

# Magnetic resonance imaging to assess ventricular remodeling

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### Abstract

Ventricular remodeling has a key role in the pathology of ventricular dysfunction. During the reaction to a myocardial insult, the ensuing genetic, structural, and biochemical changes will result in the deterioration of the functional ability of the heart in the long term. Non invasive imaging plays a central part in the diagnosis of heart failure, assessment of ventricular remodeling, prognosis, and monitoring of therapy. Cardiovascular magnetic resonance offers a unique and comprehensive assessment of patients with heart failure and has attained a role as gold standard among imaging techniques to assess myocardial anatomy, regional and global function, and viability.

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### Introduction

Heart failure is a multifaceted clinical syndrome with high rates of admissions to hospital and mortality; coronary artery disease (CAD) is its main etiology in developed countries. Ventricular remodeling leading to heart failure can have many causes, including hypertension, CAD [1], high-intensity endurance training [2], and non-CAD causes such as infiltrative myocardial diseases and viral myocarditis. Adverse ventricular remodeling has been defined as the “genomic expression resulting in molecular, cellular and interstitial changes that are manifested clinically as changes in size, shape and function of the heart after cardiac injury” [3]. An accurate quantitative assessment of ventricular remodeling is instrumental both for prognosis and to follow the effectiveness of therapeutic interventions. Cardiovascular magnetic resonance (CMR) can add novel markers of structural alterations that initiate or accompany early phases of ventricular remodeling. The integration of CMR

into the clinical work-up of patients with heart failure is furthered by its capacity to answer a range of clinical questions without the need for additional tests. A recent European survey of the clinical utility of CMR revealed a broad range of clinical indications, from myocarditis and post myocardial infarction to assessment of cardiac masses, with CMR having a direct impact on patient management in up to two-thirds of cases [4]. The current review will focus on recent developments in CMR that are relevant to the assessment of the pathophysiological changes associated with ventricular remodeling.

### Ventricular function, volume, and shape

Changes in ventricular geometry and ventricular function reflect the most obvious aspects of adverse remodeling, but may in fact reveal only the “tip of the iceberg”. Cine CMR imaging of parallel, contiguous short-axis slices covering the entire heart over

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a user-defined number of cardiac phases has become a reference standard by which to assess ventricular function and structure. Global left ventricle and right ventricle volumes and mass are derived from cine CMR without the need for any geometrical assumptions, applying to ventricles of all sizes and shapes, even to those that have experienced extensive remodeling [5]. Cine CMR with steady-state free precession (SSFP) – a relatively recent innovation with high signal-to-noise and tissue-to-blood contrast – enables an accurate identification of even subtle regional wall motion abnormalities [6].

In patients with heart failure, cine CMR demonstrates superiority over other non invasive techniques, showing less inter-study variability and better reproducibility of the volumetric results. Bellenger et al [7] argued that the excellent reproducibility of cardiac cine CMR would translate into smaller sample sizes in clinical trials. As evidence of their foresight and predictions, we point out a recent randomized study with CMR in 41 patients [8] that demonstrated that  $\beta$ -blocker therapy has antiremodeling effects on the left ventricle in patients with chronic heart failure – a result that is consistent with the highly significant decrease in mortality from worsening heart failure among 4000 patients in the Metoprolol Randomized Intervention Trial in Congestive Heart Failure (MERIT-HF) [9]. The most common measures quantifiable by cardiac cine CMR are the ventricular dimensions and volumes, myocardial mass, and derived quantities such as ejection fraction, stroke volume, and cardiac output. Additional measures relate to the shape of the ventricle, such as the ratio of the long axis to the short axis, which plays an important part in the pathogenesis of mitral regurgitation. A related measure of left ventricular shape is the sphericity index, defined as the ratio of the major axis to the minor axis of the left ventricle [10].

Flow, or wall, velocities can be quantified with CMR, using the phase-contrast technique. In the presence of a single valvular insufficiency, such as mitral regurgitation or aortic regurgitation alone, comparison of right and left ventricular stroke volumes by either cine CMR or phase-contrast blood flow measurements can accurately estimate the degree of valvular dysfunction – for example, that of stenotic aortic valves [11].

### Wall stress and strain

Wall stress has an important role in ventricular remodeling, both as a powerful stimulus for remodeling, and as a marker of the adverse ventricular adaptation [12]. Ventricular dilatation increases the radius of curvature and is accompanied by wall thinning, both changes leading to increased wall shear stress.

Estimates of regional wall stress require determination of wall thickness and wall curvature, highly accurate measures of which are accessible by cine CMR. An average measure of wall stress [13] can be obtained from the modified Laplace equation. The approach introduced by Grossman et al [14] can be adapted to CMR to estimate the regional peak systolic wall stress in the radial direction ( $\sigma_r$ ) by measuring the inner radius of the left ventricle ( $R$ ) and wall thickness ( $t$ ) at end systole:

$$\sigma_r = (0.133 \times SP \times R) / (2t \times [1 + (t/2R)])$$

where SP is peak systolic ventricular blood pressure in millimeters of mercury. In healthy individuals, the principal stress component was estimated by finite element analysis to be greatest near the base of the heart; it decreases by about 40% towards the apex of the heart, even without accounting for a ventricular pressure gradient from base to apex [15]. Using CMR, Blom et al [16] demonstrated the benefits of a ventricular constraint device that provided passive mechanical diastolic support to curb ventricular remodeling and reduce ventricular wall stress in sheep with myocardial infarction.

### Myocardial viability and infarct remodeling

Gadolinium contrast used with CMR remains confined to the extracellular space in normal myocardium. Within infarcted myocardium, the volume of distribution for gadolinium contrast is significantly expanded, reaching 60–70% in scar tissue. As early as 3 or 4 min after administration of gadolinium contrast, the expanded distribution volume can be reliably detected with CMR to demarcate non viable myocardium [17], with at least 4–6-fold greater spatial resolution and a greater contrast-to-noise ratio than can be achieved with nuclear scintigraphy. The focal signal hyperintensity of infarcted myocardium, or myocardial scar tissue, is highlighted by suppressing the signal from normal myocardium [18]. Late gadolinium enhancement (LGE) images delineate the transmural extent of infarction (*Figure 1*), thereby distinguishing between reversible and irreversible myocardial injury, regardless of the extent of wall motion at rest, the age of the infarct, or the reperfusion status [19,20]. In a landmark study of patients with CAD, the probability of improvement in regional contractility after successful coronary revascularization decreased in inverse proportion to the transmural extent of LGE before revascularization, showing that LGE provides important information regarding ventricular remodeling and recovery in function after a myocardial infarction [21].

LGE imaging is consistently more sensitive and specific than any other techniques in detecting and

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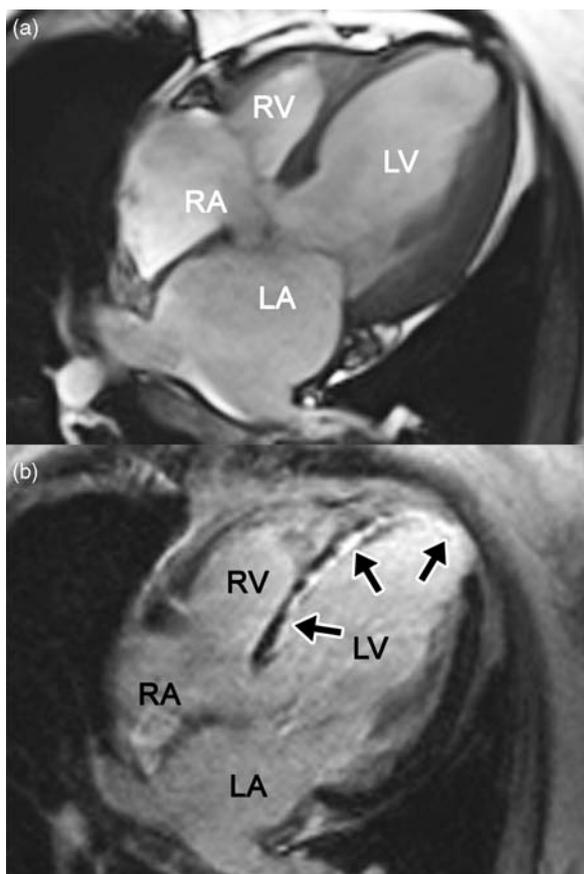


Figure 1. Cardiovascular magnetic resonance image of a patient with a myocardial infarction in the mid-left anterior descending artery territory. (a) Systolic cine steady-state free precession images demonstrating moderate left ventricular dysfunction (left ventricular ejection fraction 38%) with akinesis of anteroseptal walls. (b) Late gadolinium enhancement image showing a full-thickness myocardial infarction (arrows) matching the wall motion abnormality, and implying a very low likelihood of recovery after revascularization. LA, left atrium; LV, left ventricle; RA, right atrium; RV, right ventricle.

sizing the spatial extent of myocardial infarction [22,23]; the transmural extent of LGE can predict the response of left ventricular function to  $\beta$ -blocker therapy in patients with heart failure [24]. Orn et al [25] found that scar size assessed by CMR was the strongest independent predictor of ejection fraction and left ventricular volumes in acute myocardial infarction, and of patients with heart failure. Even in patients with suspected CAD, but without a history of myocardial infarction, LGE involving a small amount of myocardium carries a high cardiac risk, including in patients with very few signs of ventricular remodeling [26]. It was shown recently that CMR measurements of gadolinium distribution volumes in viable myocardium provide a novel marker of extracellular remodeling and diffuse fibrosis in patients with heart failure and dilated cardiomyopathy [27,28], pointing to the versatility of CMR for

extensive tissue characterization in patients with heart failure.

CMR can also assess complications after myocardial infarction, such as left ventricular mural thrombus, aneurysmal dilatation, and papillary muscle involvement causing mitral regurgitation and rupture of the interventricular septum [29]. Because thrombus is an avascular structure, on LGE images it usually appears as a mass with low signal intensity surrounded by areas of high signal intensity such as cavity blood (Figure 2).

After an acute myocardial infarction, infarct remodeling is governed by the status of coronary reflow, degree of ischemia, collateral formation, and infarct location. CMR techniques can capture and characterize the multifaceted process of infarct remodeling, and shed light on novel markers beyond infarct and scar size, cavity enlargement, and left ventricular function. The border zone of infarction with intermediate signal intensity on LGE images provides a stronger association with electrophysiological substrates of ventricular arrhythmias than with left ventricular ejection fraction. The border zone was strongly associated with post myocardial infarction mortality in a small group of patients post myocardial infarction [30]. The myocardial extent of no-reflow (microvascular obstruction) (Figure 3), despite successful coronary revascularization after acute myocardial infarction, was shown to be an independent and significant prognostic factor [31], and is associated with adverse

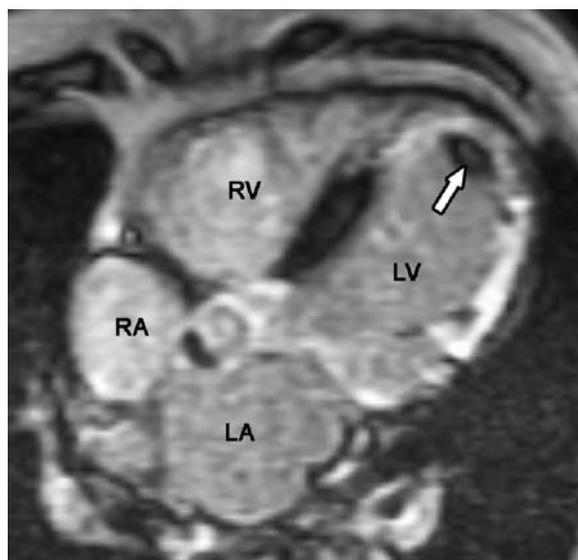


Figure 2. Four-chamber late gadolinium enhancement image of a 63-year-old man with a recent history of an anterior ST-segment elevation myocardial infarction referred to cardiovascular magnetic resonance imaging for left ventricular function. There is a transmural myocardial infarction involving the entire mid to distal anterior and anteroseptum wall of the left ventricle, associated with a large thrombus located in the left ventricular apex (arrow). LA, left atrium; LV, left ventricle; RA, right atrium; RV, right ventricle.

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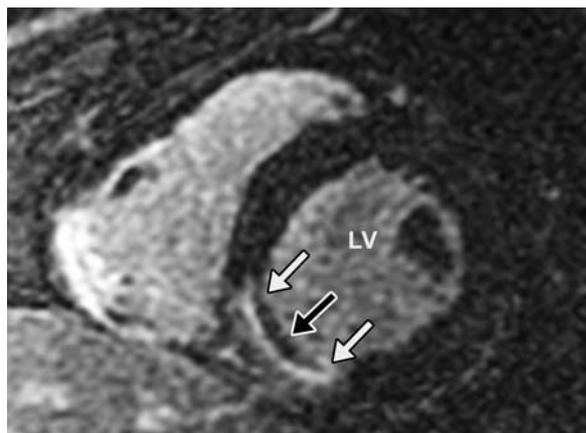


Figure 3. Late gadolinium enhancement (LGE) image in a 63-year-old man with previous inferior myocardial infarction who was referred for viability remodeling assessment. The image provides a detailed characterization of the inferior myocardial infarct, revealing near transmural LGE involving the inferior walls of the left ventricle (white arrows), with a dense area of microvascular obstruction in the core of the infarction (black arrow). LV, left ventricle.

ventricular remodeling [32]. T2-weighted imaging has been used to characterize the extent of myocardial edema as the “at-risk region” as a result of ischemia [33], and to differentiate between acute and chronic CAD [34].

## Conclusions

The application of CMR in the evaluation of patients with heart failure is bound to expand substantially in the coming years, to the point that most patients with heart failure will undergo CMR imaging as part of their diagnostic work-up, as an aid to guide management, and as a means to stratify risk. Novel CMR techniques aiming at the identification and quantification of diffuse fibrosis [27,28] will further improve in-vivo, non invasive assays of myocardial pathology. Careful application of this technology has the potential to improve both diagnostic efficiency and the care of patients with heart failure. ■

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