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# Commentary: Personalized medicine for genetically triggered thoracic aortic aneurysms

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**CENTRAL MESSAGE**

While much has been learned over the decades regarding the genetic underpinnings of thoracic aortic disease, this report emphasizes that we are far from understanding phenotypic relationships.

In this article, Brahmandam and Vallabhajosyula[1] from Yale University report on 2 patients, first-degree relatives, who presented with different forms of thoracic aortic disease.[1] The first, a young man, presented with congestive heart failure, severe aortic insufficiency, and a large aortic root aneurysm. The second case, the patient's mother, presented with acute type B intramural hematoma (IMH). Both underwent successful intervention, the first with valve-sparing aortic root operation, and the second with thoracic endovascular aortic repair. While neither patient had prominent physical features of a connective tissue disorder, genetic testing was positive for Marfan syndrome. The gene analysis revealed a novel missense fibrillin-1 gene mutation defect (c.T556C: p.C186R). The authors report that this is the first report of this specific mutation in the fibrillin-1 gene with any corresponding phenotypic description.

While much has been learned over the last several decades regarding the genetic underpinnings of thoracic aortic disease, this case report emphasizes that there is still much to be understood with respect to the genetic basis of Marfan syndrome and other connective tissue syndromes. The first association between the fibrillin-1 gene and Marfan syndrome was published in 1991.[2] In the ensuing decades, numerous additional mutations have been uncovered that led to the phenotype with common clinical characteristics for Marfan syndrome.[3] For example, the appropriate treatment for the aortic root in Marfan syndrome has evolved and now accepted therapies include Bentall composite root replacement, valve-sparing root replacement using reimplantation technique, and recent data show the Florida Sleeve technique to be durable in these patients as well.[4,5] In addition, as the authors allude to in their report, endovascular therapies are now selectively applied to patients with Marfan syndrome and thoracic aortic disease involving the descending aorta.

This report has several features that are of interest regarding the treatment of patients with connective tissue disorder and thoracic aortic disease. For one, it is unusual for patients with aortopathy to present with IMH; however, IMH is part of the spectrum of acute aortic syndromes and nevertheless may occur in patients with aortopathy. In addition, the mother's age was on the higher end of the spectrum for patients with Marfan syndrome to present with acute aortic syndrome, and this may reflect that within mutations in the fibrillin-1 gene there may be a spectrum affecting the vulnerability to aortic dissection or aneurysm formation. The authors should be commended for introducing this variant of the fibrillin-1 gene mutation and for establishing a phenotypic

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connection with Marfan syndrome. As personalized medicine evolves further, increasing understanding of the genetic basis for aortopathies will allow cardiovascular surgeons to better tailor the medical and surgical interventions to each individual patient.

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