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Should flow-mediated dilation be conducted on the legs of patients with peripheral arterial disease?

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The recent study "Local Association Between Endothelial Dysfunction and Intimal Hyperplasia: Relevance in Peripheral Artery Disease" assessed endothelial function, using flow-mediated dilation (FMD), in the legs (superficial femoral artery) and arms (brachial artery) of patients with peripheral arterial disease (PAD).1 The authors concluded that endothelial function was not impaired in the arms, but was reduced in the legs of PAD patients compared to age-matched controls. While the article supports previous research suggesting that the brachial artery may not provide a global index of endothelial health for all populations, including those with spinal cord injury,2 it is contrary to two previous PAD studies reporting reduced brachial FMD.3, 4 This publication is particularly timely as the clinical relevance of FMD has recently come under attack for reasons such as poor measurement reliability, lack of appropriate covariate analysis, concerns over expressing FMD as a ratio 5, and improper normalization to the FMD stimulus.5 We suggest each of these concerns are highlighted in this study.

First, with the between-day coefficient of variation for the standard brachial FMD test being as high as 50%,6 no mention of power analysis or variance estimates and small group sizes (n=10), the analyses potentially suffer from a lack of statistical power. Second, FMD was expressed as ratio, which can result in mathematical error propagation and allometric scaling issues.5 FMD should be expressed as the absolute change score, using baseline diameter and shear stress as covariates.5, 7 Last and perhaps most important, FMD can only be assessed if reactive hyperemia induces a sufficient shear stress stimulus to activate the endothelial cells, which may be prevented by an obstructed arterial lumen in PAD. In addition, an obstructed arterial lumen would induce a non-laminar flow profile, thereby invalidating one of the assumptions of Poiseuille's Law- based shear stress calculations.

Because of these issues, the published findings should be interpreted with caution. While we commend the authors on conducting important work in this field, we suggest additional studies are required to elucidate whether FMD in the lower limbs is a true marker of endothelial function in patients with PAD.

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Conflict of Interest:

None declared

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