subtype causes coronary vasoconstriction in mice (3,4), reinforcing our point that \( \alpha_1 \)-subtype expression is similar in the mouse and human heart and that mouse models can be relevant to human disease. We also believe that our identification of \( \alpha_{1D} \) as the major \( \alpha_1 \)-AR subtype in human coronaries (1) and \( \alpha_{1A} \) and \( \alpha_{1B} \) as the major subtypes in human myocardium (5) will facilitate much more precise studies with agonists and antagonists in large animals and humans.

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Determinants of Raised Pulse Pressure in Women

Cecelja et al. (1) conclude that increased wave reflection, not arterial stiffness, determines pulse pressure, including central pulse pressure (cPP), in women. They base this conclusion on regression analysis showing that the ratio of femoral to aortic diameter (D_{FA} [assumed an index of central-peripheral artery discontinuity and hence of wave reflection]) was a significant determinant of pressure augmentation \( \Delta P_{aug} \) whereas pulse wave velocity (PWV [a measure of arterial stiffness]) was not. However, from Table 3 in their article (1), it appears that D_{FA} accounts for only \( \approx 2\% \) of variation in \( \Delta P_{aug} \). In contrast, PWV accounts for 30% of variation in P_{1}.

In analysis of the contribution of P_{1} and \( \Delta P_{aug} \) to variance in cPP, the relative contributions (for the whole cohort) were 22% and 76%, respectively. We therefore calculate that PWV contributes 6.6% and D_{FA} 1.5% to cPP variance. From Figure 2 (1), P_{1} contributes about two-thirds of total cPP (for the whole cohort). For the whole group, the proportional contribution to cPP, therefore, is \( \approx 0.7\% \) for wave reflection and 20% for arterial stiffness (assuming PWV and D_{FA} are indeed appropriate surrogates and using results from Table 3 [1]).

These analyses suggest an entirely opposite conclusion to the authors. We believe their data are actually consistent with the proposition that arterial stiffness, not wave reflection, is the major determinant of both cPP and its variation in this cohort of women; a lack of association between PWV and T_{1} is also consistent with this interpretation.

Perhaps the "simple approach" adopted by Cecelja et al. (1) to assessing reflected pressure is overly simplistic. The authors could not formally decompose central blood pressure into forward and reverse going waves (via reflection coefficient or wave-intensity analysis), and there are problems using central T_{1} to delineate forward and reverse going waves:

1. P_{1} only represents the full magnitude of ejection wave if any reflected wave arrives after the peak (i.e., T_{1} is a local minimum rather than an inflection point). Peak ejection pressure would otherwise be lost under the reflected component.

2. \( \Delta P_{aug} \) does not correspond to the magnitude of any reflected wave; even a small reverse going wave arriving early in ventricular ejection will produce an inflection point interpreted as a large \( \Delta P_{aug} \); similarly, a large wave arriving late may result in a small \( \Delta P_{aug} \). Reflection site and PWV predominantly determine \( \Delta P_{aug} \) not the magnitude of the reflected wave.

3. It is well demonstrated that estimated central T_{1} obtained by transfer function techniques is unreliable in representing true central inflection point (2,3).

Among women \( \approx 60 \) years of age, Cecelja et al. (1) observed a small influence of aortic diameter on P_{1} with no effect of D_{FA}, supporting that aortic stiffness and diameter (4) rather than wave reflection are important in determining PP in this age group in whom it is an important predictor of cardiovascular risk.

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Reply

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