

Cardiac Magnetic Resonance in Valvular Heart Disease: Assessment of Severity and Myocardial Remodeling

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ABSTRACT: Cardiac magnetic resonance (CMR) has emerged as the gold standard in assessing ventricular mass, volume, and systolic function. Due to these and other strengths, CMR has increasingly been used to study valvular heart disease (VHD) and resultant cardiac remodeling. By using CMR to assess flow, limitations in echocardiographic assessment of VHD can be overcome, particularly in regurgitant lesions. The following article reviews the current role of CMR imaging in studying disease severity and myocardial remodeling in patients with VHD.

INTRODUCTION

There are several advantages of using cardiac magnetic resonance (CMR) to assess valvular heart disease (VHD). CMR provides a variety of unobstructed views of the heart and valves, it does not require ionizing radiation, and there is no need for contrast administration to quantify VHD severity. In addition, CMR is a powerful technique to measure forward and regurgitant flow volume, flow velocity, and tissue characteristics, particularly myocardial fibrosis. The recent American Society of Echocardiography guidelines on valvular regurgitation assessment highlight the utility of CMR, particularly when echo assessment is limited or discordant findings exist with clinical and Doppler assessment.¹ The excellent interstudy reproducibility of CMR makes it ideal for serial assessment of patients. However, patients with both VHD and arrhythmias can be challenging to study with CMR because images need to be acquired over multiple cardiac cycles. In this review, we will focus on CMR assessment of the three most commonly encountered forms of VHD: aortic stenosis, aortic regurgitation, and mitral regurgitation.

CMR ASSESSMENT OF AORTIC VALVE STENOSIS

Aortic stenosis (AS) is the most common valvular disease and affects approximately 4% of individuals over the age of 70.² Assessment of AS severity by CMR uses two independent and complementary parameters: the anatomic orifice area and the peak velocity/gradient across the aortic valve.³ These assessments can be done without the use of gadolinium-based contrast. The aortic valve is planimetered from a series of sequential high-resolution steady state free precession or gradient echo cine images acquired every 4 mm from an aortic short-axis plane. The smallest systolic opening during peak systole is planimetered to quantify the anatomic valve area. Phase-contrast velocity mapping calculates a shift of

the precession between the stationary protons and protons moving in a magnetic field. The magnitude of this phase shift is proportional to the velocity of interest; the determined peak aortic valve velocity is the highest velocity where there is no aliasing.³ The effective aortic valve area derived by the continuity equation on echocardiography can be calculated by CMR as well with high agreement (Figure 1).⁴

Aortic stenosis is a classic model of a left ventricular (LV) pressure overload state. The LV adapts to the increase in LV pressure by myocyte hypertrophy and increased wall thickness to normalize wall stress. However, maladaptive changes also occur, including inappropriate hypertrophy, fibrosis, dilatation, and contractile impairment. There is individual variability in the adaptive remodeling to AS, with important gender differences described in recent CMR investigations.⁵⁻⁷ Dweck et al. described six patterns of cardiac remodeling in 91 patients with moderate to severe AS (Figure 2). The severity of AS was unrelated to the degree and pattern of hypertrophy, and men had a higher indexed LV mass than women.⁸

In addition to accurate assessment of cavity remodeling, CMR can also measure myocardial fibrosis with late gadolinium enhancement (LGE) and extracellular volume fraction. LGE represents replacement fibrosis and is present in about half of patients with severe AS, with a noninfarct pattern in approximately one-third of them. The presence of replacement fibrosis portends a 2-fold increase in mortality even after aortic valve replacement (AVR) for severe AS.⁹ The extent of replacement fibrosis was inversely associated with LV functional improvement after AVR.¹⁰ Extracellular volume fraction (ECV) is derived from T1 mapping before and after administration of an extracellular gadolinium contrast agent. It measures the percent of the extracellular compartment of the myocardium, thus inferring interstitial fibrosis not detected by LGE. Indexed ECV or indexed matrix volume is derived from ECV fraction

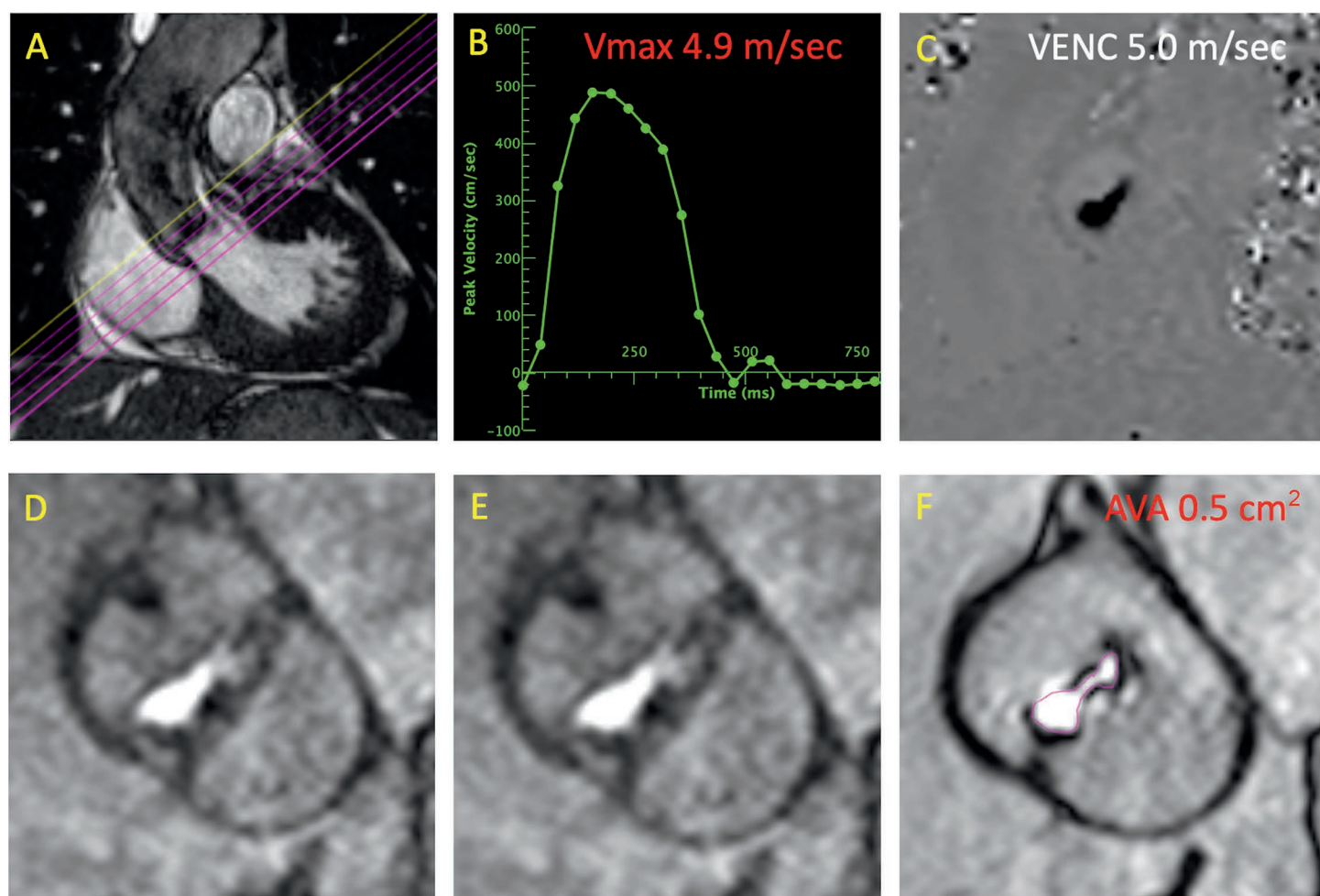


Figure 1.

Cardiac magnetic resonance imaging quantitation of aortic stenosis severity. Panel A shows localization of an appropriate short-axis cine along the long axis to measure the anatomic valve area at leaflet tips (panels D, E, F). Panel B shows calculation of the peak velocity across the aortic valve. Panel C shows a velocity-encoded phase contrast sequence with velocity set at 500 cm/sec, showing no aliasing of blood flow. VENC: velocity encoding; Vmax: peak velocity; AVA: aortic valvular area

to measure the total volume of the extracellular compartment (indexed ECV = ECV $\times$ LV end diastolic myocardial volume normalized to body surface area). Indexed ECV demonstrates good correlation with diffuse fibrosis on biopsy and predicts mortality and adverse remodeling beyond LGE.⁷ A recent CMR study showed that LGE after AVR does not resolve but that both interstitial fibrosis and cellular hypertrophy regress. However, cellular hypertrophy regresses to a greater degree by 1 year after AVR compared to interstitial fibrosis. As a result, ECV fraction may increase.^{11,12}

Gender differences have been long recognized in myocardial remodeling related to AS. However, recent CMR studies led to new insights on gender differences in ventricular adaptive processes related to myocardial cavity and tissue level. In

addition to having a lower LV mass index, women appear to have less concentric hypertrophy and myocardial fibrosis than men but develop symptoms earlier.⁵⁻⁷ An ongoing randomized clinical trial (Early Valve Replacement Guided by Biomarkers of LV Decompensation in Asymptomatic Patients With Severe AS) could answer whether replacement fibrosis guided intervention in asymptomatic severe AS patients could improve outcomes.

CMR ASSESSMENT OF AORTIC VALVE REGURGITATION

Aortic regurgitation (AR) is less common than AS and results in a combined LV pressure and volume overload. The natural history of AR has been characterized by progressive LV dilatation and hypertrophy in response to the hemodynamic load on the ventricle, with increased

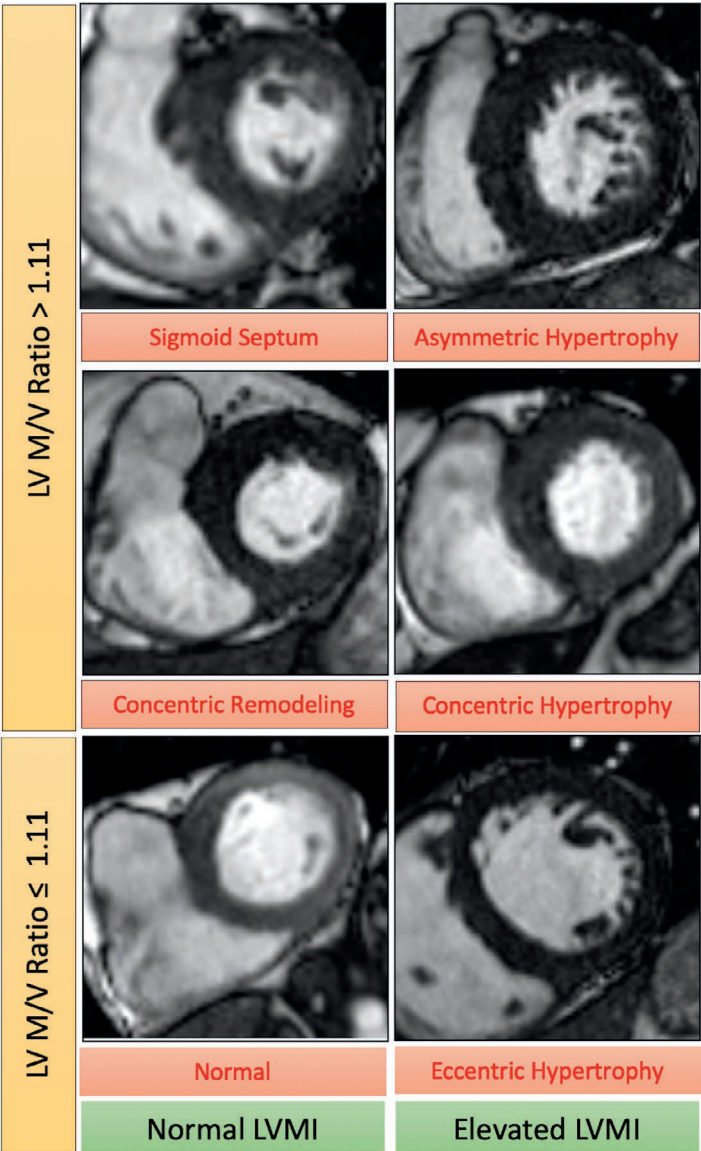


Figure 2.
Patterns of left ventricular (LV) remodeling in aortic stenosis. An abnormal mass-to-volume ratio (M/V ratio, analogous to relative wall thickness on echocardiography) was calculated as two standard deviations above a group of normal volunteers' M/V ratio. LVMI: indexed LV mass

wall stress and eventual manifest LV dysfunction. CMR can determine the mechanism of AR, assess its severity, study the resultant myocardial remodeling, and provide a comprehensive assessment of the aorta. To assess AR severity, CMR can directly measure regurgitant flow at the sinotubular junction and can also compare aortic versus pulmonary forward stroke volumes.^{1,3} CMR methods require no geometric assumptions and are highly useful in

cases with eccentric AR, multiple valve lesions, or limited echocardiographic windows (Figure 3).

There are relatively few studies of ventricular remodeling and clinical outcomes of AR using CMR. Myerson et al. studied 113 patients with moderate or severe AR with a mean follow-up of 2.6 years. A regurgitant fraction > 33% was a strong predictor of progression to symptoms or the need for AVR, while an LV end diastolic volume > 246 mL (nonindexed) had good predictive ability as well. Combining both parameters provided the best yield.¹³ Another study also showed a CMR-derived regurgitant fraction > 30% to best correlate with grade 4+ AR using echocardiography.¹⁴ A study by Harris et al. of 29 patients with chronic AR determined that a CMR regurgitant volume > 50 mL identified those meeting the end point of AVR more strongly than echocardiographic assessment (mean follow-up 4.4 ± 1.5 years).¹⁵ Furthermore, ventricular volumes were more strongly correlated with regurgitant volume than linear LV dimensions, suggesting that LV volumes better reflect ventricular remodeling in patients with AR.¹⁶ More research is needed to define the optimal cut-offs for surgery using CMR and to determine if gender affects these thresholds. To our knowledge, no CMR studies have directly assessed the impact of gender on the adaptive response to AR.

Myocardial fibrosis in AR has long been described in histopathology studies and is characterized by increased fibronectin and noncollagen components.¹⁷ In a recent study, ECV measured on CMR strongly correlated with interstitial fibrosis on histology in patients with severe AR. A small CMR study by Sparrow et al. showed that segment-based myocardial T1 mapping has the potential to show differences between relaxation times in AR versus normal hearts.¹⁸ In another study that included 9 patients with severe AR, ECV measured on 3 Tesla CMR was strongly correlated with the extent of interstitial fibrosis on histology (R = 0.79, P = .011).¹⁹ There was no significant relationship between the amount of LGE and the magnitude of fibrosis determined by histology. Conversely, in a study that included 26 patients with severe AR, LGE was present in 69% of patients and the correlation between LGE and histology was strong (R = 0.70, P < .001); ECV was not assessed.¹⁰ More research is needed to determine if LGE or ECV parameters impact outcomes in AR patients.

There are very few CMR studies on reverse remodeling after AVR for AR since this is typically assessed using echocardiography. One CMR study of 29 patient with severe AR showed a significant reduction of LV volumes and mass after AVR, with 24% of patients having persistent LV dilatation and 45% exhibiting persistent elevation of indexed LV mass at a mean of approximately 7 months after surgery. Left ventricular end diastolic volume was a significant independent predictor of

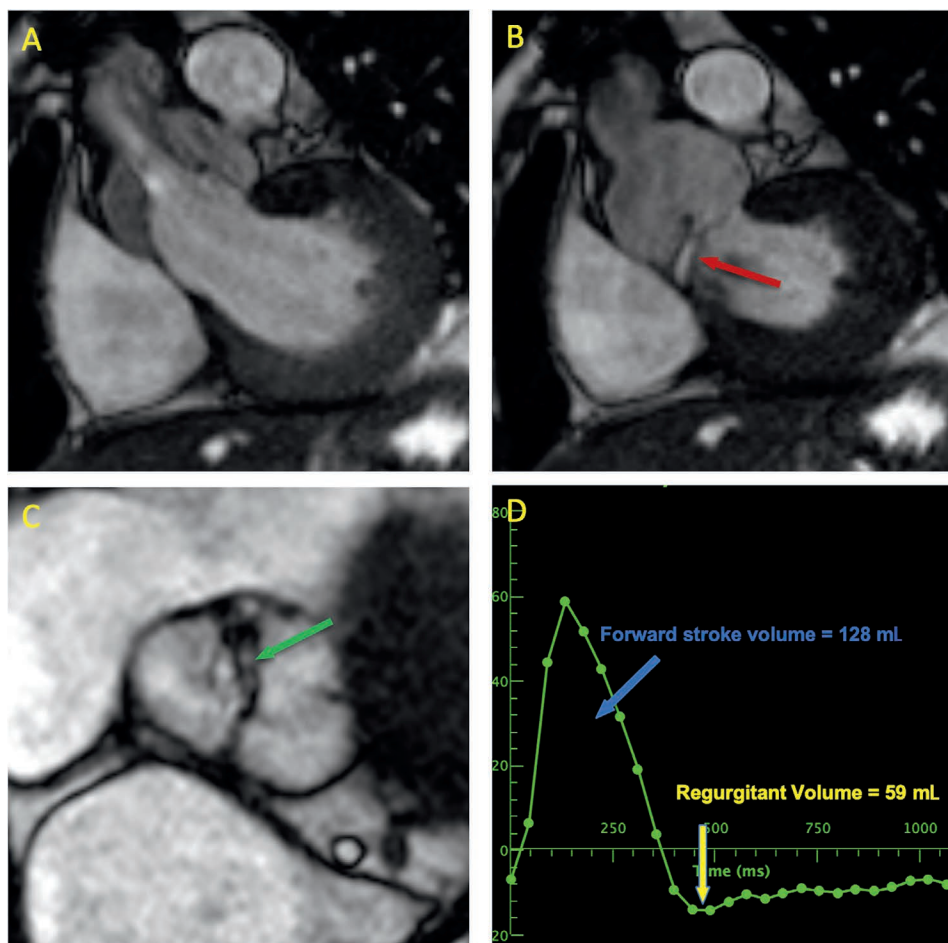


Figure 3.

Assessment of aortic regurgitation. Panels A and B show assessment of bicuspid aortic valve regurgitation with an eccentric jet (red arrow). Panel C demonstrates malcoaptation of the aortic valve leaflets in diastole (green arrow). Panel D shows direct measurement of the regurgitant volume at the sinotubular junction level.

favorable remodeling after AVR, whereas echocardiography measures were not.²⁰

CMR ASSESSMENT OF MITRAL VALVE REGURGITATION

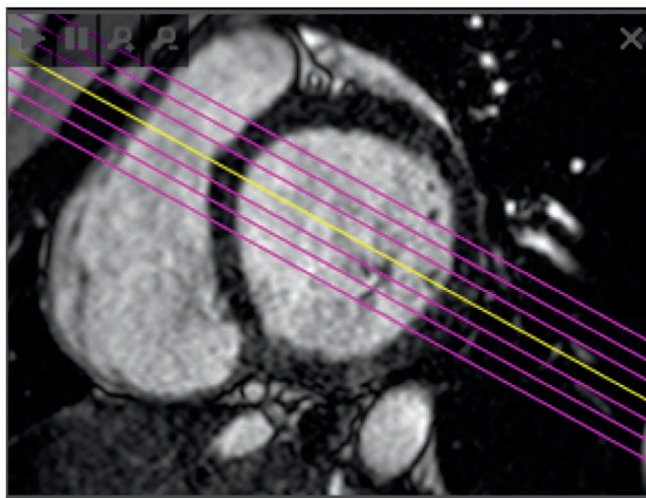
Mitral regurgitation poses a unique challenge in assessing VHD because it is complex and dynamic, with multiple mechanisms that can overlap. The recent American Society of Echocardiography guidelines recommend an integrative approach to assessment of MR severity and stress the importance of defining the mechanism of MR.¹ CMR offers several

advantages in MR assessment in that it can describe valvular pathology and quantify both MR severity and myocardial cavity and tissue remodeling. It can also differentiate primary from secondary MR via dedicated cine imaging performed through the different scallops of the MV leaflets and by studying the LV, left atrium, and mitral annulus (Figure 4).²¹ In secondary MR, CMR offers accurate assessment of LV dilation and function and identification of myocardial and papillary muscle scarring (Figure 5). The primary way to assess MR severity is to determine the difference between the

planimetered LV stroke volume and the aortic forward stroke volume obtained by phase-contrast imaging. Other methods can also be followed per the guidelines, and CMR measures are highly reproducible.¹⁶ Comparative studies of CMR and 2D echocardiographic quantitation of MR severity have shown modest concordance, and comparisons with 3D echocardiography have shown varied results.²² Furthermore, CMR regurgitant volume performs better in predicting postoperative LV remodeling.²²⁻²⁴ With regard to prognostic data, a study by Myerson et al. found that CMR regurgitant volume > 55 mL or regurgitant fraction > 40% predicted development of symptoms or need for surgery and that these measures performed better than LV volumes. In a small subgroup that underwent quantitative echocardiographic analysis by effective regurgitant orifice area, there was only a modest separation of surgery-free survival curves and it was not statistically significant.²⁵ A second study by Penicka et al. found modest concordance between an integrative echocardiography approach and CMR in patients with moderate to severe MR. Importantly, the majority of differences in severity classification were observed in patients with late systolic, eccentric, or multiple jets, where correlation between echocardiography and CMR was poor. CMR regurgitant volume had the largest area under the curve to predict mortality or need for surgery.²⁶

Similar to aortic valve disease, there is growing interest in assessing tissue characteristics in primary MR, particularly due to its association with arrhythmias. Our group studied a large cohort of primary MR patients with and without mitral valve prolapse (MVP). The prevalence of LV replacement fibrosis was high (36.7%) in the MVP group and increased with severity of MR, with fibrosis occurring in 50% of patients with MVP and severe MR. In the non-MVP group, the prevalence of

Short-axis view of the mitral valve to localize diseased scallops



4-mm high-resolution long-axis views of the mitral valve scallops

A1-P1

A2-P2

A3-P3

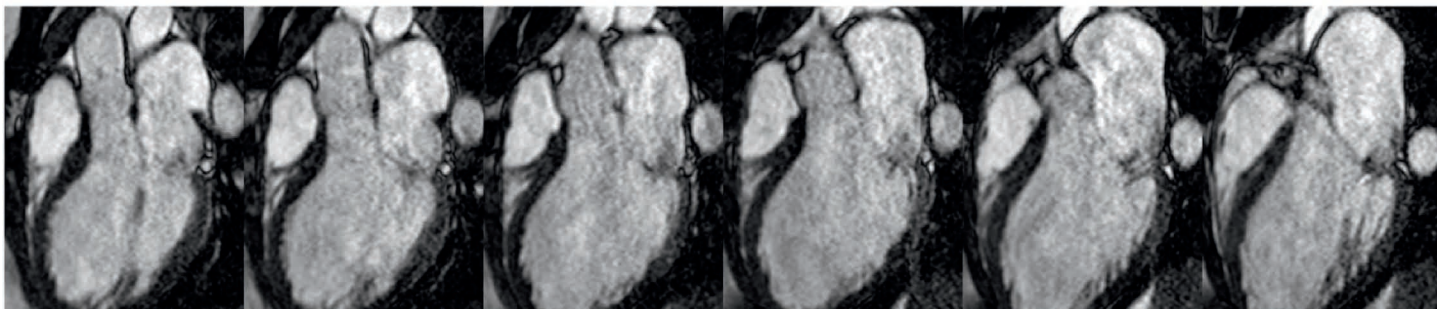


Figure 4.

Assessment of mechanism of mitral regurgitation.

fibrosis was low (6.7%) and independent of severity of MR. Replacement fibrosis was noted particularly in the segments adjacent to the posteromedial papillary muscle and was typically small in extent, occurring in mid-wall striae or patchy patterns. These findings were largely consistent with prior smaller studies.²⁷ The presence of replacement fibrosis was also associated with increased symptomatic ventricular arrhythmic events in patients with MVP (Figure 5), although these findings require confirmation in a larger multicenter study. Extracellular volume fraction also appears to increase in primary MR and is associated with reduced exercise capacity and myocardial deformation indices compared to controls.²⁸ Studies to assess whether ECV and LGE parameters can predict favorable postoperative remodeling are ongoing.

CONCLUSION

Cardiac magnetic resonance is a powerful modality to assess valvular heart disease. Its strengths emerged in valvular regurgitation, particularly in cases with eccentric lesions or limited echocardiography. CMR should be considered the gold standard in studying ventricular remodeling, which largely is the arbitrator of decision making in asymptomatic patients with severe VHD. Additionally, CMR provides insights into tissue characteristics, with important prognostic information from replacement and potentially interstitial fibrosis imaging. Prospective studies, some currently ongoing, are needed to further delineate CMR parameters that best correlate with outcomes and prevent adverse cardiac remodeling.

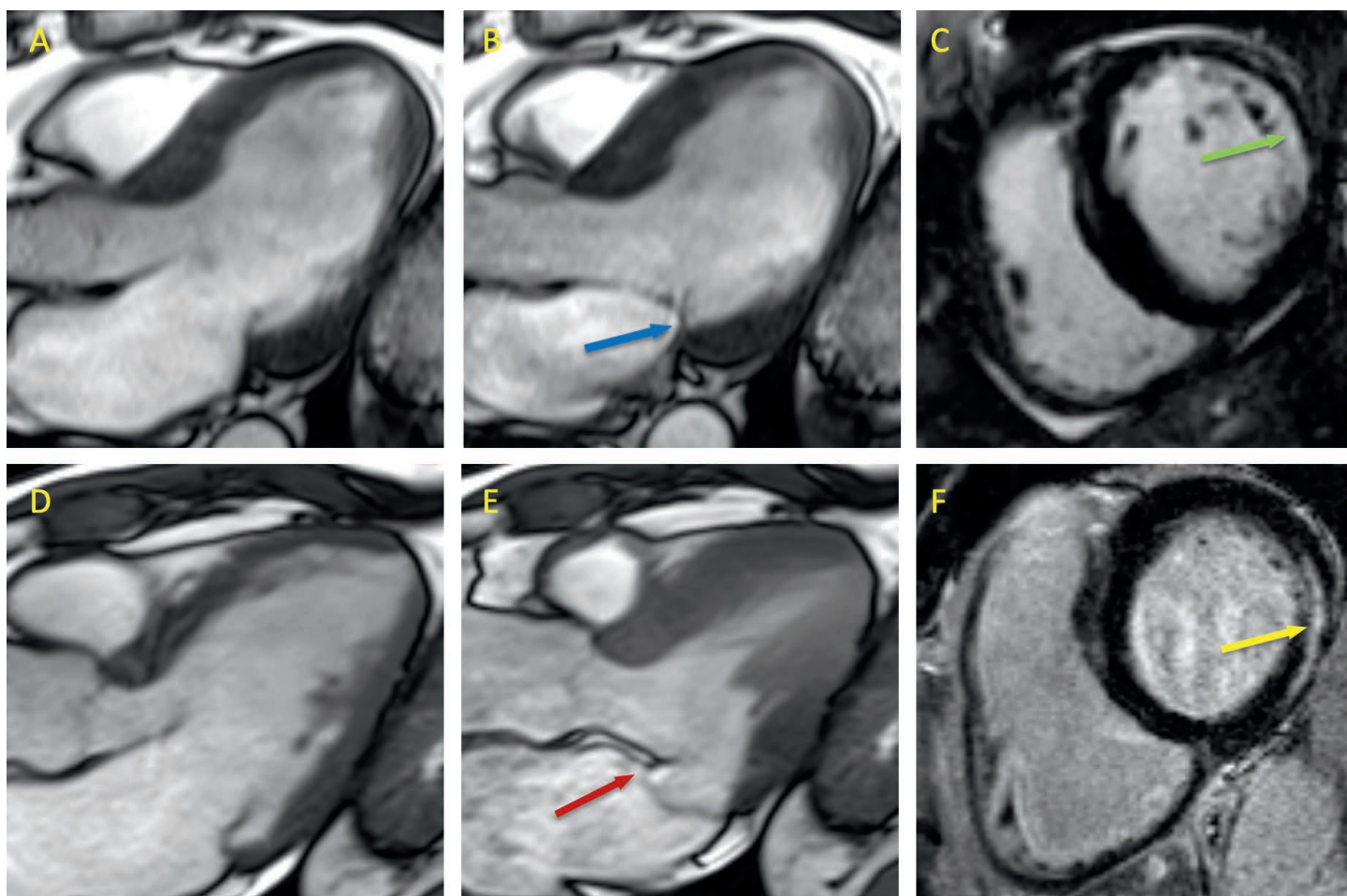


Figure 5.

Assessment of mitral regurgitation (MR) etiology and tissue remodeling. Panels A and B show secondary MR due to posterior leaflet tethering in a patient with myocardial infarction involving the left circumflex artery, with a posteriorly directed jet (blue arrow), while panel C shows subendocardial infarction in the lateral wall (C, green arrow). Lower panels show (D) primary degenerative MR during diastole, (E) systole with flail posterior leaflet causing an anteriorly directed jet (red arrow), and (F, yellow arrow) replacement fibrosis in the inferolateral wall.

KEY POINTS

- Cardiac magnetic resonance (CMR) is accurate and reproducible in assessing valvular heart disease (VHD) severity and is the gold standard in assessing myocardial remodeling.
- CMR should be considered particularly in regurgitant valvular lesions where echocardiographic assessment is limited, discordant with other findings, or in multiple/ eccentric jets.
- More research is needed to delineate CMR-specific thresholds that guide management of VHD.
- Tissue characterization by CMR is prognostic in VHD. Its role in guiding therapy warrants further research.

Conflict of Interest Disclosure:

The authors have completed and submitted the *Methodist DeBakey Cardiovascular Journal* Conflict of Interest Statement and none were reported.

Keywords:

cardiac magnetic resonance, valvular regurgitation, valvular stenosis, ventricular remodeling

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