Restrictive Cardiomyopathies: Evaluation Using Cardiac MRI and Multidetector CT

Miocardiopatías restrictivas: Valoración por resonancia magnética cardiaca y tomografía multicorte

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Pericarditis, constrictive
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Summary
Cardiomyopathies are conditions that affect the myocardium and cause alteration in the cardiac function. Within the cardiomyopathies, the restrictive subgroup has as a main finding the decrease in the ventricular filling. In this manuscript we will review the restrictive cardiomyopathies and discuss their main causes, as well as their imaging findings on cardiac magnetic resonance and computed tomography. We will also include imaging signs that help to differentiate restrictive cardiomyopathies from constrictive pericarditis.

Resumen
Las miocardiopatías son condiciones que afectan al miocardio y generan alteración en la función cardiaca. Dentro de las miocardiopatías, el subgrupo de las restrictivas tiene como principal hallazgo la disminución en el llenado ventricular. A continuación se expone una revisión acerca de las miocardiopatías restrictivas, se analizan sus principales causas, y los hallazgos por resonancia magnética cardiaca y por tomografía computarizada. También se incluyen signos por imagen que ayudan a diferenciar las miocardiopatías restrictivas de la pericarditis constrictiva.

Introduction
Restrictive cardiomyopathies are characterized by a decrease in diastolic volume, a limitation of ventricular filling, and a function normal systolic or close to normal. Although in the image evaluation there are characteristics common to all restrictive cardiomyopathies, there are some findings that differentiate them. Therefore, cardiac magnetic resonance imaging (CMRI), thanks to better tissue characterization, has become the technique of choice in the assessment of these patients, to carry out an etiological approach and direct the treatment. The following is a review of the topic of restrictive cardiomyopathy with emphasis on the main causes and their characteristics in CMRI and computed tomography (CT) assessment.

Cardiomyopathies are myocardial diseases associated with cardiac dysfunction that can be divided into ischemic or non-ischemic, according to the commitment coronary artery (1-3). Restrictive cardiomyopathies (RCM) are part of the non-ischemic group and are characterized by a restriction in filling and ventricular diastolic volume with subsequent atrial dilatation and venous stasis, normal or near-normal systolic function and thickness of the preserved wall (4,5).

MRI plays a fundamental role in the approach of patients with RCM, because it defines those who suffer from this condition, which helps determine the cause and therapeutic plan. It also allows differentiation of constrictive pericarditis (CP), which presents similar clinical manifestations, but unlike RCMs that are usually medically managed, CPs generally require surgical management.
Image modalities

Diagnostic techniques in the evaluation of RCM include: electrocardiogram, echocardiography, cardiac magnetic resonance imaging (MRI), computed tomography (CT), and angiography.

RCM echocardiography typically shows a normal or diminished-size ventricle with normal or slightly decreased ventricular function in the early stages of the disease. The atria are dilated and ventricular filling is limited (diastolic dysfunction) in the Doppler evaluation. With the progress of the disease, the pulmonary arterial pressure rises. Echocardiography, unfortunately, is limited in tissue characterization and therefore its use is limited to determine the etiology of the RCM. In the last decade, CMRI has become a noninvasive technique that allows an adequate morphological evaluation of perfusion, ventricular function and allows a tissue characterization. In addition, it helps to differentiate the RCM from the CP. CT is also useful for differentiating the RCM from the CP, since it allows the detection of calcifications in the pericardium, a frequent finding in the CP.

Angiography allows assessment of the lumen of the ventricles, their function, wall motility, and is the reference technique in the assessment of cardiac hemodynamics. However, it is not very useful to identify the cause of the hemodynamic alteration, except for some diseases that have features by angiography, such as endomyocardial fibrosis. The major advantage of percutaneous angiography is that it allows to take a histological sample.

Findings common to all RCM

Typically, it appears as normal-sized or diminished ventricles with enlarged atria. The contours of the ventricular cavities are maintained and do not appear indented, unlike the CP, in which the cavities appear tubular or indented due to the extrinsic cause of this disease. The degree of increase in atrial size is much greater in the RCM than in constrictive pericarditis (CP) (6). The myocardial thickness is frequently increased in the RCM but normal in the CP. In RCM, the pericardial thickness is usually normal, having a normal value of 2 mm or less (7), whereas in CP it is increased and sometimes with low signal calcifications in all the pulse sequences by CMRI. In some types of RCM there may be pericardial fluid, such as amyloidosis, but, unlike CP, the fluid in the RCM usually has a free distribution (8).

The RCM and CP have similar clinical and hemodynamic characteristics, but it is important to differentiate them since the management of each one is different: surgical and curable for the CP, whereas for the RCM, the treatment is medical or with a heart transplant (6, 9, 10). Currently, to distinguish them one can use imaging findings from non-invasive studies (CMRI, CT, echocardiography) for pericardial thickness measurement, septal motility analysis (including analysis of respiration changes of the interventricular septum), evaluation of systolic or diastolic myocardial function, myocardial fibrosis in late enhancement sequences, myocardial biopsy, among others. Both entities are characterized by a normal or decreased volume in the two ventricles, associated with increased binaural size, altered ventricular filling (restrictive physiology), and normal or near-normal systolic function (Figure 1) (11,12).

The following are some common causes of RCM and their imaging characteristics.

Amyloidosis

It is the extracellular deposit of insoluble proteins with alteration in the folding. Of the different causes, primary, senile and hereditary amyloidosis lead to clinically significant cardiac compromise (13). In primary amyloidosis, 50% of patients have cardiac manifestations and 25% have congestive heart failure (14). Cardiac amyloidosis can be isolated or associated with systemic compromise, in either form representing a poor prognosis.

Clinical manifestations are non-specific and include fatigue, weakness, angina, heart failure symptoms, and arrhythmias (15-17); can even elevate troponins (18).

There are multiple mechanisms by which the amyloid deposit causes myocardial dysfunction. One of them is the increase in myocardial mass and hardening of the ventricular walls by an increase in the interstitial space, which leads to alteration in ventricular filling. Also, it alters the myocardial architecture and causes a direct toxic effect on the myocyte, which alters the contractility (19).

The diagnostic standard is the endomyocardial biopsy. However, in some cases it is not possible because of its invasive nature and its possible complications (20).

CMRI is a highly specific and non-invasive technique, and therefore represents an alternative to biopsy. In a study of 33 patients with suspected cardiac amyloidosis who underwent endomyocardial biopsy and CMRI. A sensitivity of 94% and 80% specificity were found for CMRI to perform the diagnosis (21).

Using CMRI one can identify the concentric myocardial biventricular thickening associated with atrial and atrial thickening of the interatrial septum. Other findings include pleural and pericardial effusions. Some authors have reported a thickening of the interarticular septum as a characteristic finding of amyloidosis (22).

In late-enhancement images, this is usually global and predominantly subendocardial, but may also be transmural (23-25). Late enhancement is believed to be caused by interstitial expansion by deposition of the amyloid protein (26); however, the amount of amyloid has no direct relationship to the intensity of the late enhancement (27).

The pattern of late enhancement in amyloidosis is diffuse and weak. This is believed to be due to systemic amyloid binding to gadolinium by reducing its effective volume of distribution. This generates a low contrast between the suppressed myocardium and the pool of blood, because of difficulty in suppressing the myocardium without suppressing the pool of blood (26).

Amyloidosis causes an alteration in the gadolinium hemodynamics with an increase in the extracellular deposit through the body, resulting in an earlier lavage of the blood pool (21, 26). Late myocardial enhancement may be diffuse or subendocardial (Figure 2). The degree of myocardial enhancement has been directly correlated with alteration in segmental and global contractility, diastolic dysfunction and increase in atrial size (28, 29).
Figure 1. Constrictive pericarditis. a) CMRI HASTE sequence with 4 cameras. b) Sequence SSFP 4 cameras. c) Cardiac tomography with image in 4 chambers. Marked thickening of the pericardium (greater than 3 mm), mainly surrounding the ventricles, with calcification (arrow in c), indentation of lateral lateral right ventricle (arrows in a and b) and binaural growth (*).

Figure 2. Amyloidosis. a) CMRI with short-axis late enhancement sequences. b) In 2 chambers. c) SSFP in 4 chambers. Subendocardial enhancement (arrows in a and b) and thickening of the biventricular myocardium (arrow in c) with binaural dilatation. In SSFP, pericardial effusion and left pleural effusion (* in c) are identified.

Figure 3. Sarcoidosis. a and c) CMRI with short-axis late enhancement images. b) Longitudinal 2 chambers. d) in 4 chambers. Subepicardial enhancement of basal predominance (white arrows in a and b) with involvement of the right ventricle roof (arrowhead in a). In the image of 4 chambers there is also enhancement of the interatrial septum and the walls of the atria (thick arrow in d).
Sarcoidosis

Granulomatous, non-caseifying, multisystemic disease. Pulmonary involvement is the most frequent in 90% of patients (30). Cardiac involvement is frequently noted in autopsies (20-27%) (30,31), although clinically it is only detected in 5% of patients (32).

Cardiac sarcoidosis can occur before, after or simultaneously with the involvement of other organs (33). Cardiac involvement indicates poor prognosis and may be associated with cardiac failure, conduction abnormalities: atrioventricular block (26-62%) and sudden death (12-65%) (34). This is the most common cause of death in sarcoidosis (35).

The definitive test for diagnosis is the histopathological test by endomyocardial biopsy. However, because of focal involvement, biopsy is relatively unresponsive with only 10% of positive biopsies in patients with sarcoidosis and arrhythmias (36).

There are 3 successive histological stages: edema, non-caseiform granulomatous infiltration and patched myocardial fibrosis (30). In the acute inflammatory phase, there are focal areas of high T2 signaling and myocardial thickening due to edema. Granulomas are seen as low-signal foci in T1 and T2 within the areas of signal increase in T2. In the early perfusion images, a normal or increased enhancement is seen. These areas may show enhancement in late enhancement images and regional abnormalities in motility in film sequences. In patients undergoing treatment with steroids, these characteristics can be altered and appear only as a high T2 sign, without myocardial thickening or enhancement. The pathophysiology of enhancement in the acute phase is by focal myocarditis and in the late phase by fibrosis (37). The enhancement tends to be patched into a non-coronary distribution, and compromises the base more than the apex (38); more frequently the enhancement is subepicardial, non-transmural (Figure 3) (37).

Late enhancement images help guide the endomyocardial biopsy and define the prognosis. The degree of enhancement correlates with poor volume at the end of diastole in the left ventricle, volume at the end of systole in the left ventricle, increase in atrial natriuretic peptide B, and a negative correlation with ejection fraction (37,39).

Due to its great variety of morphological manifestations, sarcoidosis can simulate other entities: for example, when subendocardial enhancement may mimic ischemic lesions (40) and in advanced stages, when scarring areas present thinning of the wall and impaired motility, simulate other nonischemic cardiomyopathies (35,41).

Per tomodography the findings are not specific and include cardiomegaly, pericardial effusion and ventricular aneurysms. In the thorax there are usually findings related to the disease, such as bilateral mediastinal and hilar lymphadenopathy, involvement of the pulmonary parenchyma with nodular thickening of the interstitium, or predominant fibrosis in the upper lobes (42-45).

Löffler’s Endocarditis (LE) and endomyocardial fibrosis

The geographical distribution and clinical characteristics of these two entities are different; however, the pathological outcome is similar.

LE is associated with hypereosinophilia that may be associated with neoplasias, infections, allergies or idiopathic way (46). Endomyocardial fibrosis is found in tropical countries and is typically not associated with hypereosinophilia.

Oslen described 3 stages of LE: necrotic, necrotic thrombotic and fibrotic (47). In the necrotic phase there is eosinophilic infiltration of the myocardium, predominantly subendocardial in the apex and in the entry regions of both ventricles; generally respects the output tracts. Inflammation leads to myocardial necrosis and formation of microabscesses.

As the process progresses, subendocardial denudation leads to the formation of thrombi in the ventricular cavity. As the disease becomes chronic, subendocardial fibrosis and thrombus formation appear (48). Fibrosis leads to decreased compliance and restrictive physiology. The involvement of the papillary muscles in the entry regions can cause valvular insufficiency (49). It can compromise one or both ventricles, and when it comes to one is usually the right side.

CMRI is very useful for diagnosing endomyocardial fibrosis and defining the stage of disease. It is important to recognize the disease in early stages, since the timely administration of steroids helps prevent progression to fibrotic stages (50). Endomyocardial infiltration is seen as a high intensity signal in T2 or STIR in the endocardial and subendocardial portion of the ventricular apices and inlet regions. In the early stages this may be the only finding associated with abnormality of motility. As the disease progresses thrombus formation may appear, which are seen as a low signal band in a gradient echo sequence. In the late enhancement sequences, the thrombus gives rise to the sign of the “sandwich”, because it is a low signal between the enhancing endocardium and the blood pool (Figure 4). The compromised segments have hypokinesia or akinisia in the cinema sequences.

Endomyocardial fibrosis has a poor prognosis, and medical treatment is usually ineffective (51). Some patients benefit from surgical treatment with endocardial resection and atroventricular valve replacement. A series of surgery reported survival of 68% 10 years after surgery (49).

Iron overload cardiomyopathy

Iron deposition may be due to hemochromatosis, either primary or secondary. Common iron deposit sites include the liver, spleen and endocrine organs. Cardiac involvement is uncommon and is usually found in more advanced stages. Excessive iron deposition leads to diastolic and systolic dysfunction, initially the first. Heart failure is the leading cause of death in these patients (52,53).

CMRI plays an important role in the detection and quantification of cardiac compromise. The iron deposit causes shortening in the relaxation time in T2 star sequences (T2 star), which can be detected in gradient echo sequences. Measurements are performed on the short axis in the middle ventricle and in the interventricular septum, and it is calculated with a signal decay curve (54).
In cardiomyopathy due to iron overload the T2-weighted value typically is less than 20 milliseconds, and overloading is considered severe when the value is less than 10 milliseconds, so a shorter decay time represents less cardiac function (55). The ability of CMRI to detect iron deposition in the early-stage myocardium helps to direct iron chelation therapy and to monitor and follow up treatment, which has been shown to reduce morbidity and mortality in these patients (56).

Hypertrophic cardiomyopathy

Es la enfermedad cardiovascular hereditaria más común, con un prevalence of 1:500, and is the leading cause of sudden death in young people and athletes (57). It is an autosomal dominant disease caused by the mutation of genes that code the proteins of the sarcomere; however, it’s penetrance is incomplete and age dependent (58,59).

Symptoms include dyspnoea and chest pain with exercise, which are related to diastolic dysfunction, obstructive physiology and ischemia secondary to imbalance between supply and demand or microvascular disease (60,61).

There are multiple morphological variants that can be identified by CMRI according to the degree of wall hypertrophy (57), which, when not homogeneous, is described as asymmetrical (Figure 5).

The diagnosis is based on the morphological characteristics when finding a wall thickness of the left ventricle at the end of the diastole greater or equal to 15 mm or a ratio of the thickness of the septal wall with the lateral wall greater than 1.3 in a ventricle left non-dilated and in the absence of conditions causing this abnormality (Figure 5) (57). The disproportionate thickening in the subaortic septum leads to stenosis in the left ventricular outflow tract during systole, which increases the velocity of blood ejected in a reduced space and generates a Venturi effect that pulls the anterior leaf of the mitral valve; anterior movement of the mitral valve during systole further
reduces the left ventricular outflow tract by predisposing to sudden death (2.58).

Late enhancement is not considered a diagnostic criterion; however, it provides prognostic information. Survival is inversely proportional to the planimetric quantification of late enhancement and helps to define the need for implantation of a cardioverter-defibrillator (2).

Other conditions

Some diseases may lead to deposition of substances in the intracellular space, which increases myocardial mass with increased wall thickness and restrictive physiology. These conditions include glycogenosis types I and II, Anderson-Fabry disease, Gaucher, Neimann-Pick and galactosidosis.

Other rare conditions that cause restrictive cardiomyopathy include radiation injury and neoplasms (including cardiac carcinoma) (62-64).

Conclusions

In patients with congestive heart failure and restrictive physiology of unknown etiology, CMRI is the diagnostic modality invasive of choice.

CMRI helps to define the cause of the disease, quantify myocardial compromise, and measure ventricular function. It is also useful in monitoring these patients, to define response to treatment and prognosis; and, according to the above, to establish the need for some specific treatment, such as the implantation of a cardioverter-defibrillator.

CMRI and CT are very useful in the differentiation between RCM and CP, which is important because of the implications and prognosis of these patients, since, although the clinical picture is similar, the treatment is different: surgical for CP and doctor for the RCM.

References


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