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Author Reply to Commentary: Thinking nonlinearly about aortic biomechanics

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Drs Plestis and Rajagopal[1] have provided a commentary on our study of the relationship between aortic geometry and material properties of the aorta. Unfortunately, our work was misread. Here, we will attempt to dispel any confusion by addressing each of their 4 points.

1. "It is unclear what mathematical model the authors are using." The data were not used to fit a model. As detailed in our methods,[2-5] we made no assumptions of material model; all measures are derived directly from stress-strain curves obtained with rigorous, physically accurate, and biologically relevant mechanical tests. The specific protocol and derivation of material properties can be found in our current and previously published work.[2-5] Thus, our characterization is the most general it can be and not distorted by assumptions intrinsic to a specific material model. We distill the full biaxial stress-strain curves to metrics that efficiently describe key aspects of mechanical behavior and have clinical relevance as potentially being measurable in vivo: It is neither necessary nor useful to clinicians to apply more comprehensive material models in this context.
2. "Linearized elasticity can only be applied to small deformations." We make no assumptions of linear elasticity. Plestis and Rajagopal[1] appear to have confused Young's tangential modulus. As we defined in our study, we used the tangential modulus, which is widely used in this field. This also means that their statement that tangential modulus and hysteresis are mutually exclusive is incorrect. For further explanation on these definitions, we refer the reader to our co-Principal Investigator's textbook on biomechanics.[6] The statement that energy loss/hysteresis in the aorta is "overwhelmingly derived from left ventricular function" also points to a lack of understanding of how hysteresis is measured in biaxial tensile tests. Hysteresis is an intrinsic material property of the aorta and is independent of left ventricular function.
3. "Based upon an incorrect choice of model, one could potentially incorrectly identify a relationship between two variables." We think we have adequately addressed this bullet point already.
4. "To whatever extent correlations between aortic material properties and aortic geometry could exist, they are correlations without causation." Although the fundamental pathophysiology driving aneurysm formation and biomechanics is an active area of research in our laboratory and many others, we were extremely careful to never imply causation. The relationship between an aorta's geometry and its underlying material properties is a question of large interest and importance to those with interest in aortic disease. Plestis and Rajagopal[1] demonstrate understanding that material properties may differ in aneurysms of different sizes. They assert "pathophysiological mechanisms that underlie abnormal aortic mechanics likely are the same–or at least substantially overlapping–with those that underlie aortic dilatation." They also demonstrate understanding that "material properties are definitionally independent of material geometry." Herein lies the crux of our study: Diameter is the standard all surgeons continue to use, including in the most recent 2022 American Heart Association/American College of Cardiology/American Association for Thoracic Surgeon aortic guidelines,[7] because it can actually be routinely measured. Length has recently garnered increasing interest.[5,8-10] Geometric variables have served cardiac surgeons reasonably well as surrogates of wall stress and disease severity. Thus, as scientists do, we used rigorous experiments to understand the actual relationships between clinically measurable metrics against tissue material properties that define failure risk. We found that there is indeed a relationship between aortic diameter and energy loss, albeit not strong, and not between length and any of the biomechanical metrics we tested. This can then be tied together with our previous work that links biomechanical metrics, including energy loss and histopathology.[2,3]

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Therefore, for at least the above 4 interrelated issues, the Commentary is not relevant to our study.

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