Map to the future of cardiac magnetic resonance in myocarditis

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Cardiac magnetic resonance (CMR) imaging is an excellent tool for the diagnosis of acute myocarditis and to differentiate acute myocarditis from ischemic events in acute coronary syndromes. CMR has therefore been included in recent guidelines for the management of patients with acute myocarditis. Monitoring of healing or persistence of myocardial inflammation in patients with acute myocarditis is important, since persistent myocardial inflammation is perceived as a key factor for the development of dilative cardiomyopathy. Accurate monitoring of the healing process of myocardial inflammation by non-invasive means is therefore highly desirable since endomyocardial biopsy (EMB), the gold standard technique to demonstrate myocardial inflammation, is limited by its invasiveness, availability of experienced centres, cost and rather low sensitivity.

‘Lake-Louise’ CMR criteria have been widely used to diagnose myocarditis: the diagnosis is likely if two of the three criteria are present: (i) myocardial oedema (T2-weighted imaging); (ii) late Gadolinium enhancement (LGE) in a mid-wall noncoronary pattern; and (iii) hyperaemia/capillary leak (increased early Gadolinium enhancement). Radunski et al. have shown that LGE together with extracellular volume (ECV) quantification significantly improved the diagnostic accuracy to 90% [95% confidence interval (CI): 84–95%] compared with 79% [95% CI: 71–85%; P = 0.0043] for the ‘Lake-Louise’ CMR criteria.

Bohnen et al. report on their study of 48 patients with infarct-like or cardiomyopathy-like acute myocarditis who underwent a CMR study during the acute stage, 3 and 12 months later. The CMR protocol included standard ‘Lake-Louise’ sequences as well as T1, T2, and ECV mapping. It could be shown that (i) native T1 and T2 values normalized during healing; (ii) a combination of native T1 and T2 values could differentiate acute from healed stages of myocarditis with high accuracy; and (iii) combined analysis of LGE images and ECV values had the best diagnostic accuracy to identify diseased patients independent from the disease stage. The authors conclude that healing of myocarditis can be monitored by native myocardial T1 and T2 and that both native myocardial T1 and T2 provide an excellent performance for assessing the stage of myocarditis by CMR.

Native T1, post-contrast T1, and ECV in fibrosis detection

Native T1 values are a composite signal from myocytes and ECV. The two most important determinants of an increase in native T1 are oedema and collagen (fibrosis) or amyloid deposition.

Unlike native T1 relaxation times, contrast-enhanced T1 values are much shorter, more variable and dependent on contrast agent dosing, the time elapsed between contrast agent administration and T1 measurement and finally renal clearance.

Estimation of the ECV is derived from the ratio of myocardial and blood T1 before and after administration of contrast agents and the patient’s haematocrit value. It may therefore be more reproducible between different field strengths, vendors, and acquisition techniques than both native and post-contrast T1. ECV as a marker of myocardial tissue remodelling is supposed to reflect the collagen content, as well as the degree of fibrosis.

Native T1, post-contrast T1, and ECV mapping allow for more sensitive identification and quantification of diffuse myocardial fibrosis and oedema than LGE. ECV showed better agreement with histological collagen volume fraction than post-contrast T1 alone.

Native T1 vs. T2 mapping for oedema detection

Native T1 values have been shown to correlate well with T2-weighted signal intensity ratios and demonstrated high-diagnostic accuracy (AUC = 0.94, sensitivity and specificity of 92%) in the differentiation between oedema and normal myocardium. T1 mapping may suffice to detect myocardial oedema, but T2 values are much less affected by myocardial fibrosis than T1 values and are therefore more specific for oedema detection. Elevated native T1 values can be caused by myocardial oedema and fibrosis: A presumed region of myocardial oedema might be additionally substantiated with T2

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mapping, a presumed region of myocardial fibrosis with ECV mapping and LGE.

Ferreira et al.\textsuperscript{10} have recently demonstrated higher sensitivity of T1 mapping compared with T2-weighted imaging and LGE imaging techniques. High-diagnostic performance (~90% overall sensitivity, specificity, and diagnostic accuracy) has been reported for detecting changes in myocarditis using an absolute T1 cut-off of 990 ms using a ShMOLLI sequence at 1.5 T.\textsuperscript{10} T2 mapping has been shown to better depict myocardial involvement in myocarditis than LGE imaging\textsuperscript{11} and traditional T2-weighted imaging with its inherent susceptibility for artefacts.\textsuperscript{12}

In a direct comparison of T1 and T2 mapping, the MyoRacer-Trial\textsuperscript{13} showed that T2 mapping more reliably detected myocarditis than T1 mapping in patients with acute and chronic myocarditis. This may be explained by the higher sensitivity of T2 mapping to detect myocardial oedema.

**General aspects of multi-parametric imaging**

Absolute values for native T1 depend on scanner field strength, pulse sequence used, cardiac phase, vendor, and region of interest.\textsuperscript{14} Thus, they are specific to the local set-up, cannot be universally applied and need to be reassessed if one of the acquisition parameters has been altered.

Major advantages of novel parametric T1 and T2 mapping techniques are that they are not in need of a reference region of interest such as LGE techniques or the T2-weighted short-tau inversion recovery sequence. In addition, they can be used in patients with severe renal impairment.

A major disadvantage of novel parametric mapping techniques is that poor-breath holding can significantly impair the quality of both T1 and T2 maps, which partially can be corrected with automatic or manual motion correction.\textsuperscript{15}

**Concluding remarks**

Although the potential of tissue characterization with native T1, T2, and ECV mapping is very promising in acute and healing myocarditis, there is a substantial overlap between myocarditis and different cardiomyopathies and some overlap with T1 values of normal myocardium.

In the future, standardization of T1 mapping protocols might help to apply T1 and ECV values. Nevertheless, abnormalities in T1, T2, and ECV have to be interpreted in regard to their clinical context, pre-test probabilities, and in conjunction with established CMR techniques.

Parametric tissue characterization techniques such as native T1, T2, post-contrast T1, and ECV maps can guide invasive EMB to a diseased myocardial region at interest and with other yet to be discovered CMR mapping techniques may have the potential to supplement or once even replace EMB in patients with viral myocarditis.

Regarding the present study\textsuperscript{5} the authors have to be commended on their work: One of the major results of this study is that monitoring of disease activity in myocarditis might be possible with parametric CMR imaging techniques and potentially even without the need of contrast agents. Endomyocardial biopsies would have been helpful to some extent in order to prove CMR findings. On the other hand, standardized markers for the histochemical assessment of disease activity in EMB specimens with viral infection are still missing for clinical routine.

In order to prove that multi-parametric imaging techniques provide important information on the course and eventually will impact on therapeutic decisions of myocarditis further trials are needed.

**Conflict of interest:** None declared.

**References**


