

# LA RM NELLA DIAGNOSI DIFFERENZIALE DELLA MIOCARDITE IN CARDIOLOGIA

## ROLE OF MR IN THE DIFFERENTIAL DIAGNOSIS OF MYOCARDITIS

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Cardiovascular Magnetic Resonance (CMR) is non-invasive tomographic imaging technique. Its intrinsic advantages are the ability to acquire images in multiple planes without limitation of the acoustic window and patients' body habitus, lack of radiation exposure, high contrast-to-noise ratios, and true 3D volumetric coverage with no geometric assumptions. But the unique ability of CMR is the non-invasive myocardial tissue characterisation.

CMR offers the unique opportunity to perform non-invasively myocardial tissue characterisation by exploiting the magnetic properties of hydrogen nuclei protons within a determined magnetic field. Myocardial tissue characterisation can be achieved in health and disease by imaging the native magnetic properties of the heart (T1 longitudinal relaxation time and T2 transverse relaxation time) with several pulse sequences and by using a gadolinium-chelate contrast agent. CMR can identify the presence and extent of myocardial oedema/inflammation, as well as focal, replacement and interstitial myocardial fibrosis. Myocardial replacement fibrosis is imaged using a T1-weighted inversion-recovery gradient echo sequence after the administration of a gadolinium-chelate contrast agent. These are extracellular contrast media which accumulate in the increased myocardial extracellular space due to a pathological process. This leads to increased signal intensity compared to the normal myocardium (Late Gadolinium Enhancement, LGE).

The pattern of contrast distribution tends to follow the underlying pathophysiological processes of disease. In fact, in ischemic heart disease the pattern is either subendocardial or transmural (which reflects the ischemic-necrotic wave-front phenomenon). In non-ischemic cardiomyopathies the pattern varies among the different etiologies. In myocarditis LGE is typically epicardial, particularly of the lateral wall or septum. Mid-wall LGE of the basal inferolateral wall is a more aspecific pattern as it is observed in myocarditis, sarcoidosis, Anderson-Fabry's disease; in amyloidosis, the pattern of LGE is diffuse

and patchy, or alternatively diffusely subendocardial<sup>1</sup>. LGE-CMR is a very established technique to image focal myocardial fibrosis in both ischemic and non-ischemic cardiomyopathies<sup>2</sup>. Myocarditis is a challenging diagnosis due to the heterogeneity of clinical presentations, from acute coronary syndromes to acute heart failure to cardiomyopathies or an arrhythmic event. Several studies have shown that the commonest underlying etiology of patients presenting with suspected ACS and unobstructed coronary arteries is myocarditis. The typical CMR protocol included short- and long-axis cines, LGE and edema images (T2-STIR images). The cine images are used to calculate LV/RV volumes, EF and the presence of regional wall motion abnormalities. Assessment of the T2-STIR and LGE images will delineate the presence and extent of myocardial edema and fibrosis, respectively. The final diagnosis is reached by the integration of the information from the various sequences.

Recently, a consensus paper has defined the recommendations on the use of CMR in myocarditis which led the establishment of the Lake Louise diagnostic criteria<sup>3</sup>. In particular, the CMR findings are consistent with the diagnosis of myocarditis if two of three sequences demonstrating myocardial edema, hyperemia, and fibrosis are positive. These criteria offer also an opportunity for a semi-quantitative analysis of the image signal intensity that can aid in more difficult borderline cases.

However, in the pool data from published literature, the prevalence of this diagnosis on CMR is highly variable, ranging from 15 to 75%<sup>4</sup>. This variation is likely due to: 1) the different CMR sequences used in the different studies; 2) the different timing of CMR from the acute presentation. The most adequate time-window to image myocarditis from its presentation has not been determined. However, it should be considered that of myocardial edema/inflammation are transient and resolve with time (up to 3 months). Therefore, to be able to image myocardial edema the CMR protocol containing the T2-weighted images should be carried out reasonably early after the onset of symptoms.

The diagnosis of myocarditis and myocardial inflammation could be challenging with other imaging modalities such as echocardiography, given that it is based on indirect signs like myocardial swelling, wall motion abnormality, and pericardial effusion<sup>5</sup>. A recent position paper of the ESC postulates that although CMR is a useful non-invasive tool, Endomyocardial Biopsy (EMB) still represents the gold standard for the diagnosis of myocarditis<sup>6</sup>.

Recently, several studies have validated CMR against EMB, suggesting that CMR can have a promising role in the diagnostic pathway of these patients<sup>7</sup>. Whilst CMR cannot replace EMB, there is agreement that it can be offered in clinically stable patients prior to EMB. In fact, Mahrholdt et al. have demonstrated that when biopsy is guided by the CMR (i.e. the myocardial sampling is directed in areas of myocardial inflammation/scar detected by CMR), the diagnostic accuracy of EMB increases<sup>8</sup>. Novel parametric mapping techniques, like native T1 mapping, ExtraCellular Volumes of distribution (ECV) and T2 mapping, currently mainly used for research, have recently shown promising results in the diagnostic assessment of myocarditis.

In brief, T1 mapping offers the opportunity to detect and quantify diffuse myocardial processes adding a new dimension in the assessment of cardiac injury with and without the need of a contrast agent. In general terms, the native (non-contrast) T1 relaxation time in the heart is prolonged with fibrosis,

edema and amyloid and reduced in lipid accumulation (Anderson-Fabry disease), cardiac siderosis, and hemorrhage in acute infarction<sup>9</sup>. Therefore the calculation of the native T1 times can provide an indication about myocardial changes. T2 mapping is a particularly promising new technique to assess myocardial edema with a higher degree of reproducibility compared to traditional sequences for myocardial edema<sup>10</sup>.

Recent studies by Ferreira and Piechnik et al.<sup>11</sup> demonstrated that native T1 mapping has a superior diagnostic role compared to conventional T2-weighted imaging, and an equivalent performance to LGE, and without the need for gadolinium contrast agents<sup>12</sup>.

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