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Commentary: The mutation matters: Improving precision for surgical management of hereditary aortic syndromes

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Hereditary aortic diseases can present challenging surgical management decisions for clinicians. To date, clinical expert guidelines have lacked precision. Guidelines often fail to consider important pathophysiological differences between different inherited thoracic aortic diseases and how underlying cellular and molecular mechanisms can influence surgical outcomes.¹ The exponential growth of computing power combined with the evolution of high resolution, multimodal advanced imaging technologies offers the promise of more precise diagnostic and predictive tools to assess disease progression and in so doing, influence surgical approaches. With further advances in molecular biology, we gain an increased understanding of disease pathogenesis at the level of the gene, protein, and cell. We now have an opportunity to achieve personalized treatment strategies for the surgical management of thoracic aortic disease.

Bicuspid aortic valve-associated aortopathy, once considered a milder version of Marfan syndrome (MFS), is increasingly understood as triggered by hemodynamic aberrations. Clinical expert recommendations for prophylactic aortic resection in bicuspid-associated aortopathy have become more conservative over time, recognizing this less-aggressive disease pathway compared with genetic connective tissue diseases.² Emerging methods will validate and improve patient risk stratification such as 4-dimensional-flow magnetic resonance imaging

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CENTRAL MESSAGE

An improved understanding of hereditary aortic syndromes reveals a need for more precise and individualized surgical treatment approaches.

measures of flow-mediated wall shear stress and novel circulating biomarkers.^{3,4}

Loeys-Dietz Syndrome (LDS), previously classified as a subset of MFS, is recognized as a unique clinical condition. However, contemporary medical and surgical treatment recommendations for LDS are similar to those made for MFS.^{5,6} Sieke and colleagues⁷ develop more precise surgical management strategies for people with LDS and MFS.⁷ Following an index surgical procedure, the study results show a significantly higher incidence of reoperation and dissection in LDS patients compared with MFS patients. Specifically, the need for aortic arch reoperations is substantially increased with LDS. The investigators appropriately suggest that more aggressive surgical resection is warranted in LDS patients. We should give greater consideration to prophylactic aortic arch intervention at the time of initial operation. The lower incidence of reoperation in MFS suggests that a comparatively conservative surgical approach, particularly without associated aortic dissection, is prudent.

Current management strategies for prophylactic aortic resection employ aortic diameter measures to predict the future risk of acute aortic catastrophe. Aortic diameter as a predictive tool has significant inherent limitations.⁸ Aortic size alone may be particularly imprecise for gene mutations of connective tissue regulation, like MFS and LDS because aortic tissue biomechanics and vascular wall tensile strength may be highly abnormal at smaller diameters. Alternate measures of biomechanical properties may improve prediction of acute aortic events.^{1,9}

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The mutation matters. Advanced imaging modalities and concomitant use of circulating biomarkers may improve our ability to predict an individual's risk of future aortic events. Improving precision in our decisions for prophylactic aortic resection is an excellent opportunity for surgeons interested in collaborative, multidisciplinary research. Rigorous clinical follow-up with formal reporting of surgical outcomes for all cases of hereditary aortic diseases, as achieved by Sieke and colleagues,⁷ should be implemented by all surgical programs of excellence.

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