# Should everyone have an MRI in heart failure?

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## Definition and epidemiology

Heart failure (HF) is a complex clinical syndrome characterized by typical symptoms and signs caused by a structural and/or functional cardiac abnormality, resulting in a reduced cardiac output and/or elevated intracardiac pressures at rest or during stress. HF patients can be classified into three categories based on left ventricular systolic function: HF with reduced ejection fraction (<40%, HFrEF), HF with mid-range ejection fraction (40–49%, HFmrEF), and HF with preserved ejection fraction (≥50%, HFpEF). Despite recent advances in disease prevention and treatment, HF remains a public health problem worldwide associated with substantial morbidity and mortality, reduced health-related quality of life, and significant burden on health care systems. HF affects around 26 million people worldwide with an estimated prevalence of 1–2% of the adult population in developed countries and a steep increase with increasing age, rising to above 10% among people >70 years of age and above 15% in people >80 years of age (1,2). Although the incidence of HF is decreasing, the overall prevalence and hospitalization rates have increased and are expected to rise substantially in the next two decades due to the ageing population, better survival of patients with ischemic heart disease and cardiomyopathies, and a growing proportion of patients presenting with HFpEF (3,4). There is a wide range of abnormalities of the myocardium, pericardium, endocardium, and heart valves, cardiac rhythm disorders or systemic diseases that can cause HF. Determining the underlying cause is central to the diagnosis and treatment planning of HF (1,5).

## Imaging in HF: magnetic resonance imaging pros, cons, and appropriateness criteria

The recent rapid growth and evolution of cardiovascular imaging techniques has helped clinicians gain important diagnostic and prognostic information on many cardiac pathologies. The judicious utilization of the different imaging modalities in clinical practice requires an assessment of their strengths and limitations. Other factors that can influence the selection of the appropriate cardiac imaging techniques are local availability and expertise, cost, and patient characteristics (6). Cardiac magnetic resonance (CMR) provides high quality images in any desired imaging plane without making geometrical assumptions and without the use of ionizing radiation. It is acknowledged as the gold standard for the assessment of cardiac anatomy, function, and viability. Its unique capability of tissue characterization remains unsurpassed and is continuously evolving (7).

CMR has been proven cost-effective as the initial imaging modality in different clinical scenarios; however, it is not as cost-effective as echocardiography in patients with HF (8) and remains unsustainable by health care systems in many parts of the world (9). CMR is contraindicated in patients with MR unsafe metallic implants and devices, including conventional, not MR-conditional cardiac pacemakers/ defibrillators (10). Gadolinium-based contrast agents should be avoided in patients with end-stage renal failure (estimated glomerular filtration rate <30 mL/min/1.73 m$^2$) due to a small risk of nephrogenic systemic fibrosis, unless the expected benefits outweigh the risks and patient-informed consent has been obtained (11). This limitation can be overcome by using

the novel parametric T1 and T2 mapping techniques for tissue characterization without the administration of contrast agent (12). Another limitation of CMR is the relatively long scan times (approximately 45 minutes), which may be an issue for patients with decompensated HF. Moreover, a proportion of patients with HF have cardiac arrhythmias rendering the scan technically challenging and in rare cases non-diagnostic. Claustrophobic patients constitute a minority of patients referred for CMR (13); however, the administration of mild sedatives or simple measures such as reassuring the patient and using blindfold eye-masks may be necessary to facilitate the scan.

In patients with HF, transthoracic echocardiography (TTE) is the modality of choice in the initial diagnostic evaluation in urgent, elective and screening settings, as it is widely available and can provide useful information even on the bedside on a 24/7 basis. CMR is considered the best alternative imaging technique when the echocardiographic study is non-diagnostic and is the method of choice in patients with right ventricular (RV) pathology, congenital heart disease and for tissue characterization in cases of suspected myocardial inflammation, or infiltrative cardiomyopathies. CMR is considered appropriate for patients presenting electively for the diagnosis of HF etiology, for the assessment of myocardial ischemia/ viability, valve disease, cardiotoxicity from chemotherapy, congenital heart disease, and for treatment planning with revascularization or devices. It is considered inappropriate in the initial assessment of patients with HF, when the severity of valvular heart disease explains the clinical presentation and for follow-up of patients with cardiac resynchronization devices (1,5,14).

## Role of CMR in HF

### Anatomy and function

CMR offers accurate and reproducible measurements of cardiac volumes and function. Left ventricular ejection fraction (LVEF) is thus far the single imaging parameter guiding HF medication optimization and device treatment as it has been shown to have prognostic implications in patients with ischemic and non-ischemic cardiomyopathy (1). Compared with echocardiography, CMR can better demonstrate left ventricular (LV) and RV regional wall motion abnormalities, and the presence of regional RV akinesia or dyskinesia especially in patients with suspicion of arrhythmogenic cardiomyopathy. CMR can also

provide accurate measurements of wall thickness and demonstrate the exact pattern of hypertrophy in patients with hypertrophic cardiomyopathy (HCM) or restrictive cardiomyopathies who usually present with HFpEF or HFmrEF.

### HF etiology

CMR with late gadolinium enhancement (LGE) imaging and parametric mapping can help identify the underlying etiology in patients with HF, by providing an *in vivo* assessment of the pattern and extent of myocardial scarring/ fibrosis. Patients with ischemic cardiomyopathy typically have subendocardial or transmural hyperenhancement in an area perfused by an epicardial coronary artery on LGE images. On the contrary, non-ischemic cardiomyopathies usually cause subepicardial, mid-wall or even transmural (but not in keeping with coronary artery distribution) LGE in specific patterns (15). For example, a mid-wall band of enhancement, most usually seen in the septum is found in about one third of patients with dilated cardiomyopathy (DCM), corresponding to local fibrosis (16). The typical LGE pattern in patients with cardiac sarcoidosis is sub-epicardial and mid-wall enhancement along the basal septum and/or inferolateral wall; however, subendocardial or transmural LGE can be observed (17). Patients with arrhythmogenic cardiomyopathy demonstrate RV enhancement and/or sub-epicardial or mid-wall LV enhancement in cases with LV involvement, correlating well with fibroadipose replacement of the myocardium (18). The usual LGE pattern in HCM is patchy or hazy midwall enhancement mainly seen in the areas of hypertrophy and enhancement of the LV-RV junctions (19). T1 mapping can detect fibrosis in patients with HCM, even when the fibrotic process is diffuse and undetected on LGE imaging (20). Patients with cardiac amyloidosis have characteristic LGE appearances with circumferential, mainly subendocardial LV enhancement with some transmural and patchy areas, possible enhancement of the RV, the atrial walls and the valves, and presence of a dark blood pool (21). T1 mapping in patients with cardiac amyloidosis demonstrates significantly elevated T1 values and can help differentiate cardiac amyloid from other causes of LV hypertrophy (22).

CMR is the only imaging modality that can non-invasively identify possible reversible causes of HF. In patients with ischemic HF, CMR can guide revascularization by demonstrating the extent of reversible ischemia and the presence of viable myocardium (23). In patients with

valvular heart disease, CMR provides an added value to echocardiography in the assessment of the mechanism and severity of the disease, and of the consequences on the relevant ventricle, especially in patients with inadequate echocardiographic quality or discrepant results (24,25). Moreover, CMR can evaluate the presence of acute myocardial oedema/inflammation in cases of acute myocarditis, Takotsubo or other inflammatory cardiomyopathies using T2-weighted imaging and T2-mapping (26). Furthermore, CMR is valuable in infiltrative cardiomyopathies. Iron overload cardiomyopathy can be non-invasively diagnosed by assessing the T2* relaxation time which is shortened in patients with iron loading and with T1 mapping which shows low myocardial T1 values in patients compared to healthy controls. Native myocardial T1 values are also characteristically low in patients with cardiac involvement in Anderson-Fabry disease (27).

### HF prognosis and treatment planning

CMR can identify various parameters associated with adverse clinical outcomes in patients with HF, such as LV ejection fraction, impaired myocardial strain, microvascular obstruction and intramyocardial hemorrhage in patients with acute or recent myocardial infarction, inducible ischemia on stress perfusion CMR, and extent of fibrosis on LGE, T1 mapping and extracellular volume (ECV) quantification.

LGE predicts cardiovascular and all-cause mortality, ventricular arrhythmias, sudden death, and major adverse cardiovascular events, independently of LVEF in both ischemic and non-ischemic cardiomyopathy (28). More specifically, in patients with DCM, LGE predicts all-cause, cardiovascular and arrhythmic mortality, and HF hospitalization. Even small amounts of LGE, especially septal and free wall are associated with a significant increase in the risk of death and sudden cardiac death (SCD) events, while the absence of LGE predicts LV reverse remodeling with treatment (29,30). In HCM patients, the extent of LGE is predictive of arrhythmias, SCD and end-stage systolic dysfunction. Even in patients considered to be at lower risk, late enhancement of ≥15% of LV mass is associated with a 2-fold increase in SCD event risk (31). Moreover, the presence of LGE correlates with increased all-cause mortality and arrhythmogenic events in patients with cardiac sarcoidosis (32).

The extent and location of myocardial scarring on LGE can guide catheter ablation therapy in HF patients with arrhythmias, and lead positioning away from myocardial scar for maximizing response to cardiac resynchronization therapy (CRT) (33). Furthermore, the presence of mid-wall fibrosis on LGE can improve patient selection for device therapy in DCM patients, as treatment with an implantable cardioverter defibrillator (ICD) and CRT-D (CRT-Defibrillator) was proven beneficial only in patients with myocardial scarring (34).

ECV is another strong predictor of adverse cardiovascular events, HF hospitalization and mortality in patients with ischemic and non-ischemic cardiomyopathies, whereas the value of T1 mapping as a prognostic marker remains uncertain (35,36). T1 and T2-mapping can also detect and monitor cardiotoxicity from chemotherapy and radiotherapy in cancer patients (37).

### Metabolic cardiac imaging

Finally, CMR can detect altered myocardial energetics and changes in metabolism *in vivo*, using Magnetic Resonance Spectroscopy and Dynamic Nuclear Polarisation. Although these techniques are still evolving and are currently being used mainly for research purposes, they can help our understanding of cardiac metabolism and energy homeostasis in different types of HF and guide individualized prevention and treatment of cardiovascular disease (38,39).

## Conclusions

In conclusion, CMR plays a complementary but rapidly expanding role to echocardiography in the evaluation of HF patients. With its unsurpassed accuracy to detect cardiac anatomy and function, and its unique capability for myocardial tissue characterization, CMR aids in the diagnosis, treatment planning and prognostication of patients with HF. Promising novel MRI techniques such as Magnetic Resonance Spectroscopy and Dynamic Nuclear Polarisation may shape the future for precision medicine. Thus, excluding patients with absolute contraindications to MRI, it would not be provocative to paraphrase the original question to '*Shouldn't every patient with HF have a CMR*?'.

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