Through Thick and Thin Collagen Fibrils, Stress, and Aortic Rupture
Another Piece in the Jigsaw
Janet T. Powell, MD, PhD; Toste Länne, MD, PhD

This century has seen a leap forward in both treatment and understanding of the molecular and pathogenetic mechanisms underlying aortic dissection. The advantages of endovascular stenting are becoming obvious, and results from the Investigation of Stent Grafts in Patients With Type B Aortic Dissection (INSTEAD) trial are pending. Molecular and pathogenetic advances include genetic defects mapped to several chromosomes in familial thoracic aortic dissection, including splice and missense mutations in the TGFBR2 gene on chromosome 3 associated with a Marfanoid syndrome. Indeed, evidence is increasing that dysregulated transforming growth factor–β signaling is an underlying mechanism in aneurysm formation. The small leucine-rich proteoglycans, including biglycan, bind transforming growth factor–β and regulate collagen fibrillogenesis in vitro. The current article by Heegaard and colleagues, as well as the recent work of Takaluoma et al, uses mouse models to further our understanding of the weaknesses in collagen fibrils that can provoke the aortic dissection characteristic of Ehlers-Danlos syndrome.

Heegaard et al elegantly demonstrate the altered morphology of aortic collagen fibrils in the absence of bgn, the biglycan core protein gene, which is encoded on the X chromosome in both mice and men. Absence of aortic biglycan leads to smaller collagen fibrils and a reduced resistance of the aorta to passive stress. In particular, the role of the adventitia in resisting passive stress is highlighted. The magnitude of these changes in fibril diameter and resistance to passive stress was much greater in males than in females, and only males were susceptible to death from aortic rupture. The authors speculate about the role of estrogens and the mechanism in aneurysm formation. The small leucine-rich proteoglycans, including biglycan, bind transforming growth factor–β and regulate collagen fibrillogenesis in vitro. The current article by Heegaard and colleagues, as well as the recent work of Takaluoma et al, uses mouse models to further our understanding of the weaknesses in collagen fibrils that can provoke the aortic dissection characteristic of Ehlers-Danlos syndrome.

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arteries, it may not be possible to translate the findings of altered aortic wall mechanical properties from mice to humans. In addition, the pathology of these mouse models is very different from the classic cystic medial necrosis and mucoid degeneration (with proteoglycan accumulation) commonly observed in the presentation of idiopathic aortic dissection in humans. Nevertheless, the work of Heegaard et al is a very important step in understanding structure-function relationships in the aorta.

Disclosures
None.

References

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