EDITORIAL COMMENT

T1 Maps in Nonischemic DCM
Do They Show Us the Way?*

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True navigation begins in the human heart.
It's the most important map of all.
—Elizabeth Kapu'uwailani Lindsey (1)

Cardiac magnetic resonance (CMR) is increasingly used in the diagnostic and prognostic workup of cardiomyopathy. Beyond accurately quantifying biventricular size and systolic function, the main current strength of CMR is the characterization of myocardial tissue. The technique of late gadolinium enhancement (LGE), or transient accumulation of paramagnetic extracellular contrast agent in areas of myocardial scar and/or necrosis, was developed more than 2 decades ago primarily for the visualization of ischemic infarct. In the chronic setting, LGE occurs because of localized increased interstitial space (and therefore contrast volume of distribution) within the scar (2). It has been long known that it is also possible to use this technique to depict scar in a variety of nonischemic cardiomyopathies. In the specific setting of nonischemic dilated cardiomyopathy (NIDCM), LGE can assist in determining the underlying etiology, and its presence and extent have been associated with increased risk of death, malignant arrhythmia, and heart failure events (3).

Strengths of LGE include excellent spatial resolution, which enables the visualization of very small scars, and high contrast to noise ratio that makes differentiation of fibrotic and normal myocardium simple; however, the technique relies on the presence of normal (or seemingly normal) myocardial tissue. When fibrosis is diffuse, such as in cases of reactive as opposed to replacement fibrosis, LGE has an inherent weakness to detect an enlarged extracellular compartment (2). In the last few years, alternative approaches that rely on the quantification of tissue magnetic properties, specifically T1 times, have been developed in an attempt to overcome this limitation. Myocardial T1 mapping can be performed before or after contrast administration, and histology validation studies have demonstrated correlations of T1 times with the extent of interstitial fibrosis (4,5). Whereas an increasing body of evidence indicates that T1 mapping can detect subclinical myocardial abnormalities in multiple clinical scenarios, data on the potential prognostic implications of these findings are scant (6,7).

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In this issue of *iJACC*, Puntmann et al. (8) explored the use of T1 mapping to predict outcome specifically in NIDCM. At 4 centers, the investigators prospectively enrolled 713 patients with a clinical and echocardiographic diagnosis of NIDCM and no evidence of coronary disease, significant valvular disease, infiltrative or deposit disorders, inflammation, or other primary cardiomyopathies. Using a highly standardized modified look locker imaging sequence on 1.5- or 3-T magnets, they performed myocardial T1 mapping before and 15 min after the administration of 0.1 to 0.2 mmol/kg of a single contrast agent. Measured indexes included native (pre-contrast) T1 times, post-contrast T1 times, and extracellular volume (ECV), which combines blood and myocardial pre- and post-contrast T1 times as well as hematocrit. After exclusion of 53 patients lost to follow-up and 23 with nondiagnostic studies, a total of 637 patients were included and monitored for the development of all-cause death (primary endpoint) or a combination of heart failure death or hospitalization (composite secondary endpoint). During a median follow-up of 22 months, there were 28 deaths and 68 secondary endpoint events. In

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univariate analyses, all T1 mapping indexes (increased native T1 times and ECV and reduced post-contrast T1 times) were associated with events, with the exception of post-contrast T1 time and mortality. Based on statistical criteria, the investigators selected native T1 mapping for subsequent multivariate analyses that considered clinical characteristics, biventricular ejection fraction, left ventricular volume and mass, and LGE presence and extent. Native T1, together with LGE extent, was independently associated with mortality (hazard ratio per 10-ms change: 1.1; 95% CI: 1.05 to 1.13). Native T1, together with right ventricular ejection fraction, also predicted heart failure events (hazard ratio: 1.1; 95% CI: 1.04 to 1.11).

Puntmann et al. (8) are to be congratulated for providing important new evidence on the prognostic significance of diffuse myocardial abnormalities in NIDCM, as well as the potential of T1 mapping for improving our understanding of cardiomyopathy. Although an association of T1 maps with impaired outcomes had been reported in all-comers to CMR (6,7), this is the first large, multicenter study to specifically test this question in NIDCM. The evaluation of myocardial abnormalities using different T1 map indexes is another strength of the paper. Although current consensus documents recommend ECV as the preferred approach (4), potential clinical superiority of one method versus another will need to be determined from clinical studies such as this. Although ECV methodology has been optimized for the quantification of predominantly interstitial expansion, native T1 times likely reflect a combination of changes in vascular, interstitial, and cellular compartments and may provide different or complementary information. Conversely, although the investigators selected native T1 mapping for ultimate testing in their multivariate models, this should not be interpreted as proof of superiority either. It is important to note that only 1 method was selected to avoid collinearity and that it only marginally outperformed the others. Post-contrast T1 mapping is inherently more sensitive to inaccuracies, which may have been exaggerated by the use of varying contrast doses in this study. Similarly, hematocrit values for ECV quantification were missing in a substantial proportion of patients and were not collected at the time of CMR, limitations that may have had some impact on the accuracy of the technique and the observed findings.

A few other aspects of the study deserve consideration. Given the small number of events, adjustments were made for only a limited number of confounders. Although T1 maps remained in the models after powerful markers of outcome such as ejection fraction or LGE were considered, full adjustment unfortunately could not be performed, and the prognostic value of T1 maps in NIDCM will require confirmation in larger series. Explicitly, given that many prior studies in NIDCM tested the prognostic significance of septal LGE, the complementary value of T1 mapping over this specific LGE pattern needs to be further evaluated. It would also be interesting to explore if these subclinical indexes of myocardial disease are additive to other prognostic markers of subclinical disease, such as myocardial deformation (9). Of note, none of the patients underwent transplant or ventricular assist device implantation, suggesting that this cohort was not representative of the sickest patients with NIDCM and that the findings should not be extrapolated to end-stage disease.

Undoubtedly, many uncertainties remain. T1 maps are starting to show us new ways for the evaluation of myocardial disease; we will need to better understand what they are telling us and whether they point us in the right directions. The outcomes study by Puntmann et al. is an important step forward and provides reassurance that these maps are not misleading us. The journey has just started and there is long road ahead, but it promises to be worthy!

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