Dr Eleftheriades is a principal and founder of CoolSpine and serves on the data and safety monitoring boards of Jarvik Heart and Terumo. These have no direct relevance to this academic submission. All other authors have nothing to disclose with regard to commercial support.

BICUSPID AORTIC DISEASE: “MARFAN LIGHT”?

Reply to the Editor:

We thank Dr Sundt for his kind comments. We always welcome his insightful perspectives on all aspects of cardiac disease and cardiothoracic surgery.

As it turns out, we agree very strongly with Dr Sundt on the excellent points that he raises. It appears that our cryptic, telegraphic words in Box 2 of Figure 6 in our article were interpreted as indicating routine operation for all patients with bicuspid valve and aortas in the 4.0 to 5.0 cm size range.¹ This was contrary to our intended meaning, which was simply to indicate common accompanying conditions (including chest pain, strong family history, severe connective tissue disease, and disease of a bicuspid aortic valve) that often contributed to our decision to operate on this category of patients. We have adjusted this figure (and its corresponding text citation) to correct this innate susceptibility to misinterpretation.¹

We have never practiced routine bicuspid aortic resection in the size range of 4.0 to 5.0 cm. We have never advocated this. In fact, as the Letter to the Editor points out, we were one of the first groups to report that the bicuspid aorta was behaving in a more benign fashion than expected at the

time. In our 2007 article, “Natural History of Ascending Aortic Aneurysms in the Setting of an Unreplaced Bicuspid Aortic Valve,” we concluded that “patients with BAV have similar rates of aortic rupture, dissection, and death [to those with nonbicuspid valves] and improved long-term survival.”² In that article, we were countering the impression of the era that the bicuspid aorta had severe intrinsic disease, amounting to a sort of “Marfan light.” The early impression, that the bicuspid aorta had a susceptibility approaching that of the aorta in Marfan disease, has since been dispelled by multiple avenues of evidence. In fact, one of us (J.A.E.) was a member of the writing group and a participating author of the recent consensus paper in the *Journal of Thoracic and Cardiovascular Surgery* that advocated return to a criterion of 5.5 cm for the bicuspid aorta (5.0 at expert centers).³ Our approach to aortic replacement in the size range 4.0 to 4.9 is shown in Figure 1.

Although aortic dissection is a catastrophic event, our team has written extensively on how to time aortic intervention, in terms of aortic size, precisely to avoid operating earlier than needed. In the *Journal*, our most recent publication on this topic presents a detailed chart of the exact aortic risk for patients depending on aortic size and patient height. This manifests our commitment to guiding aortic resection so that it is performed before dissection, but not earlier than necessary.⁴

That being said, however, we must recognize that size criteria are imperfect. Nature does not respect an artificial “dividing line” criterion, despite the great effort and huge patient numbers brought to bear in its creation. Sobering in this regard is the well-known graph from the International Registry of Acute Aortic Dissection article of Pape and colleagues,⁵ which shows that a full 50% of aortic dissections occur *before* a size criterion of 5.5 cm has been reached (Figure 2, A). We have analyzed the detailed

FIGURE 1. Approach to moderate aortic enlargement in patients with bicuspid aortic valve (BAV). AVR, Aortic valve resection.

FIGURE 2. A, International Registry of Acute Aortic Dissection demonstration of the “paradox” that many aortic dissections occur at small aortic sizes exemplifies this issue. (Modified with permission.⁵) B, Ascending aortic size follows a modified bell curve distribution in the general population. The number of individuals at risk increases dramatically the closer one moves leftward from the right “tail” of the bell curve. A huge population is thus at risk at small aortic sizes; so, although dissections do occur, the relative risk is very low compared to the huge “at risk” population. (Modified with permission from: Elefteriades JA, Farkas EA. Thoracic aortic aneurysm clinically pertinent controversies and uncertainties. *J Am Coll Cardiol*. 2010;55:841-57.) C, The relative risk of an adverse aortic event is more than 6000-fold higher for large aortas than for small ones. (Reprinted with permission.⁶)

population dynamics of this article diligently, and size remains a powerful predictor when both the numerator (dissections) and denominator (patients in a certain aortic size range) are taken into account (Figure 2, B and C).⁶

It is important to note, as we review in a recent article,⁷ that multiple observations will argue for a “left shift” (to smaller sizes) in future position papers on criteria for aortic intervention. Most importantly, we now recognize that the aorta grows 7 to 8 mm at the moment of aortic dissection. This means that the postdissection aortic measurements we have been using to determine evidence-based criteria for intervention have been misleading us; the aorta was, when it dissected, nearly a centimeter smaller than we thought on the basis of the postevent images.

The important considerations brought up in this response to the letter to the Editor should not distract from the key message of our article.¹ Our article determines the effectiveness of a size-based algorithm in determining who needs aortic surgery and who does not. We are not aware of any previous article that examines the actual clinical effectiveness of an evidence-based algorithm for aortic decision making. In our study, the patients algorithmically triaged to medical therapy did well. The patients triaged to surgery who did not undergo surgery did very poorly, with a high

rate of aortic events.¹ This strongly suggests that the algorithm effectively identifies patients at risk of the “sudden killer” and protects those safe patients with “innocent” aortas from surgery sooner than required.

Ayman Saeyeldin, MD
Bulat A. Ziganshin, MD, PhD
Mohammad A. Zafar, MD
John A. Elefteriades, MD, PhD (hon)
Aortic Institute at Yale-New Haven Hospital
Yale University School of Medicine
New Haven, Conn

References

1. Saeyeldin A, Zafar MA, Li Y, Tanweer M, Abdelbaky M, Gryaznov A, et al. Decision-making algorithm for ascending aortic aneurysm: effectiveness in clinical application? *J Thorac Cardiovasc Surg*. 2019;157:1733-45.
2. Davies RR, Kaple RK, Mandapati D, Gallo A, Botta DM Jr, Elefteriades JA, et al. Natural history of ascending aortic aneurysms in the setting of an unreplaced bicuspid aortic valve. *Ann Thorac Surg*. 2007;8:1338-44.
3. Borger MA, Fedak PW, Stephens EH, Gleason TG, Girdauskas E, Ikonomidis JS, et al. The American Association for Thoracic Surgery consensus guidelines on bicuspid aortic valve-related aortopathy: full online-only version. *J Thorac Cardiovasc Surg*. 2018;156:e41-74.
4. Zafar MA, Li Y, Rizzo JA, Charilaou P, Saeyeldin A, Velasquez CA, et al. Height alone, rather than body surface area, suffices for risk estimation in ascending aortic aneurysm. *J Thorac Cardiovasc Surg*. 2018;155:1938-50.

5. Pape LA, Tsai TT, Isselbacher EM, Oh JK, O'Gara PT, Evangelista A, et al; International Registry of Acute Aortic Dissection (IRAD) Investigators. Aortic diameter ≥ 5.5 cm is not a good predictor of type A aortic dissection: observations from the International registry of acute aortic dissection (IRAD). *Circulation*. 2007;116:1120-7.
6. Paruchuri V, Salhab KF, Kuzmik G, Gubernikoff G, Fang H, Rizzo JA, et al. Aortic size distribution in the general population: explaining the size paradox in aortic dissection. *Cardiology*. 2015;131:265-72. Erratum in: *Cardiology*. 2015;132:44.
7. Ziganshin BA, Zafar MA, Elefteriades JA. Descending threshold for ascending aortic aneurysmectomy: is it time for a "left-shift" in guidelines? *J Thorac Cardiovasc Surg*. 2019;157:37-42.

<https://doi.org/10.1016/j.jtcvs.2018.12.048>

WITNESS PROTECTION FOR AUTHORS OF CONTROVERSIAL GUIDELINES

Reply to the Editor:

For many years, Thoralf M. Sundt has shared his concerns about the premature prophylactic replacement of the aortic root and ascending aorta in patients with a bicuspid aortic valve. In a recent letter to the Editor,¹ he shares his perspective on the article by Saeyeldin and colleagues (including Elefteriades),² which presents their latest thoughts. Elefteriades and colleagues³ have long been at the forefront of enhancing the understanding of the natural history of aortic aneurysm and dissection. Their efforts have included a nuanced examination of patients with bicuspid aortic valves, published in 2007, which suggested that the risk of negative events dramatically increases when aneurysms reach a diameter of 5 cm or more.⁴ Over the next decade, this analysis and others helped shift the needle toward intervention at a lower diameter-based threshold.⁵ This shift was controversial, and mediation was needed for conflicting practice guidelines.⁶

In their most recent analysis, Saeyeldin and colleagues² again dive headlong into this continuing controversy. Should the diameter-based threshold for surgical intervention in patients with bicuspid aortic valves be lowered even further, to 4 cm? Although the authors make a convincing argument for a lower threshold,² Sundt points out weaknesses in their decision-making algorithm and expresses concern that reducing the threshold of repair to a new low could ensnare those with "innocent" aortas (ie, those that would not dare dissect or rupture) as unnecessary surgical victims.¹

At the heart of the matter is the balance between maintaining an adequately functioning bicuspid aortic valve for as long as possible and avoiding a life-threatening aortic dissection. The facts remain that elective aortic root replacement in patients with a bicuspid aortic valve is typically a low-risk operation that usually entails little further intervention. In contrast, acute ascending aortic dissection is a life-threatening event, repairing it is a high-risk operation, and if the residual dissection is extensive, further aortic intervention is often necessary.

Dr Coselli participates in clinical research trials conducted by Edwards Lifesciences and Bolton Medical; consults for, receives royalties and a departmental educational grant from, and participates in clinical trials for Terumo Aortic; and consults and participates in clinical trials for Medtronic Inc and W.L. Gore & Associates.

Factors to include in this decision include meeting the needs of an informed patient relative to the expected outcome, based on the demonstrated skill of an experienced surgeon.

Much like bioprosthetic valves, which are typically reserved for older patients because of the valves' limited durability but are sometimes used in younger patients with a strong preference for them, there should be some flexibility in the 4- to 5-cm diameter threshold. Ultimately, a balance is struck for clinicians and patients because the actual risk for an individual is impossible to determine; one could argue that patient discomfort and surgical experience may be worth a centimeter of leeway.

Joseph S. Coselli, MD

Division of Cardiothoracic Surgery

Michael E. DeBakey Department of Surgery

Baylor College Medicine

Houston, Tex

Department of Cardiovascular Surgery

Texas Heart Institute

Houston, Tex

References

1. Sundt T. Silent killer or victim of mistaken identity? *J Thorac Cardiovasc Surg*. 2019;157:e239.
2. Saeyeldin A, Zafar MA, Li Y, Tanweer M, Abdelbaky M, Gryaznov A, et al. Decision-making algorithm for ascending aortic aneurysms: effectiveness in clinical application? *J Thorac Cardiovasc Surg*. 2019;157:1733-45.
3. Elefteriades JA. Natural history of thoracic aortic aneurysms: indications for surgery, and surgical versus nonsurgical risks. *Ann Thorac Surg*. 2002;74:S1877-80.
4. Davies RR, Kaple RK, Mandapati D, Gallo A, Botta DM Jr, Elefteriades JA, et al. Natural history of ascending aortic aneurysms in the setting of an unreplaced bicuspid aortic valve. *Ann Thorac Surg*. 2007;83:1338-44.
5. Hiratzka LF, Bakris GL, Beckman JA, Bersin RM, Carr VF, Casey DE Jr, et al. 2010 ACCF/AHA/AATS/ACR/ASA/SCA/SCAI/SIR/STS/SVM guidelines for the diagnosis and management of patients with thoracic aortic disease: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines, American Association for Thoracic Surgery, American College of Radiology, American Stroke Association, Society of Cardiovascular Anesthesiologists, Society for Cardiovascular Angiography and Interventions, Society of Interventional Radiology, Society of Thoracic Surgeons, and Society for Vascular Medicine. *Circulation*. 2010;121:e266-369.
6. Hiratzka LF, Creager MA, Isselbacher EM, Svensson LG, Nishimura RA, Bonow RO, et al. Surgery for aortic dilatation in patients with bicuspid aortic valves: a statement of clarification from the American College of Cardiology/American Heart Association task force on clinical practice guidelines. *J Am Coll Cardiol*. 2016;67:724-31.

<https://doi.org/10.1016/j.jtcvs.2018.12.060>