is that age-related changes explain these differences. A proportional decrease in aortic collagen with advancing age has been previously described.[2] In our laboratory, we have looked at messenger RNA expression in dilated aortas with microarray gene chip analysis. Looking at expression of tenascin, for example, we have found similar expressions in tissues from patients with aneurysms and older control subjects (mean ages 63.3 ± 6.4 years, 95% confidence interval 59.8-66.9 years, and 48.8 ± 4.9 years, 95% confidence interval 35.3-62.3 years, respectively). We too have struggled to obtain appropriately age-matched control tissue for obvious reasons; however, appreciation of these age-related changes may be crucial to understanding the pathophysiology and genetic basis of BAV and aortic aneurysms and should not be overlooked.

Again, Cotrufo and colleagues are to be commended for their comparative study of expression of extracellular matrix proteins within dilated aortas among patients with BAV. Their comparisons between regurgitant and stenotic BAV and between the concavity and convexity of dilated aortas are valuable contributions to the field and should be in the foreground of discussions, whereas the comparisons between patients with disease and control subjects should remain in the background.

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## References

1. Cotrufo M, Della Corte A, De Santo LS, Quarto C, De Feo M, Romano G, et al. Different patterns of extracellular matrix protein expression in the convexity and concavity of the dilated aorta with bicuspid aortic valve: preliminary results. *J Thorac Cardiovasc Surg*. 2005;130:504-11.
2. Cattell MA, Anderson JC, Hasleton PS. Age-related changes in amounts and concentrations of collagen and elastin in normotensive human thoracic aorta. *Clin Chim Acta*. 1996; 245:73-84.

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### *Reply to the Editor:*

We appreciate the comments made by McKellar and colleagues regarding our study on extracellular matrix (ECM) proteins in the dilated ascending aorta of patients with bicuspid aortic valve (BAV) disease.[1] We agree with their words of caution about the comparison between patients and control subjects unmatched for age. Unfortunately, the only setting in which we could obtain normal aortic tissue was multiorgan harvesting, and heart donors are usually younger than patients with aortic aneurysms.

Scarce information is available concerning age-related changes in aortic ECM composition in healthy subjects: in rats, the collagen amount per square millimeter decreases with age,[2] and similarly in human aortas, according to the study of Cattell and associates[3] cited by McKellar and colleagues,[3] the collagen amount per sample (in this case the amount in a tissue surface area 1 cm in diameter) decreased by 80% between the ages of 14 and 90 years. However, both in rats[3] and in human beings,[4] the concentration of collagen—that is, the amount per unit of tissue mass—increases with age, because of a predominant loss of other media constituents. In our study, as acknowledged in the Methods section,[1] the presence of collagen in both normal and diseased aortas was not quantified as amount per sample, which could have been affected by the differences in specimen thickness between diseased (thinner wall) and normal vessel, but in terms of the amount of collagen separated from a constant mass of total proteins. Therefore the difference in collagen between patients with BAV and control subjects could have been rather reduced than emphasized by a possible interference of age. Nevertheless, the actual impact of age differences cannot be discerned, and we are trying in our ongoing research to obtain study groups as properly matched for age as possible.

Indeed, our suggestion that the synthesis and degradation of each ECM protein may be differently regulated by different types and degrees of rheologic and mechanical disturbances[1] was derived from the comparison between patients with stenotic and regurgitant BAVs (with comparable mean ages) and not that between patients and control subjects. Our most important finding, as recognized by McKellar and colleagues, was the different expressions of ECM proteins in the convexity and the concavity of dilated aortas, with typical signs of the "flow-induced vascular remodeling" process prevailing at the convexity. If further confirmed, this evidence could exclude that a congenital defect of some wall component may be the prime mover for aortic dilation in BAV disease, because a genetic disorder capable in itself of causing dilatation should be equally expressed along the circumference of a given tract of the vessel. On the contrary, wall stress, which is known to promote vascular remodeling,[1] has been found to unevenly involve the vessel when the valve is bicuspid, with maximal burden at the convex aspect of the ascending tract.[5]

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## References

1. Cotrufo M, Della Corte A, De Santo LS, Quarto C, De Feo M, Romano G, et al. Different patterns of extracellular matrix protein expression in the convexity and concavity of the dilated aorta with bicuspid aortic valve: preliminary results. *J Thorac Cardiovasc Surg*. 2005;130:504-11.
2. Bruel A, Oxlund H. Changes in biomechanical properties, composition of collagen and elastin, and advanced glycation endproducts of the rat aorta in relation to age. *Atherosclerosis*. 1996;127:155-65.
3. Cattell MA, Anderson JC, Hasleton PS. Age-related changes in amounts and concentrations of collagen and elastin in normotensive human thoracic aorta. *Clin Chim Acta*. 1996; 245:73-84.
4. Marque V, Kieffer P, Atkinson J, Lartaud-Idjouadiene I. Elastic properties and composition of the aortic wall in old spontaneously hypertensive rats. *Hypertension*. 1999;34: 415-22.
5. Robicsek F, Thubrikar MJ, Cook JW, Fowler B. The congenital bicuspid aortic valve: how does it function? Why does it fail? *Ann Thorac Surg*. 2004;77:177-85.

doi:10.1016/j.jtcvs.2005.09.034