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ELASTIN DEFICIENCY IN WILLIAMS SYNDROME MAY EXPLAIN POSTOPERATIVE MAJOR ADVERSE CARDIAC EVENTS

To the Editor:

Dr Christoph P. Hornik and colleagues¹ established, in their paper published in the *Journal* in June 2015, that major adverse cardiac events after cardiac surgery are common in patients who have Williams syndrome. They suggest a multifactorial explanation.

Williams syndrome is now recognized as a clinical manifestation of elastin deficiency,² with a mutation sequenced in chromosome 7q11.23. Elastin, an extracellular matrix protein, is the major component of elastic fibers responsible for the elastic and rheologic properties of arteries.^{3,4} Normal deposition of elastin is a critical event in vessel development.⁵ Defective elastin has been implicated in aortic dissection for some time.⁶

Therefore, consideration of pathologic elastin as one factor that may explain the findings of Dr Hornik and colleagues is prudent.

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COMBINING CLINICAL DATABASES WITH GENETIC STUDIES TO HELP ADVANCE THE CAUSATION MODEL OF CONGENITAL HEART DISEASE

Reply to the Editor:

We thank Dr Protopapas for his thoughtful comments on our article “Major Adverse Cardiac Events in Children With Williams Syndrome Undergoing Cardiovascular Surgery: An Analysis of the Society of Thoracic Surgeons Congenital Heart Surgery Database.” The hypothesis brought forward that elastin pathology is at the source of the abnormal vascular development seen in some patients with Williams syndrome seems well founded and worthy of continued study.¹

The promise of genetic information driving clinical decision making in congenital heart disease is appealing, particularly in high-risk patients with variable outcomes, such as those with Williams syndrome.² Turning this promise into reality first requires establishing strong genotype–phenotype relationships. This will best be accomplished by routinely collecting and analyzing genetic data from large patient cohorts.³ In a subsequent step, the identified genetic information will need to be linked to a clinical outcome. Although the routine collection of genetic information is undoubtedly complex and requires a strong infrastructure, the overall task may be simplified by using existing clinical outcomes data sources. The Society of Thoracic Surgeons Congenital Heart Surgery Database, as the largest and most comprehensive congenital heart surgery data repository in the world, is an excellent source of such data.⁴

Given the variability in clinical outcomes described in our study and the potential genetic mechanism hypothesized by Dr Protopapas and others, patients with Williams syndrome may be an ideal population in whom to prospectively study genetic sample collection combined with standard of care clinical outcomes data. If successful in identifying a genotype–phenotype relationship, such a study might demonstrate the feasibility and efficiency of a novel mechanism to help advance the causation model of congenital heart disease.

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