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EDITOR'S PAGE

Multiparametric CMR in Cardiomyopathies

Beyond Diagnosis and Toward Prognosis

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In the past 2 decades, cardiac magnetic resonance (CMR) imaging, with its versatility in tissue characterization with late gadolinium enhancement (LGE) and T1 and T2 mapping, has made major inroads in differentiating among the underlying causes of heart failure (1). The presence of prior myocardial infarctions can establish the diagnosis of ischemic cardiomyopathy in the appropriate setting (2). Myocarditis can be readily identified in a patient presenting acutely (3). It is also becoming important in assessing vascular changes underlying coronary artery disease, including evidence for a vulnerable vasculature (4-5). Cardiomyopathies such as hypertrophic cardiomyopathy, amyloidosis, and sarcoidosis can be differentiated by their pattern of hypertrophy and LGE, and native T1 signal and iron overload can be demonstrated by reductions in T2* (1). Multiparametric CMR can do much more than simply identify the cause of of disease. In addition, identification of the extent and location of both LGE and extracellular volume (ECV), as well as measurement of myocardial and/or coronary flow reserve are demonstrating their utility for assessment of prognosis in cardiomyopathies and coronary artery disease (6-8). CMR continues its rapid development, and in this issue, *iJACC* has focused on showing its utility further in a number of conditions.

CMR plays an important role in identifying inflammation (9). An area of previously untapped potential for multiparametric CMR is in the detection of heart transplant rejection. Several papers in this issue of *iJACC* describe advances in this field. Imran et al. (10) demonstrated the potential role of T1 mapping in transplant patients who underwent 112 myocardial biopsies, of which more than one-half had no rejection and 17 of 112 patients (15%) who had grade 2 or clinically diagnosed rejection. In patients with grade 2 rejection, native T1 was higher than in those with no or lower grades of rejection, and a cutoff of 1,029 ms yielded a sensitivity and specificity of 93% and 79%, respectively. This suggests that native T1 alone shows promise but may not be quite "ready for prime time" as the single measurement for identification of clinically significant rejection.

Another group added echocardiographic strain mapping to T1 mapping in a 2-part study in 49 patients (11). Both global longitudinal strain (GLS) and circumferential strain were independent predictors when used alone. When CMR was added in the second part of the study, the cutoff values for native T1 and ECV along with GLS and GCS had 100% sensitivity and 100% negative predictive value to define clinical grade rejection with variable positive predictive values. GLS >−16% and native T1 >1,060 ms had a sensitivity and specificity of 91% and 92%, respectively, clearly improving upon the results of Imran et al. (10). An issue for using an absolute value of T1 as a cutoff is the fact that the values presented in these 2 papers are specific for these 1.5-T scanners. Values would be, on average, 200 ms greater at 3.0-T, and ideally, each laboratory needs to set its normal value range as well as cutoffs that suggest rejection. This may limit ultimate clinical utility of native T1 values alone.

The study by Dolan et al. (12) goes beyond native T1 alone, adding T2 and ECV measurements to the

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mixture in a study of 58 transplant recipients who underwent 97 CMRs and 14 control patients. A combined model of age at CMR, global T2, and ECV was predictive of clinical grade rejection with an area under the receiver operator curve of 0.84. Increased ECV was more specific for acute rejection than T2, which was elevated in both acute and chronic cases of rejection.

Multiparametric CMR is gaining additional traction in its ability to assess various tissue pathology signatures (13), including collagen volume or extracellular space expansion (14) and, thus, prognosis in heart failure. Halliday et al. (15) studied 874 patients with nonischemic dilated cardiomyopathy (NIDCM) and followed them for almost 5 years. A total of 34% of the patients had a nonischemic pattern of LGE. There were stepwise increases in all-cause mortality and sudden cardiac death based on the extent of LGE, although even small amounts of LGE substantially increased the risk over those with none. The location of LGE was also important as septal LGE was associated with mortality and septal and lateral wall LGE were associated with sudden cardiac death.

Location of fibrosis also turned out to be important in the study by Vita et al. (16). They studied 240 patients with NIDCM, 36 of whom (15%) suffered heart failure hospitalization or death over a median of nearly 4 years. ECV was strongly associated with major adverse cardiac events (MACE), and values from 6 locations around the left ventricle were significantly associated with MACE, with the anteroseptum being the most significant. Every 10% increase in ECV was associated with a 2.8-fold increase in MACE and was incremental to LGE or native T1 mapping. Carefully mapping the location of both LGE and ECV in NIDCM is becoming increasingly important in assessing prognosis. Ongoing studies may offer insight into how these can be used to assess the need for implantable cardioverter-defibrillators and other therapies aimed at reducing event rates (17).

One factor that may contribute to adverse prognosis in NIDCM is microvascular dysfunction. The group at the Brompton studied 65 patients with NIDCM and 35 control subjects using adenosine stress CMR (18). Patients had higher rest and lower stress myocardial blood flow and resultant much lower myocardial perfusion reserve compared to controls. This was especially true for those with left ventricular ejection fraction ≤35%. The authors speculate that a mechanism contributing to microvascular and systolic dysfunction is stress-induced repetitive stunning, as rest flow is paradoxically higher than in controls.

Abnormal flow reserve is prognostically important in coronary artery disease as well. Indorkar et al. (19) demonstrated this by measuring coronary flow reserve in the coronary sinus by using phase-contrast imaging at rest and after stress in 507 patients with suspected ischemia. Eighty patients experienced a MACE over 2.1 years. Coronary flow reserve less than the median was an independent predictor of MACE after adjusting for ischemia, LGE, and left ventricular ejection fraction. Because this measure can be readily added during a stress CMR, it could be used to identify markers of adverse prognosis in patients without ischemia and LGE. Finally, a study looks at the evolution of T1 in Fabry's disease (which is classically low due to sphingolipid accumulation) and shows that there are definable phases in the disease and that there is a sex difference in T1 response as the disease evolves (20).

In summary, the utility of CMR in cardiomyopathies and coronary artery disease is rapidly expanding beyond the evaluation of LV volumes and function and identifying the presence and pattern of LGE. Multiparametric mapping is showing promise in identifying heart transplant rejection. The location and extent of both LGE and ECV are important in assessment of prognosis in NIDCM. In addition, measurement of myocardial and/or coronary flow reserve is demonstrating utility in both mechanistic and prognostic studies. The breadth of CMR in the evaluation of heart disease continues to expand.

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