EDITORIAL COMMENT

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Trying to overcome the ‘chicken or egg’ impasse in bicuspid aortopathy research

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A reliable parameter for measuring the severity of an aortopathy is currently lacking, probably because of the lack of knowledge of what defines the presence of an aortopathy. Is it just increased aortic diameters? Or is it the evidence, with or without dilatation, of altered mechanical properties of the aortic wall? Or presence of histological/biomolecular alterations? Most probably, different experts would answer differently to these questions, but the correct answer is unknown.

About 10 years ago, having studied the intrinsic stenotic-like kinematics of the echocardiographically normo-functional bicuspid aortic valve (BAV) in magnetic resonance imaging (MRI) examinations, my colleagues and I looked for a method to quantify the restriction of the systolic opening motion of the fused leaflet: 2D true-Fast Imaging with Steady-state Precession (true-FISP) and phase-contrast sequences suggested that conjoint cusp hypomobility, that is, restricted motion in opening phase, was responsible for flow-jet deflection from the vessel’s axis [1]. In a small, selected cohort of patients with morphologically and functionally ‘homogeneous’ BAVs, all right-coronary-left-coronary type, all non-stenotic and non-regurgitant, the cusp opening angle (COA, between the long-axis section of the central part of the fused leaflet and the ventricular-aortic junction plane, in systole), was significantly narrower than in matched tricuspid aortic valve (TAV) of healthy subjects, showing a significant correlation with the yearly aortic growth rate in subsequent prospective follow-up [1], thus proving to be a promising tool for prognostic stratification. Since then, we have expanded that cohort, confirming the results also in the right-coronary-non-coronary type of BAV.

The study by Girdauskas et al. [2] similarly proposes novel 2D-MRI parameters to quantify flow derangement in the ascending aorta of BAV patients, but focuses on a different setting, that is, severe aortic stenosis. By choosing normally functioning BAV patients, our aim [1] was to identify early imaging markers, whereas Girdauskas’ study [2] sought to transfer the concept to the surgical decision-making process: an effective MRI predictor of aortopathy severity could help in the choice of whether to replace the ascending aorta at the time of aortic valve replacement for BAV stenosis, regardless of the diameter.

Observing a significant association, however, does not mean identifying a causal relationship. In our abovementioned study [1], the two groups of patients (BAV and TAV) were well matched for all clinical variables except ascending aorta dimensions (larger in BAV), so we wondered whether the skewed flow pattern in BAV subjects could be a consequence rather than a determinant of the aortopathy: given that differences in diameter and mechanical properties can affect flow patterns, we were faced with the typical ‘which came first the chicken or the egg’ dilemma. Thus, we used computational fluid dynamics to reproduce the flow pattern associated with BAV (restricted COA) and TAV motion (normal COA).
but scaling the dimensions and properties of the ascending aorta to be equal in the two models; thus, we could confirm that restricted cusp opening was enough to explain the BAV-related flow patterns observed in-vivo through MRI [1]. In Girdauskas’ study, the left ventricle/aorta angle (LV/aorta) was significantly correlated with what they considered as ‘parameters of aortopathy severity’, that is, aortic indexed diameter and histological sum-score: but was the LV/aorta determining or determined by the aortopathy? The ascending aorta tends to elongate in BAV aortopathy [3], with the heart passively assuming a more horizontal position as a consequence: aortic length was not measured [2]; thus, it cannot be excluded that elongation consistently accompanied wall degeneration, in turn causing the widening of the LV/aorta angle. Again, the chicken and egg question. Intuitively, in the setting of BAV stenosis, the valve orifice geometry should represent the most downstream determinant of flow-jet direction; therefore, the evidence of good correlation of the histological score with the LV/aorta angle (representing the ‘first obstacle’ to flow jet, as underscored by Girauskas et al. [2]) but not with valvular variables (the ultimate obstacle) seems to support the idea that the angle could be determined by the aortopathy rather than having a causal role.

Several studies have recently employed the more sophisticated 4D-Flow-MRI [3–6]: although not as widely available as standard 2D-MRI, it not only allows for the visualization of flow vectors and streamlines in 3D, but also for the estimation of wall shear stress (WSS) and other flow-related parameters. In BAV patients, Bissell et al. [4] have suggested that wider flow-jet angles induce greater amount of rotational flow, with consequent increase of the in-plane component of WSS: importantly, this appeared as a stronger contributor to aortic dilatation than the through-plane WSS component. Of note, the flow-jet angle in 4D-Flow-MRI-based studies [4, 5] is measured as the angle between the mean flow vector and the root central axis, thus being in fact a bidimensional measurement directly quantifying the phenomenon that was indirectly measured by the COA [1]. Girdauskas’ jet/aorta angle [2] is the angle between the jet and the vessel axis at the level of the impact: this level can vary widely (i.e. be more proximal or distal along the ascending) depending on both valve orifice orientation and aorta morphology and curvature.

In the end, the ‘severity’ of the aortopathy in an individual patient should define (or be defined by) the individual risk of a catastrophic aortic event. In this perspective, classical histology might be not reliable as a metric of aortopathy severity: for example, Roberts et al. [7] reported that severe rarefaction of medial elastic fibres was rarely associated with acute type A aortic dissection. Moreover, Bechtel’s score includes features of both medial degeneration and atherosclerosis, which may be misleading [8]. However, the incidence of acute aortic events in the BAV population is low (<0.3% per year) [9]; therefore, very large series and long follow-up periods would be necessary to verify the predictive value of any functional risk marker. In smaller series with a shorter follow-up, the growth rate of the aorta is commonly accepted as a surrogate parameter for the clinical severity of the aortopathy [1, 5]. A longitudinal study is strongly warranted before any conclusion about usefulness of functional MRI parameters in risk prediction can be made: quoting the common saying again, one must start with the egg only and then wait to see if the chicken comes.

Future studies should compare the previously proposed/validated parameters of root function and flow derangement [1, 2, 4, 5, 10] in terms of their ability to predict aortic events or the rate of dilatation progression.

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**REFERENCES**


