Current Role of Cardiac Magnetic Resonance Imaging in Hypertrophic Cardiomyopathy

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Introduction

The purpose of this paper is to provide a brief review of the use of Cardiac Magnetic Resonance Imaging (CMRI) in the risk stratification of patients with Hypertrophic Cardiomyopathy (HCM).

HCM has historically been the most common hereditary cardiomyopathy and affects one in every 500 individuals. It is believed that with the availability of new diagnostic tools, such as the recognition of new phenotypes by CMRI and genetic testing with new subtypes of genes that do not manifest a specific phenotype, this prevalence can reach one in every 200 individuals.[1]

The diagnosis is always a challenge to the different phenotypes of HCM, in addition to genotypes that did not manifest the disease in diagnostic imaging methods. Regarding the prognosis, we must value not only the clinical symptoms and myocardial thickness, but also the presence or absence of fibrosis in CMRI, since outcomes that include Sudden Cardiac Death (SCD) and Heart Failure (HF) are more frequent in individuals presenting myocardial fibrosis, particularly in the group with fibrotic areas greater than 15% of the Left Ventricular (LV) mass.[2]

Faced with a prevalent cardiomyopathy with fatal outcomes, its stratification should be refined after initial diagnosis, including advising the patient on the risks and the need for family investigation.

Due to its high spatial resolution images and tissue characterization techniques, CMRI is currently an important tool in the evaluation of this pathology. However, CMRI is not widely accessible to the population because it is a complex method. In addition, we must remember the possible limitations and contraindications of the method: in claustrophobic individuals, anesthesia will probably be necessary; the presence of cochlear implants, clips or metal fragments, in addition to Pacemakers (PM), Implantable Cardioverter-Defibrillators (CDI) or other devices that are not compatible with the magnetic field (http://www.mrisafety.com). It is important to note that there are currently PM and CDI compatible with CMRI. Besides, gadolinium-based contrast injection is required to perform the Late Enhancement (LE) which, although it rarely causes allergic reactions, it should be used with caution in patients with advanced renal impairment.

Keywords

Cardiomyopathy, Hypertrophic, Familial; Magnetic Resonance Imaging/methods; Endomyocardial Fibrosis; Heart Failure; Echocardiography/methods; Electrocardiography/methods.

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Definition of hypertrophic cardiomyopathy

HCM is an autosomal dominant genetic disease characterized by ventricular hypertrophy, preserved systolic function and diastolic dysfunction, in the absence of secondary causes that may promote myocardial hypertrophy, such as systemic arterial hypertension, aortic and subaortic valve disease, infiltrative cardiomyopathies, etc.[3,4] Its development is determined by mutations in the genes encoding the cardiac sarcomere, the most common being heavy chain beta-myosin and myosin-bound protein C.

Epidemiology

It is the most common hereditary heart disease. It is present on all continents and, consequently, in all races and ethnicities and is equally distributed among men and women.

Despite its high prevalence in the literature, it appears to be infrequently diagnosed at a medical level. This apparent discrepancy suggests that most patients are not being diagnosed, probably because of the absence of symptoms or findings in early diagnostic methods, believed to be the "tip of the iceberg."[5]

Screening for CMRI is recommended worldwide among first-degree relatives. The first option for evaluation of these patients is by means of imaging methods (echocardiography and CMRI) and resting electrocardiography, which must be performed since adolescence, a period in which the manifestation of myocardial hypertrophy is frequent.[5] Echocardiography screening should begin at approximately 12 years of age and should be performed every 12 to 18 months until physical maturity is reached, near the age of 20 or in the presence of symptoms. Due to the low probability of manifestation in adulthood, follow-up with echocardiography can be performed every 5 years, between 20 and 50 years of age.[6] CMRI should always be considered in cases where electrocardiography presents evidence of myocardial hypertrophy that has not been documented on the echocardiography.[7]

Stratification of risk for sudden cardiac death

Although SCD in individuals with HCM is infrequent (~1% per year), it is the most serious complication. SCD results mainly

from ventricular arrhythmias, dynamic LV outflow tract (LVOT) obstruction, microvascular ischemia, myocyte derangement and myocardial fibrosis. The main risk factor for SCD is previous history of cardiac arrest, ventricular fibrillation or sustained ventricular tachycardia, with a mortality of approximately 10% per year.

The biggest challenge is to identify which patient is at greater risk of SCD, HF, dynamic LVOT obstruction and severe ventricular arrhythmias, since its presentation varies from childhood to adulthood.

Electrocardiography and echocardiography are initial diagnostic methods. However, CMRI offers an accurate evaluation of myocardial hypertrophy, ventricular function and potential gradients of dynamic LVOT obstruction, in addition to the detection of areas of myocardial fibrosis. When the secondary etiology of ventricular hypertrophy is ruled out, the presence of fibrosis is directly related to a higher probability of an unfavorable cardiovascular event, such as MSC and severe ventricular arrhythmia, especially in individuals with fibrotic areas greater than 15% of the LV mass.[2]

Aspects of hypertrophic cardiomyopathy in cardiac magnetic resonance imaging and its prognostic impact

Phenotypes of hypertrophic cardiomyopathy

Through high resolution CMRI, it is possible to identify the different patterns of hypertrophy (Figures 1 to 7) and, in some cases, the HCM phenotype. It is a test of great importance, especially in cases where hypertrophy is located in areas where echocardiography is less precise (anterolateral wall and apex), allowing diagnosis in cases where echocardiography was considered borderline or ambiguous.

In addition, it allows to rule out differential diagnoses, such as hypertensive cardiomyopathy, athlete's heart, infiltrative or depositional cardiomyopathy (amyloidosis, hemochromatosis, Fabry's disease and endomyocardial fibrosis), uncompressed cardiomyopathy, etc.[8]

Regarding the prognostic findings, a phenotype associated with apical aneurysm formation, usually accompanied by severe mean ventricular hypertrophy associated with local obstruction and LVOT obstruction, is considered a risk factor for SCD and thromboembolic events.[9]

Left ventricular mass and maximum thickness

Excessive LV hypertrophy (with thickness ≥ 30 mm) is associated with higher risk of SCD, and is considered an independent risk factor for SCD, even in the absence of other conventional risk factors. However, measurement of LV mass did not prove to be an independent predictor of SCD.[9]

CMRI is of great importance in these cases, because it is able to provide precise measurements of myocardial thickness due to its high spatial resolution.

Left atrial dilation

Left atrial measurement was included in the risk score of the European Society of Cardiology (ESC).[10] However, the independent relationship between left atrial size and risk of SCD is not well established and is not used by the guideline of the American College of Cardiology/American Heart Association (ACC/AHA) as a criterion to dictate the preventive management of SCD these days.[7]

Obstruction of left ventricular outflow tract

Dynamic LVOT obstruction is associated with increased cardiac morbidity and mortality.[11] Patients with non-obstructive HCM have a better prognosis, except in cases whose phenotype evolves with severe ventricular dilation and dysfunction.[3]

Through CMRI, it is possible to identify flow vortexing in the LVOT secondary to septal hypertrophy (Figure 8) and/or abnormal mitral subvalvular apparatus, which may also lead to mitral regurgitation by Anterior Systolic Motion (ASM). It is also possible to see the mobility of the mitral and aortic valve leaflets and the mitral and aortic valve planes by direct planimetry in cine-mode resonance imaging.

In addition, short-axis direct planimetry in the LVOT makes it possible to measure the LVOT area, in which values ≤ 2.7 cm^2 present a higher correlation with severe LVOT gradient.[12]

Ventricular dysfunction

A subgroup of patients with non-obstructive HCM develops systolic dysfunction (LV ejection fraction < 50%) secondary to disordered remodeling associated with extensive fibrosis. This subgroup is subject to a higher risk of SCD due to ventricular arrhythmia and advanced HF. The risk factors associated with this condition are positive family history and LE ≥ 20% of the total LV mass.[2]

Myocardial edema

T2-weighted black blood images (sequence for evaluation of myocardial edema) can identify the presence of edema (Figure 9) in areas that generally coincide with the presence of myocardial fibrosis (Figure 10). The presence of myocardial edema in individuals with HCM is associated with advanced levels of heart disease and a higher incidence of cardiac arrhythmia.[13]

Myocardial fibrosis

Detection and quantification of myocardial fibrosis is performed using the LE technique, which uses gadolinium-based contrast media, as it accumulates in the myocardial areas with increased extracellular space.[14]

The LE pattern in HCM is variable and it is not possible to use the pattern found as a predictor of risk. In addition to the heterogeneous distribution pattern (Figure 11), another pattern often found in these patients is the junctional (Figure 12) LE (right and left ventricular confluence area) pattern, but none of them is associated with worse prognosis and is not exclusive to the pathology.

The heterogeneous pattern of fibrosis distribution in HCM may be difficult to quantify, and it is necessary to establish a gray scale pattern (6 standard deviation above mean signal intensity for the normal myocardium) to optimize its accuracy. Studies have shown that the presence of ventricular arrhythmias with worse prognosis is more frequently associated with ≥ 15% fibrosis of the total myocardial mass and, consequently, higher risk of CSD.[2,15]

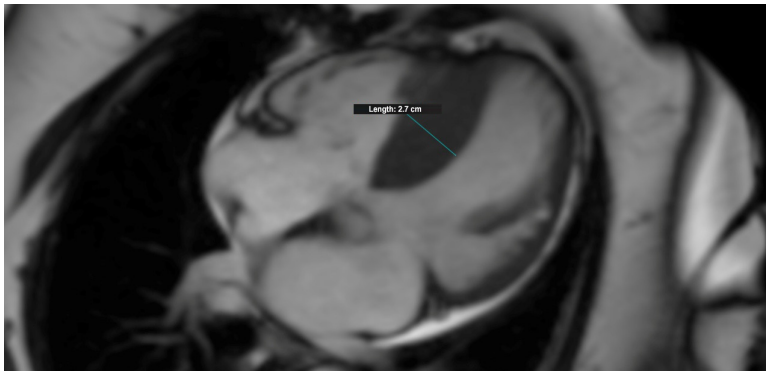

Figure 1 – *Four-chamber cine-mode magnetic resonance imaging. Asymmetric septal hypertrophy is observed with a maximum thickness of 2.7 cm.*

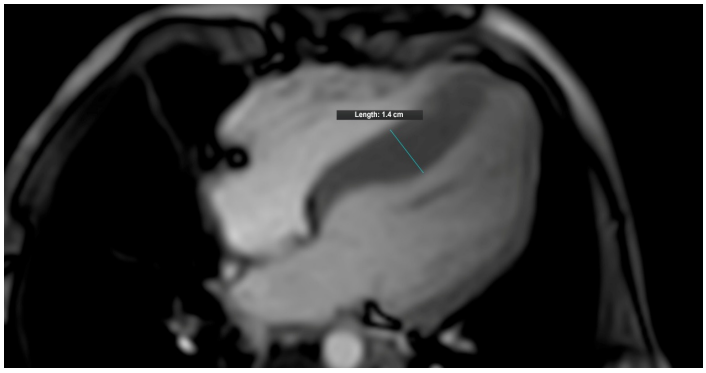

Figure 2 – *Four-chamber cine-mode magnetic resonance imaging. Male patient, 3 years old, with family history of hypertrophic cardiomyopathy. Asymmetric septal hypertrophy is observed with maximum thickness of 1.4 cm.*

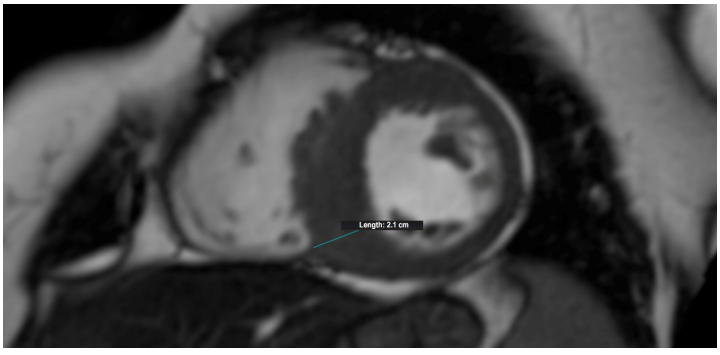

Figure 3 – *Short-axis cine-mode resonance imaging. Asymmetric septal hypertrophy is observed, with maximum thickness in the basal inferosseptal segment of 2.1 cm.*

T1 Map

T1 myocardial map consists of a technique that compares pre- (native T1) and post-contrast T1 values, whose value is used to quantify the extracellular space and estimate myocardial fibrosis, even those of heterogeneous pattern, using the measurement of extracellular volume fraction. The latest studies with Map T1 have shown a difference between HCM and other causes of ventricular hypertrophy, and have found extracellular volume fraction values significantly higher in HCM, compared to cases of cardiac amyloidosis or Fabry's disease.[16] This technique may be highly useful in the future for the stratification of the risk of patients with HCM.[3]

Conclusion

Cardiac magnetic resonance imaging, through the different techniques for the evaluation of anatomy and tissue characterization, allows an accurate evaluation of patients with hypertrophic cardiomyopathy, currently consisting of the gold standard method for the evaluation of patients with HCM.

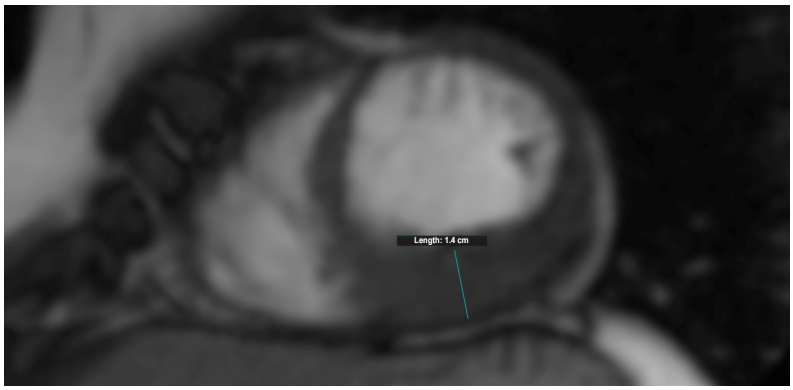

Figure 4 – *Short-axis cine-mode resonance imaging. Asymmetric hypertrophy is observed in the lower middle segment, with maximum thickness of 1.4 cm.*

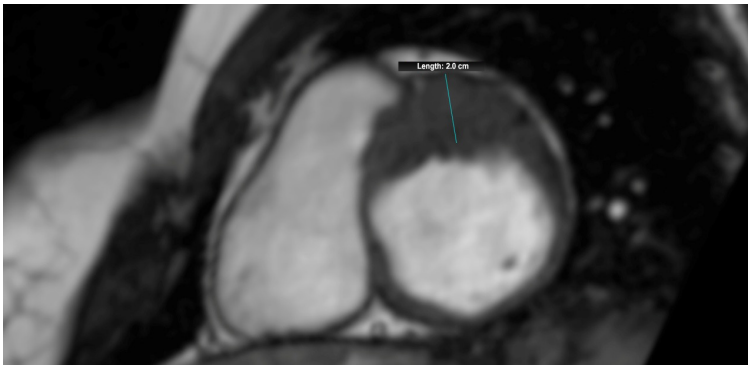

Figure 5 – *Short-axis cine-mode resonance imaging. Asymmetric hypertrophy is observed in the anterior basal segment, with maximum thickness of 2.0 cm.*

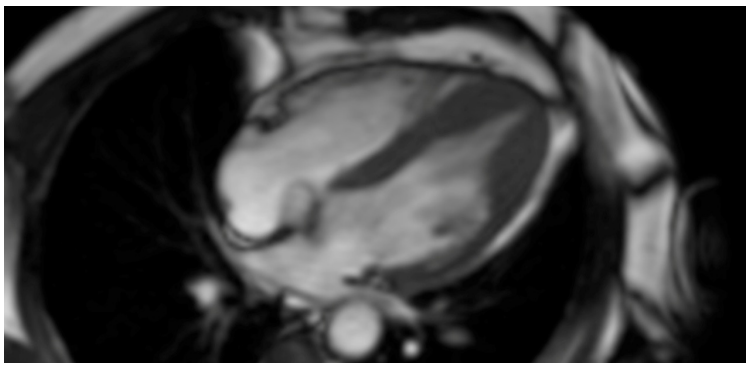

Figure 6 – *Four-chamber cine-mode resonance imaging – diastole. Myocardial hypertrophy of apical predominance is observed – Yamaguchi.*

In the difficult task of risk stratification for primary prevention of sudden death in patients with hypertrophic cardiomyopathy, quantification of myocardial fibrosis using cardiac magnetic resonance imaging suggests that individuals with intermediate risk for classic risk factors can be re-stratified as a higher risk, and can be of great help in the clinical decision to recommend implantable cardioverter defibrillator for primary prevention in patients with hypertrophic cardiomyopathy.[10,14]

Authors' contributions

Manuscript writing Fernandes FV, Bello JHSM; Critical revision of the manuscript for important intellectual content: Fernandes FV, Bello JHSM, Shiozaki AA, Cury RC.

Potential Conflicts of Interest

There are no relevant conflicts of interest.

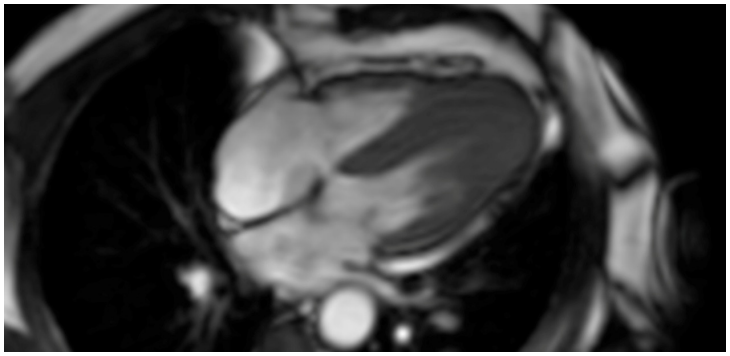

Figure 7 – *Four-chamber cine-mode resonance imaging – systole. Myocardial hypertrophy of apical predominance with collapse during ventricular systole.*

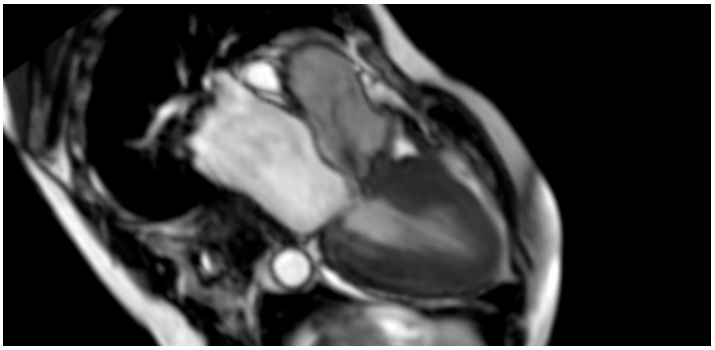

Figure 8 – *Three-chamber cine-mode resonance (left ventricular outflow tract). Left ventricular outflow tract obstruction during ventricular systole (systolic jet in the left ventricular outflow tract).*

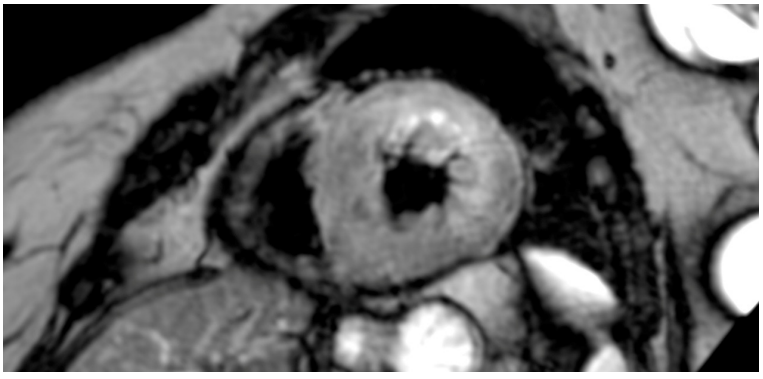

Figure 9 – *T2-weighted black blood image (triple edema). Hypersignal (edema) is seen in the anterior and lateral walls of the left ventricle.*

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This study was self-funded.

Academic Association

This study is not associated with any graduate programs.

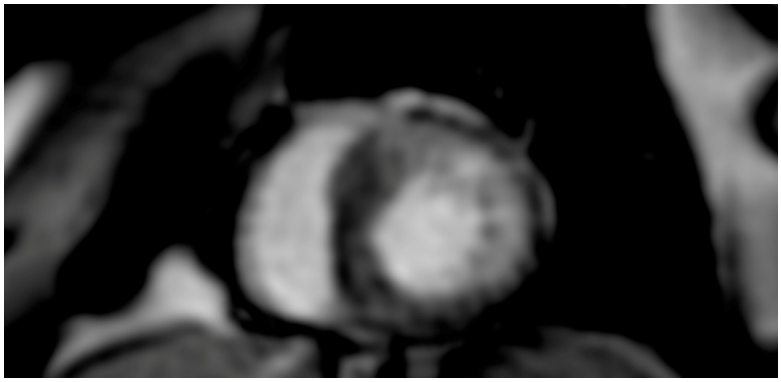

Figure 10 – *Late enhancement. There is accumulation of gadolinium in the anterior and lateral walls of the middle portion, matching the area of myocardial edema (Figure 8).*

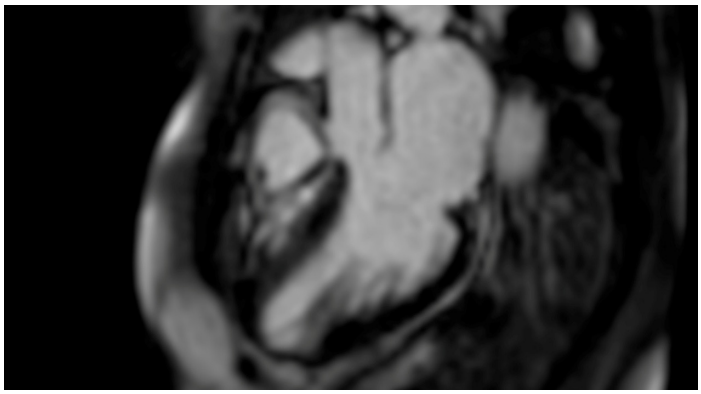

Figure 11 – *Three-chamber late enhancement (left ventricular outflow tract). Note the enhancement in the anteroseptal segment of the middle and basal portions of the left ventricle.*

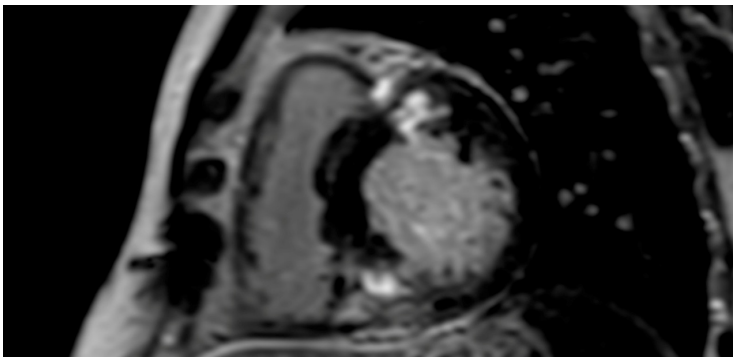

Figure 12 – *Short-axis late enhancement. Junctional, anteroseptal and inferosseptal enhancement patterns are observed.*

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