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Comment on 'Numerical assessment and comparison of pulse wave velocity methods aiming at measuring aortic stiffness'

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Abstract.

A recent numerical study investigated the potential utility of peripheral PWV measurements for assessing aortic stiffness by simulating pulse wave propagation through the arterial tree. In this Comment we provide additional analysis of the simulations in which arterial compliances were changed. The analysis indicates that relationships between aortic and peripheral pulse transit times (PTTs) may not be constant when compliances change. Consequently, peripheral PWV measurements may have greatest utility in particular clinical settings in which either: an assumption can be made about possible changes in compliance, allowing aortic PTT to be estimated from peripheral PTT; or, one wishes to assess changes in peripheral PWV over time.

We read with interest the recent paper by Obeid *et al.* [1]. In this paper a numerical model of pulse wave propagation was used to investigate the clinically important issue of whether pulse wave velocity (PWV) measurements obtained from peripheral sites are reliable indicators of aortic stiffness. Strong correlations were observed between the aortic pulse transit time (aPTT) and PTTs obtained peripherally (hereafter, peripheral PTTs). This was shown by \mathbb{R}^2 values of 0.95 for the finger-toe PTT (ft-PTT), and 0.96 for the brachial-ankle PTT (ba-PTT). These were observed in a set of pulse wave simulations in which resistance, heart cycle length, and maximal heart elastance were varied (Fig. 5 of [1]). The strong correlations in this set of simulations, hereafter set (a), suggest that under these conditions peripheral PTTs could be used to estimate aPTT.

The paper also presented data from three additional sets of simulations in which: (b) peripheral compliances were varied; (c) central compliances were varied; and (d) all compliances were varied simultaneously (Fig. 6 of [1]). Figure 1 summarises the data from all four sets of simulations, showing the relationships between aortic and peripheral PTTs for each set of simulations. The gradients of the best-fit lines changed when arterial compliances were changed, indicating that the relationships between



Figure 1. The relationships between aortic pulse transit time (aPTT) and peripheral PTTs for the four sets of simulations presented in [1]. Best-fit lines are shown for brachial-ankle (ba-PTT) on the left, and finger-toe (ft-PTT) on the right. The four sets of simulations were generated by: (a) holding compliances constant whilst varying resistance, heart cycle length, and maximal heart elastance; (b) varying central compliances; (c) varying peripheral compliances; and (d) varying all compliances. The gradients of the best-fit lines, and therefore the relationships between aPTT and peripheral PTTs, appear to be influenced by the relative nature of changes in compliances of central and peripheral arteries.

aortic and peripheral PTTs were dependent on how compliances were varied in the simulations. This indicates a potential limitation in inferring aPTT from peripheral PTTs: the relationships between them may not be constant when compliance changes. In particular, the relative nature of changes in compliances of central and peripheral arteries appears to impact the relationships, as illustrated by the arrows in Fig. 1. If this remains the case in *in vivo* studies, then peripheral PTTs may have greatest clinical utility in two scenarios. Firstly, peripheral PTTs could be used to estimate aPTT if an assumption can be made about the relative nature of changes in central and peripheral PTTs. Secondly, it may be useful to assess changes in peripheral PTTs over time in an individual, even if the resulting PTTs cannot be used to estimate aPTT.

Previous numerical studies have also investigated whether peripheral PWVs can be used as reliable indicators of aortic stiffness. Willemet *et al.* performed a study in which several cardiac and arterial parameters were varied to create a database of virtual healthy subjects, containing pulse waves at several arterial sites [2]. By measuring PWVs across several arterial paths, the authors found that peripheral PWVs were not reliable indicators of aortic stiffness. They concluded that ba-PWV is influenced by the properties of both the aorta and peripheral arteries, and overestimates aPWV. This is to be expected since the arterial path used in ba-PWV measurements includes both the aorta and peripheral arteries. In addition, they observed that carotid-radial (cr) and femoral-ankle (fa) PWVs do not capture stiffening of the aorta. This is to be expected since the arterial paths used in cr-PWV and fa-PWV measurements do not contain the aorta. Furthermore, a recent study by Xiao *et al.* found that even carotid-femoral PWV, the current gold standard for assessment of aortic stiffness, is influenced by factors other than aortic stiffness such as left-ventricular ejection time and peripheral resistance [3].

To conclude, numerical studies such as that presented by Obeid *et al.* provide opportunity to investigate the performance of methods for assessing aortic stiffness in a systematic manner which cannot be easily performed *in vivo*. In our view, the results presented in [1] indicate that peripheral PWV measurements may have particular utility in certain clinical settings, since relationships between aortic and peripheral PTTs may not be constant when compliances change. Further *in vivo* studies are required to assess their utility in such settings.

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Data Access Statement

The code and data used in this research are provided as a supplementary Matlab (\mathbb{R}) file. Further information can be found by emailing *research.data@kcl.ac.uk*.

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