MRI to Evaluate Cardiomyopathies and Inflammatory Cardiac Disease

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**Background.** Earlier classifications of cardiomyopathies described them in terms of their morphologic characteristics (dilated, hypertrophic) or functional consequences (restrictive). The current classification of cardiomyopathies has recently been updated [1] as diseases of the myocardium that are associated with mechanical and/or electrical dysfunction that exhibit inappropriate ventricular hypertrophy or dilatation. The causes are numerous, but an increasing number are being recognized as genetic in etiology. Cardiomyopathies may be primary, i.e. confined to the heart:

- a) genetic (hypertrophic, arrhythmogenic right ventricular dysplasia, glycogen storage, mitochondrial, ion channel diseases),
- b) mixed (dilated cardiomyopathy, restrictive cardiomyopathy), or
- c) acquired (inflammatory-myocarditis, stress, tachycardia induced, infants of insulin dependent mothers).

The second category of cardiomyopathies is those that are secondary, as a result of systemic diseases. There are dozens of secondary cardiomyopathies, but examples of those that are more common include infiltrative disorders (e.g. primary or secondary amyloidosis, Gaucher disease), storage disorders (e.g. hemochromatosis, glycogen storage disease) toxic (heavy metals), inflammatory-granulomatous (sarcoidosis).

In the case of both primary and secondary cardiomyopathy, MRI is increasingly being applied to both for primary diagnosis as well as for characterization of the extent of disease.

**MRI techniques and applications for cardiomyopathy evaluation.** Rather than a single technique, cardiac MRI for cardiomyopathy consists of several techniques that may be performed separately or in various combinations during a patient examination. Major techniques include:

- a) **Cine-MRI is the using steady state free precession**, performed in the short and long axis planes (including the aortic outflow tract). This series of scans provides accurate depiction of myocardial global morphology and function. For right sided disorders in particular, MRI offers superior depiction of wall motion abnormalities as well as better/more accurate quantification of right heart function compared to echocardiography.

- b) **Inversion-recovery prepared myocardial 10-20 min delayed enhancement sequences**, also acquired in the short and long axis planes following 0.15-0.2 mmol/kg intravenous gadolinium administration. These sequences are identical to those used for evaluation of myocardial scar due to coronary artery disease. For evaluation of the right ventricle, inversion recovery times are typically shortened by 25 msec to obtain improved suppression of the right ventricle. Unlike scar from myocardial infarction, scar associated with nonischemic conditions may be intermingled with normal myocardium, so that relatively lower signal intensity (than dense scar) is present. Our current standard is to use delayed gadolinium enhancement images for all patients referred for nonischemic cardiomyopathy.

The contrast enhancement patterns for nonischemic cardiomyopathy are distinct in most cases from those associated with myocardial infarction. Myocardial infarction scar involves the endocardial border extending towards the epicardial surface of the myocardium. Scars are in an anatomic distribution, i.e., in territories related to the coronary arterial tree. By comparison, nonischemic cardiomyopathy scar shows a) non-anatomic distribution, frequently involving multiple coronary artery territories, b) mid-wall as well as epicardial scar location (although endocardial scars may also be present). Scars that are confined to the mid-wall and epicardial surface alone are not known to be associated with coronary artery disease.

- c) **Double inversion recovery turbo/fast spin echo imaging.** These sequences are used primarily for arrhythmogenic right ventricular dysplasia (proton density weighted with/without fat suppression) and hypertrophic cardiomyopathy (T2 weighted with fat suppression). Optimization of the sequence is difficult in order to achieve black blood, particularly for long axis views in diseased ventricles with low rates of blood flow. Imaging is optimized by synchronizing the image acquisition period to the rest period of the cardiac cycle.

- d) **T2* weighted gradient echo images for evaluation of iron deposition.** These sequences are specifically added for patients for iron overload evaluation only.

- e) **First pass myocardial perfusion.** Stress imaging is usually not used in the setting of nonischemic cardiomyopathy. We have routinely obtained first pass perfusion images for nonischemic cardiomyopathy but their diagnostic yield is low. This sequence should be considered optional at present, although quantification may improve the utility of this method.
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 electrophysiologic 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 [2]. Scar tissue can be detected using contrast enhanced MRI and is becoming a major application for the evaluation of patients with arrhythmia. Several nonischemic cardiomyopathies are summarized below as examples for MRI evaluation:

**Dilated cardiomyopathy.** Cine MRI usually a uniform wall thickness that seems thin due to increased ventricular volumes. However, there is increased left ventricular (LV) mass, reduced stroke volume and ejection fraction, and usually diffuse hypokinesis as wall motion abnormality, although this is not mandatory [3]. 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. MRI using gadolinium contrast can be used to define the absence of ischemic etiology in patients with dilated cardiomyopathy. Wu et al [5] showed 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 finding was confirmed by McCrohon et al. [6], who demonstrated that subendocardial or transmural enhancement occurs in all cases of ischemic etiology in heart failure patients. Although absence of enhancement was the most common finding (59%), midwall striae or patches of enhancement were present in 28% of the cases. By comparing 42 dilated cardiomyopathy patients and 42 controls, Zimmermann et al [7] demonstrated that delayed enhancement 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.

**Hypertrophic cardiomyopathy.** 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 [8]. 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.

Echocardiography is the standard technique for the evaluation of this entity [8]. MRI is an appropriate alternative to confirm the diagnosis or identify atypical cases[9] [10]. CMR has high accuracy in wall thickness measurements. Echocardiography may be limited by the acoustic window available and is limited in the evaluation of the LV apex, a common site of hypertrophy. Rickers et al [11] published a series of 48 cases in which 6% were only diagnosed by CMR. Delayed myocardial enhancement is variable, as is increased signal on T2 weighted images, occurring in the midwall and as patchy or multiple foci. Delayed enhancement has been reported in up to 80% of cases, but the implication on patient prognosis is currently unknown.

**Arrhythmogenic right ventricular dysplasia (ARVD).** ARVD is 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 [12]. Fibrofatty tissue might have a role on the development of cardiac arrhythmias. 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% [13]. Desai et al [14] found that the TI for myocardial signal suppression appears to be different between left and right ventricles. Potential mechanisms include partial volume averaging with fat or blood pool (related to increased trabeculation) in the RV. The primary diagnostic features of ARVD are a) enlargement and dysfunction of the right ventricle out of proportion to LV dysfunction, b) regional aneurysm formation or wall motion abnormalities. Fatty infiltration is not considered a definitive sign of disease in any case, because it can occur in other circumstances.[15] 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 [16], [17].

2. Spector PS. Diagnosis and management of sudden cardiac death. *Heart* 2005;91:408-413


