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Increased Extracellular Volume and Altered Mechanics Are Associated With LVH in Hypertensive Heart Disease, Not Hypertension Alone

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ABSTRACT

OBJECTIVES The goal of this study was to assess the relationship among extracellular volume (ECV), native T1, and systolic strain in hypertensive patients with left ventricular hypertrophy (HTN LVH), hypertensive patients without LVH (HTN non-LVH), and normotensive controls.

BACKGROUND Diffuse myocardial fibrosis in HTN LVH patients, as reflected by increased ECV and native T1, may be an underlying mechanism contributing to increased cardiovascular risk compared with HTN non-LVH subjects and controls. Furthermore, increased diffuse fibrosis in HTN LVH subjects may be associated with reduced peak systolic and early diastolic strain rate compared with the other 2 groups.

METHODS T1 mapping was performed in 20 HTN LVH (mean age, 55 ± 11 years), 23 HTN non-LVH (mean age, 61 ± 12 years), and 22 control subjects (mean age, 54 ± 7 years) on a Siemens 1.5-T Avanto (Siemens Healthcare, Erlangen, Germany) using a previously validated modified look-locker inversion-recovery pulse sequence. T1 was measured pre-contrast and 10, 15, and 20 min after injection of 0.15 mmol/kg gadopentetate dimeglumine, and the mean ECV and native T1 were determined for each subject. Measurement of circumferential strain parameters were performed using cine displacement encoding with stimulated echoes.

RESULTS HTN LVH subjects had higher native T1 compared with controls ($p < 0.05$). HTN LVH subjects had higher ECV compared with HTN non-LVH subjects and controls ($p < 0.05$). Peak systolic circumferential strain and early diastolic strain rates were reduced in HTN LVH subjects compared with HTN non-LVH subjects and controls ($p < 0.05$). Increased levels of ECV and native T1 were associated with reduced peak systolic and early diastolic circumferential strain rate across all subjects.

CONCLUSIONS HTN LVH patients had higher ECV, longer native T1 and associated reduction in peak systolic circumferential strain, and early diastolic strain rate compared with HTN non-LVH and control subjects. Measurement of ECV and native T1 provide a noninvasive assessment of diffuse fibrosis in hypertensive heart disease. (J Am Coll Cardiol Img 2015;8:172–80) © 2015 by the American College of Cardiology Foundation.

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Hypertension (HTN) is a common cause of morbidity and mortality in the United States affecting 1 in 3 adults (1). Patients with long-standing or poorly controlled HTN are at increased risk for developing left ventricular hypertrophy (LVH) and diastolic dysfunction (2). LVH is an independent risk factor for cardiovascular morbidity and mortality in hypertensive patients (3,4). Diffuse fibrosis has been detected in subjects with HTN with LVH in both biopsy (5) and autopsy studies (6) and has been linked to the development of LVH and diastolic dysfunction (7). Concentric LVH portends higher cardiovascular morbidity and mortality compared with other hypertrophy subtypes (8). The presence of diffuse fibrosis may confer increased cardiovascular risk in HTN LVH patients.

Diffuse myocardial fibrosis in hypertensive LVH is not detected by conventional late gadolinium enhanced (LGE) cardiac magnetic resonance (CMR). T1 mapping is a novel CMR approach that is able to detect diffuse fibrosis in diseases such as aortic stenosis and hypertrophic cardiomyopathy as validated against myocardial biopsy (9). By measuring the T1 relaxation times of the blood and myocardium both pre- and post-contrast, one can determine the partition coefficient (λ) of gadolinium and, subsequently, the extracellular volume (ECV).

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We hypothesized that HTN LVH patients would show diffuse myocardial fibrosis as measured by T1 mapping and ECV compared with HTN non-LVH and normotensive controls. We also postulated that subjects with HTN LVH would have greater fibrosis and reduced systolic strain, and early diastolic strain rate compared with the other 2 groups.

METHODS

Twenty subjects with HTN LVH (mean age, 55 ± 11 years), 23 subjects with HTN non-LVH (mean age, 61 ± 12 years), and 22 normotensive controls (mean age, 54 ± 7 years) were enrolled between November 2010 and October 2013 under an institutional review board-approved protocol. All subjects signed informed consent. Patients with a history of HTN and evidence of LVH by any imaging modality were considered for this study. Patients with any other causes of LVH, known coronary disease, significant valvular disease, renal impairment with glomerular filtration rate <45 ml/min/1.73 m^2 or reduced systolic function (ejection fraction [EF] <45%) were excluded. Subjects with a history of HTN with systolic blood pressure >140 mm Hg or diastolic blood pressure >90 mm Hg on at least 2 office readings (10), or taking 1 or more medications for hypertension, were included. Subjects were then classified as having LVH if their left ventricular mass indexed by body surface area (LVMI) as measured by cardiac magnetic resonance imaging was >81 g/m^2 for men or >61 g/m^2 in women as defined by Olivotto et al. (11). Hypertensive subjects not meeting criteria for LVH as defined in the preceding text were included in the HTN non-LVH group. Healthy volunteers who were normotensive and did not have a history of HTN were enrolled in the control arm.

CMR PROTOCOL. CMR was performed on a 1.5-T magnetic resonance scanner (Siemens Avanto, Erlangen, Germany).

Cine Imaging. Left ventricular (LV) mass and function were assessed by steady-state free-precession cine imaging using the following sequence parameters: repetition time (TR) 2.7 ms, echo time (TE) 1.3 ms, flip angle 70°, field of view (FOV) 300 to 350 mm, and in-plane resolution 1.8 × 1.4 mm, TR 40 to 50 ms, slice thickness 8 mm. Images were obtained in short-axis and standard long-axis orientations. Analyses were performed (R.J., S.K.) using Argus software (Siemens Healthcare, Princeton, New Jersey) on a Leonardo workstation (Siemens Healthcare, Erlangen, Germany). End-diastolic and end-systolic endocardial and epicardial cavity areas were planimetered for each short-axis slice. The LV mass, end-diastolic volume, and end-systolic volumes were determined and indexed to body surface area. LV mass was measured from the end-diastolic image frames using the validated Q-Mass version 7.5 (Medis Medical Imaging, Leiden, the Netherlands) program (12). Papillary muscles were included when measuring LV mass as per recent Society for Cardiovascular Magnetic Resonance guidelines (13).

T1 mapping. T1 mapping was performed using a reduced breath-hold variant of the modified look-locker inversion recovery (MOLLI) technique (14), which was previously validated by our group (15). This protocol yields 8 T1-weighted source images over 11 heartbeats. The starting TI (to the first image readout) was chosen to be 100 ms, with an increment of 80 ms for the subsequent look-locker trains. The pulse sequence parameters included: TE 1.1 ms, TR 2.5 ms, flip angle 35°, FOV 340 × 260 mm, resolution 1.8 × 1.8 mm and slice thickness of 8 mm.

T1 maps (**Figure 1**) were obtained in basal and mid-ventricular short axis slices pre-contrast and at 10, 15, and 20 min after a bolus intravenous injection of

ABBREVIATIONS AND ACRONYMS

CMR = cardiac magnetic resonance
ECV = extracellular volume
EF = ejection fraction
FOV = field of view
Hct = hematocrit
HTN = hypertension
LGE = late gadolinium enhancement
LV = left ventricle
LVH = left ventricular hypertrophy
LVMI = left ventricular mass index
MOLLI = modified look-locker inversion recovery
TE = echo time
TR = repetition time