MRI to Assess Arrhythmogenic Cardiomyopathy

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Introduction

Cardiomyopathies are diseases of the myocardium associated with cardiac dysfunction. The latest report of the World Health Organization classifies them according to the dominant pathophysiology (Table 1).1 The diagnosis of cardiomyopathy has been greatly improved in recent years by non-invasive imaging techniques. Cardiovascular magnetic resonance, or CMR, is now firmly established in clinical and research cardiovascular medicine as a tool for evaluating cardiomyopathy.2

The presence of scar tissue in cardiomyopathy has been related to the genesis of arrhythmia, particularly in ischemic heart disease, but some cardiomyopathies are also associated with severe arrhythmias that can be life threatening. The electrophysiological effects of cardiomyopathy have been studied in several different animal models as well as in human tissue from biopsies and explanted hearts. These studies reveal that electrical remodeling occurs in myopathic hearts. Globally there is cell necrosis and replacement of myocytes with scar tissue. Remaining cells develop hypertrophy and altered ion channel and gap junction expression. These changes affect ventricular mechanical function as well as promoting arrhythmia.3 Scar tissue can be detected using delayed enhancement-CMR. This review will focus on CMR for the evaluation of arrhythmogenic cardiomyopathy.

Table 1: WHO classification of cardiomyopathy

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<th>Category</th>
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<td>Dilated</td>
<td>Hypertrophic</td>
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<td>Restrictive</td>
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<td>Arrhythmogenic Right Ventricular Cardiomyopathy</td>
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<td>Neuromuscular disorders</td>
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<td>Sensitivity and toxic reactions</td>
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<td>Peripartum cardiomyopathy</td>
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Dilated cardiomyopathy

Dilated cardiomyopathy (DCM) is characterized by left ventricular or biventricular dilatation and impaired contraction. Although a significant proportion of cases is of unknown etiology, viral, genetic, toxic, immune and some other pathological conditions can lead to this condition. The clinical presentation usually involves heart failure, which is often progressive. Recently, myocardial tagging has been reported to provide evidence of severe reductions in fiber shortening and the absence of normal systolic LV wall thickening from base to apex.4

Recent publications have described the utility of DE-CMR in the evaluation of patients with dilated cardiomyopathy in which ischemic heart disease must be excluded. CMR using gadolinium contrast can be used to define the absence of ischemic etiology in patients with dilated cardiomyopathy in which this differential diagnosis needs to be done. Wu et al5 were the first to report that DE-CMR may hold promise in differentiating ischemic dilated cardiomyopathy from DCM. In their study, nearly all patients with ischemic heart disease and prior myocardial infarction had myocardial hyperenhancement, whereas none of the patients with idiopathic DCM or the normal volunteers had hyperenhancement. This notable finding was confirmed and expanded by McCrohon et al.,6 who demonstrated that subendocardial or transmural enhancement occurs in all cases of ischemic etiology in heart failure patients. In addition
this group reported that, although absence of enhancement was the most common finding (59%), they could identify midwall striae or patches of enhancement in 28% of the cases. A distribution of fibrosis similar to the one seen in ischemic patients was present in 13%. This finding further expands the capability of CMR in evaluating minor quantities of fibrous tissue. Soriano et al.\textsuperscript{7} confirmed these findings and noted that in some cases, midwall enhancement was present in ischemic patients, but never in a region perfused by a diseased vessel. By comparing 42 dilated cardiomyopathy patients and 42 controls, Zimmermann et al.\textsuperscript{8} has recently demonstrated that delayed enhancement after contrast injection occurred only in the first group and that, in 50% of the cases, the midwall distribution was present and in 17% patchy distribution could be seen. The pattern suggestive of ischemic heart disease (involving the subendocardium) appeared in only 1 case.

Arrhythmias and sudden death are common and may occur at any stage. Ventricular arrhythmias are common, but syncope and sudden death are rarely the initial manifestations of the disease.\textsuperscript{9} Current guidelines propose placement of internal defibrillators to patients with low LV ejection fraction for prevention of sudden death. Using CMR can reduce measurements errors and better select patients for the procedure. Atrial fibrillation is present in fewer than 25 percent of such patients,\textsuperscript{10} and is mainly due to increased dilatation of the atria and resulting disorganized electrical conduction of the stimulus from the sinus node. Atrial dilatation is secondary to dysfunction of the ventricles with augmented preload volumes.

**Hypertrophic cardiomyopathy**

Hypertrophic cardiomyopathy (HCM) is characterized by left and/or right ventricular hypertrophy. This results from an inherited defect in the protein components of the cardiac sarcomere. The pathologically characteristic feature is localized but otherwise unexplained myocardial hypertrophy associated with significant myofibrillar disarray. Accurate and early diagnosis of HCM is essential as many of these patients are at risk for recurrent arrhythmias, premature cardiac death. The genetic nature of the disorder has important implications with respect to the screening of family members.\textsuperscript{11}

In cases where hypertrophy occurs at basal septal location, obstruction of the left ventricle outflow tract due to systolic anterior movement of the anterior leaflet of the mitral valve can be present, as well as mitral regurgitation. From a clinical point of view this pathology is challenging since the first manifestation may be sudden cardiac death at early age.

A potential advantage of CMR that can turn it the standard of care exam in this disease is the use of DE-CMR. Choudhury et al.\textsuperscript{12} recently described the presence of DE in the hypertrophied regions only, occurring in the midwall and as patchy or multiple foci. Most of the times fibrosis can be seen in the regions close to the attachments of the right ventricle. Necropsy studies have already shown the same pattern of distribution and these findings have been confirmed by others.\textsuperscript{13,14} This latter series could also demonstrate DE in nearly 80% of the cases.

Life threatening arrhythmias occurs at a rate of 5% per year for primary prevention and double that in secondary prevention cases in a longitudinal study published recently.\textsuperscript{15} This same study confirmed ventricular tachycardia or fibrillation as the arrhythmias leading to sudden cardiac death. Although not definitive proven, slow conduction and reentry occurring in the presence of scar tissue are possible mechanisms of these arrhythmias. Varnava et al\textsuperscript{16} have demonstrated in a series of 75 patients that the risk for reentry arrhythmias was related to the degree of fibrosis. Teraoka et al\textsuperscript{17} also showed that ventricular tachycardia (VT) by Holter monitoring occurred more frequently in those patients with larger amounts of hyperenhancement.

In summary, CMR represents a promising non-invasive technique for diagnosis, risk stratification and perhaps monitoring therapeutic interventions in HCM.

**Arrhythmogenic right ventricular cardiomyopathy**

Arrhythmogenic right ventricular cardiomyopathy (ARVC) is a disease characterized by enlargement, dysfunction and fibrofatty infiltration of the right ventricle (RV). It is recognized clinically
by ventricular tachyarrhythmia, abnormal RV morphology and RV dysfunction. Although rare, it may be responsible for 10-20% of sudden cardiac death due to arrhythmias among young people in certain populations.18

There are many methods to assess the RV, but techniques like CMR that facilitate comprehensive coverage of the RV are essential.19 Combined with its ability to characterize fatty/fibrofatty infiltration of the right ventricle, CMR has rapidly evolved into the diagnostic standard for identifying ARVC in experienced centers.20-22

Fibrofatty tissue might have a role on the development of cardiac arrhythmias. Several investigators have looked at the clinical value of tissue characterization in ARVC. Tandri et al. assessed 30 consecutive patients referred for diagnostic evaluation. Of the patients identified as having ARVC by RV biopsy, RV late gadolinium enhancement was observed in 100%.23 Furthermore, DE-CMR was found to predict inducible sustained ventricular tachycardia at EP study, although the prognostic value of this finding remains unclear.24 DE-CMR for fibrosis/scar assessment in the RV has to be done with optimized techniques. Desai et al.25 evaluated the time inversion (TI) for signal suppression in RV compared to LV. The TI for myocardial signal suppression appears to be different between LV and RV. Potential mechanisms include partial volume averaging with fat or blood pool (related to increased trabeculation) in the RV. Alternatively, increased blood pool signal (within Thesbian veins or arterioluminal communications) in RV compared to LV leads to alter TI times due to similar partial volume effects.

ARVC evaluation with MRI can be difficult. Problems occur if the scans are overinterpreted, because the right ventricle shows substantial normal variations, including reduced regional wall motion in the region of the moderator band insertion, highly variable trabeculation, and substantial fat around the coronary vessels and epicardium. Sufficient experience of the normal variants is therefore important. In addition, it is important to recognize the limitations of CMR, because poor-quality breath-holds with fast spin-echo images may lead to the misinterpretation of wall thinning, because epicardial fat may not be distinguished clearly from right ventricular myocardium, and artifacts may give rise to an increased right ventricular wall signal that mimics fat. Fatty infiltration is not considered a definitive sign of disease in any case, because it can occur in other circumstances. Small amounts of RV fat with normal RV function are seen in normal individuals, but individuals with large amounts of RV fatty infiltration and normal function may be seen.26,27

One of the main differential diagnoses for ARVC is idiopathic right ventricular outflow tachycardia (RVOT). Tandri et al. evaluated 20 patients with idiopathic RVOT for structural abnormalities using MRI and compared them with 20 controls. There were no differences in incidence of qualitative MRI findings in patients compared with controls. The results did not favor an association between anatomic abnormalities and arrhythmia in those patients.22 The outcomes of this study confirms and extends the outcomes of a previous study by Grimm et al.28 but are in contrast to several other clinical studies that have reported structural abnormalities limited to the right ventricle in patients with idiopathic VT.29-31 In conclusion, more studies needs to done to verify if MRI is useful or not to diagnose idiopathic RVOT.

**Acute inflammatory cardiomyopathy - Myocarditis**

Myocarditis is defined as inflammation of the heart muscle. Myocarditis can result from exposure to a number of different pathogens, toxins, and systemic ailments. The diagnosis of myocarditis is generally made on a clinical basis, in part because of the inadequacies of currently available diagnostic strategies. Endomyocardial biopsy, considered the gold-standard for diagnosing myocarditis, is limited by inadequate sensitivity and specificity and large interobserver variability in histological interpretation.32 Patients with myocarditis have been reported to develop refractory ventricular tachycardia, torsade de pointes, or sudden cardiac death.33,34 No prospective randomized trials have evaluated the natural history and spontaneous resolution of these arrhythmias. Myocarditis has been reported in some athletes succumbing to sudden cardiac death.35 Recently, refractory atrial fibrillation has been associated with
inflammatory infiltrates in the atrium. The electrocardiogram is almost always abnormal in patients with myocarditis and may display changes of acute injury. More typical, however, are the presence of nonspecific ST-T wave changes. Any form of atrial or ventricular arrhythmia can be demonstrated, including atrial or ventricular premature beats, atrial or ventricular tachycardia, and atrioventricular fibrillation. In addition, patients with myocarditis may display atrial, ventricular, or intraventricular conduction delays.

Noninvasive imaging techniques have been used in an attempt to diagnose myocarditis, including CMR. CMR shows focal increases of myocardial signal in patients with acute myocarditis. DE-CMR with early imaging at 1 to 2 minutes can show relative myocardial enhancement compared with skeletal muscle. Abnormal myocardial signal is also seen with T2-weighted spin-echo CMR images. Normalization of signal intensity occurs with healing, unless cell death has occurred, in which case late gadolinium imaging may show patchy enhancement. DE 4 weeks after the onset of symptoms has been predictive for the functional and clinical long-term outcomes.

The study by Friedrich et al. was the first to systematically evaluate DE-CMR in patients with myocarditis. The authors showed that DE in patients with myocarditis evolves during the first 2 weeks after the onset of symptoms and concluded that CMR may hold promise for diagnosing inflammatory heart disease. However, regions of DE had image intensities that were on average only 40–50% higher than normal regions. Utilizing segmented inversion recovery gradient-echo pulse sequences (IR-GRE), Mahrholdt et al. evaluated 32 consecutive patients with clinically diagnosed myocarditis and performed histological examination of abnormal regions. The IR-GRE technique increased contrast between normal and abnormal segments by almost 500% compared to the imaging strategies employed by previous investigators. In 88% percent of patients, some region of contrast enhancement was observed, frequently only seen in epicardial layer of the lateral free wall. This pattern of enhancement is consistent with postmortem studies. A major achievement of this study was guided endomyocardial biopsy in 21 patients from regions of DE. Using this strategy, histological evidence of myocarditis was seen in over 90% of subjects.

We observed that hyperenhancement in the setting of myocarditis has a ‘non-ischemic’ pattern, typically affecting the epicardial quartile of the ventricular wall, that decreases during healing and can be almost invisible after recovery.

Sarcoidosis

Myocardial sarcoidosis is relatively uncommon, but sudden death due to arrhythmia may be its initial clinical presentation. However, cardiac involvement is clinically evident in only 5% of patients as current diagnostic tools are insensitive. Accurate diagnosis of cardiac sarcoidosis can be difficult but it is essential as immunosuppressive therapy can improve prognosis. Currently used techniques, including echocardiography, scintigraphy, and myocardial biopsy are often inadequate, particularly in identifying disease in its early stages. In patients with sarcoidosis suspected of cardiac involvement, CMR may provide a diagnostic alternative and a method by which disease activity can be followed. Several authors have emphasized the occurrence of MR abnormalities (especially on T2-weighted images) in patients with ongoing systemic sarcoidosis. CMR may be of value, with gadolinium enhancement occurring in presumed areas of fibrosis.

Assessment of pulmonary veins and right atrium in patients with atrial fibrillation

There is an estimative of 2 million persons in US with atrial fibrillation. One of the options to treat atrial fibrillation besides pharmacology intervention is catheter ablation. Over the years, the technique of catheter ablation of atrial fibrillation (AF) using pulmonary vein (PV) approach is a procedure performed in many electrophysiology laboratories. PV stenosis has been identified as a unique complication of this procedure. Increasing evidence suggests that the risk of PV stenosis may be minimized and the success maximized by delivery of radiofrequency (RF) energy to the ostial portion of the PV. The importance of PV anatomy to the success of PV ablation is now appreciated. MRI has the
potential to provide accurate images and render 3D reconstruction for precise characterization of each PV.

This manuscript was excerpted from reference 2.

References