hemodynamic effects mediated through pulse wave velocity is the important pathophysiological factor. Furthermore, the issue still remains whether this phenomenon acts either as a primary determinant of adverse outcomes or simply as a biomarker of systemic disease. The increase in ascending aortic diameter (decreasing pulse wave velocity) and increase in regional length (increasing transit time at a given pulse wave velocity) with very little change in other segments, as reported by Hickson et al. (1) (their Fig. 4), would have a significant effect on the relative timing of any reflected pressure wave within the cardiac cycle and therefore on central blood pressure. The net influence of these changes would be to delay return of any reflected wave; although these could be seen as compensatory changes, they apparently generally fail, as aging is associated with earlier (systolic) pressure augmentation. It therefore remains uncertain whether the established deleterious effect of aortic stiffening (age or disease related) is mediated by the effect of local changes in mechanics and geometry as has been suggested (5), secondary effects related to suboptimal hemodynamic coupling, or whether increased aortic stiffening is merely acting as a biomarker of a progressive systemic condition (e.g., ageing, atherosclerosis, arteriosclerosis).

The influence of aortic diameter as opposed to wave reflection and pulse wave velocity in determining cardiovascular risk have been debated, and we would suggest that the most relevant issue is how these factors are related to central blood pressure. The work by Hickson et al. (1) offers further insight into these issues and, equally relevant, highlights the potential for cardiac magnetic resonance to individualize cardiovascular risk prediction and management.

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REPLY

We thank Dr. Nelson and colleagues for their interest in our recent work concerning the effect of age on the biomechanical properties of the human aorta (1). We observed the greatest age-related difference in the aortic pulse wave velocity in the distal abdominal aorta, and the least in the aortic arch, suggesting that the distal aorta stiffened most with age. As we noted in our discussion, and as Dr. Nelson and colleagues reiterate, others have reported the converse, that is, that the ascending aorta stiffens most with age (2,3). No doubt, there are several explanations for these discrepant observations, not least the very small sample sizes reported by some authors (2,3), the use of differing techniques to estimate regional stiffness, methodological issues such as the use of nonsimultaneous, peripheral pressure when calculating distensibility/compliance (3), and technical issues such as inaccurate edge detection with cardiac magnetic resonance with varying sequences (4). Interestingly, a recent postmortem analysis of a relatively large collection of human aortae suggests that the abdominal aorta may indeed stiffen most with age (5). However, further carefully conducted studies employing large sample sizes, with prospective in vivo observations are required.

We would agree with Dr. Nelson and colleagues that it is unclear how changes in aortic stiffness alter cardiovascular risk. However, we believe that changes in aortic pressure probably play an important role. Although the ascending aorta may stiffen less with age, changes in the stiffness of the first part of the aorta are likely to have a more profound effect on aortic pressure than do changes in the more distal parts. This is because most of the volume buffering (or windkessel effect) occurs in the first part of the aorta. Therefore, we hypothesized that dilation of the aorta helps to offset the detrimental effect of aortic stiffening on peak systolic pressure by increasing the capacitance of the aorta. Despite this potential protective effect, stiffening and dilation will still lead to a loss of elastic recoil and fall in diastolic pressure. Since coronary perfusion occurs mainly in diastole, such an effect is likely to be detrimental to the myocardium. Unfortunately, we did not assess the windkessel effect in our original study because of the limitation of the cardiac magnetic resonance technique we employed with respect to accurate edge detection, but this could be done with alternative approaches.

Finally, we believe that determining which part of the aorta stiffens most with age remains an important question, because the structure of the aorta changes considerably along its length. Thus, we may have a better knowledge of the processes involved in age-related stiffening, or arteriosclerosis, if we can first define the region of the aorta this affects most, and then relate stiffness of the structural and biochemical changes at this and other locations, which some authors have already attempted to do. Ultimately, these data may help provide targets for future antiarteriosclerotic interventions.

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