FIGURE 1. Multidisciplinary collaboration and specialized care in an “aortic center” are important to improve outcome and individualized risk assessment for family members of patients with aortic dissections. With the advance of genetic testing and international registries, we are in an area of personalized medicine to save lives.

a modifiable risk factor for aortic dissection.⁸ Until we have further data, we would like to propose that the annual flu vaccine should become part of the toolbox used in the care for

patients with aortic disease. In summary, after recovery from aortic dissection, which is in large part due to timely and skillful surgery, patients benefit from an interdisciplinary and multispecialty care in an aortic center that addresses the many aspects of cardiovascular health (Figure 1).

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See Article page 39.

Check for updates

Commentary: Thoracic aortic disease: One step closer to precision medicine

Teng C. Lee, MD, and Tom C. Nguyen, MD

Despite recent advances in management, aortic dissection and rupture continue to be life-threatening conditions. More than 60% of individuals are not diagnosed before

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CENTRAL MESSAGE

Screening family members with thoracic aortic disease may allow the detection of otherwise asymptomatic disease and the planning of appropriate prophylactic surgery based on size and specific pathogenic genetic variants.

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death, based on data from the Jesse E. Edwards Registry

of Cardiovascular Disease.¹ Among those who survive to undergo repair, mortality and morbidity are still very high.² Therefore, the best prevention is identification of asymptomatic but at-risk individuals.

The etiology of aortic dissection is multifactorial, involving both physiologic and anatomic factors. It is commonly known that aneurysms result in dissection/rupture. We have traditionally used aortic diameter as a criterion for prophylactic repair; however, up to 40% of patients who experienced dissection and were listed in the International Registry of Aortic Dissection database had an aortic dimension <5 cm.³ This is especially prevalent in patients who have syndromic hereditary thoracic aortic diseases (HTAD). Recent publications have espoused the value of other predictors of dissection/rupture, such as aortic length⁴ and its surrogate, aortic volume.⁵ Regardless of which anatomic criteria is better, the majority of patients with dissection/rupture have no knowledge of their aortic size. A recent commentary in the *Journal*⁶ stressed the importance of screening and better primary prevention with hypertension management. Without screening, even the best therapy would be moot. Societal guidelines for screening are confusing and have not been updated since 2010.⁷ The US Preventive Services Taskforce still does not have any guideline on screening for thoracic aortic disease.

Thoracic aortic aneurysm and dissection (TAAD) has a strong genetic component compared to abdominal aortic aneurysm. A recent systematic review by Mariscalco and colleagues⁸ revealed that 33% of first-degree relatives and up to 24% of second-degree relatives also have HTAD. In the current issue of the *Journal*, Roman and De Backer⁹ highlight the importance of family history in HTAD and advocated for cascade screening to allow for timely referral for elective aortic surgery to save lives. Their premise is based on 2 recent large population-based estimates of dissection risks in first-degree relatives who have sustained an aortic dissection,^{10,11} showing that their overall relative risks are extremely high.

In their algorithm of screening, Roman and De Backer use a phenotype-first approach with imaging and clinical evaluation of all first-degree relatives. Genetic screening and counseling are advocated only if HTAD is found. Some others favor a genotype-first approach and obtain imaging only if a pathogenic variant is found.¹² There are pros and cons to each approach.

Over the past 2 decades, our understanding of the genetic basis of HTAD has advanced significantly, and the number of known pathogenic variants continues to increase yearly. Currently, more than 30 genes have been associated with HTAD. The aortopathy working group of the Clinical Genome Resource (ClinGen) evaluated 53 candidate genes selected from the literature and summarized the cumulative evidence as of 2018 for 11 genes that cause highly penetrant

HTAD.¹³ Currently, only approximately 30% of familial nonsyndromic HTAD are attributable to known pathogenic variants.¹⁴ These can be detected through various types of available aortopathy panel testing. With decreasing costs of genetic testing and next-generation sequencing technologies, whole exome and whole genome sequencing are becoming more common. Although whole exome sequencing is tempting as it provides us with a lot of data, we must be careful about how to interpret and use these data. Genetic counselors must be available as part of the team that relay the information to the patient and their family members. Even if a pathologic variant is identified, the presentation in each individual could be substantially different due to variable penetrance. Insurance coverage for such tests is also inconsistent. The consequences of the information obtained are unclear, because the Genetics Information Non-Discrimination Act in the United States, which provides protection against genetic discrimination by health insurers and employers, does not provide protection against genetic discrimination for life insurance, disability insurance, and other long-term care insurance.

In recent years, with the work done by the GenTAC Alliance and the Montalcino Aortic Consortium, our understanding of genotype–phenotype interactions has improved significantly. Different pathogenic variants present differently, and certain genes, such as *MYLK*, can result in aortic dissection with minimal aortic enlargement.¹⁵ Another recent study looking at *SMAD3* pathogenic variants show that different variants are associated with different ages at presentation of aortic complications.¹⁶

In summary, as we move toward identifying more family members with HTAD via cascade screening, and as we improve our understanding of different genotype–phenotype interactions among different pathogenic variants, we will be able to move closer toward the holy grail of precision medicine.¹⁷

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See Article page 39.

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,