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Native T1 Mapping in Differentiation of Normal Myocardium From Diffuse Disease in Hypertrophic and Dilated Cardiomyopathy

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OBJECTIVES The aim of this study was to examine the value of native and post-contrast T1 relaxation in the differentiation between healthy and diffusely diseased myocardium in 2 model conditions, hypertrophic cardiomyopathy and nonischemic dilated cardiomyopathy.

BACKGROUND T1 mapping has been proposed as potentially valuable in the quantitative assessment of diffuse myocardial fibrosis, but no studies to date have systematically evaluated its role in the differentiation of healthy myocardium from diffuse disease in a clinical setting.

METHODS Consecutive subjects undergoing routine clinical cardiac magnetic resonance at King's College London were invited to participate in this study. Groups were based on cardiac magnetic resonance findings and consisted of subjects with known hypertrophic cardiomyopathy (n = 25) and nonischemic dilated cardiomyopathy (n = 27). Thirty normotensive subjects with low pre-test likelihood of cardiomyopathy, not taking any regular medications and with normal cardiac magnetic resonance findings including normal left ventricular mass indexes, served as controls. Single equatorial short-axis slice T1 mapping was performed using a 3-T scanner before and at 10, 20, and 30 minutes after the administration of 0.2 mmol/kg of gadobutrol. T1 values were quantified within the septal myocardium ($T1_{native}$), and extracellular volume fractions (ECV) were calculated.

RESULTS $T1_{native}$ was significantly longer in patients with cardiomyopathy compared with control subjects ($p < 0.01$). Conversely, post-contrast T1 values were significantly shorter in patients with cardiomyopathy at all time points ($p < 0.01$). ECV was significantly higher in patients with cardiomyopathy compared with controls at all time points ($p < 0.01$). Multivariate binary logistic regression revealed that $T1_{native}$ could differentiate between healthy and diseased myocardium with sensitivity of 100%, specificity of 96%, and diagnostic accuracy of 98% (area under the curve 0.99; 95% confidence interval: 0.96 to 1.00; $p < 0.001$), whereas post-contrast T1 values and ECV showed lower discriminatory performance.

CONCLUSIONS This study demonstrates that native and post-contrast T1 values provide indexes with high diagnostic accuracy for the discrimination of normal and diffusely diseased myocardium. (J Am Coll Cardiol Img 2013;6:475–84) © 2013 by the American College of Cardiology Foundation

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Myocardial fibrosis is a fundamental process in the development of myocardial dysfunction in various cardiomyopathies, leading to myocardial remodeling and poor outcomes (1–5). Cardiac magnetic resonance (CMR) is increasingly applied as the first-line investigation into the causes of cardiomyopathies (6). Visualization of fibrosis by CMR is based on a greater distribution volume and slower washout of gadolinium contrast agents within tissues with greater extracellular space due to edema or fibrosis (7). Whereas regional fibrosis after ischemic injury is readily distinguished by well-delineated areas of increased signal intensity on T1-weighted images by late gadolinium enhancement (LGE) (8), it may be impossible to define an area of clearly unaffected myocardium as a "nulled" reference in diffuse fibrotic processes (Figs. 1A and 1B) (9). As a consequence, such images may null the signal in areas of fibrosis, obscuring the finding or result in images with various gray values, not allowing a clear "yes or no" decision (9,10). Recently, several studies have proposed the measurement of T1 relaxation as potentially valuable for the quantitative assessment of myocardial fibrosis (11–16). In these studies, native myocardium with ischemic scar showed longer T1 values compared with unaffected remote myocardium. After contrast administration, regional and also diffusely scarred myocardium showed shorter T1 relaxation and delayed normalization of T1 times with gadolinium washout. Whereas these observations show the potential of T1 mapping for the evaluation of myocardial fibrosis, these studies used a variety of imaging methodologies and post-processing approaches. The ability of T1 mapping to differentiate between normal and abnormal myocardium is yet to yield a clinically robust application. In the present study, we aimed to examine the value of native and post-contrast T1 relaxation in the differentiation of healthy and diffusely diseased myocardium in 2 model conditions, hypertrophic cardiomyopathy (HCM) and nonischemic dilated cardiomyopathy (NIDCM).

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ABBREVIATIONS AND ACRONYMS

CI = confidence interval

CMR = cardiac magnetic resonance

HCM = hypertrophic cardiomyopathy

HR = heart rate

LGE = late gadolinium enhancement

LV = left ventricular

NIDCM = nonischemic dilated cardiomyopathy

ROI = region of interest

METHODS

Consecutive subjects undergoing routine clinical CMR at King's College London were invited to participate in this study. Groups were based on CMR findings and consisted of subjects with known HCM (n = 25) and NIDCM (n = 27) and controls (n = 30). Diagnosis of HCM was based on the demonstration of a hypertrophied left ventricle associated with a nondilated left ventricle (LV) in the absence of increased LV wall stress or another cardiac or systemic disease that could result in a similar magnitude of hypertrophy (17,18). All patients with HCM had an expressed phenotype with typically asymmetric septal hypertrophy of increased LV wall thickness, permitting unequivocal clinical diagnoses. NIDCM was defined as an increase in LV volumes, a reduction in global systolic function, and absence of evidence of ischemic-like LGE (18). Thirty normotensive subjects with low pre-test likelihood for LV cardiomyopathy, not taking any regular medications and, consequently, with normal CMR findings including normal LV mass indexes, served as the control group (19). Additional exclusion criteria for all subjects were the generally accepted contraindications to CMR (implantable devices, cerebral aneurysm clips, cochlear implants, severe claustrophobia) or a history of renal disease with a current estimated glomerular filtration rate <30 ml/min/1.73 m^2. The study protocol was reviewed and approved by the institutional ethics committee, and written informed consent was obtained from all participants.

CMR protocol. We integrated native and post-contrast myocardial T1 mapping into our routine imaging protocol for the determination of the underlying etiology of cardiomyopathy; an outline is provided in Figure 2. The CMR studies were performed with the patient supine, using a clinical 3-T scanner (Achieva TX, Philips Healthcare, Best, the Netherlands) and a 32-channel coil. After standardized patient-specific planning (20), volumetric cavity assessment was obtained by whole-heart coverage of gapless short-axis slices. Thereafter, cine images of 3 long-axis views (4-chamber, 2-chamber, and 3-chamber views) and transverse axial views were acquired. All cine-images were acquired using a balanced steady-state free precession sequence in combination with parallel imaging (SENSitivity Encoding, factor 2) and retrospective gating during a gentle expiratory breath-hold (echo time [TE]/repetition time [TR]/flip-angle: 1.7 ms/3.4 ms/60°, spatial resolution 1.8 × 1.8 × 8 mm). LGE imaging was performed in a gapless whole heart coverage of short axis slices 20 min after administration of a cumulative dose of 0.2 mmol/kg body weight gadobutrol using a mid-diastolic inversion prepared 2-dimensional gradient echo sequence (TE/TR/flip-angle 2.0 ms/3.4 ms/25°, interpolated voxel size 0.7 ×