spectrum? Could this variation inform our understanding of the embryology of the bicuspid aortic valve?^{9,10} Could this possible variation in atherosclerotic risk across the phenotypes for valve and proximal aorta stimulate a more personalized approach to medical and surgical therapy?^{11,12} The thoughtful interpretation of variations in lipid metabolism and atherosclerotic risk across the bicuspid aortic valve spectrum could provide important molecular, cellular, and morphological perspectives to foster more precise and personalized care for our patients.¹⁰⁻¹³

In conclusion, Weininger and colleagues³ are to be congratulated for highlighting the relative absence of atherosclerosis in ascending aortic aneurysms and its importance as a milestone in our understanding. It is likely that future advances in thoracic aortic aneurysms will be significantly influenced by this observation.

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Commentary: Current understanding of the role of atherosclerosis in aneurysmal disease is incomplete

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The group at Yale has extensive experience with treatment of aortic disease and has widely published on the topic. In

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CENTRAL MESSAGE

A propensity-matched analysis demonstrates an inverse relationship between LDL levels and odds of ascending thoracic aortic aneurysm, but the implication for statin use remains unknown.

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the current brief report,¹ they address a hypothesis that differs distinctly from the common belief that aortic aneurysms are generally associated with atherosclerotic disease. While the aorta is considered a single entity, it has been observed to behave differently in various anatomic sections. Having observed that their patient population operated for ascending thoracic aortic aneurysms (ATAA) less frequently had grossly apparent atherosclerotic disease in the aneurysmal segments compared with those operated for descending thoracic aortic aneurysms, the authors undertook to examine the relationship between low-density lipoproteins and the presence or absence of ATAA. Of note, the authors have previously quantified other markers of atherosclerosis, such as total body calcium, coronary atherosclerosis, and intimal media thickness, finding that these were also low in patients with ATAA. We suspect that many aortic surgeons have observed these clinical differences but have not previously considered the relevance, particularly in terms of guideline therapy for ATAA including statins.

The authors' finding of lower low-density lipoprotein association with greater odds of ATAA is concordant with the surgical experience of finding nonatheromatous ascending aortas at surgery and highlights that ATAA is of degenerative rather than atheromatous/inflammatory etiology. How this impacts the decision for statin therapy in patients with ATAA is another matter. While 63% of the ATAA cohort¹ were on statins, the indications for and intensity of such therapy in this brief report is not known. The 2010 guidelines on thoracic aortic disease recommend statin use only for atherosclerotic aortic aneurysm and atheromas.² However, statins are felt to have pleiotropic effects. In animal models, a protective effect appears to be related to alteration of matrix

metalloproteinase activity in the thoracic aorta.³ Similar effects have been shown in human abdominal aortic aneurysms,⁴ but human tissue data in thoracic aortic aneurysms are lacking. Nevertheless, improved clinical outcomes have been observed with statins in patients with ascending aortic aneurysm.⁵⁻⁷ In short, while this report per se offers little in the way of clinical relevance, it is certainly hypothesis-generating. Further study may clarify the relationship between lipoproteins and structural integrity of the aorta.

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