hematic effects mediated through pulse wave velocity is the
important pathophysiological factor. Furthermore, the issue still
remains whether this phenomenon acts either as a primary deter-
minant 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 employ-
ing 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 impor-
tant 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 detrimen-
tal 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 myocard-
ium. 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 inter-
ventions.

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