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Commentary: Endothelial nitric oxide synthase in unicuspid aortic valve-related aortopathy: Cause or consequence?

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CENTRAL MESSAGE

Dysregulated endothelial nitric oxide synthase is a primary feature in unicuspid valve disease-related aortopathy.

In a carefully conducted study, Balint and colleagues[1] demonstrate that dysregulated endothelial nitric oxide (eNOS) is a cause and not a consequence in unicuspid aortic valve aortopathy.[1] These findings mirror patterns of dysregulated eNOS in closely related conditions, including bicuspid aortic valve disease related aortopathy.[2,3]

Thoracic aortic aneurysm disease is common and represents a significant risk in those with congenital malformations of the aortic valve.[4] Although the risks that aortic aneurysms pose to patients with bicuspid and unicuspid aortic valve disease are clear, the precise molecular mechanisms underpinning these complex valvular-aortic traits remain poorly understood. Whether or not aortic dilation in this population is a product of altered valve hemodynamic parameters, a consequence of an embryologic event, or a combination of both remains unknown. Understanding the precise mechanism is important because it could potentially alter surgical strategy for replacement of mildly aneurysmal ascending aorta during surgery for bicuspid or unicuspid aortic valve disease as well as extent of aortic replacement. One can argue that aneurysmal changes are secondary to altered valve hemodynamic status and a valve replacement only would suffice. The study by Balint and colleagues[1] represents a significant advance by demonstrating that dysregulation of eNOS in the aortic wall of patients with a unicuspid aortic valve is not a consequence of altered valve hemodynamic status. Although a role for eNOS in unicuspid aortic valve aortopathy is evident at the molecular level, more work is needed to clearly define the genetic underpinnings of this phenomenon and how that translates to clinical practice and surgical strategy for patients with aortopathy.

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