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EDITOR'S PAGE


Is it Time to Look Beyond the Valve and Ventricular Function for Assessing Patients With Aortic Stenosis?

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The decision to perform aortic valve replacement is driven by symptoms, the severity of the stenosis, assessed primarily using echocardiography (valve area and pressure gradient), and ejection fraction, also assessed largely using echocardiography. The logic behind recommendations for aortic valve replacement (surgical or transcatheter) is to reverse an abnormality that is sufficiently severe that it affects survival, left ventricular (LV) function, and symptoms. This paradigm, unchanged for decades and although effective, may not be optimal. The current indication for surgery may be to detect late-stage valve disease, and advanced imaging (looking at more than valve severity and global LV function) reveals significant LV damage (maladaptive remodeling at the myocyte, wall, and chamber levels, increased fibrosis, and expansion of extracellular matrix components) in patients presenting for intervention (1). It is likely that identifying these maladaptive components at an earlier stage might help in stratifying risk and deciding on the timing of intervention, with the aim of improving prognosis.

Advanced imaging has already gained significant traction in many areas of valve disease. Transcatheter aortic valve replacement procedures are routinely planned on the basis of images obtained by cardiac computed tomography (CT). Leaflet calcification as measured by cardiac CT has been shown to predict outcome and speed of deterioration. In patients with insufficient echocardiographic windows, the assessment of valve area by cardiac CT or cardiac magnetic resonance (CMR) is a validated alternative. More advanced uses of CT published in this journal include predicting unfavorable anatomy before intervention (2) and complications post-intervention (3). CMR, although less used in valvular heart disease, is showing increasing utility in complex situations (e.g., assessing prosthetic valve function [4], planning intervention [5]).

However, the power of imaging has not been fully harnessed in other areas of potential benefit, especially in defining subsets that can benefit from early intervention. As an example, despite an increasing amount of data on the prognostic value of late gadolinium enhancement (LGE) and diffuse abnormalities of the myocardium itself as measured by T1 mapping in this patient group, the assessment of these parameters is not (yet) recommended in the guidelines.

Two papers in this issue add to the value of imaging in understanding aortic stenosis (AS).

Fibrosis, both replacement as well as interstitial, detected with CMR has prognostic value in AS (6-8), and it has been postulated that these patterns can help classify patients independent of valvular dysfunction alone (8). Forty percent to 50% of patients with severe AS demonstrate LGE representing irreversible regional damage. In large cohorts of patients with various forms of cardiomyopathies, LGE has been shown to be an independent predictor of

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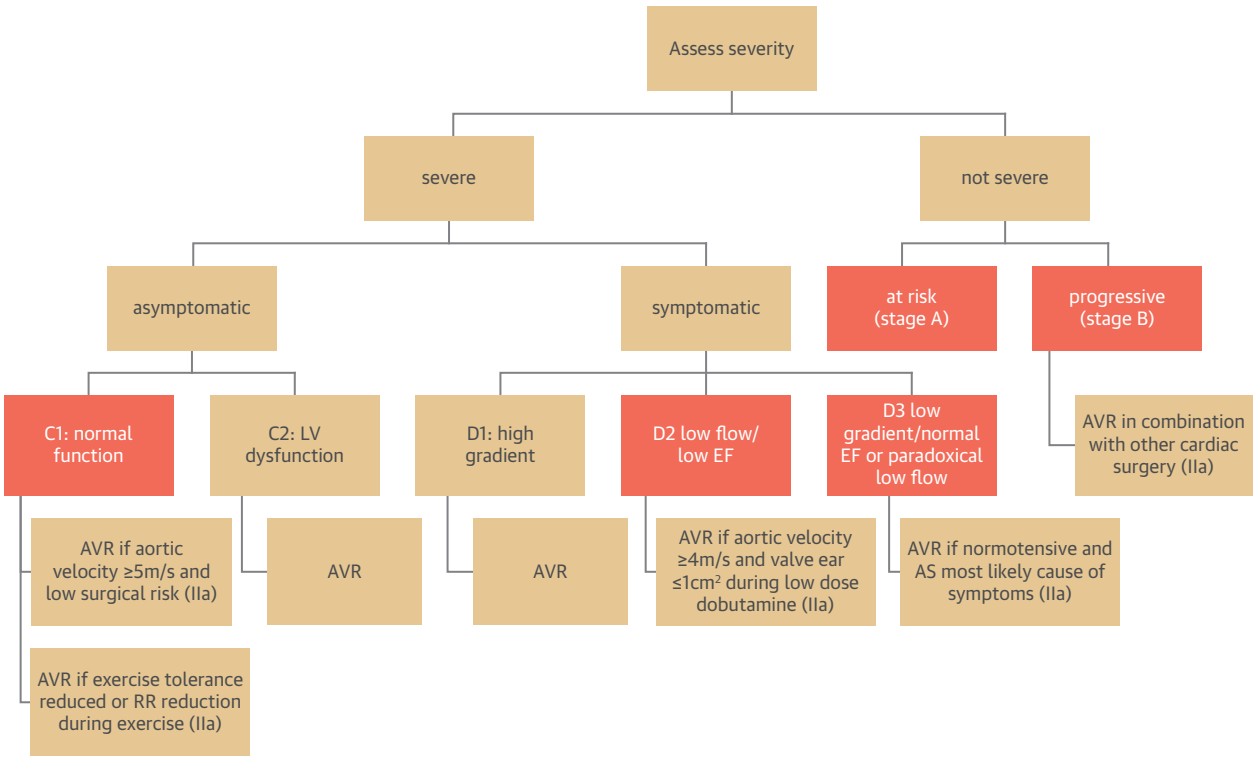
FIGURE 1 Aortic Stenosis Subsets That Might Benefit from CMR



Potential areas where cardiac magnetic resonance (CMR) might help in stratifying patients with aortic stenosis **(orange boxes)**. Future studies focused on these subsets will clarify the exact added value of CMR. AS = aortic stenosis; AVR = aortic valve replacement; EF = ejection fraction; LV = left ventricular.

outcomes beyond ejection fraction (8). In patients with moderate to severe AS, the presence of midwall fibrosis as imaged by CMR portends a negative prognosis over 2-year (7) and 5-year (8) follow-up and is a stronger predictor than ejection fraction or wall thickness. In patients with bicuspid aortic valve, the presence of LGE is an important predictor of valve replacement within the next year (9). In addition, there are increasing data that diffuse fibrosis as imaged by T1 mapping further adds to risk assessment (8). Increasing T1 and extracellular volume (ECV) values correlated with greater hypertrophy, myocardial injury, diastolic dysfunction, and longitudinal systolic dysfunction consistent with progressive LV decompensation and predicted adverse prognosis. In this issue of *iJACC*, Lee et al. (10) take this forward with a focus on the prognostic importance of T1 mapping; they convincingly demonstrate that one-third of patients with AS have increased native T1 values and that these patients are at significantly higher risk for mortality or heart failure.

It is well known that men and women respond differently to pressure overload. Women present later and with fewer symptoms than men with a similar degree of AS. Men develop more scar and show faster deterioration of ejection fraction with similar severity of AS compared with women (11). Once remodeling has occurred, women have a worse prognosis than men. In this issue, Treibel et al. (12), using comprehensive CMR evaluation, shed further light on the impact of sex dimorphism. Men and women have a normal gradient of difference in mass-to-volume ratio (sex dimorphism), but this seemed to be exaggerated in patients with severe AS presenting for intervention. Echocardiographic studies had hinted at hypertrophic remodeling in women, but this was not conclusive; the present CMR study conclusively shows that remodeling is much more maladaptive in men (concentric and eccentric hypertrophy) compared with women (more concentric remodeling) with similar degree of severity of AS. This had consequences: lower ejection fraction, as well as higher N-terminal pro-brain natriuretic peptide, LGE, and ECV. CMR classified geometry better than echocardiography, which underestimated LV remodeling. Given the strong prognostic value of scar and ejection

fraction as described earlier, women may tolerate a similar amount of AS better than men but are at higher risk once remodeling is present. It is interesting that the same group previously found that native T1 and ECV worsen proportional to the severity of remodeling, but T1 and ECV levels remained rather sex independent. This might make its utility more meaningful. Future studies should urgently investigate whether intervening early in patients starting to demonstrate maladaptive remodeling is helpful.

Deciding when to intervene is a fine art, and experience in transcatheter aortic valve replacement shows that outcomes are worse after intervention once certain patterns of maladaptation on imaging are present (13). However, relevant subsets may not be clearly discernable in lesser stages of AS severity (14). Both these papers in this issue of *iJACC* thus advance this field further. It might be time to critically evaluate the integration of advanced imaging in analyzing risk and timing of intervention in patients with valvular heart disease (e.g., the assessment of LGE and diffuse fibrosis into the standard algorithm of patients with AS) (**Figure 1**). Specifically, patients at stage A or B, asymptomatic patients with normal LV function (stage C1), and symptomatic patients with low flow and low ejection fraction (stage D2) or low gradient and normal ejection fraction (stage D3) could potentially benefit from earlier consideration of aortic valve replacement by identifying those with higher risk on the basis of the presence of diffuse or midwall fibrosis. As women remain more frequently asymptomatic and preserve the ejection fraction longer, they may benefit most from such an approach. Although comparative effectiveness data demonstrating the benefit of such an algorithm are lacking, the strength of the prognostic data and the close relationship of the imaging results with our understanding of pathophysiology strengthen the case for the clinical use of CMR in decision making for patients with AS.

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