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EDITORIAL

Multivalvular diseases: look beyond the valves—no way home

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This editorial refers to 'Alterations in left atrial and ventricular coupling in mixed aortic valve disease', by M. Sooriyakanthan *et al*., https://doi.org/10.1093/ehjci/jeae199.

Significant mixed aortic valve disease (MAVD), characterized by concurrent aortic stenosis (AS) and aortic regurgitation (AR), poses a unique clinical challenge due to its complex pathophysiology and diverse haemodynamic effects. AS leads to obstruction of blood flow from the left ventricle (LV) to the aorta, increasing pressure overload, whereas AR results in diastolic backflow of blood into the LV, causing volume overload.[1] This combination exacerbates the myocardial wall stress on the LV, often leading to progressive ventricular dilation, hypertrophy, and adverse cardiovascular events if untreated.[2] Echocardiography remains the cornerstone for diagnosing and assessing the severity of both AS and AR, providing detailed haemodynamic data and anatomical insights. However, none of the classic echocardiographic parameters adequately reflect the overall haemodynamic burden associated with the sum of AS and AR.[3] Atrioventricular (AV) coupling understanding is valuable not only for establishing the pathophysiological mechanisms of mixed valvular diseases but also for the prevention of related adverse cardiovascular events and for an optimal targeted treatment. Managing significant MAVD as well as the best timing of the intervention remains an unresolved clinical challenge. Very limited clinical evidence is available in the field of combined valvular disease.[3]

In this issue of *European Heart Journal: Cardiovascular Imaging*, Sooriyakanthan *et al*.[4] address MAVD from a pathophysiological point of view, and comparatively assess AV coupling on the basis of isolated or combined presentation and severity of aortic valvulopathy. They retrospectively identified 46 patients with moderate MAVD (MMAVD) from echocardiographic data and they compared them with 81 isolated moderate AS (mAS), 50 isolated severe AS (sAS), 48 moderate AR (mAR), 35 severe AR (sAR) cases, and 66 controls. Participants had normal LV function and were in sinus rhythm. Prior valve intervention or concomitant significant valve disease was exclusion criteria. Peak longitudinal strain (LS) of LV and left atrium (LA) were evaluated. AV coupling was determined both by AV strain (AV-S), calculated as the sum of the absolute values of LV GLS and LA reservoir strain, and LA:LV end-systolic volumetric ratio. The study confirmed good reproducibility for strain measurements. Among 260 patients, in MMAVD cohort, LV strain was comparable to the patients with mAS and sAS and significantly lower compared with controls and moderate and severe isolated AR. Very interestingly, they reported that AV-S was significantly lower in MMAVD as compared with the control group and the isolated moderate valvulopathies (mAS and mAR) but on the other hand, it remained similar to the values found for isolated severe valvulopathies (sAS and sAR).

As previously mentioned, there is a lack of data on combined or multiple-valve disease, which prevents the formation of evidence-based recommendations. When stenosis and regurgitation are equally severe, decisions regarding interventions should be guided by symptoms and objective consequences such as presence of LV dilatation or dysfunction, rather than the severity indices of either condition.[1,3] Intervention may be considered for non-severe multiple lesions if they are associated with symptoms or result in LV impairment.[3] This particular situation is not addressed by existing guidelines, which is why it is crucial to evaluate the overall impact of the lesions, including a thorough assessment of ventricular volumes and pulmonary pressure.[1,3] Symptomatic MAVD patients rarely meet the criteria of LV impairment that would indicate the need for valve replacement such as and LV end-systolic diameter of 50 mm or greater,[1,3] indicating that LV hypertrophy might prevent the LV from dilating due to the volume overload. Additionally, the rise in stroke volume due to the regurgitant flow may exacerbate severe pressure overload, even if the aortic valve area is >1 cm^2.[1] Limitations in the accurate echocardiographic quantification of MMAVD have led to new imaging parameters such as AV coupling potentially providing useful insights into this knowledge gap.

As of today, there is no universally accepted left AV coupling index definition. The most widely described approach in scientific literature is the ratio of LA end-diastolic volume to LV end-diastolic volume known as the left atrioventricular coupling index (LACI), both evaluated by transthoracic echocardiography and by cardiac magnetic resonance (CMR). It has been correlated with adverse cardiovascular events.[5–7] Meucci *et al.*[6] suggested an uncoupling cut-off point of 40% based on the risk excess of new-onset AF in a cohort of patients with hypertrophic cardiomyopathy. Pezel *et al.* have even developed a fully automated LACI measurement algorithm using artificial intelligence that predicts heart failure admissions and cardiovascular mortality in patients undergoing stress CMR who showed LGE or perfusion defects. This innovative research shows promising results independent of classical prognostic factors.[7] Otherwise, Cameli *et al.*[8] assessed AV coupling through global AV-S measured by speckle-tracking echocardiography and resulting from the algebraic sum of absolute peak atrial LS

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and LV LS strain value. Similarly, Hinojar *et al*. reported the predictive role of a new index named STREI combining right atrial and ventricular strain in the setting of significant tricuspid regurgitation as a predictor of adverse events. This index is calculated as the algebraic sum of two times the absolute value of the RV free wall strain and one time the reservoir RA strain and proved to have an independent prognostic impact on all-cause mortality and heart failure episodes.[9] Zhou *et al*.[10] also evaluated AV coupling by means of Pearson's correlation coefficient for longitudinal LV and LA strain over the entire cardiac cycle. The LA/LV strain ratio was defined as the slope of the regression line of the strain–strain loop. However, this approach is complex and not very applicable to clinical practice.

In the article covered by this editorial, AV coupling was evaluated from two perspectives. First, from a volumetric approach with the AV telesystolic-volume ratio and, secondly, from the mechanical assessment of myocardial deformation with the global strain.[4] One aspect to take into account is that Sooriyakanthan *et al.* performed measurements only in apical four-chamber view, while other studies included both four- and two-chamber views.[4,8] Given that the patients of this cohort did not present with regional wall motion abnormalities, the reproducibility of the results may be improved. Concerning the AV-S, the ventricle:atrium relative value given to the global sum of both strains was 1:1, whereas other authors adopted alternative ratios.[9] To the best of our knowledge, no study has assessed AV coupling to date through AV-S evaluated by CMR feature tracking techniques. Moreover, this novel paper introduces the ratio LA:LV end-systolic volumes (ESV) and demonstrates in the study cohort that it was lower than in the control group and severe isolated valvular heart disease and higher than in the sAR, with no differences found with the mAR group.[4] This ratio is mainly modified by the increase in LV ESV and therefore by volume overload,[3] so we hypothesize that the LV end-systolic volumetric ratio is better suited for the assessment of the LV impairment in this particular scenario.

MMAVD represents a major clinical challenge given the complete lack of clinical evidence for the optimal timing of early intervention. Sooriyakanthan *et al.* article demonstrates that the impact on left cardiac chambers might be similar to that in isolated severe aortic valve disorders. AV coupling is a promising indicator of cardiac left chambers performance currently under clinical study in several disorders. Different definitions and calculations have been reported by various authors, including measurements using a variety of imaging technologies and techniques. For this reason, there is still a long way to travel towards a more accurate definition of the concept and systematic measurement. Specifically in the field of MAVD, it may represent a milestone as shown in this work. The results encourage further research in order to give light in this field full of shadows.

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Data availability

The data that support the findings of this study are available from the corresponding author, upon request.

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