Cardiomyopathies (hypertrophy and failure): What can offer cardiac magnetic resonance imaging?

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Summary

In routine, cardiomyopathy, confirmed or not, is a frequent reason for cardiac MRI evaluation. Step by step, by using a wide panel of sequences, cardiac MRI is able to characterize cardiomyopathies by their morphologic and functional phenotype as well as by tissue characterization. Cardiac-MRI is also considered as the most appropriate technique for the follow-up of this disease.

The purpose of this article is to browse an overview of the main MRI features of cardiomyopathy, focusing the purpose on hypertrophic forms and myocardial diseases leading to cardiac failure.

Cardiomyopathies are diseases of the myocardium which may lead to cardiac failure. The term cardiomyopathy was introduced by Harvey and Brigden four decades ago [1,2]. In the classification of the World Health Organization (WHO), the term “cardiomyopathy” is reserved for myocardial diseases of unknown etiology, while other diseases that affect the myocardium, but are of known cause or are part of a generalized systemic disorder, are termed specific heart muscle diseases. However, since the clinical presentation of a given cardiomyopathy and a specific heart muscle disease is often similar, it is preferable to use the term secondary cardiomyopathy to identify those patients with a specific heart muscle disease that clinically, closely simulates an idiopathic or primary cardiomyopathy. The etiology and pattern of the most frequent myocardial diseases causing cardiomyopathies are shown in Table 9.1. Three basic types of cardiomyopathies have been described by the WHO: hypertrophic cardiomyopathies (HCM), dilated cardiomyopathies (DCM) (formerly called congestive), and restrictive cardiomyopathies [3]. Each type of cardiomyopathy corresponds with a basic type of functional impairment. However, overlap between the different types may exist. HCM are characterized by an inappropriate LV hypertrophy, usually...
with a preserved contractile function; DCM are characterized by ventricular dilatation and a contractile dysfunction; while in restrictive forms, impaired diastolic filling is the most prominent finding.

**Hypertrophic Cardiomyopathy**

The characteristic finding of HCM is an inappropriate myocardial hypertrophy in the absence of an obvious cause for the hypertrophy, such as systemic hypertension or aortic stenosis. Familial clustering is often observed, and the disease is genetically transmitted in about half of the cases \[4,5\]. The natural history and clinical presentation of HCM are variable. Symptoms are caused by intraventricular, usually left ventricular outflow tract (LVOT) obstruction, myocardial ischemia and reduced coronary vasodilator flow reserve, diastolic dysfunction, and arrhythmias. Although patients might be completely asymptomatic, HCM is the most common identified cause of sudden cardiac death in young people, due to arrhythmia \[4\]. Histologically, HCM is characterized by a disorganization and malalignment of the myofibrils, i.e., myofibrillar disarray, which is not unique to HCM but is clearly more extensive in this disorder than in secondary myocardial hypertrophy from pressure overload or congenital heart disorders \[6,7\]. The combination of inappropriate myocardial hypertrophy, intimal hyperplasia of intramural coronary arteries and endothelial dysfunction causes myocardial ischemia and spontaneous myocardial infarction in the absence of abnormalities of epicardial coronary arteries. It is likely that the capillary density in the hypertrophied heart is inadequate relative to the increased myocardial mass.

Hypertrophic cardiomyopathy is a morphologically heterogeneous cardiac disease, which appears in a multitude of diverse patterns and shows a wide range in the magnitude of wall thickening. Different morphologic types of HCM are described including diffuse as well as focal patterns of myocardial hypertrophy. HCM classically produces marked asymmetrical hypertrophy of the left ventricle (LV). The end-diastolic LV wall thickness is usually greater than 15 mm (figure 1). In some patients, HCM might be associated with massive myocardial hypertrophy (wall thickness of 45–50 mm). In 70% of patients, the ventricular septum and anterior LV wall are involved. Abnormalities are usually most prominent in the basal segments (previously called “idiopathic hypertrophic subaortic stenosis” and “muscular subaortic stenosis”). Less frequent locations of myocardial hypertrophy include the mid- and lower portion of the ventricular septum, and the apex. In a recent study by Soler et al. using MRI \[8\], three types of apical HCM were described: (a) true apical form (“spadelike” configuration), (b) involvement of the apex and symmetric hypertrophy of the four ventricular wall segments, and (c) involvement of the apex with asymmetric involvement of the wall segments (“non-spade” apical HCM) \[9\]. Severe concentric as well as papillary muscle hypertrophy may also occur in HCM. According to the definition of the WHO, HCM might also involve the right ventricle (RV). The LV volumes are normal or might be reduced. Secondary, left atrial enlargement is usually found \[10\]. Approximately 25% of patients with HCM have a dynamic outflow tract obstruction caused by a narrowed LVOT and abnormal systolic anterior motion of the mitral valve \[11,12\]. In nearly all patients with LVOT obstruction, the outflow tract area is smaller than 4.0 cm\(^2\) (mean: 2.6 \(\pm\) 0.7 cm\(^2\)) \[13\]. In patients without obstruction and normal subjects, the outflow tract area is 5.9 \(\pm\) 1.6 cm\(^2\) and 10.4 \(\pm\) 1.2 cm\(^2\), respectively. During onset of cardiac systole, deformation and bulging of the hypertrophied septum into the LVOT contributes to the flow acceleration in the narrowed LVOT. The subsequent pressure drop leads to an anterior movement and eventually apposition of the anterior mitral valve leaflet to the septum during systole contributes to the outflow obstruction (the “Venturi effect”). The LVOT obstruction may be present at rest (resting obstructive HCM) or may be provoked by exercise.
Valsalva maneuver, or administration of amyl nitrite (latent obstructive HCM). The anterior mitral valve leaflet motion causes a secondary mitral valve regurgitation, occurring in mid-late systole. In some patients, mitral regurgitation might be severe and contributes substantially to symptoms of heart failure. The pressure gradient in the LVOT is used to determine the hemodynamic relevance of the LVOT obstruction. Pressure gradients can be calculated by a modified Bernoulli formula, according to which maximal flow velocities across a stenosis reflect the severity of obstruction. In midventricular hypertrophy patients may exhibit a gradient between the LV apical region and the remainder of the chamber. This may progress to a non-contractile apical aneurysm with apical thrombus formation [14]. The less common apical form of HCM has a high prevalence in Japan. These patients have no outflow obstruction but present with a severe apical LV hypertrophy, giant negative T-waves on their ECG, and a typical spade-shaped LV cavity [14]. Because of near-field problems of the echo probe, apical HCM is often difficult to assess on echocardiography, and MRI should be considered the preferred imaging technique [15]. It is clearly recognized that not all HCM patients have severe outflow tract pressure gradients, while abnormalities in diastolic function are common [16]. Currently, diastolic dysfunction is thought to be one of the major pathophysiologic mechanisms in all patients with HCM, frequently leading to diastolic heart failure. HCM patients usually display a combination of increased chamber stiffness and impaired ventricular relaxation.

At present transthoracic echocardiography is considered the standard imaging modality for the clinical diagnosis of HCM. However, CMRI is the only diagnostic technique which permits the simultaneous assessment of myocardial morphology and function, coronary flow reserve, contractility, tissue perfusion (contrast-enhanced first-pass perfusion MRI), and distinction between viable myocytes and fibrotic tissue (delayed contrast-enhanced MRI). Therefore, cardiac MRI is a useful adjunct in the reproducible assessment of cardiac abnormalities.

The distinction between HCM and physiological hypertrophy, as seen in athletes’ hearts, is a difficult task in clinical practice. Given the fact, that most exercise-related sudden cardiac deaths in athletes from HCM occur during adolescence (14–18 years old), individuals at risk should be closely monitored. Whenever LV wall thickness is greater than 12 mm in a male or greater than 11 mm in female athlete in combination with a small or normal-sized LV, HCM should be strongly considered until proven otherwise [17]. Accuracy of measurements of LV volume and LV wall thickness is essential for differentiating HCM from athletes’ hearts. Using MRI it was shown that athletes’ hearts could be distinguished from HCM and other forms of pathologic cardiac hypertrophy with 99% specificity by means of a receiver operating curve-determined cut-off value for diastolic wall-to-volume ratio of less than 0.15 mm × m² × mL⁻¹ [18]. Additionally, recent data indicates, that diagnosis of HCM may be established de novo by CMR in certain HCM subgroups with focal involvement of the apex and the anterolateral free LV wall [19], typical regions which may be difficult to assess by echocardiography. Therefore, patients with a high clinical likelihood of HCM (e.g. positive family history for HCM or sudden cardiac death in relatives) or typical ECG pattern (e.g. giant negative T-waves) and normal or inconclusive echocardiography findings should undergo CMR for further investigation. Moreover, Rickers et al. [19] showed that echocardiography appeared to underestimate the absolute magnitude of LV wall thickening and therefore it might be advisable to use CMR in certain patient collectives where accurate determination of wall thickness is crucial [19].

The arsenal of MRI sequences usable in HCM includes: SE MRI; cine MRI; velocity-encoded MRI; MRI tagging; CE-IR MRI; and MR spectroscopy. The presence, distribution, and severity of the hypertrophic process can precisely be evaluated with SE MRI and cine MRI [20–25]. An advantage of MRI over other cardiac imaging modalities is the use of angled planes, which allows accurate measurement of the myocardial wall thickness [26]. In the asymmetric septal form of HCM, the mean ratio of septal-to-free wall thickness is higher than 1.5 ± 0.8, compared with 0.9 ± 0.3 in normal volunteers and 0.8 ± 0.2 in patients with LV hypertrophy [20].

Using cine MRI sequences, obstructive can be differentiated from non-obstructive forms of septal HCM [24,27]. Flow acceleration and turbulence in the narrowed LVOT causes a dispersion of spin magnetization, generating a signal void in the LVOT during systole [24]. Presence of signal void in early systole is indicative of severe obstructive HCM. Mid-systolic signal voids usually represent less severe (latent) obstructions. In non-obstructive forms of HCM and in normal subjects, usually no signal voids are found. The presence and severity of signal void, however, is closely related to the length of the echo time. With the advent of the b-SSFP cine MRI techniques, the precise relation between signal void and flow acceleration need to be reassessed. The concomitant regurgitant jet through the mitral valve is also visible as an area of signal void. Velocity-encoded cine MRI can be used to quantify flow velocities in the narrowed LVOT, and to assess the mitral valve regurgitation. A combination of imaging planes is required to optimally image the LVOT and mitral valve abnormalities. These include longitudinal views through the LVOT; combined LV in- and outflow views; horizontal and vertical long-axis views through the mitral valve; views perpendicular through the LVOT (to measure the LVOT area), and views through the mitral valve plane (to quantify the mitral regurgitation).

The impact of myocardial hypertrophy on global and regional LV and RV function can be precisely assessed with cine MRI. The global functional values in HCM are often increased with high ejection fractions (EF) and low end-systolic values. During cardiac contraction, incomplete compression of the ventricular...
cavities may occur in patients with severe HCM. In the thickened myocardial regions, however, systolic wall thickening is markedly reduced, which is related to muscle disorganization [26,28,29]. Myocardial MRI tagging techniques have been used to study the strain or deformation in HCM patients [30–33]. In the hypertrophied myocardium, the systolic myocardial strains are invariably diminished with reduced longitudinal and circumferential shortening as well as diminished/absent systolic wall thickening. The functional abnormalities are inversely related to the local thickness. Conversely, these studies show that the ventricular torsion significantly increases in patients with HCM. Moreover, MRI tagging techniques may be helpful to differentiate focal HCM from true cardiac masses [34]. Suzuki et al. reported assessment of diastolic dysfunction of the RV in patients with HCM by means of cine MRI [35]. Nowadays, velocity-encoded cine MRI sequences assessing the flow patterns in the caval and pulmonary veins, as well as the diastolic inflow in the tricuspid/mitral valve can be used to evaluate the cardiac diastolic function. Flow measurements in the coronary sinus at rest and after administration of vasodilating agents (e.g. dipyridamole or adenosine) allow determination of the coronary flow reserve. Using breath-hold velocity-encoded cine MR Kawada et al. reported a severely depressed flow reserve ratio in patients with HCM compared with that in healthy subjects (1.72 ± 0.49 vs. 3.01 ± 0.75; P < 0.01) [36]. In agreement, using stress/rest first-pass MR perfusion imaging global reduction of first-pass reserve index (1.12 ± 0.35 vs. 1.80 ± 0.58, P = 0.015) was described in HCM patients compared to healthy controls [37]. Decreased first-pass reserve index was correlated negatively with maximal LV wall thickness and LV mass [37]. Furthermore, preliminary data suggests that contrast-enhanced MR first-pass perfusion at rest alone allows the detection of microvascular dysfunction via perfusion deficits at rest in hypertrophied and non-hypertrophied myocardial segments in HCM patients [38].

Up to now, the diagnosis of myocardial disarray in HCM was based on invasive methods. 3D diffusion tensor MR imaging is a recently developed, promising technique for the assessment of myocardial fiber architecture. In combination with 3D strain-rate MRI using velocity-sensitive phase-contrast sequences, relations between myocardial disarray and dysfunction can be non-invasively assessed in human subjects [39]. Myocardial disarray in HCM was found to be correlated with abnormalities of both diastolic and systolic function, with a more severe disturbance of diastolic function. The decrease of systolic function was related to a deranged pattern of both fiber circumferential shortening and radial thickening [39].

Use of gadolinium (Gd)-DOTA to differentiate normal from disorganized myocardial tissue in HCM patients was reported in the mid-1990s [40]. After Gd-DOTA administration, the hypertrophic myocardium in patients with HCM shows a higher signal intensity ratio than non-hypertrophic regions and than myocardium in normal subjects, and a delayed decay of the signal intensity is present. It has been hypothesized that the areas of abnormally high signal intensity in LV myocardium reflect myocardial ischemia and brosis due to small-vessel disease, or myocardial degeneration and necrosis [41]. A major limitation of the MRI techniques at this time was the insufficient contrast between normal and abnormal (e.g. infarcted) myocardium. With the advent of CE-IR MRI sequences with late imaging, the selective nulling of the signal of normal myocardium by appropriate choice of inversion-time has enabled the differences in contrast between normal and abnormal myocardium to be substantially increased. For instance, infarcted myocardium can be differentiated from normal viable myocardium with differences in signal intensity of nearly 500% [42,43]. Recently, several groups have reported promising results characterizing the hypertrophied regions in patients with HCM using CE-IR MRI [29,42,44–46]. Abnormal late enhancement is found in the majority of HCM patients, ranging from 79%, in a selected group of patients (n = 53) [45], to 81% in a non-selected group of patients (n = 21) [44]. Mean volume of enhancement was 8 to 11% of LV mass. While enhancement is primarily associated with increased wall thickness, involvement of non-hypertrophied myocardial regions has been reported [38]. The pattern of enhancement is usually diffuse or confluent patchy with multiple foci, predominantly involving the middle third of the ventricular wall; and the junction of the ventricular septum and RV free wall is the most frequently involved area of enhancement [44] (figure 1). The extent of enhancement is positively correlated with the wall thickness, and inversely with systolic wall thickening in the hypertrophied region [29,44]. Since late enhancement is a non-specific phenomenon that can reflect a variety of myocardial disorders [47], the question remains – What is the histopathologic correlate of late enhancement in HCM? At present, it is generally believed that enhanced regions represent scarred myocardium [42] or are related to myocardial disarray and local interstitial expansion [45]. In this context it is interesting that the amineterinal propeptide of type III collagen (PIIINP), a marker of collagen scar formation, was shown to be increased in patients with HCM compared to control subjects, pointing towards an increased synthesis or turnover of soft-tissue collagen in HCM patients [37]. The pattern of enhancement corresponds to the typical pattern of myocardial scarring found in necropsy studies. A pattern that does not correspond to any epicardial coronary artery distribution and is often limited to the mid-wall or subepicardium, with a predominant involvement of the junction of the ventricular septum and RV free wall (most prominent myocardial scarring and myocardial fiber disarray) [48,49]. Moreover, it is suggested by Moon et al., studying a highly selected group of patients with HCM, that myocardial enhancement in HCM is associated with progressive disease (i.e., progressive adverse LV remodeling), and increased risk for...
sudden cardiac death [45]. They found specific patterns of enhancement associations with the clinical phenotype. For instance, patients with diffuse enhancement had a higher risk for sudden cardiac death than patients with confluent enhancement. It is likely that the degree of diastolic dysfunction is linked to the extent of myocardial fibrosis, quantified by means of CE-IR MRI [50]. Secondary cardiomyopathies such as sarcoidosis- or pheochromocytoma-induced hypertrophic myocardial involvement for instance exhibit specific enhancement patterns (figure 2).

Cine MRI and CE-IR MRI are also useful in the evaluation of HCM patients with a dynamic LVOT obstruction after non-surgical septal reduction (NSSR), also called percutaneous transluminal septal myocardial ablation (PTSMA) [42,46,51]. The procedure consists in selectively inducing a localized myocardial infarct by infusion of ethanol into one or several septal branches of the left anterior descending (LAD) coronary artery [52–54]. Subsequent scarring of the induced infarct and thinning of the ventricular septum results in a widening of the LVOT, a decrease in the pressure gradient and symptomatic improvement. Ethanol causes a significant microvascular obstruction such that the penetration of Gd-DTPA is extremely slow. CE-IR MRI performed shortly (i.e., within days) after the procedure shows a large perfusion deficit with patchy enhancement on delayed imaging. With time, the extent of microvascular obstruction decreases with a less severe first-pass perfusion defect, and more pronounced delayed enhancement [42]. Since CE-IR MRI allows detailed evaluation of the size and location of the septal infarct induced by NSSR, CE-IR MRI might be helpful in predicting the final outcome. Infarcts that are too small or are located outside the target area may not achieve the necessary reduction in LVOT gradient. Large infarcts may cause potentially hazardous conduction abnormalities or ventricular arrhythmias [46]. Moreover, the infarct created by the septal myocardial ablation is not infrequently located exclusively on the right ventricular side of the ventricular septum (7/24 patients in the study by van Dockum et al. [46]). These patients have smaller infarction size and less reduction in LV outflow tract gradient. In some patients, no symptomatic improvement is reported. CE-IR MRI has been used recently to evaluate differences in lesion morphology and the extent of the infarct in patients treated with embolic septal infarction using microparticles versus alcohol.

**FIGURE 2**

*Pheochromocytoma-related cardiomyopathy.*

As the previous figure, end-diastolic short-axis SSFP cine image shows concentric thickening of the ventricle wall (A). Thickening is observed on end-diastolic four and three-chambers views (C and D). The focal hyperenhancement observed in the mid-myocardium of the lateral left ventricle wall is highly suggestive of adrenergic myocarditis.
induced necrosis [51]. While the clinical outcome was similar (i.e., improvement in NYHA class), infarct size and infarct transmurality were smaller in the emboli group compared with the alcohol group. Cine MRI can be applied to evaluate the impact of the NSSR procedure on the improvement of the LVOT area [51], and on changes in LV mass and volumes [46,55]. The LVOT area gradually increased from 1.3 ± 0.1 cm² before septal myocardial ablation to 3.5 ± 0.6 cm² one year after the procedure, representing a 128 ± 12% improvement, while the LVOT gradient dropped from 88 ± 10 mm Hg to 31 ± 11 mm Hg [51]. At six months after the septal myocardial ablation not only septal mass (58 ± 19 g vs. 75 ± 23 g, P < 0.001) but also non-septal, remote myocardial mass decreased significantly compared to baseline values (111 ± 27 g vs. 141 ± 41 g, P < 0.001). Reduction of remote LV mass was found to be significantly correlated with alcohol-induced infarct location and reduction of the LVOT pressure gradient at six months (P < 0.03) [55]. These findings indicate that myocardial hypertrophy in HCM may be partially or exclusively caused by the genetic disorder.

Dilated Cardiomyopathy

Dilated cardiomyopathy (DCM) is the most common cardiomyopathy and is characterized by impaired systolic function and by enlargement of the LV or both LV and RV. DCM has to be distinguished from ventricular enlargement, which can be seen with athletes with normal systolic function. There are many known causes of DCM amongst which figure ischemic heart disease and excessive alcoholic consumption as the most frequent causes. However, in almost half of the cases, the cause remains unknown, and DCM is denominated idiopathic cardiomyopathy (ICM). Between extremes, ischaemic cardiomyopathy (ICM) on one hand and in the other, IDC, many etiologies with sometimes specifics treatments must be sought. In this group, called non-ischaemic cardiomyopathy (NICM), causes are numerous such as Chagas’ disease, sarcoidosis or chronic myocarditis.

In this review, we will focus on how cardiac magnetic resonance (CMR) imaging is became a major tool to identify cardiac enlargement and how the use of delay contrast enhancement (DCE) sequence may help to distinguish ICM to NICM.

DCM diagnosed by CMR imaging

In clinical routine, transthoracic echocardiography (TTE)-2D is considered as the standard method to confirm or not an enlargement of one or two ventricles. Its check-list includes many geometric criteria (e.g. LV structural’s modification from ellipsoidal to spherical shape) leading to the final echo’ definition: LV diameter greater than 27 mm/m² and/or EF less than 40%. However, even if this method is more than helpful in routine, several limitations encourage the exploration of new techniques. Among those limitations, it has been proved that the low apical visibility leads to an approximate measurement of ventricles volumes [56], and inter- and intra-observer reproducibility are low, depending on physician’s experience and on patient’s echogenicity. New imaging techniques such as real-time 3-dimensional echocardiographic (RT3DE) analysis of LV volumes are now investigated, but this technique is still suffering of a poor differentiation between myocardium and trabeculae [57]. So far, CMR imaging has been shown to be a more reliable tool than TTE-2D and RT3DE techniques in order to measure LV volume, wall thickness, and LV mass and EF [21,51,58]. Real-time CMR imaging is obtained by using a balanced steady-state free precession (SSFP) gradient-echo sequence. While resulting in T1/T2-weighted signal intensities, this sequence emphasis the contrast between bright blood and dark myocardium allowing an excellent delineation of the inner border of ventricles. In addition, its excellent temporal resolution allows quantitative and qualitative approaches of global and regional wall motion. LV dilatation is diagnosed when LV end-diastolic volume exceeds 235 mL or 112 mL/m² in males and 174 mL or 99 mL/m² in females [59].

ICM versus NICM: is CMR imaging should have a place?

Most of the time, regional wall motion abnormalities and reduction of wall thickness may help to distinguish ICM to NICM. However, in the case of advanced ICM, because LV remodeling leads to a global hypokinetic motion the distinction from NICM appears more difficult. In order to go further than simple morphologic analysis, delayed contrast enhancement sequence has been tested (figure 3). In 2001, Wu et al. were the first to highlight the role of DCE sequence in order to differentiate patients with healed myocardial infarction, patients with non-ischaemic cardiomyopathy and healthy volunteers [42]. All the patients with healed myocardial infarction imaged after 14 months displayed an hyperenhancement areas on DCE while none patients with non-ischaemic cardiomyopathy and healthy volunteers showed an hyperenhancement. Two years later, McCrohon et al. confirmed the major role played by DCE sequence but also demonstrated the interest of the enhancement location [60]. In this study, all the patients with ICM had myocardial hyperenhancement and surprisingly, 41% of patients with idiopathic-DCM, meaning in this study no past history of myocardial infarction, normal coronarography, presented a pathological hyperenhancement as well. This latest group was divided in two, in 32% of those patients, an ischemic type hyperenhancement was observed whereas in 68% had a non-ischaemic hyperenhancement pattern. Instead of having a subendocardial hyperintensity, idiopathic-DCM displayed a mid-myocardium enhancement of the LV wall. In both cases, coronaryography was normal, and authors evoked the hypothesis of vulnerable plaque unknown on angiography in order to explain the subendocardial intensity.
Cardiac sarcoidosis

The hallmark of cardiac sarcoidosis is a discrepancy between cardiac clinical symptoms and autopsy results. Cardiac involvement are clinically silent, symptoms appear in only 5% whereas non-caseating granulomatous infiltration of the myocardium have been found in 20–50% at the autopsy [61]. Its early diagnosis is an indication of corticosteroid therapy in order to prevent arrhythmia (sudden death accounts for 60% of the fatalities from cardiac sarcoidosis) and to improve left ventricular function. Cardiac involvement takes place in three stages: acute myocardial inflammation, post-inflammatory pattern and replacement scarring [62].

During the first stage, focal myocardial thickening is often seen and may mimic hypertrophic cardiomyopathy. Nodules display high signal intensity on T2-weighted sequence and on DCE sequence. Those inflamed nodules are located in the basal portion of the septum and into the left ventricular wall. Because any others type of myocarditis could mimic those signal features, the location of signal abnormalities present a good indicator of disease. The second stage is a stage of transition. Thickening of the ventricle wall and delayed hyperenhancement decrease whereas the signal on T2-weighted sequence can remain slightly intense. This postcard is often observed with patient during or after corticosteroid treatment. As a result of natural evolution or of specific treatment, the latest stage is the time of the replacement scarring. At this time of the diagnosis, patient history, normal angiography and location of delayed gadolinium uptake are the only evidences of sarcoidosis cardiac involvement.

Chagas’ disease

South-America is celebrating the 100th year anniversary of discovery of the disease by the Brazilian scientist Carlos Chagas. The WHO considers Chagas’ disease, infectious caused by Trypanosoma cruzi, as the most serious parasitic threat in South-America with a number of infected people between 10 to 13 million [63]. Chagas’ disease is characterized by three phases: acute, latent, and chronic. The heart is the most severely and frequently involved organ and cardiac symptoms can vary between asymptomatic to severe. The duration of the latent phase is between 10 to 30 years and it is characterized by the absence of clinical symptom and by the absence of electrocardiogram abnormality except some minor cardiac rhythm disturbances. In 30% of the infected people, late manifestations can occur, and in those symptomatic people 94.5% of the clinical signs are cardiac. In 58%, congestive heart failure is the cause of death whereas cardiac arrhythmias is involved in 36.5%. The pathogenesis of chronic chagasic cardiomyopathy is still unclear, chronic fibrosing myocarditis and alterations in the myocardial microcirculation seem to be the main two corner stones of the disease [64]. Elective sites of the disease are located at the apex and at the basal infero-lateral region, explaining the great value of CMR compare to TTE-2D. In those areas, aneurysm, intra-ventricle thrombus and delayed contract enhancement have to be sought. It has to be underlined that even if this disease seems far away from western countries, traffic people around the world must aware clinicians and radiologist about this disease.

Idiopathic dilated cardiomyopathy

Idiopathic dilated cardiomyopathy (IDC) is evoked after known causes have been excluded such as excessive alcohol exposure, severe hypertension, autoimmune disease (figure 4) and, of course, ICM. This occurs in almost 50% of the patients with a diagnosis of DCM. IDC is probably multifactorial, including autosomal dominant mode of inheritance [65] and environmental exposures. The incidence is 40 cases per 100,000 populations per year in United-States. Approximately half of
patients with recently diagnosed IDC die within the first year. The main causes of death are lethal arrythmias and sudden cardiac death. With the advent of implantable cardioverter defibrillators ICD implantable it is now possible to prevent this fatal outcome and especially to prevent sudden cardiac death. However, right now, the main issue is to identify the patient who needs the most of this device independently of its cost. Many risk stratifications have been studied and MRI could be one of the accurate tools in a near future. In a study, patients for whom the diagnosis of IDC was made with LVEF less than 35% underwent CMR before placement of a device. Patients with myocardial hyperenhancement had an eight times greater risk of sudden cardiac death [66,67]. However, the value of DCE sequence still needs further studies since its presence is variable in different studies.

**Restrictive Cardiomyopathy**

Restrictive cardiomyopathy (RCM) is the least common cause of cardiomyopathy and is characterized by diastolic dysfunction with relative preservation of systolic function and wall thickness. RCM can be defined by three physiological patterns: stiffening of ventricular walls, restrictive filling and reduced diastolic volume of LV or both ventricles. The main consequence is typically described as an abrupt premature cessation of ventricular filling in early diastole, causing a dip-plateau pattern on ventricular pressure tracing. The ultimate result in decreased compliance of ventricles is the development of atrial dilatation. The overlap with others cardiomyopathies is wide and restrictive filling patterns of LV can as well be seen with pure restrictive form or with patients with HCM or DCM. RCM can be associated with several diseases such as amyloidosis (AL), hemosiderosis, hypereosinophilia, endocardial fibroelastosis, systemic sclerosis (figure 5) and secondary to radiation therapy and certain medications.

**Amyloidosis (AL)**

Cardiac involvement is seen in primary AL and in senile systemic AL with a frequency of 60 and 25% respectively. Half of the death of the patients with primary AL is attributed to cardiac failure or arrythmias [68]. When cardiac symptoms are identified, median survival is strongly shortening, about 4 months while senile form is less aggressive with a median survival of 75 months [69]. The disease is due to amyloid deposit into the myocardium (with a preference for the subendocardial layer).
disturbing contractile function and electrical conduction. Although myocardial biopsy can make the diagnosis, this procedure is invasive and the risk of sampling error limits its application. In routine, the diagnosis is made by ETT associated with an extracardiac biopsy. However, ETT have some limitations, previously discussed, and particularly if hypertrophy from other causes is observed. Other non-invasive techniques also have limitations such as ECG and scintigraphy with the use of radiolabeled serum amyloid P component.

Beside the morphological abnormalities of the RCM, MR findings in AL involvement are observed after injection of gadolinium. Those abnormalities of signal are the direct consequences of amyloid deposition. The first consideration depends on the gradient of amyloid deposition between the subendocardial layer and subepicardial layer, with a high prevalence for the inner border. The exact inversion time for the perfect dark myocardium is thus unobtainable (figure 6). The second consequence of the presence of the amyloid depots is the increase of the extracellular space. So, when delayed contrast enhancement sequence (after 10 min) is acquired, a hyperenhancement as a regular ring is observed into the subendocardial layer. This MR finding appears specific of the cardiac AL and combined with the value of the entire signal uptake of the myocardium an accuracy of 97% in patients with biopsy proven AL is yield [70].

Anderson-Fabry disease
Fabry disease is an X-linked lysosomal storage disease that is caused by deficient activity of lysosomal enzyme a-galactosidase A. Cardiac involvement is common, and usually develops in the fourth decade of life. In brief, glycosphingolipids accumulate in the lysosomes of numerous cells owing to a-galactosidase A deficiency. This accumulation leads to cells and tissue ischemia and fibrosis. In case of cardiac involvement, the accumulation concerns the cardiomyocytes, the valve and the vascular endothelium. The result is a concentric cardiac hypertrophy, which has to be differentiating of LV hypertrophy. Anderson-Fabry disease would represent 3% to 6% of the patients with diagnosed HCM. Delayed hyperenhancement is characterized by an elective location in the midventricular and subendocardial layers of the basal and infero-lateral myocardium [71]. This MR finding has been found in 92% of the case of cardiac involvement [71].

Hemosiderosis
Schematically two types of disease must be differentiated. First, the classic haemochromatosis, inherited or not, its diagnosis can be mad on the basis of history, clinical examination, laboratory abnormalities such as elevated serum iron, ETT and CMR showing DCM. Second, cardiac siderosis, encountered later, and where ventricular dimensions may be normal until the late stage of disease. Moreover, conventional markers for iron overload such as serum ferritin and liver iron have been shown to bear no relation to myocardial iron deposition in the classic form of acquired myocardial siderosis, and especially in β-thalassemia major. Here, CMR may be a new modality to evaluate myocardial iron overload burden, even if it’s not a quantitative tool as it has been established for liver. Its principle is based on iron deposition that reduced the relaxation rates of T1- and T2- weighted sequences by introducing local magnetic field inhomogeneities.
The decrease is observed on $T_2^*$, and preferentially measure into the septum [72]. Now, beside the right ventricular myocardium, which is usually spared, LV and both atrium are more often affected. CMR could also be used as an indicator of iron chelation therapy efficiency.

Endomyocardial disease and hypereosinophilic syndrome

Both diseases are directly related to the cardiac toxicity of activated eosinophils. There are three stages: necrotic, thrombotic, and fibrotic. The acute necrotic stage is often asymptomatic including eosinophils and lymphocytes infiltration within the myocardium, lesions of the subendocardial layer and necrosis. During the intermediate stage, thrombus formation occurs along necrotic endocardium. The latest stage is the fibrotic stage, because of the endomyocardial replacement scarring, the thickening of the LV wall is observed. A restrictive pattern is typical of the late stage of the disease.

RCM versus constrictive pericarditis

CMR imaging enables to distinguish RCM to constrictive pericarditis, which is the main differential diagnosis for clinicians.

The main MR finding observed in case of pericarditis is the thickening of the pericardium, up to 4 mm (normal < 2 mm). Its signal is also quiet different, hyperintense on $T_2$-weighted sequence and enhanced after gadolinium. However, because pericardium can also be infiltrated in few cases of RCM, as it can be seen in AL, others MR findings must be sought. With real-time cine imaging, the early diastolic interventricular septal flattening or inversion (the so-called paradoxical septal movement) during inspiration can be observed in cases of constrictive pericarditis. Phase encoded flow velocity imaging is helpful in order to measure constrictive inflow patterns in the caval veins. However this sequence is time consuming and not use in routine. This type of sequence can also be used in RCM in order to show LV diastolic dysfunction. With RCM, diastole is characterized by increased early LV filling velocity (E-wave) and decreased atrial filling velocity (A-wave) leading to an elevated E/A ratio. With RCM, others anatomical MR findings can be observed, normal ventricular size with or without wall thickening and bi-atrial enlargement, with systolic function almost preserved.

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Figure 6

51-year-old patient with systemic AL amyloidosis. Top row shows the thickening of the LV wall on short-axis $T_2$-weighted image (A) and on short-axis diastolic cine image (B). Still at the top row, short (C) and four-chambers (D) delayed-contrast enhancement sequence show a diffuse biventricular concentric subendocardial enhancement. Bottom row show how the system failed to select the right inversion-time, from E to H image.
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