Article

Acute clinical presentation of nonischemic cardiomyopathies: early detection by cardiovascular magnetic resonance

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Nonischemic cardiomyopathies include a wide range of dilated, hypertrophic and arrhythmogenic heart muscle disorders, not explained by coronary artery disease, hypertension, valvular or congenital heart disease. Advances in medical treatments and the availability of implantable cardioverter defibrillators to prevent sudden cardiac death have allowed a substantial increase in the survival of affected individuals, thus making early diagnosis and tailored treatment mandatory. The characterization of cardiomyopathies has received a great boost from the recent advances in cardiovascular magnetic resonance (CMR) imaging, which, to date, represents the gold standard for noninvasive assessment of cardiac morphology, function and myocardial tissue changes.

An acute clinical presentation has been reported in a nonnegligible proportion of patients with nonischaemic cardiomyopathies, usually complaining of acute chest pain, worsening dyspnoea or palpitations; 'hot phases' of cardiomyopathies are characterized by a dynamic rise in high-sensitivity troponin, myocardial oedema on CMR, arrhythmic instability, and by an increased long-term risk of adverse remodelling, progression of myocardial fibrosis, heart failure and malignant ventricular arrhythmias. Prompt recognition of 'hot phases' of nonischemic cardiomyopathies is of utmost importance to start an early, individualized treatment in these high-risk patients. On the one hand, CMR represents the gold standard imaging technique to detect early and typical signs of ongoing myocardial remodelling in patients presenting with a 'hot phase' nonischemic cardiomyopathy, including myocardial oedema, perfusion abnormalities and pathological mapping values. On the other hand, CMR allows the differential diagnosis of other acute heart conditions, such as acute coronary syndromes, takotsubo syndrome, myocarditis, pericarditis and sarcoidosis. This review provides a deep overview of standard and novel CMR techniques to detect 'hot phases' of cardiomyopathies, as well as their clinical and prognostic utility.

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Introduction

Nonischemic cardiomyopathies include primary heart muscle disorders characterized by a dilated (DCM), hypertrophic (HCM) and/or arrhythmogenic (ACM) phenotype, not explained by coronary artery disease, hypertension, valvular or congenital heart disease.[1] An acute clinical presentation (sometimes referred to as a 'hot phase') has been reported in a nonnegligible proportion of patients with nonischemic cardiomyopathies, characterized by a dynamic rise in high-sensitivity troponin and myocardial oedema on cardiovascular magnetic resonance (CMR). From a pathophysiological perspective, myocardial oedema is the result of a mechanical, ischemic, infective, inflammatory or toxic insult and manifests as an impairment of fluid homeostasis, which relies on a complex interplay between microvascular, interstitial, cardiomyocyte, endothelial, leukocyte and lymphatic components. Intracellular and extracellular fluid accumulation disrupts myocardial architecture, intercellular communication, and metabolic pathways, decreasing contractility and increasing myocardial stiffness. Intracellular oedema may be mirrored by a dynamic troponin release, either because of a transient increase in cell membrane permeability or because of cell membrane disruption and necrosis. From a clinical perspective, 'hot phases' of cardiomyopathies may manifest with acute chest pain, worsening dyspnoea or palpitations, but also with more threatening conditions such as syncope and sudden death.

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Recent advances in cardiac imaging and its increased availability have improved anatomical, functional and tissue characterization of almost all cardiac diseases, including nonischemic cardiomyopathies. While echocardiography remains the first-line imaging tool for the management of patients with cardiomyopathies and has been implemented with more advanced features (speckle tracking strain, stress echocardiography, contrast-enhanced echocardiography), CMR represents the gold standard technique for myocardial anatomy and tissue characterization.[2] The widespread use of CMR enables the identification of myocardial oedema as a clinically relevant imaging finding with diagnostic and prognostic implications in several types of heart diseases. Indeed, myocardial oedema can be detected as an increased myocardial signal intensity on conventional T2-weighted fast spin-echo sequences [including short-tau inversion recovery (STIR) and fat-suppressed (FAT-SAT) T2-weighted sequences], which are sensitive to an increased intracellular and/or extracellular water content in tissue. Native (i.e. precontrast) T1- and T2-mapping sequences provide a quantitative assessment of myocardial tissue changes, both being increased by the presence of either intracellular or extracellular oedema: while native T1 is also increased by fibrosis, amyloidosis and hyperaemia, T2 mapping is more specific to myocardial oedema and inflammation, and has demonstrated a higher sensitivity and reproducibility than T2-STIR sequences in both ischemic and nonischemic cardiac diseases.[3] According to a recent meta-analysis, T2 mapping values are higher in patients with myocardial infarction (MI), heart transplantation, sarcoidosis, systemic lupus erythematosus, amyloidosis, HCM, DCM and myocarditis;[4] however, reference values differ between centres and disease differentiation seems limited, since changes in T2 values are similar in most cardiomyopathies.[5] Although some pathological conditions are characterized by a predominant intracellular oedema (such as in the very early phases of MI), in most cases myocardial oedema results in an increased extracellular space that can be detected as a subtle myocardial signal hyperintensity on late gadolinium enhancement (LGE) imaging and can be quantified with extracellular volume (ECV) mapping. Indeed, the resolution of myocardial oedema typically occurring weeks or months after an ischemic or nonischemic event can be seen on CMR as the disappearance of myocardial hyperintensity on T2-weighted images, but also as a 'shrinkage' of LGE areas, which in the chronic phase solely represent fibrotic scars (without the surrounding extracellular oedema that was present in the acute phase).

The aim of the present review is to describe the typical CMR features of patients presenting with a 'hot phase' nonischemic cardiomyopathy, including myocardial oedema, perfusion abnormalities and pathological mapping values, and their clinical and prognostic implications. Moreover, a CMR-based algorithm for the differential diagnosis from other acute cardiac disorders will be provided, including acute coronary syndromes, takotsubo syndrome, myocarditis, pericarditis and sarcoidosis.

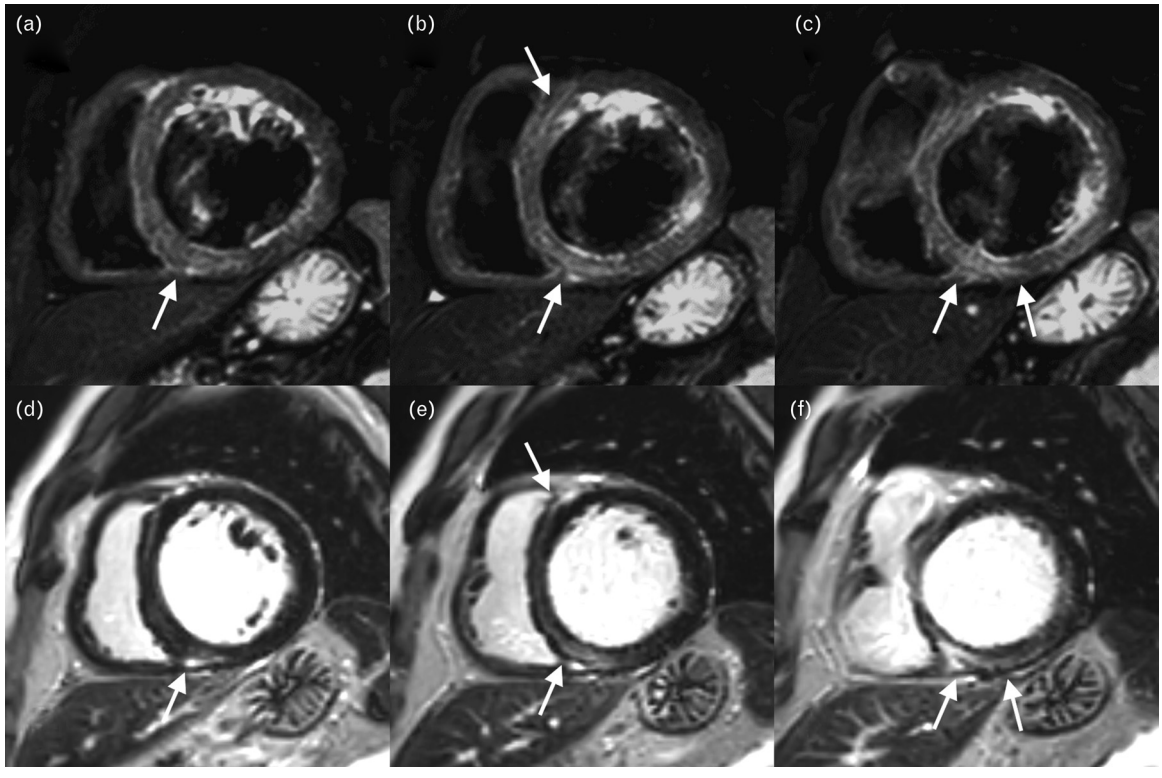
Dilated cardiomyopathy

DCM is a common clinical condition characterized by left ventricular (LV) dilation and dysfunction in the absence of ischemic heart disease or pressure/volume overload. CMR is now acknowledged as the gold standard technique for the quantification of biventricular volumes, mass, and ejection fraction (EF) with cine steady-state free-precession (SSFP) sequences, and for the assessment of myocardial fibrosis with LGE sequences.[6] LGE can be found in about 25–50% of DCM patients, typically in a patchy, midwall or subepicardial distribution. Since the first prospective longitudinal study conducted in 2006 by Assomull *et al.*[7] midwall fibrosis detected by LGE has emerged as a predictor of adverse prognosis, including all-cause mortality, cardiovascular mortality, sudden cardiac death (SCD), appropriate ICD therapy and ventricular arrhythmias (VA), independently from LVEF.[8,9] In particular, while the relationship between LVEF and VA or SCD is weak in DCM patients, a strong, significant association has been demonstrated between LGE and VA or SCD, even in patients with LVEF above 35%. Different LGE location, pattern or extent presents a different prognostic impact, even though further larger investigations are needed.[10,11] The absence of LGE predicts the occurrence of reverse remodelling on optimized medical therapy,[12,13] while the presence and transmurality of LGE in the LV lateral wall predict a poor response to cardiac resynchronization therapy (CRT).[14,15] Native myocardial T1 and ECV mapping have been shown to track myocardial fibrosis and interstitial remodelling, and have recently emerged as independent markers of poor outcome.[16–18] Recently, global longitudinal strain (GLS) measured by feature-tracking analysis of cine SSFP images was found to correlate better than LVEF and BNP with the composite of cardiac death, heart transplantation and appropriate ICD shock.[19] Moreover, right ventricular (RV) systolic dysfunction on CMR is an important predictor of all-cause mortality or cardiac transplantation.[20,21] DCM is also characterized by microvascular dysfunction, whose severity is associated with the degree of LV impairment: in a recent study on 65 DCM patients studied with quantitative perfusion mapping CMR, absolute rest perfusion was slightly more elevated in DCM than controls; during adenosine vasodilation, on the other hand, absolute stress perfusion and myocardial perfusion reserve were both reduced compared with controls.[22] Myocardial perfusion was further decreased in patients with severe LV systolic dysfunction, and in LV segments affected by myocardial fibrosis.

Several CMR studies have reported the presence of myocardial oedema in patients with DCM, particularly in those with biohumoral evidence of acute myocardial injury. In a study on 31 DCM patients, T2-weighted STIR images showed a higher normalized global signal intensity ratio compared with controls (2.2 ± 0.6 and 1.8 ± 0.3, respectively, $P = 0.0006$), consistently with global myocardial oedema; there was an inverse correlation between the signal intensity ratio on T2-weighted images and EF.[23] In a study on 26 DCM patients, myocardial oedema was detectable with both T2-weighted imaging and T2-mapping compared with 15 healthy controls and it was further increased in patients with severe dysfunction (LVEF $\leq$ 35%).[24] In a small study on 12 DCM patients, circumferential strain was inversely related to myocardial T2 values, suggesting that myocardial dysfunction was tightly linked to myocardial inflammation.[25]

In patients with acute heart failure, myocardial oedema can be detected as patchy hyperintense areas involving the RV insertion points both in T2-STIR and/or LGE imaging, particularly in cases presenting with pulmonary hypertension (Fig. 1): insertion point oedema and LGE has been linked to myocardial fibre derangement and the relative increase in the extracellular water content secondary to RV overload,[26] but holds little prognostic role[27,28] and can even disappear during follow-up as long as reverse remodelling occurs. Chronic myocardial injury in DCM patients may also be caused by postinfectious immune or autoimmune processes and can be detected by plasma troponin rise and/or positive T2 imaging. In a study on 42 DCM patients undergoing EMB (36% positive for inflammation), both CMR and hs-cTnT assay showed modest performance in the diagnosis of biopsy-proven inflammatory cardiomyopathy. Nonetheless, both CMR and hs-cTnT assessment were predictors of the clinical outcome.[29] In 66 children undergoing CMR within 2 weeks after the diagnosis of DCM, inflammatory cardiomyopathy (defined as the presence of at least two CMR criteria among oedema, hyperaemia and late enhancement) was found in 31/66 children (CMR positive). Myocardial inflammation and elevated troponin levels at baseline were predictors of LV function recovery.[30] In a recent study by Spieker *et al.*[31] global myocardial T2 was

Fig. 1



'Hot phase' in a patient with DCM. Top row (a–c): short-axis T2-STIR CMR images showing midwall hyperintensity in the interventricular septum and basal inferior wall (white arrows), suggesting intramyocardial oedema with a nonischemic pattern. Bottom row (d–f): corresponding LGE images showing midwall enhancement in the interventricular septum and basal inferior wall (white arrows), consistent with an increased extracellular volume due to fibrosis, necrosis and/or extracellular oedema. Please note that the myocardial signal changes extended well beyond the interventricular insertion points, represented by very small point-like hyperintense areas at the interventricular hinge points. CMR, cardiac magnetic resonance; DCM, dilated cardiomyopathies; LGE, late gadolinium enhancement; STIR, short-tau inversion recovery.

higher in 70 DCM patients (65.9 ± 6.2) than 62 controls (60.0 ± 4.2 ms; $P < 0.001$); moreover, DCM patients with the presence of inflammatory cells at endomyocardial biopsy exhibited further T2 elevation (68.8 ± 5.8) than DCM patients without inflammation (64.7 ± 5.9 ms; $P = 0.02$). The Authors concluded that although there is an overlap of T2 values between patients and healthy controls, T2 mapping may facilitate the identification of patients who may benefit from EMB for therapeutic decision-making. An acute clinical presentation with recurrent VA, mild troponin rise, myocardial oedema and LGE at CMR has been described also in a case of DCM due to light-chain deposition disease.[32]

Hypertrophic cardiomyopathy

In patients with HCM, CMR represents an essential tool for the morphological assessment of cardiac chambers,[33] including unusual patterns of hypertrophy (lateral, apical or RV distribution), myocardial crypts, papillary muscle abnormalities, elongated mitral valve leaflets and apical aneurysm, which are not always easily visualized by echocardiography.[34–36] CMR is of utmost importance also for the differential diagnosis of hypertrophic phenocopies, including cardiac amyloidosis,[37] Anderson-Fabry disease,[38] hypertensive cardiomyopathy,[39] athlete's heart[40] and iron overload cardiomyopathy.[41,42] Myocardial fibrosis detected by LGE imaging is a common finding in HCM, occurring in up to 80% of HCM patients,[43] so that only quantitative analysis is a robust marker of unfavourable prognosis: a LGE threshold of 10–15% of the LV mass identifies patients at high risk of VA,[44] even in the absence of other major risk factors and also in those with a low-intermediate ESC risk score[45,46] and has been listed among the criteria to be considered in ICD patient selection in the recently updated HCM guidelines by AHA/ACC.[47] Also scar heterogeneity (expressed as 'dispersion map of LGE'),[48] scar channels (assessed with an advanced postprocessing analysis to differentiate the scar core and the border zone of LGE images),[49] impaired global longitudinal strain,[50] myocardial oedema,[51] native T1 and ECV mapping[52–54] are emerging as prognostic markers in HCM patients. Myocardial T2$*$ values, an index of magnetic field inhomogeneities, are reduced in HCM patients compared with controls, and have been suggested to provide further information to characterize myocardial fibrosis.[55]

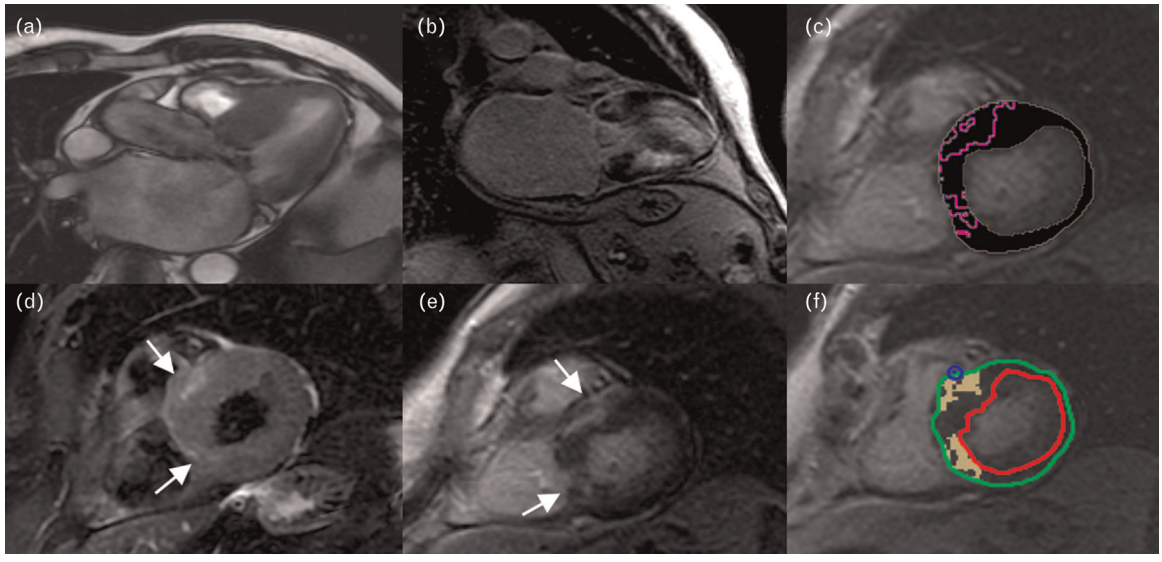
From a pathophysiological perspective, colocalization of myocyte disarray[56] and intramural arteriolar dysplasia[57,58] has been demonstrated at histology, suggesting that myocardial ischemia might be a dominant contributor to the development of fibrosis. Similar results have been found in imaging studies, using stress perfusion CMR and PET,[59,60] even though inducible ischemia at CMR typically involves the sub-endocardial layer, while LGE and T2 hyperintensity usually involve the mid-myocardial and sub-epicardial layers;[61] most tissue abnormalities are more prominent in the hypertrophied segments. The global severity of ischemia in HCM has been associated with progressive adverse remodelling, suggesting that tissue ischemia may be related downstream to an increasing burden of fibrosis, occurring over years.[62] T2$*$-BOLD (blood oxygen level dependent) CMR represents another method for assessing myocardial oxygenation and perfusion: HCM patients with ΔT2$*$ ratio $\geq 10\%$ had higher values of ECV than those without,[63] and this may suggest that the progression of myocardial fibrosis over time is related to repeated episodes of hypoxia and myocardial ischemia.

Another hallmark of HCM is represented by myocardial oedema, which may be detected in a 20–40% of HCM patients using T2-weighted (T2W) sequences, often matching LGE areas.[51,64,65] Differently from ischemic heart disease, where hyperintense areas on T2W images are larger than LGE areas, T2W hyperintensity areas in hypertrophic cardiomyopathy typically show good matching or smaller size than LGE (Fig. 2). The pathophysiological explanation for regional T2-signal hyperintensity in HCM is unknown: acute ischemic bouts are the most likely mechanism, also because perfusion defects usually match with T2 hyperintensity, but inflammatory injuries, myocyte disarray and scar heterogeneity may represent further explanations for T2 hyperintensity. T2 imaging has been proposed as a marker of disease activity ('hot phase') in HCM and, similarly to the extensive literature on the prognostic role of LGE in HCM, T2 imaging has been investigated as a marker of disease progression and prognosis. Indeed, the presence of myocardial oedema on T2 imaging has been associated with other established markers of adverse remodelling and prognosis, including LGE, elevated troponin levels and nonsustained ventricular tachycardia.[51] In a pilot study, HCM patients with high T2 were more likely to be at intermediate-high risk, with projected SCD rates 1.5-fold higher than in patients with normal T2;[65] among patients with extensive LGE, those with hyperintense areas at T2-weighted sequences experienced more life-threatening VA than those without.[64] Besides a qualitative assessment with conventional T2-STIR or T2-FAT-SAT imaging, T2 mapping resulted in an excellent quantitative method for assessing myocardial water content. Amano *et al.*[66] demonstrated greater T2 values in hyperintense areas observed on conventional T2-weighted images than in LGE-positive areas, and these abnormalities were associated with increased levels of troponin T and brain natriuretic peptide, reflecting active myocardial injury and probably cardiac stiffness and diastolic dysfunction in HCM.

Arrhythmogenic cardiomyopathy

ACM is a heart muscle disease characterized by loss of ventricular myocardium, which is replaced by fibrofatty tissue, and the occurrence of malignant VA, which occasionally causes SCD, particularly in the young.[67] Initially

Fig. 2



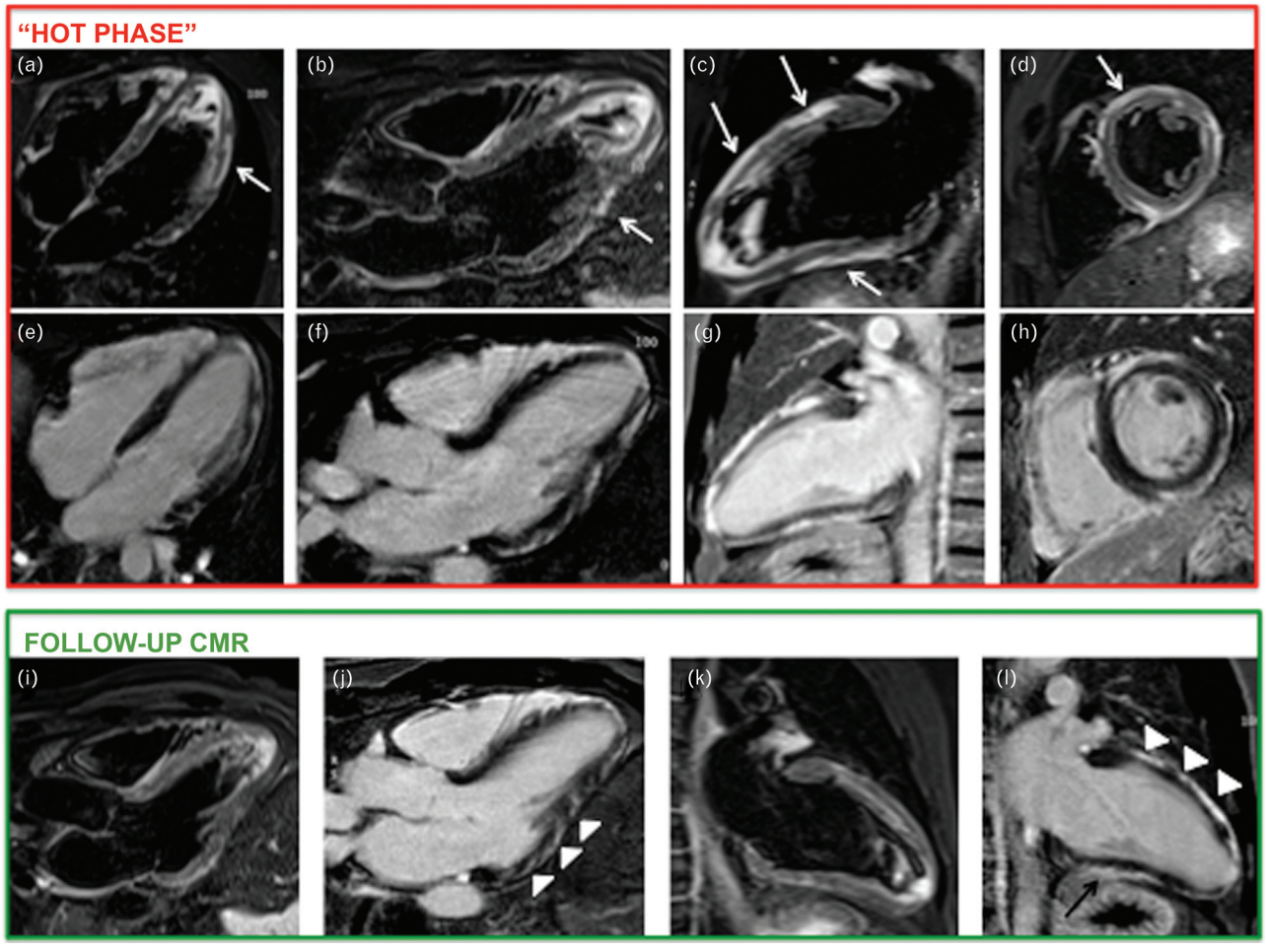
'Hot phase' in a patient with obstructive HCM. The patient, carrier of a known myosin binding protein C-3 (MYBPC3) mutation, presented nonsustained ventricular arrhythmias. CMR imaging showed extensive myocardial fibrosis on LGE and hyperintense areas on T2-weighted imaging. (a) Three-chamber cine SSFP imaging; (b) two-chamber LGE imaging; (c) LGE dispersion map in a short-axis view, with dispersion contours highlighted in purple; (d) short-axis T2 STIR imaging; (e) short-axis LGE imaging; (f) quantification of LGE, highlighted in yellow. CMR, cardiac magnetic resonance; HCM, hypertrophic cardiomyopathies; LGE, late gadolinium enhancement; SSFP, steady-state free-precession; STIR, short-tau inversion recovery.

described as a disease with a predominant RV involvement, the increasing use of CMR allowed the recognition of the biventricular and left dominant variants, involving respectively the myocardium of both ventricles or the LV only.[68] The disease can express with a large spectrum of clinical phenotypes, ranging from asymptomatic individuals without overt morpho-functional abnormalities and arrhythmias, to symptomatic patients presenting with syncope or chest pain episodes, but also with malignant VA and sudden cardiac arrest.[69,70]

Different phases of the disease have been hypothesized. Preclinical and presymptomatic phases occur when the first histological changes of the myocardium (myocyte death and fibro-fatty replacement) and the first electrical/structural abnormalities manifest, respectively, in the absence of overt clinical signs and symptoms. Symptomatic phases, more commonly occurring in adolescents and young adults, include several different clinical manifestations: syncope, chest pain and cardiac arrest by ventricular fibrillation (VF) are mostly reported during the earlier phases of ACM, whereas dyspnoea and sustained ventricular tachycardias (VTs) occur more commonly later in the disease course. Pathobiological explanations for this course may be related to the progressive nature of the disease, which modifies the myocardial lesions over time. While sustained monomorphic VTs are caused by re-entry circuits around stable fibrofatty myocardial scars, as a result of a healing process taking place in more advanced stages of the disease, chest pain and life-threatening VA may be the result of myocarditis-mediated bouts of acute myocyte necrosis.[71] In particular, probands and healthy gene mutation carriers (mostly desmoplakin) may exhibit a particular susceptibility to suffer from 'hot phases' of chest pain and release of troponins, closely resembling clinically acute myocarditis with infarct-like presentation.[72] Virus-negative myocarditis is reported in a high proportion of histologically proven ACM and myocardial inflammation has been documented in transgenic animal models with ACM, as a response to myocyte necrosis.[73] Moreover, recent data proved the presence of autoimmunity in ACM probands and affected relatives and it was associated with more severe forms of disease.[74]

CMR can help study all different phases of the natural history of ACM, given its accuracy in morpho-functional evaluation and the unique capability of myocardial tissue characterization.[75] Although the routine use of T2 techniques is not mandatory in patients with ACM, T2-weighted imaging should be recommended in ACM patients presenting with severe VA or myocarditis-like symptoms, to demonstrate an acute phase, characterized by inflammation and oedema (Fig. 3).[2] In a recent study by Bariani *et al.*[76] a myocarditis-like picture (chest pain, high troponin, ST-T changes) was an uncommon clinical presentation of ACM, with a 5% prevalence, more often occurring in children and in carriers of desmoplakin gene variants. CMR was able to demonstrate myocardial

Fig. 3



'Hot phase' in a patient with ACM. Top panel, 'hot phase': T2-weighted four-chamber (a), three-chamber (b), two-chamber (c) and mid-cavity short-axis (d) showing diffusely increased subepicardial signal intensity (white arrows), partially sparing the interventricular septum, consistent with nonischemic myocardial oedema. Corresponding postcontrast images (e–h) showing extensive nonischemic LGE in the oedematous areas. Bottom panel, 6-month follow-up CMR, showing complete regression of myocardial oedema on three-chamber (i) and two-chamber (k) T2-weighted images, with persistence of nonischemic LGE of the basal to mid-cavity inferolateral (j, arrowheads), basal to apical anterior (l, arrowheads) and mid-cavity inferior (l, black arrow) walls. ACM, arrhythmogenic cardiomyopathies; CMR, cardiac magnetic resonance; HCM, hypertrophic cardiomyopathies; LGE, late gadolinium enhancement; STIR, short-tau inversion recovery.

oedema in 7 out of 12 patients (58%) presenting with a hot phase. Accordingly, the Authors concluded that CMR is the first-choice examination for the differential diagnosis between ACM and acute myocarditis, yet reserving to endomyocardial biopsy a second-line role, mostly in selected cases with sporadic variants. Of course, familiar and clinical history plays a pivotal role in the diagnostic assessment, together with genetic testing. Regarding the prognostic role of T2 abnormalities in ACM patients, data are scant. In recent work, Chun *et al.*[77] investigated the application of T2 mapping in an ACM cohort, demonstrating the association of high T2 values and heart-failure events (a composite of hospitalization, heart transplantation and cardiac death due to systolic dysfunction) during follow-up. Further data are needed, however, to confirm these findings.

Differential diagnosis from alternative causes of acute myocardial injury

The fourth universal definition of MI introduced a clear differentiation between acute myocardial injury, defined by significant and dynamic rise and fall of troponin, and acute MI when clinical evidence of acute myocardial ischemia is associated.[78] Sepsis, pulmonary embolism, acute myocarditis, takotsubo syndrome, cardiac contusion and 'hot phase' cardiomyopathies are all possible causes of acute myocardial injury. On the other hand, acute MI comprises acute coronary syndromes and MIs with nonobstructive coronary arteries (MINOCAs), a term that should be reserved for patients with myocardial ischemia unrelated to recognizable atherothrombotic coronary occlusions and that should exclude patients with nonischemic myocardial injury (myocarditis,

cardiomyopathies, takotsubo).[79] Moreover, chronic heart failure, chronic cardiomyopathies, amyloidosis and chronic kidney disease are all possible causes of chronic myocardial injury, characterized by persistently elevated troponin levels in the absence of dynamic changes.

Based on its multiparametric capability to assess cardiac pathology, CMR allows the identification of myocardial areas of acute damage and may also assist in differentiating between ischemic and nonischemic aetiologies.[75,80] Current clinical guidelines recommend the use of CMR in all patients with a provisional diagnosis of MINOCA.[81,82] Multicentre registries reported that as many as 10% of patients with suspected acute MI have no evidence of obstructive coronary artery disease.[83] In patients with a provisional diagnosis of MINOCA, conflicting prognostic data have been reported when compared with typical cases of MI and obstructive coronaries; currently, the prevalent opinion is to not consider MINOCA as a benign condition and to reserve careful assessment and treatment for these patients.[84]

When applied to patients with initial diagnosis of MINOCA, CMR is able to identify specific entities responsible for the clinical presentation in a large majority of cases and, most importantly, to differentiate between a true MINOCA (showing ischemic myocardial lesions) and alternative diagnoses. In a systematic review of studies using CMR to characterize patients with suspected MINOCA, the most common final diagnoses were acute myocarditis (33% of cases), true MINOCA (24%) and takotsubo cardiomyopathy (18%).[85]

In recent years, CMR has become the noninvasive diagnostic test of choice to support a clinical suspicion of acute myocarditis and to guide further management of these patients.[86] Indeed, noninvasive imaging with CMR may reveal typical findings of focal or diffuse myocardial oedema, inflammatory hyperaemia and myocardial damage, including presence of LGE with subepicardial and/or midwall distribution. Current indications recommend that at least a T1-based criterion (including LGE and T1 mapping) should be combined with at least a T2-based criterion (T2 weighted imaging and T2 mapping) to obtain a diagnosis of acute myocarditis with CMR.[87] Conversely, true MINOCA can be recognized on CMR images by the demonstration of an area of myocardial damage with a typical ischemic pattern (subendocardial-to-transmural involvement with a coronary distribution) and coexisting functional impairment.

CMR has emerged also as a first-line diagnostic tool for the assessment of takotsubo syndrome, particularly in confirming cases with nonclassic involvement of basal or mid-ventricular segments or with persisting systolic dysfunction after the first few days from initial symptoms.[88] Extensive myocardial inflammation, classically involving the LV apical segments, without evidence of necrosis or scar on LGE images represents a consistent CMR finding in patients with takotsubo syndrome.

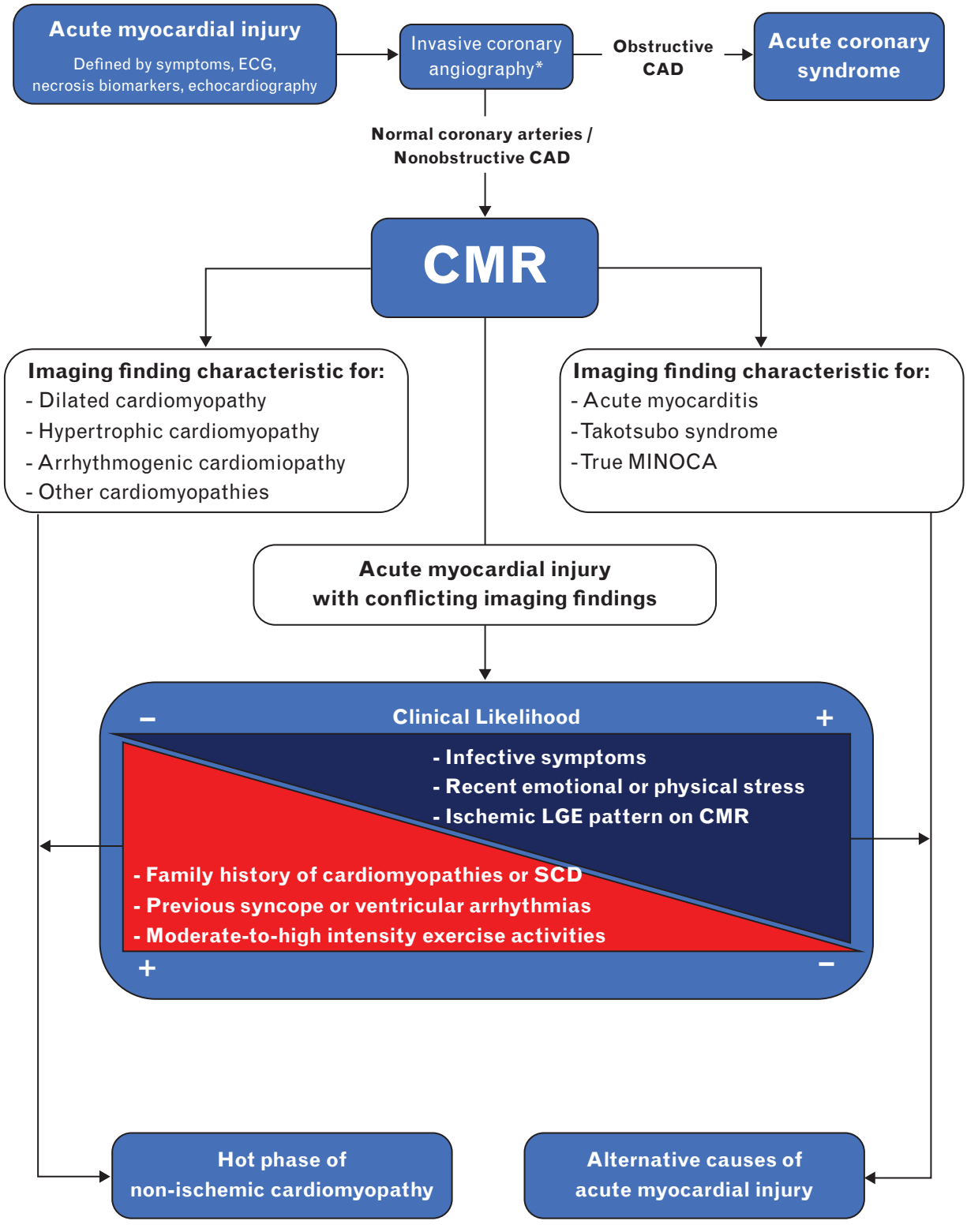
Many reports focusing on MINOCA include a variable proportion of patients with a final diagnosis of nonischemic cardiomyopathy, mainly DCM and HCM. Until recently, the possibility to observe such acute events as part of the natural history of nonischemic cardiomyopathy was not widely acknowledged, probably contributing to a lower prevalence reported in older studies than in more recent reports (5% vs. 25%, roughly).[85,89,90] In small prognostic studies describing the various causes of MINOCA-like clinical presentation as identified by CMR, the sub-group with structural cardiomyopathy showed the worst outcome in terms of major adverse cardiac events and all-cause mortality.[89,90] In order to take full advantage of the diagnostic and prognostic potential of CMR, patients presenting with acute myocardial injury should be evaluated no later than a few weeks after the onset of symptoms and using an adequate imaging protocol, with the inclusion of mapping techniques.[91]

A flowchart emphasizing the role of CMR to distinguish the hot phase of nonischemic cardiomyopathies from alternative causes of acute myocardial injury is suggested in Fig. 4. More commonly, CMR will demonstrate characteristic imaging findings, with the possibility of obtaining a definite diagnosis of cardiomyopathy (including DCM, HCM and arrhythmogenic cardiomyopathy) or, alternatively, to recognize clinical entities such as acute myocarditis, true MINOCA and takotsubo syndrome. At the time of CMR evaluation, however, some cases of nonischemic cardiomyopathy may be in a stage of incomplete or atypical phenotypic expression or, in other circumstances, the observed imaging features may show partial or complete overlap with other pathologies (e.g. acute myocarditis vs. arrhythmogenic cardiomyopathy, takotsubo syndrome vs. HCM, etc.), making a differential diagnosis particularly challenging. In some of these cases, details on family history and on clinical presentation or, when deemed appropriate, a repetition of the CMR study after a few months may lead to a specific diagnosis (see Fig. 4).

Conclusions and perspectives

Cardiomyopathies are characterized by different clinical phases, from chronic 'silent' periods to acute 'hot' phases. The latter are often characterized by worsening of the clinical status, including chest pain, dyspnoea, palpitations and life-threatening arrhythmias. Serum biomarkers, such as troponins and B-type natriuretic peptides, generally present a dynamic rise during these acute phases and represent a simple, reproducible, sensitive tool to track disease course. From a pathophysiological perspective, 'hot phases' of cardiomyopathies are characterized by myocardial oedema, fibrosis and adverse remodelling that should be differentiated from other acute cardiac conditions, such as infarction, MINOCA,

Fig. 4



Role of CMR in recognizing the acute clinical presentation (hot phase) of nonischemic cardiomyopathies from alternative definite causes of acute myocardial injury. CAD, coronary artery disease; CMR, cardiac magnetic resonance; ECG, electrocardiogram; MINOCA, myocardial infarction with nonobstructive coronary arteries; SCD, sudden cardiac death. ∗If indicated based on clinical setting. Note that this diagram does not include chronic myocardial injury, characterized by persistently elevated troponin levels in the absence of dynamic changes, typically occurring in patients with chronic heart failure, chronic cardiomyopathies, amyloidosis or chronic kidney disease.

myocarditis and takotsubo. Symptoms, biomarkers and ECG modifications are fundamental hallmarks to decide whether and when to perform a CMR examination. Indeed, CMR is a unique diagnostic tool to correlate these clinical signs of disease activity to the morphological and tissue changes occurring in the myocardium, but also to assist the clinician in the differential diagnosis of most common acute cardiovascular diseases. Furthermore, the presence of specific abnormalities on CMR, such as myocardial oedema and extensive LGE (particularly with a 'ring-like pattern' involving most LV myocardial segments), has been associated with a worse prognosis; in selected cases, these 'high-risk' features not only should raise the suspicion of specific gene mutations, but also should prompt early medical and device treatment. The inclusion of CMR in the clinical management of patients with nonischemic cardiomyopathies, besides providing important diagnostic and prognostic information, could help the clinician in improving patient treatment: in a pharmacological era, where 'precision' aetiological therapies, in addiction to 'symptomatic' therapies, are being developed, CMR may play a crucial role in increasing the effectiveness of such patient-tailored approaches.

Acknowledgements

Conflicts of interest

There are no conflicts of interest.

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