The effect of aortic root anatomy and vortex flow induced shear stress on the aortic valve leaflets

Arash Kheradvar¹, Mani A. Vannan²*, Lakshmi P. Dasi³, and Gianni Pedrizzetti⁴

¹Edwards Lifesciences Center for Advanced Cardiovascular Technology, Department of Biomedical Enginnering, University of California, Irvine, CA, USA; ²Marcus Heart Valve Center, Piedmont Heart Institute, Atlanta, GA, USA; ³Department of Biomedical Engineering, Georgia Institute of Technology, Atlanta, GA, USA; and ⁴Department of Engineering and Architecture, University of Trieste, Trieste, Italy

This editorial refers to 'Influence of aneurysmal aortic root geometry on mechanical stress to the aortic valve leaflet', by H. Hayashi et al. doi:10.1093/ehjci/jeab006.

'Vortex reigns, having expelled Zeus'

Aristophanes, Clouds (423 BC), Strepsiades speaking.

[tr. Hickie 1853, vol. 1, Perseus]

The anatomy of aortic root and its components has been shown to significantly affect the flow through the aorta. Aberrant flows in the ascending aorta are mainly due to aortic abnormalities of the aortic root or the aorta, which can be corrected by surgical repair.^{1–4} However, the effect of the aberrant flow on the aortic root and the aorta is less clear, although this has been previously explored. What is certain is that there is a dynamic interaction between the flow and the adjacent aortic root tissue that leads to continuous exchange of momentum between the two. From a mechanistic perspective, blood flow interacts with the adjacent tissue through the exchange of forces, as represented by either pressure or wall shear stress (WSS). The role of pressure in the cardiovascular system is already well known. However, effects of WSS on the neighbouring structures are more elusive.

Vascular atherogenesis is an example where the role of WSS has been recognized since the early sixties.⁵ *Low* values of WSS were initially considered to simply facilitate lipid deposition on the vessel walls and buildup of atherosclerotic plaques. However, more recent studies suggest that the interplay between the flow and the endothelium is more complex than what was thought before. Plaque buildup is regulated at the cellular level such that the *abnormal* WSS can trigger proinflammatory responses through mechano-transduction that leads to atherosclerosis.⁶ Similarly, degradation of the endothelial layer can occur in the regions where WSS is *high* (e.g. when blood jet across a stenosis or bicuspid aortic valve (AV) deviates and impacts the adjacent wall in the aortic root).⁷ Thus, it is possible that abnormal WSS on the AV leaflets may eventually trigger endothelial dysfunction and inflammation, which ultimately leads to calcification.⁸ The sinuses of Valsalva play a crucial role in the fluid dynamics of the aortic root and in the interaction between the flow and AV leaflets. Preserving the protection that is facilitated by the fluid dynamic of sinuses of Valsalva is one of the basis for valve-sparing aortic root replacement (VSARR).^{9,10} Figure 1 compares computer simulation of aortic root's blood flow pattern in presence or absence of sinuses of Valsalva. In early and peak systole, the vortex flow that develops along with the jet in the Valsalva sinuses creates a cushion between the leaflets and the wall preventing the leaflets from smashing against the wall of the aorta. This vortex flow may regulate WSS on the AV's fibrosa layer. The central jet stream of aortic flow through the open AV regulates the WSS on the ventricularis surface of its leaflets. In late systole, the vortices in the sinuses of Valsalva mitigate the forces at which the leaflets appose during diastole, thus minimizing trauma to the leaflets. Therefore, the intricate fluid dynamics of the normal aortic root is in part intended to sustain the durability of the AV leaflets.

The recent study by Hayashi *et al.*¹¹ investigates the effect of aortic root geometry on WSS measured directly over the valve leaflets prior to and post-VSARR. Their results indicate that the abnormal WSS on the AV leaflets in an aneurysmal aortic root is reversed post-VSARR, when a Valsalva graft is used to replace the aneurysmal aortic root. The post-VSARR WSS on the AV leaflet was found similar to a control group of patients who underwent coronary artery bypass grafting surgery in whom the aortic root geometry was normal. These results suggest that preserving the sinuses of Valsalva during VSARR may improve durability of the native AV leaflets, although this remains a matter of debate. From a methodological standpoint, the authors have calculated WSS using blood velocities and estimations of velocity gradients obtained by colour flow Doppler-based vector flow mapping (VFM). This simplistic approach entails limitations because it is based

The opinions expressed in this article are not necessarily those of the Editors of European Heart Journal – Cardiovascular Imaging, the European Heart Rhythm Association or the European Society of Cardiology.

^{*} Corresponding author. Tel: +17143647056. E-mail: mvannan2560@gmail.com

Published on behalf of the European Society of Cardiology. All rights reserved. © The Author(s) 2021. For permissions, please email: journals.permissions@oup.com.

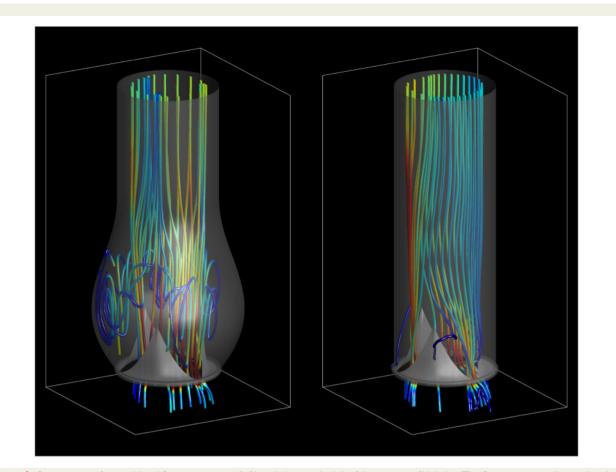


Figure I Comparison of aortic blood flow in presence (left) and absence (right) of the sinuses of Valsalva. The flow is numerically simulated with streamlines (coloured according to shear stress) drawn at the peak systole. In the presence of the sinuses of Valsalva, blood flow leads to the formation of a vortex that acts as a cushion separating the leaflets from aortic wall. In contrast, in the absence of the sinuses of Valsalva (right). In both cases, shear stress develops over the ventricular side of the leaflets is predominantly rectilinear with small deviations because of leaflets. In both cases, shear stress develops over the ventricular side of the leaflets (*ventricularis*), which is markedly higher than the one on the aortic side of the leaflets (*fibrosa*).

on 2D colour flow Doppler images, which does not capture the complexity of the 3D flow across the AV. Furthermore, VFM's spatial resolution is insufficient to evaluate the velocity gradient adjacent to the thin moving leaflets. In fact, even 4D flow magnetic resonance imaging does not have the required resolution for accurate calculation of the vessel WSS.¹² Furthermore, the attempts to measure WSS on the moving leaflets poses even more challenges, which are difficult to overcome even in the controlled settings of fluid dynamics laboratories.¹³ An alternative solution is to use surrogate parameters that are grounded on variables less susceptible to measurement errors. These options include volume-averaged measures of flow properties that are closely related to AV WSS, e.g. Reynolds stresses in the aortic anatomical segments. Lastly, the role of coronary flow and the location and position of the coronaries in the different cohorts cannot be ignored as they significantly impact the overall vortex dynamics and the magnitude of WSS on the leaflets.¹⁴

Despite these methodological limitations, the study by Hayashi et al.¹¹ highlights the interaction between blood flow and surrounding tissue and how this can be used as a guide for improvements in VSARR. More specifically, this work reminds us

of the limitations of the current approach to characterize blood flow by only using blood flow velocity acquired from conventional imaging methods. In fact, the aberrant interaction between blood flow and the surrounding tissue has emerged as important epigenetic trigger responsible for a host of perturbations in cellular and structural physiology, which may lead to a range of cardiovascular disease.^{15,16} The ability to analyse blood flow patterns is the next frontier to find ways to predict and detect occult cardiovascular dysfunction, even before changes in the structural anatomy appear. As Abraham Lincoln brilliantly stated: 'the best way to predict the future is to create it'.

Conflict of interest: none declared.

References

- Kheradvar A, Rickers C, Morisawa D, Kim M, Hong G-R, Pedrizzetti G. Diagnostic and prognostic significance of cardiovascular vortex formation. J Cardiol 2019;74:403–11.
- Guala A, Teixido-Tura G, Dux-Santoy L, Granato C, Ruiz-Muñoz A, Valente F et al. Decreased rotational flow and circumferential wall shear stress as early markers of descending aorta dilation in Marfan syndrome: a 4D flow CMR study. *J Cardiovasc Magn Reson* 2019;21:63.

- 3. Rodríguez-Palomares JF, Dux-Santoy L, Guala A, Kale R, Maldonado G, Teixidó-Turà G et al. Aortic flow patterns and wall shear stress maps by 4D-flow cardiovascular magnetic resonance in the assessment of aortic dilatation in bicuspid aortic valve disease. J Cardiovasc Magn Reson 2018;20:28.
- Fatehi Hassanabad A, Burns F, Bristow MS, Lydell C, Howarth AG, Heydari B et al. Pressure drop mapping using 4D flow MRI in patients with bicuspid aortic valve disease: a novel marker of valvular obstruction. *Magn Reson Imaging* 2020; 65:175–82.
- Caro CG, Fitz-Gerald JM, Schroter RC. Arterial wall shear and distribution of early atheroma in man. *Nature* 1969;**223**:1159–61.
- 6. Chen P-Y, Qin L, Li G, Wang Z, Dahlman JE, Malagon-Lopez J et al. Endothelial TGF- β signalling drives vascular inflammation and atherosclerosis. *Nat Metab* 2019;**1**:912–26.
- Dux-Santoy L, Guala A, Teixidó-Turà G, Ruiz-Muñoz A, Maldonado G, Villalva N et al. Increased rotational flow in the proximal aortic arch is associated with its dilation in bicuspid aortic valve disease. Eur Heart J Cardiovasc Imaging 2019;20: 1407–17.
- Fernández Esmerats J, Heath J, Jo H. Shear-sensitive genes in aortic valve endothelium. Antioxid Redox Signal 2016;25:401–14.
- Gaudino M, Piatti F, Lau C, Sturla F, Weinsaft JW, Weltert L et al. Aortic flow after valve sparing root replacement with or without neosinuses reconstruction. J Thorac Cardiovasc Surg 2019;157:455–65.

- Oechtering TH, Sieren MM, Hunold P, Hennemuth A, Huellebrand M, Scharfschwerdt M et al. Time-resolved 3-dimensional magnetic resonance phase contrast imaging (4D flow MRI) reveals altered blood flow patterns in the ascending aorta of patients with valve-sparing aortic root replacement. J Thorac Cardiovasc Surg 2020;159:798–810.e1.
- Hayashi H, Itatani K, Akiyama K, Zhao Y, Kurlansky P, DeRoo S et al. Influence of aneurysmal aortic root geometry on mechanical stress to the aortic valve leaflet. *Eur Hear J Cardiovasc Imaging* 2021;doi:10.1093/ehjci/jeab006.
- Garcia J, Barker AJ, Markl M. The role of imaging of flow patterns by 4D flow MRI in aortic stenosis. JACC Cardiovasc Imaging 2019;12:252–66.
- Yap CH, Saikrishnan N, Tamilselvan G, Yoganathan AP. Experimental technique of measuring dynamic fluid shear stress on the aortic surface of the aortic valve leaflet. J Biomech Eng 2011;133:061007.
- Flemister DC, Hatoum H, Guhan V, Zebhi B, Lincoln J, Crestanello J and Dasi LP. Effect of Left and Right Coronary Flow Waveforms on Aortic Sinus Hemodynamics and Leaflet Shear Stress: Correlation with Calcification Locations. Annals of Biomedical Engineering 2020;48:2796–2808.
- Pedrizzetti G, La Canna G, Alfieri O, Tonti G. The vortex—an early predictor of cardiovascular outcome? Nat Rev Cardiol 2014;11:545–53.
- Arvidsson PM, Kovács SJ, Töger J, Borgquist R, Heiberg E, Carlsson M et al. Vortex ring behavior provides the epigenetic blueprint for the human heart. Sci Rep 2016;6:22021.