methodology.

Another issue that probably lead to misclassification of PAD is related to the author's definition of an ankle brachial pressure index >1.3 as criteria for PAD. Non-compressible peripheral arteries are most commonly associated with Mönckeberg's sclerosis. Mönckeberg's is a form of arterial sclerosis where the tunica media becomes calcified. However, non-compressible arteries are not necessarily associated with occlusion. Generally, non-compressible systolic pressure and ABPI >1.30 are considered unreliable. So, in the study, these subjects, or the arteries that were non-compressible should have been excluded.

Another source of concern is a prior cut point for systolic ankle pressure, toe pressure, toe brachial index, and transcutaneous oxygen measurements that the authors selected to define disease. Some of these may be cited and used by convention. There does not seem to be robust data to support these selections. The authors could have used their data to establish criteria for the seven tests that could then be used to define PAD by finding better cut points.

This paper by Vriens *et al.* (4), asks important questions concerning which non-invasive test is best to use to assess PAD in the neuropathic diabetic with a foot ulcer. While they found that the toe-brachial index and the tibial waveform were most useful in detecting PAD in this population, the concerns raised here should be taken into account going forward. Tools to diagnosis PAD and to predict wound healing continue to be an unmet need. New technology in this area such as various approaches to hyperspectral imaging and combinations of established tests may help us meet these needs in the near future.

Cite this article as: Lavery LA, Crisologo PA. Non-invasive vascular screening test to diagnose peripheral vascular disease. *Ann Transl Med* 2018;6(Suppl 2):S108. doi: 10.21037/atm.2018.11.54

Acknowledgements

None.

Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

References

1. Brownrigg JR, Hinchliffe RJ, Apelqvist J, et al. Performance of prognostic markers in the prediction of wound healing or amputation among patients with foot ulcers in diabetes: a systematic review. *Diabetes Metab Res Rev* 2016;32 Suppl 1:128-35.
2. Brownrigg JR, Hinchliffe RJ, Apelqvist J, et al. Effectiveness of bedside investigations to diagnose peripheral artery disease among people with diabetes mellitus: a systematic review. *Diabetes Metab Res Rev* 2016;32 Suppl 1:119-27.
3. Williams DT, Harding KG, Price P. An evaluation of the efficacy of methods used in screening for lower-limb arterial disease in diabetes. *Diabetes Care* 2005;28:2206-10.
4. Vriens B, D'Abate F, Ozdemir BA, et al. Clinical examination and non-invasive screening tests in the diagnosis of peripheral artery disease in people with diabetes-related foot ulceration. *Diabet Med* 2018;35:895-902.