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T1-Mapping and Outcome in Nonischemic Cardiomyopathy

All-Cause Mortality and Heart Failure

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ABSTRACT

OBJECTIVES The study sought to examine prognostic relevance of T1 mapping parameters (based on a T1 mapping method) in nonischemic dilated cardiomyopathy (NIDCM) and compare them with conventional markers of adverse outcome.

BACKGROUND NIDCM is a recognized cause of poor clinical outcome. NIDCM is characterized by intrinsic myocardial remodeling due to complex pathophysiological processes affecting myocardium diffusely. Lack of accurate and noninvasive characterization of diffuse myocardial disease limits recognition of early cardiomyopathy and effective clinical management in NIDCM. Cardiac magnetic resonance (CMR) supports detection of diffuse myocardial disease by T1 mapping.

METHODS This is a prospective observational multicenter longitudinal study in 637 consecutive patients with dilated NIDCM (mean age 50 years [interquartile range: 37 to 76 years]; 395 males [62%]) undergoing CMR with T1 mapping and late gadolinium enhancement (LGE) at 1.5-T and 3.0-T. The primary endpoint was all-cause mortality. A composite of heart failure (HF) mortality and hospitalization was a secondary endpoint.

RESULTS During a median follow-up period of 22 months (interquartile range: 19 to 25 months), we observed a total of 28 deaths (22 cardiac) and 68 composite HF events. T1 mapping indices (native T1 and extracellular volume fraction), as well as the presence and extent of LGE, were predictive of all-cause mortality and HF endpoint ($p < 0.001$ for all). In multivariable analyses, native T1 was the sole independent predictor of all-cause and HF composite endpoints (hazard ratio: 1.1; 95% confidence interval: 1.06 to 1.15; hazard ratio: 1.1; 95% confidence interval: 1.05 to 1.1; $p < 0.001$ for both), followed by the models including the extent of LGE and right ventricular ejection fraction, respectively.

CONCLUSIONS Noninvasive measures of diffuse myocardial disease by T1 mapping are significantly predictive of all-cause mortality and HF events in NIDCM. We provide a basis for a novel algorithm of risk stratification in NIDCM using a complementary assessment of diffuse and regional disease by T1 mapping and LGE, respectively. (J Am Coll Cardiol Img 2016;9:40-50) © 2016 by the American College of Cardiology Foundation.

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Nonischemic dilated cardiomyopathy (NIDCM) is an increasingly recognized cause of cardiovascular morbidity and mortality (1-3). In NIDCM, a number of diverse influences promote intrinsic myocardial impairment and remodeling via complex pathophysiological processes including extracellular matrix remodeling, myofibroblast transformation, and cardiomyocyte cell loss, affecting the myocardium diffusely (4,5). The lack of accurate and noninvasive characterization of diffuse myocardial disease limits its early recognition and effective clinical management. Endomyocardial biopsy is the suggested gold standard for detection and classification of myocardial tissue abnormalities, yet its invasiveness, low diagnostic yield, and paucity of proven consequential management pathways limit its widespread use in guiding clinical management (6). Cardiac magnetic resonance (CMR) is able to visualize regional myocardial disease by late gadolinium enhancement (LGE) and has gained relevance in clinical management of cardiomyopathies by informing on the underlying etiology and supporting risk stratification in NIDCM (7,8). Because LGE relies on regional differences in tissue composition, it is an imperfect measure of diffuse interstitial disease underlying myocardial impairment in NIDCMs (9,10). Myocardial T1 mapping is emerging as the noninvasive method of choice in assessment of diffuse myocardial disease allowing quantification of altered magnetization properties, which relate to the pathophysiological changes in the myocardium. Studies have shown that T1 mapping measurements correlate with extracellular collagen volume fraction (9,11-14), are raised in a number of NIDCMs and relate to the severity of left ventricular (LV) remodeling in NIDCM (9-11,15). The relationship with outcome of these novel parameters in NIDCM and their comparative value against conventional markers of adverse outcome remain unknown.

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METHODS

STUDY DESIGN. This is a prospective longitudinal observational multicenter investigator-led study of the prognostic value of noninvasive T1 mapping measures in a cohort of adult patients with NIDCM. The multicenter consortium has been described previously (16). Standardization of T1 mapping acquisition was performed at all participating centers prior to the onset of patient recruitment. Participating centers support large CMR clinical service (>1,000 patients a year) and provide clinical care compliant with international guidelines and recommendations on patient management. The study protocol was reviewed and approved by the respective institutional ethics committees and written informed consent was obtained from all participants. All procedures were carried out in accordance with the Declaration of Helsinki (2000).

Consecutive subjects (n = 713) fulfilling the accepted diagnostic criteria for NIDCM (1-3) were enrolled between January 2011 and July 2014. Prior to enrolment, the diagnosis was confirmed by CMR on the basis of increased LV end-diastolic volume indexed to body surface area and reduced LV ejection fraction (EF) compared with published reference ranges normalized for age and sex (7). Patients were excluded (based on previous medical history, other investigations or CMR findings) if they had evidence of: 1) ischemic heart disease, defined as significant documented coronary artery disease, previous coronary revascularization, previous history of myocardial infarction, or evidence of ischemic type LGE, or inducible ischemia on stress testing (17); 2) myocardial infiltration due to amyloidosis, iron accumulation, lipid-storage disease, hypertrophic or arrhythmogenic right ventricular (RV) cardiomyopathy (1-3), or myocardial inflammation (18); or 3) significant primary valvular heart disease (1-3).

Additional exclusion criteria were the generally accepted contraindications to CMR (implantable devices, cerebral aneurysm clips, cochlear implants, severe claustrophobia), history of renal disease with a current estimated glomerular filtration rate <30 ml/min/1.73 m^2, unable to receive gadolinium contrast agent, and inability to provide informed consent. Clinical metadata were collected for all

ABBREVIATIONS AND ACRONYMS

CMR = cardiac magnetic resonance

ECV = extracellular volume fraction

EF = ejection fraction

HF = heart failure

IQR = interquartile range

LGE = late gadolinium enhancement

LV = left ventricular

NIDCM = nonischemic dilated cardiomyopathy

NYHA = New York Heart Association

RV = right ventricular

SAX = short axis

SD = standard deviation

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