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HOW TO

How to evaluate cardiomyopathies by cardiovascular magnetic resonance parametric mapping and late gadolinium enhancement

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Background

Cardiomyopathies (CMPs), defined as a myocardial disorder in which the heart muscle is structurally and functionally abnormal, in the absence of coronary artery disease, hypertension, valvular disease, and congenital heart disease sufficient to cause the observed myocardial abnormality are broadly classified in dilated CMP (DCM), hypertrophic CMP (HCM), restrictive CMP, and arrhythmogenic CMP (ACM). The aetiology is heterogeneous, both genetic as well as (or triggered by) acquired causes. Genetic causes include the known DCM, HCM, and ACM mutations, but also lysosomal (e.g. Anderson-Fabry disease etc.), infiltrative (amyloidosis, sarcoidosis, and haemochromatosis), and neuromuscular diseases (e.g. Duchenne muscular and Becker dystrophy etc.). Acquired causes include toxins (e.g. alcohol, cocaine etc.), drugs (e.g. chemotherapy such as anthracyclines etc.), infectious/inflammatory diseases (viruses, or autoimmune mediated), and peripartum CMP. Cardiovascular magnetic resonance (CMR) imaging is now firmly established for comprehensive evaluation of CMPs. Its unique advantage over other imaging techniques is the ability to provide comprehensive tissue characterization. Focal necrosis/fibrosis and amyloid infiltration and oedema can be identified by late gadolinium enhancement (LGE), whereas diffuse fibrosis and, amyloid can be detected by increased T1 and extracellular volume (ECV) fraction. Oedema increases T2 values. Fat and lysosomal storage disease decrease T1 times while iron infiltration lowers T1, T2, and especially T2*. Furthermore, CMR is the gold standard for the assessment of myocardial volumes, mass, wall thickness, and trabeculation for both the left and right ventricle. These features not only allow differential diagnosis of different types of CMPs but were also shown to have important prognostic value in many of such CMPs.

Indications for CMR in evaluation of CMPs

The usefulness of CMR in evaluating CMP mostly relies on its tissue characterizing ability. The latest European Society of Cardiology (ESC) guidelines recognize CMR as, a Class 1 level C indication for tissue characterization in suspected infiltrative disease, Fabry disease, inflammatory disease (myocarditis), left ventricular (LV) non-compaction, amyloid, sarcoidosis, and iron overload. In addition, a CMR should be considered (Class IIa, Level C) in DCM, to distinguish between an ischaemic or non-ischaemic aetiology, and in HCM, for the differential diagnosis, and assessment of the diagnostic criteria (cardiac anatomy, ventricular function, the presence and extent of LGE, and the presence of diffuse fibrosis or proteins/fat accumulation by T1 mapping). Other indications not yet mentioned in the guidelines include evaluation of endomyocardial fibrosis (such as hyper eosinophilic syndromes etc.), vasculitis, and transplant CMP. Therefore, judicious interpretation of CMR data in conjunction with clinical and other laboratory data is essential.

Imaging protocol

For characterization of CMPs, a comprehensive standardized CMR imaging protocol according to published guidelines[1] (*Figure 1*) should be used.

Imaging should always include

- LV and right ventricular (RV) structure and function images by means of balanced steady-state free precession (bSSFP) long-axis cine imaging in LV two-, three-, and four-chamber views and a stack of short-axis cine images acquired from the base of the left ventricle to the apex.

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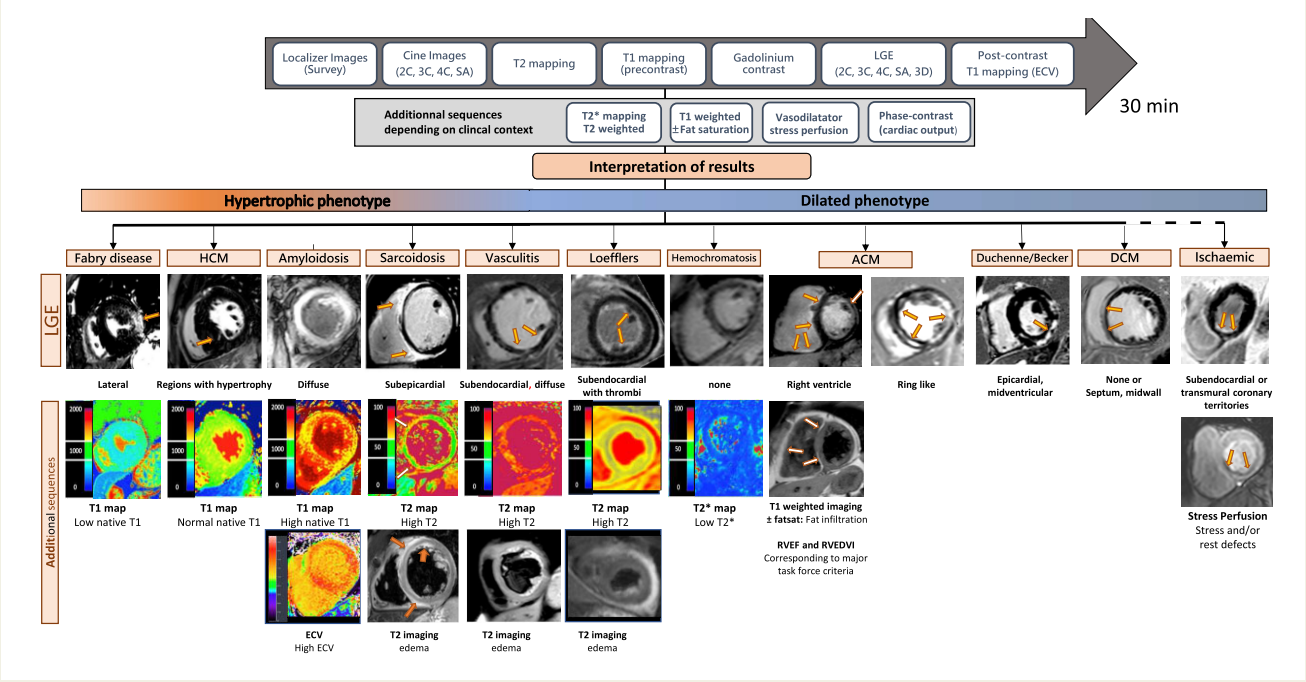

Figure 1 Image protocol and interpretation algorithm with examples of different types of cardiomyopathies. ACM, arrhythmic cardiomyopathy; DCM, dilated cardiomyopathy; HCM, hypertrophic cardiomyopathy; LGE, late gadolinium enhancement.

- If available, native T1 mapping by modified Look-Locker Inversion recovery (MOLLI) or shortened MOLLI (ShMOLLI) sequences in at least four slices (basal, mid, and apical short-axis slice, one long-axis slice to visualize patchy disease). A four-chamber view long-axis slice is recommended to visualize base-to-apex gradient In Amyloidosis, ACM, endomyocardial fibrosis, apical hypertrophy or infarction, a three-chamber long-axis slice in Anderson-Fabry disease, to assess basal inferolateral scarring.
- Native T2 mapping using either T2 prepared single-shot bSSFP or gradient spin echo of at least three source images, in similar views as for the T1 mapping.
- LGE images acquired at least 8–10 min after a gadolinium-based contrast injection (0.1–0.2 mmol/kg body weight) with either 2D, 3D inversion recovery gradient recalled echo of bSSFP or single short imaging adapted with inversion delay to null normal myocardium in the same views as for the cine images (short- and long-axis views); phase-sensitive inversion recovery imaging is recommended to avoid errors in inversion time.
- Post-contrast T1 mapping should be repeated in the same slices as native T1 mapping at least 15 min after contrast administration. Haematocrit should be measured within 24 h of imaging to allow computation of ECV fraction.

Additional sequences can be used depending on the specific question asked

- Suspected iron overload CMP: T2* mapping images with single breath-hold, gradient-echo, multi-echo scan (using eight equally spaced echos) in short-axis view, with a preference for the dark-blood approach.
- Suspected ACM: Axial and short-axis T1-weighted turbospin-echo images with optional fat-saturation.
- Suspected inflammatory diseases (cardiac sarcoidosis, myocarditis, post-heart transplantation, cancer, or drug-induced CMPs): T2-weighted short-axis turbospin-echo images
- Vasodilator stress perfusion imaging to rule out an ischaemic aetiology.
- Phase contrast imaging in the aortic root to allow computation of cardiac output and evaluation of mitral regurgitation severity.

Imaging report

Images should be postprocessed interpreted and reported according to guidelines.[2] Report of images should mention

- Dimensions and mass (corrected for body surface area) as well as ejection fraction of both the left and right ventricle. The interpretation of values should take the patients age and sex into account. Evaluation of dimensions and mass allows to distinguish dilated vs. hypertrophic phenotype.
- LV and RV regional function should be reported using a standardized 17 segment model and using a 4-point Lickert scale as normal, hypokinetic akinetic or dyskinetic. Dyssynchronous contraction and presence of apical rocking and septal flash should also reported.
- In patients with HCM, the type of hypertrophy (concentric, eccentric) and the maximal thickness of segments should be evaluated. If present, LV outflow tract obstruction with possible systolic anterior movement of the mitral valve should be reported.
- Similarly, the presence of increased hypertrabeculation should be reported in case of suspicion of non-compaction CMP and the ratio of non-compacted to compacted myocardium should also be measured according to reported criteria.

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- Measurements of native T1, T2, and T2* times should be performed in the septal segment and reported with normal references values relative to the scanner and sequence. ECV should be calculated using the same slice on the native T1 and post-contrast T1 images. The source images and quality control maps should be checked first, to ensure sufficient quality, and to exclude significant artefacts (such as motion- or wrap-around artefacts).
- LGE images should report on the presence of focal LGE. LGE is present if confirmed on 2 matching different (long- and short-axis) axis views. LGE extent is clearly associated with worse prognosis in various non-ischaemic CMPs. However, a variety of quantification methods are currently being used, which influences the LGE extent greatly, and unfortunately there is no consensus yet on which quantification method to use.
- In case of suspicion of ACM, the interpretation should report whether imaging features respond to major or minor criteria of the modified 2010 Task Force ACM guidelines.
- The presence of extracardiac findings should be reported especially if they are helpful in diagnosis of the CMP (i.e. increased adenopathy or hepatosplenomegaly in infiltrative diseases such as sarcoidosis or pleural or pericardial effusions).

Interpretation of results

The interpretation and diagnosis consider morphological features, but LGE and tissue mapping (*Figure 1*) play the largest role in differentiating between CMPs. LGE locations and patterns are often specific of the type of CMP and, in combination with the clinical presentation, allow therefore the differential diagnosis.[3] Further differential diagnosis is allowed by parametric measurements of native T1,[4] T2, and T2* times and ECV.[5] The main principles of parametric mapping are as follows: (i) fibrosis, amyloid, oedema, and inflammation cause moderate degrees of increase of native T1 times; (ii) oedema is identified by concomitant important increase in native T2 times; and (iii) amyloid and fibrosis is identified by increased ECV.

Ischaemic aetiology is suggested by sub-endocardial or transmural LGE pattern in areas corresponding to coronary artery distribution territories. LGE is present in about half of patients with non-ischaemic DCM (ranging from 21% to 70%), most often mid-wall septal LGE, with or without LV free wall involvement. Acute inflammatory CMPs (myocarditis etc.) typically present with epicardial or mid-wall LGE, and elevated T1 and T2 values. Sarcoid is characterized by LGE in multiple epicardial, or transmural regions (which do not follow coronary artery distribution), predominantly at the hinge points and extending towards the RV. In endomyocardial fibrosis disease (such as in hyper eosinophilic syndromes), global endocardial LGE is typically present in the apex and the inflow tract. Anti nuclear cytoplasmic antibodies (ANCA)-associated vasculitis patients often present with endocardial LGE covering up to the whole LV circumference, whereas non-ANCA vasculitis patients commonly have mid-wall LGE (most often in the basal, posterolateral segments). Patients with Chagas disease typically have inferolateral or posterior subendocardial or transmural or apical scar with aneurysms, which can mimic ischaemic disease. Ring like LGE has recently been described in ACM from desmosome mutations. HCM due to sarcomere mutations often present with asymmetrical hypertrophy, and LGE is frequently visible in the hypertrophic areas. They may also present ventricular crypts and in apical HCM with apical aneurysms. Native T1 times are normal or only slightly increased in HCM of genetic origin outside of areas with LGE or in hypertensive disease. Patients with neuromuscular disease often present with a DCM, and LGE typically starts in the infero- and anterolateral basal segments from the epicardium towards the endocardium, progressing downward to the apex. Anderson-Fabry disease is characterized by concentric hypertrophy, with a greater relative contribution of papillary muscle mass (up to 20% of the total LV mass), and in around half of patients basal inferolateral LGE is present. Although the lipid accumulation in these patients lower T1-values, accumulation triggers an inflammatory response, and later on hypertrophy and fibrosis, which can sometimes lead to pseudonormalization of T1-values. Amyloidosis presents with diffuse subendocardial or transmural LGE, including hyperenhancement of the atrial walls. It may also be identified by a typical pattern on T1 scout (look-locker images) in which myocardial inversion precedes blood pool inversion. Further differential diagnosis is allowed by measurement of native T1 T2, and T2* times and measurement of ECV. Marked T1 lengthening as well as increase of ECV is a hallmark of cardiac amyloid deposition. In contrast, iron overload leads to reduction in T1- and T2* values. In this setting the severity of iron overload should be classified as mild ($30 > T2 > 20$ ms), moderate ($20 > T2^* > 10$ ms), or severe ($T2^* < 10$ ms).

Conclusions

A comprehensive approach of combined tissue mapping LGE imaging and functional imaging allows characterization of various types of non-ischaemic CMPs.

Conflict of interest: none to be declared.

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