

# Letters to the Editor

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## Effects of Ramipril on Arterial Stiffness

To the Editor:

The study by Ahimastos et al<sup>1</sup> described reduction in aortic pulse wave velocity (PWV) with 10 mg daily ramipril; this was not associated with any fall in mean brachial artery pressure. There is a curious anomaly in this study, which casts doubt on the conclusions. Whereas the authors report no change in mean pressure with 10 mg ramipril compared with placebo, there was a highly significant reduction in brachial systolic (5.4 mm Hg) and diastolic (6.3 mm Hg) pressures. How is it possible for both systolic and diastolic pressures to fall but mean pressure to be maintained? We have never seen such a phenomenon. We do, however, have serious reservations about using the Dinamap Vital Signs Monitor to measure cuff brachial pressure, because this device has been shown to be inaccurate in a number of studies, especially for diastolic blood pressure.<sup>2</sup> If related to diastolic pressure at the foot of the waveform (from which PWV is measured), the fall in aortic PWV may be largely attributed to passive reduction in distending pressure. We, and others, certainly have noted this.<sup>3–5</sup> Further, the authors calculated carotid systolic pressure from brachial mean and diastolic pressure. Such calculation is based on equivalence of mean pressure and diastolic pressure in the carotid and brachial arteries. If one is incorrect, such a calculation will be erroneous.

Views on direct effects of ramipril and other drugs on aortic stiffness will remain unclear until these technical issues are addressed. There is no doubt that ramipril and similar drugs reduce aortic augmentation<sup>3–5</sup> and, hence, arterial compliance as measured by Ahimastos et al.<sup>1</sup> There is, however, doubt on any direct effect on aortic PWV, especially when based on anomalous recordings of arterial pressure.

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## Response: Ramipril Reduces Large Artery Stiffness

We thank Prof O'Rourke and colleagues for their interest in our article,<sup>1</sup> but there are no anomalies in our data. Our pulse wave velocity measurements do not rely on calibration of the carotid arterial waveform.<sup>1</sup>

We determined the time difference in the systolic upstroke of the pressure waveform at the carotid and femoral arteries; the issue of brachial blood pressure measurement is therefore irrelevant to this parameter.

In our study, ramipril reduced systolic/diastolic blood pressure by 5/6 mm Hg,<sup>1</sup> a magnitude similar to that reported with 2 years of ramipril therapy at the same dose (10 mg) in the Heart Outcomes Prevention Evaluation (HOPE) trial (4/3 mm Hg).<sup>2</sup> In our study and the HOPE trial, blood pressure measurements were made the day after the last dose. We neglected to mention that all measurements were made approximately 24 hours after the last dose of ramipril in our original manuscript and are grateful to Prof O'Rourke and his coauthors for giving us the opportunity to correct this omission. The rationale for the timing of blood pressure measurements was to minimize the acute effects of ramipril on blood pressure and enable us to assess chronic (potentially structural) effects on arterial stiffness.

Mean blood pressure was also reduced in our study (by 2.3 mm Hg, Table 2 in Ref. 1), but this was not significantly different from the placebo group.<sup>1</sup> The 5/6 mm Hg reduction in systolic/diastolic blood pressure in conjunction with a 2 mm Hg reduction in mean pressure is certainly plausible. This likely results from changes in the morphology of the arterial pressure waveform, including changes in wave reflection as indicated by the reduction in augmentation index with ramipril treatment (Table 2).

All blood pressure measurements have their limitations, but the Dinamap Vital Signs Monitor (model 1846SX) used in our study is better than most in assessing mean arterial pressure.<sup>3</sup> This model is distinct from the 8100 portable model quoted by O'Rourke and colleagues.<sup>4</sup> In a study by Lehmann et al, the correlation coefficient between Dinamap 1846SX and direct aortic mean blood pressure was 0.909.<sup>3</sup> Furthermore, the Dinamap 1846SX demonstrated a smaller absolute error for both mean and diastolic pressure and a trend toward smaller error with systolic pressure in relation to direct aortic pressures than other devices tested.<sup>3</sup> The fact that the change in systolic blood pressure measured with manual sphygmomanometry during ankle-brachial index measurements in our study gave the same result as the Dinamap 1846SX (Table 2)<sup>1</sup> also validates our measurements. Brachial mean and diastolic blood pressures were used to calibrate the carotid arterial waveform, so our central systolic pressure measurements and systemic arterial compliance calculations are reliable. Finally, all our data are reported as change in pressure within patients so that any systematic error would be minimized.

In conclusion, our data clearly show that 6 months treatment with ramipril increases systemic arterial compliance and reduces pulse wave velocity and augmentation index.<sup>1</sup> Mean blood pressure was not significantly reduced by ramipril, but we agree that slight reductions may contribute to reduced arterial stiffness in some individuals. Our cell culture data suggest that structural changes to the elastic matrix are also a likely mechanism.

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