

The author reported no conflicts of interest.

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using patient-specific metrics as a means to improve the ability to predict aortic dissection risk and better guide prophylactic aortic repair than the current dimension-based guidelines. Aortic dissection represents biomechanical failure of the aortic wall, and currently the most promising clinical tool to allow measurement of aortic wall stress would appear to be 4-dimensional-flow magnetic resonance imaging of the aorta,<sup>5</sup> which likely represents the future of “patient-specific” guideline-based prophylactic aortic surgery rather than any aortic dimension-based guideline.

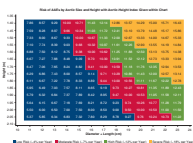
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## REPLY: FUTURE PROSPECTS FOR THORACIC AORTIC PREDICTION

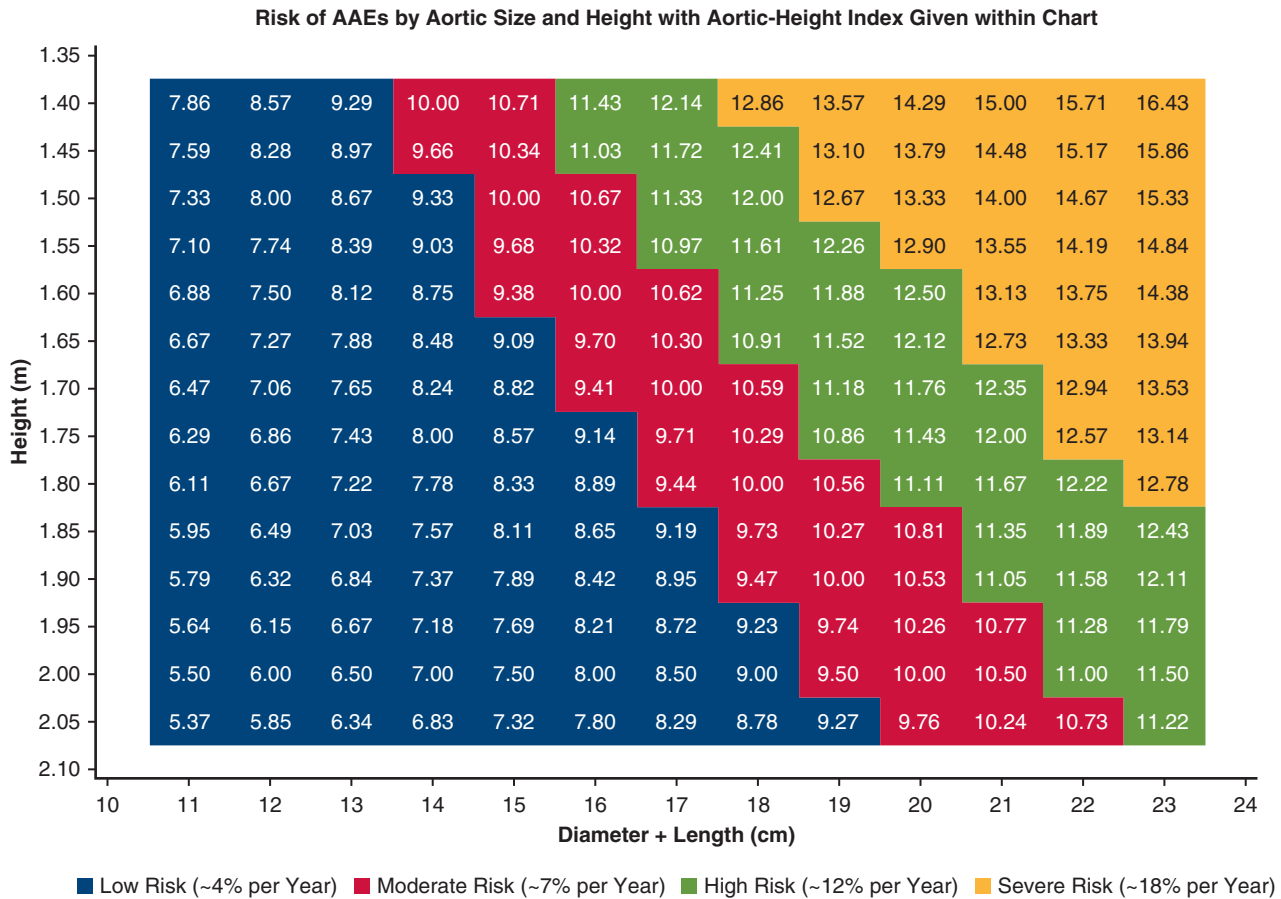
### Reply to the Editor:

We are in agreement with the points that are made by Drs Acharya, Mariscalco, and Jahangiri.<sup>1</sup> We hasten to emphasize,

however, that in any cross-sectional criteria, the only patient variable is the radius of the aorta; the rest is just an arithmetic manipulation of that number.

In terms of prospects for future enhancement of the predictive ability for adverse events, we have the following points to make:

1. Combined morphologic criterion. Aortic length used to be thought of as unimportant, given the benign-sounding moniker of “tortuosity” or “uncoiling.” Our group<sup>2</sup> and others<sup>3-5</sup> have begun to focus on length as a newly recognized important parameter. We find that elongation of the ascending aorta (from annulus to innominate artery) is an important predictor of adverse events. In a novel parameter, we add ascending aortic diameter to ascending aortic length and divide by the patient’s height.<sup>2</sup> This leads to a parameter that is quite accurately predictive. This accounts for the impact of diameter, of length, and of body size, and body size to some extent accommodates the sex contribution. This produces a simple predictive nomogram (Figure 1).<sup>2</sup> This criterion is based on retrospective analysis of our large database. We look forward to “test driving” this criterion prospectively.
2. Clinical genetics. It is becoming abundantly clear that once a family member dissects, the risk of dissection for other family members increases dramatically. We saw this in our studies (2.7-fold increase compared with aneurysm families without dissection),<sup>6</sup> and it was seen by Raunsø and colleagues<sup>7</sup> and Chen and colleagues<sup>8</sup> (nearly 9-fold and 6.3-fold increase compared with the general population, respectively). Accordingly, we see no reason to wait for the nearly inevitable dissection event in an aneurysm-bearing (almost any size) family member of a known dissector. The very high safety of elective aortic surgery adds to the impetus for such prophylactic intervention.
3. Molecular genetics. The proliferation of whole-exome sequencing permits identification of a specific causative variant for about one-third of our patients with ascending aortic aneurysm.<sup>9</sup> This percentage is certain to increase rapidly as new mutations are identified each year. Remarkably, ascending thoracic aortic aneurysm is mostly a single-gene, single-allele disease, that is to say, a mutation in 1 single letter among the 2.2 billion letters of our genetic code produces the thoracic aortic aneurysm. As our “dictionary” of causative variants expands, we can provide personally tailored intervention criteria for each patient based on their individual mutation. Each mutation has its own size criterion for intervention. Each year, we publish in the journal *Aorta* a “timeline” of the recommended size criterion for each specific mutation (Figure 2).<sup>10</sup>



**FIGURE 1.** AHI nomogram as a function of aortic size (diameter + length) (x-axis) and height (y-axis), with the AHI given within cells. The table has a 4-tier, color-coded warning system, with yellow representing the most severe, followed by green, red, and blue. AAEs, Aortic adverse events. Reprinted with permission from Wu and colleagues.<sup>2</sup>

Such personalized aortic decision making is likely to expand dramatically.

- Artificial intelligence. We and others are making initial efforts to apply the tremendous (and mysterious) power of artificial intelligence to enhance our predictions of the best size at which to intervene to prevent dissection of the ascending aorta. This exciting modality, which can search and identify relationships and predictors not dependent on human clinical intuition, provides the promise of continued enhancement of our predictive accuracy and ability.<sup>11</sup>

We believe that the future is bright for additional progress in predictions of the behavior of the aneurysmal ascending aorta.

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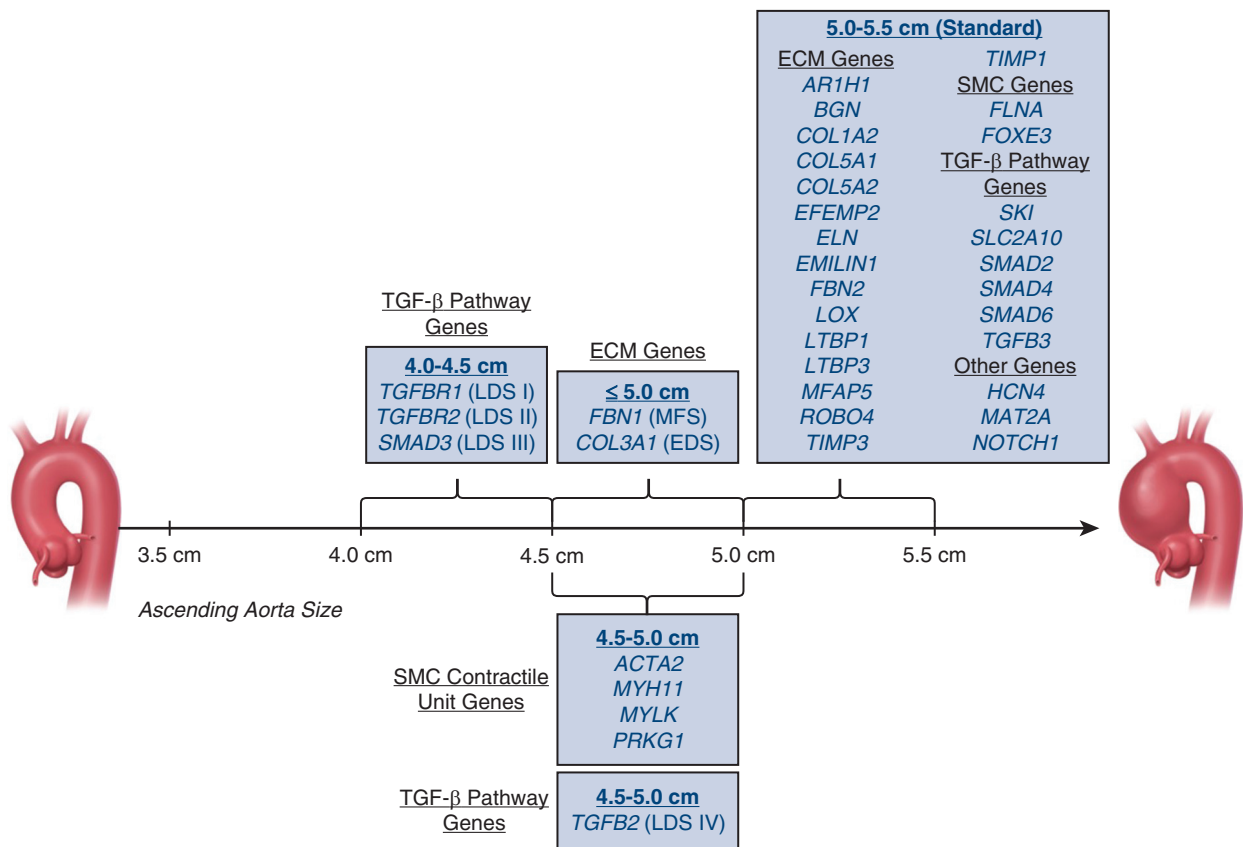
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Dr Elefteriades reported principal, CoolSpine, consultant for CryoLife, Data/Safety Monitoring Board for Terumo. Dr Ziganshin reported no conflicts of interest.

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**FIGURE 2.** Ascending aortic dimensions for prophylactic surgical intervention in the setting of a specific mutated gene. *TGF-β*, Transforming growth factor  $\beta$ ; *ECM*, extracellular matrix; *SMC*, smooth muscle cell. Reprinted with permission from Faggion Vinholo and colleagues.<sup>10</sup>