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Commentary: Ascending aortic aneurysms: A marker for freedom from atherosclerosis and a milestone in our understanding

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Ascending aortic aneurysms have important clinical complications.^{1,2} The absence of atherosclerosis in their genesis compared with the thoracoabdominal aorta has been highlighted in an intriguing report by Weininger and colleagues.³ This atherosclerotic heterogeneity in the thoracic aorta may be due to differences in their embryologic origins.³⁻⁵ The ascending aorta and aortic arch are derived from the embryonic neural crest, whereas the thoracoabdominal aorta is derived from embryonic somites and splanchnic mesoderm.^{4,5}

The systematic observations by Weininger and colleagues³ have demonstrated that atherosclerotic markers such as calcium scores, carotid intima-media thickness, and coronary artery disease are conspicuously attenuated in patients with ascending aortic aneurysms.³⁻⁵ In an elegant case-control analysis, this group has now demonstrated that elevated low-density lipoprotein levels are unlikely to be associated with ascending aortic aneurysms.³ Given that elevated low-density lipoprotein levels predict atherosclerosis, this inverse relationship is consistent with their prior published observations pointing to freedom from atherosclerosis in this aortic phenotype.³⁻⁵

Although this association is indeed a “silver lining” for these patients, could it also advance our understanding and management of thoracic aortic aneurysms? First,

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Financial Support: Institutional.

Disclosures: The author reported no conflicts of interest.

The *Journal* policy requires editors and reviewers to disclose conflicts of interest and to decline handling or reviewing manuscripts for which they may have a conflict of interest. The editors and reviewers of this article have no conflicts of interest.

Received for publication Sept 27, 2021; revisions received Sept 27, 2021; accepted for publication Sept 28, 2021; available ahead of print Sept 30, 2021.

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J Thorac Cardiovasc Surg 2022;163:e133-4
0022-5223/\$36.00

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<https://doi.org/10.1016/j.jtcvs.2021.09.042>

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CENTRAL MESSAGE

Ascending aortic aneurysms are unlikely to be associated with atherosclerosis. This phenotypic relationship may yield important clues for more personalized therapeutic options for our patients.

further trials could confirm this association and examine whether it also applies to the aortic arch, given that it shares a common embryonic origin with the ascending aorta.⁴⁻⁶

Second, this observation could be integrated with the expanding horizons in hereditary thoracic aortic disease.⁷ This disease group offers opportunities for multiple important pathophysiologic and therapeutic breakthroughs.⁷ The knowledge gaps in this setting include underlying genotypes in nonsyndromic presentations and effective medical therapies in non-Marfan conditions. The observation by Weininger and colleagues³ could inform future genomic investigation with detailed consideration of relevant nonatherogenic genotypes.^{3,7} Their observation could also direct searches for pharmacologic targets through further molecular investigations of ascending aortic aneurysms, including the role of endothelial dysfunction.^{3,7,8}

Third, because ascending aortic aneurysms are part of the aortopathy associated with bicuspid aortic valve disease, the observations by Weininger and colleagues³ also could be explored in this context.^{2,3,7,8} A recent international consensus has defined 3 presentations for the bicuspid aortic valve (partial-fusion type, fused type, 2-sinus type) and 3 presentations for the associated aortopathy (root, ascending, and extended phenotypes).³ Does the risk for associated atherosclerosis vary significantly across this phenotypic

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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Disclosures: The authors reported no conflicts of interest.

The *Journal* policy requires editors and reviewers to disclose conflicts of interest and to decline handling or reviewing manuscripts for which they may have a conflict of interest. The editors and reviewers of this article have no conflicts of interest.

Received for publication Oct 5, 2021; revisions received Oct 5, 2021; accepted for publication Oct 7, 2021; available ahead of print Oct 12, 2021.

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J Thorac Cardiovasc Surg 2022;163:e134-5

0022-5223/\$36.00

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<https://doi.org/10.1016/j.jtcvs.2021.10.008>