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Authors' reply

We thank Hersant and colleagues for their interest in our work [1].

Our study was principally designed to address the utility of clinical examination and adjunctive tests to exclude peripheral artery disease (PAD) in people with diabetes related foot ulceration. We emphasise the importance of negative likelihood ratio (and sensitivity) throughout as a missed diagnosis has potentially more severe consequences. The study demonstrated that the majority of clinical and bedside tools are unreliable in excluding PAD. This is an extremely important finding for the multidisciplinary teams caring for these individuals.

We acknowledge that specificity and to a lesser extent sensitivity correlate indirectly with disease prevalence due a variety of factors including spectrum effects. Broadly speaking this equates to disease severity [2]. Readers therefore need to know disease prevalence and severity for interpretation of applicability to their patients. For this reason we have already stated in the manuscript that 20 (33%) participants had PAD as defined by our gold standard. We also detail the distribution of SINBAD SVS WifI scores for study participants. Hersant and colleagues suggestion that reporting the number of abnormal screening, as opposed to gold standard, test responses would directly aiding interpretation is incorrect.

Monophasic flow in distal tibial arteries demonstrated the most favourable negative likelihood ratio to exclude PAD. The question of whether infection or exercise could have led to misclassification of hyperaemic flow as monophasic is therefore important. It must be emphasised that hyperaemic flow can be differentiated from monophasic flow as it is a variant of the normal triphasic waveform in which the third component extends as forward flow throughout diastole. This was classified as no PAD in the analysis. Additionally, as they state the proportion of participants with severe infection in our cohort was low. The highlighted difference between those classified as with and without infection using the SVS Wifi and SINBAD is due to differences in definition used by the two systems. We do not use cotton socking of the limb. We understand the concern regarding the reporting of monophasic flow as a screening tool. We make it clear in the manuscript that although an interesting result the tester was unblinded. We also explain why the specificity and positive predictive value are 1 i.e. because the gold standard definition included this finding. We would state therefore that further studies should be performed before widespread adoption of distal tibial waveforms as a screening tool for exclusion of PAD.

Whilst it is correct to say that TcPO2 is influenced by the microcirculation, it is still used pragmatically to screen for PAD by many groups. Our study demonstrates that such utilisation is ill advised. The appropriateness of TcPO2 to predict ulcer healing is a separate and more complex question that was not part of our study design. We selected a TcPO2 of below 60mmHg as the cut off for PAD precisely because the normal value lies between 50 to 70mmHg. We are testing TcPO2 as a screening tool rather than a prediction of healing tool, where the 30mmHg would apply. The use of the higher cut off would have improved negative likelihood ratio and impaired the positive likelihood ratio. However, it should be noted that the area under the receiver operator characteristic curve (AUC) for this modality was only 0.55, suggesting that an alternative cut-off would be unlikely to significantly improve the discriminatory ability of the test. With such a poor AUC we suspect that the influence of participant position on the outcome would be very limited.

The overall conclusion of the study is that clinical and device based screening for PAD in people with established ulceration is limited. Even the two most promising tools, distal tibial waveform analysis and toe brachial index, need to be used with caution and formal diagnostic imaging requested if there is no response to best medical and wound care.

References
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Vriens B[1], D'Abate F[2], Ozdemir BA[3], Fenner C[2], Maynard W[2], Budge J[2], Carradice D[3], Hinchliffe RJ[4].

Corresponding Author:
Baris Ata Ozdemir
drbaozdemir@gmail.com

1 Vascular Department, Colchester General Hospital, Colchester Hospital University NHS Foundation Trust, Colchester.
2 St. George's Vascular Institute, St. George's Hospital, St. George's University NHS Foundation Trust, London.
3 Southmead Hospital, North Bristol NHS Trust, Bristol, UK
3 Academic Vascular Surgical Unit, Hull York Medical School, Hull.
4 Bristol Centre for Surgical Research, University of Bristol, Bristol, UK.