

EDITORIAL COMMENT

The Promise of Myocardial Fibrosis Assessment by T1 Mapping*

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Two intertwined needs have promoted the development of T1 mapping in cardiac magnetic resonance (CMR) during the past decade. The first need relates to the desire for greater spatial granularity as investigators venture outside the infarct- and scar-sizing paradigm to probe the regional heterogeneity of myocardial damage associated with diverse disease processes (1–3), the substrate of arrhythmias (4,5), and the possibility of CMR-guided arrhythmia ablation (6), as well as stem cell therapy (7). The second need, also rooted in the desire to investigate tissue structure using CMR, results in large part from the dependence on contrast kinetics that imposes significant limitations to a more complete understanding of basic cardiac disease processes (8,9). In this issue of *JACC*, the report by Puntmann et al. (10) gets us closer to both goals by demonstrating that T1 mapping, carefully performed at 3-T, not only advances our knowledge of differences in the size and/or type of myocardial extracellular space associated with different diseases, but perhaps allows us to perform such assessment without or before contrast administration.

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The investigators compared measures of T1 mapping obtained from 25 patients with known asymmetric hypertrophic cardiomyopathy and from 27 patients with known dilated nonischemic car-

diomyopathy with a group of 30 normotensive controls of similar age and sex distribution and with low pre-test probability of developing left ventricular cardiomyopathy. They measured T1 in the interventricular septum before and at 10, 20, and 30 min after contrast administration using an established steady-state free precession Look-Locker imaging pulse sequence at 3-T, with motion correction during data processing. They found differences in pre-contrast and post-contrast T1 times up to 30 min after gadolinium administration between controls and patients with cardiomyopathy, whereas no differences were found between the 2 groups of patients with hypertrophic and dilated nonischemic cardiomyopathies. Moreover, when pre-contrast and 20-min post-contrast measures were integrated and represented in relation to parallel measures in blood, the derived extracellular volume (ECV) indexes obtained from patients with hypertrophic (0.31 ± 0.10) and nonischemic dilated (0.30 ± 0.05) cardiomyopathy were greater than those obtained from patients in the control group (0.20 ± 0.06). Similar relationships were found for ECVs at 10 and 30 min after contrast administration, as well as for the partition coefficients calculated before adjustment for blood cell intravascular volume at each of the post-contrast times. The investigators conclude that T1 mapping allows the differentiation of myocardial tissue characteristics between patients with cardiomyopathies compared with normotensive controls of similar age and sex distributions. Moreover, they highlight the fact that differences between patients with cardiomyopathy and controls could be detected from T1 values obtained before contrast administration, underscoring the method's power to elicit different tissue signatures in the absence of a selective extracellular indicator.

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The latter finding has implications beyond its potential use to differentiate patients with myopathic processes from those without such processes. Does it mean that extracellular matrix alterations can be quantified by T1 mapping even when diluted by the presence of larger intracellular spaces presumed similar between cardiomyopathy patients and controls? Or does it mean that they parallel intracellular alterations, leading to a greater magnitude of pre-contrast T1 signal detectable at 3-T by the methods used in this work? If so, what kind of alterations would those be, and what kind of myocardial pathological processes would they reflect beyond the substitution of myocytes for fibroblasts and corresponding increase in collagen deposition that accompany the well-described extracellular matrix alterations associated with cardiomyopathy? The findings do suggest that the primary changes are extracellular, given the accompanying differences in post-contrast times and ECV values and that they are of such magnitude in patients with cardiomyopathy that they can be detected by T1 mapping at 3-T before contrast administration. However, as the power of CMR technology increases, mitochondrial structural abnormalities and/or other potential intracellular alterations associated with myocardial disease processes should be kept in mind as potential contributing mechanisms for differences detected before contrast administration. In the meantime, the very possibility of differentiating between normal and diseased myocardium for purely diagnostic purposes should not be underestimated given the limitations of administering gadolinium-based substances to patients, particularly those with renal dysfunction.

The study results should of course be interpreted in light of its potential limitations, in large part discussed by the investigators. When comparing groups of patients with known disease against nondiseased controls, differences tend to be magnified, whereas borderline situations and milder disease presentations tend to be reduced, potentially resulting in overestimation of the ultimate diagnostic method's power. Prospective studies using intention to diagnose will ultimately demonstrate the diagnostic power of T1 measures to distinguish patients with cardiomyopathy from those without disease within a pool of patients with suspected disease. Moreover, the choice of sampling from the interventricular septum, although based on valid

technical considerations highlighted in previous studies (11,12), may have magnified differences between patients with asymmetric hypertrophic cardiomyopathy and controls, while potentially reducing differences between the latter and those with dilated cardiomyopathy. Myocardial fibrosis alterations are known to be more pronounced in the septum as opposed to other left ventricular wall segments in patients with asymmetric hypertrophic cardiomyopathy. The latter theoretical concern does not diminish the validity of the diagnostic findings reported, but should be kept in mind when patients with other types of hypertrophic cardiomyopathy are being considered for diagnostic T1 mapping.

The investigators should be congratulated for the performance of such sophisticated studies at high field strength, including the careful reproducibility of post-contrast times and the methods customized for motion correction used for data analysis. In addition to the practical applicability of the main results, the study has many implications beyond the detected pre-contrast differences and the potential extracellular versus intracellular abnormalities they may reflect. The fact that no differences in the ECVs (or T1 times) of patients with hypertrophic versus dilated nonischemic cardiomyopathies were found is thought provoking in many ways. Does it mean that the extracellular matrix is altered in a similar manner in both processes? Does the absence of differences reflect advanced septal disease in both processes? Do the measured indexes of ECV enlargement reflect true ECV size augmentation, a change in the relaxivity of water associated with collagen in the extracellular space, or both? The investigators discuss the potential influence of processes that could alter T2 relaxation times as well as several other potential implications of this work. The future and potential of CMR T1 mapping is certainly enhanced by this study. Hopefully, patients with suspected cardiomyopathy will be detected and treated earlier as a result of this investigation and other similar efforts in this field.

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