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Commentary: How to save and improve the lives of families with heritable aortic diseases

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As our understanding of the genetics underlying heritable aortic disease (HAD) grows, so too does the complexity increase with respect to managing this growing population.¹ In this issue of the *Journal*, Roman and De Backer² review the contemporary management of HAD, outline the minefield of knowledge gaps facing clinicians, and propose a reasonable pathway forward. The concise recommendation for family screening of first-degree relatives for those with aortic dissection under age 60 years is a clear wayfinder for the multidisciplinary teams managing these patients and their families.

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A repaired ascending aortic aneurysm in a patient with a heritable aortopathy.

CENTRAL MESSAGE

A useful and informative framework for management of heritable aortic disorders is offered in this comprehensive review.

The greatest strength of the offered discourse is the excellent summary of known genetic variants for HAD and their clinical implications. Staying informed about the myriad of genetic advancements is a daunting task. This focused review highlights the importance of geneticists in the care paradigm of aortic disease.³ In the flurry of acute management of aortic dissection, the focus is on reducing morbidity and mortality for the affected patient,

and the foundational nature of a robust family history easily can be forgotten or dismissed. We are reminded by the authors to avoid a myopic focus on the immediate surgical task at hand, as it could cost us many more future lives than the single life that we are trying to save in the moment.

In the past, a binary evaluation for those with aortic dissection, Marfan or non-Marfan, was the standard of care.⁴ First-degree relative screening using advanced imaging and genetic phenotyping were isolated events. Family members were triaged into discrete categories, either affected or not affected.⁵ Roman and De Backer remind us of how this simple approach lacks precision and depth, and encourage us to challenge our assumptions. They emphasize the importance of longitudinal care for affected families, given that variants of unknown significance can become significant over time.

Will this proposal be feasible and provide value? Genetic testing is becoming more accessible and efficient, but the complex challenge of managing patients in resource-poor settings remains an unsurmounted barrier.⁶ Advocating for longitudinal imaging screening of first-degree relatives is laudable, but the cost-effectiveness of screening needs more consideration.⁷

A diagnosis of HAD is a life-changing event. Individuals are forced to confront their own mortality while simultaneously managing the stress and grief that comes from supporting a family member with a complication from a heritable disease. The impact of psychological distress on adherence to treatment and long-term follow-up should be a research priority moving forward. For example, expert consensus led us to counsel women with Loeys–Dietz

syndrome that their average life expectancy was 26 years, and that pregnancy carried a high risk of severe complications.⁵ Longitudinal cohort studies and data from wider genetic testing efforts have now informed us that these estimates and recommendations were likely too conservative. Counseling has since changed, and we must now confront the real-world implications of past recommendations on affected women.⁸ As such, more precise screening and management of families with heritable aortopathy is needed. Future research should assess the cost-effectiveness, psychological burden, and feasibility of the proposed management strategy.

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