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.
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 (Δ) of gadolinium and, subsequently, the extracellular volume (ECV).

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 m² 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/m² for men or >61 g/m² 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
FIGURE 1 Example T1 Maps

T1 maps pre-contrast (left) and post-contrast (right). T1 maps are generated from a collection of T1 images obtained at different inversion times during the same phase of the cardiac cycle.

Values were compared between groups using 1-way analysis of variance, the Scheffe method was used to control for multiple pairwise corrections. Age and number of blood pressure medications for the 3 groups were calculated. Left ventricular mass was higher in the HTN LVH group by 0.15 mmol/kg gadopentetate dimeglumine (Gd-DTPA) (Magnevist, Bayer Healthcare, Berlin, Germany). Hematocrit (Hct) was measured in all subjects.

Late gadolinium enhancement. LGE images were acquired approximately 10 to 15 min after bolus injection of 0.15 mmol/kg of Gd-DTPA. A phase sensitive inversion recovery sequence was used (TR 7.1 ms, TE 3.4 ms, flip angle 25°, FOV 300 to 340 mm, resolution 1.8 × 1.3, slice thickness 8 mm). LGE images were scored visually by 2 experienced observers (S.K., M.S.).

Strain imaging. A spiral cine displacement encoding with stimulated echoes-pulse sequence was used to quantify circumferential strain and strain rate. Sequence parameters included: TR 17 ms, TE 1.8 ms, flip angle 20°, FOV 350 mm², resolution 2.5 mm, slice thickness 8 mm, number of spiral interleaves 6, temporal resolution 34 ms (16,17). Images were obtained in basal and mid short-axis locations.

Baseline Characteristics of HTN LVH Subjects, HTN Non-LVH Subjects, and Controls

<table>
<thead>
<tr>
<th></th>
<th>Normotensive Controls (n = 22)</th>
<th>Hypertensive Non-LVH (n = 23)</th>
<th>Hypertensive LVH (n = 20)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td>15 F, 7 M</td>
<td>13 F, 10 M</td>
<td>14 F, 6 M</td>
</tr>
<tr>
<td>Age (yrs)*</td>
<td>54 (48-61)</td>
<td>64 (56-71)</td>
<td>55 (44-66)</td>
</tr>
<tr>
<td>Systolic BP (mm Hg)</td>
<td>123 ± 14</td>
<td>135 ± 16*</td>
<td>151 ± 21††</td>
</tr>
<tr>
<td>Diastolic BP (mm Hg)</td>
<td>71 ± 11</td>
<td>77 ± 11</td>
<td>84 ± 16*</td>
</tr>
<tr>
<td>Heart rate (beats/min)</td>
<td>73 ± 12</td>
<td>73 ± 14</td>
<td>71 ± 10</td>
</tr>
<tr>
<td>Number of HTN medicines</td>
<td>0</td>
<td>2.1 ± 1.1*</td>
<td>3.6 ± 1.2††</td>
</tr>
<tr>
<td>LV mass (g)</td>
<td>92 ± 20</td>
<td>115 ± 31</td>
<td>171 ± 39††</td>
</tr>
<tr>
<td>LVMI (g/m²)</td>
<td>49 ± 7</td>
<td>55 ± 9</td>
<td>83 ± 14††</td>
</tr>
<tr>
<td>LV mass/volume ratio</td>
<td>0.71 ± 0.19</td>
<td>0.87 ± 0.21</td>
<td>1.30 ± 0.40††</td>
</tr>
</tbody>
</table>

Values are n, median (interquartile range), or mean ± SD. *p < 0.05 vs. controls. †p < 0.05 vs. non-LVH groups.

BP = blood pressure; F = female; HTN = hypertension; LV = left ventricular; LVH = left ventricular hypertrophy; LVMI = left ventricular mass index; M = male.

Results

Table 1 shows the baseline characteristics of the 3 groups. The groups had similar values for heart rate, LVEF, and Hct. The systolic and diastolic blood pressures were significantly higher in the HTN LVH group than the HTN non-LVH and control subjects. LV mass was higher in the HTN LVH group by study design. Two subjects (both in the HTN non-LVH group) had focal areas of late enhancement: 1 subject had right ventricular insertion site hyperenhancement, and the other had a focal area of midwall enhancement in the distal inferior wall, considered to be nonischemic in origin. These regions were not included on T1 mapping analysis to minimize potential bias from including regions with focal fibrosis. Left ventricular mass/volume ratios for the 3 groups were calculated. Left ventricular...
mass/volume ratios were higher in the HTN LVH groups compared with the other 2 groups (Table 1) (Online Appendix).

**ECV.** ECV was significantly higher in HTN LVH subjects versus controls (0.29 ± 0.03 vs. 0.26 ± 0.02, p < 0.01) and HTN non-LVH subjects (0.29 ± 0.03 vs. 0.27 ± 0.02, p = 0.05) (Table 2, Figure 2). There were no differences in ECV (p = 0.6) between HTN non-LVH and control subjects. Similar findings were seen with partition coefficient (λ) (Table 2) (Online Appendix).

**NATIVE T1.** The native T1 of the patients with HTN LVH was longer than that of control subjects (996 ± 32 vs. 967 ± 35, p = 0.007) (Table 2). Although the point estimate of native T1 in the HTN non-LVH group was higher than that of controls, this difference was not statistically significant (Table 2). Post-contrast T1 values are provided in the data supplement.

**RELATIONSHIP AMONG ECV, NATIVE T1, AND LVMI.** A positive association was noted between LVMI and ECV (Figure 3A) (Spearman rho = 0.26, p = 0.03). However, ECV was not linearly related to an increase in LVMI. HTN non-LVH subjects had similar LVMI and ECV levels to those of controls. HTN LVH subjects had higher LVMI levels as expected and had higher ECV levels. However, subjects with the highest LVMI did not show a proportional increase in ECV. Furthermore, certain HTN LVH subjects with relatively lower LVMI had significantly higher levels of ECV (>0.30). Similarly, a positive association was noted between native T1 levels and LVMI (Figure 3B) (Spearman rho = 0.36, p = 0.03).

**ECV, NATIVE T1, CIRCUMFERENTIAL STRAIN, AND STRAIN RATE.** Figure 4A shows average circumferential strain-time curves from the 3 groups. The average early diastolic circumferential strain rate (e\(_{SR}\)) was reduced in HTN LVH subjects compared with both controls and HTN non-LVH subjects (Table 3). ECV correlated with peak circumferential strain (R = 0.44, p < 0.0001) (Figure 6A). Native T1 also correlated significantly with e\(_{SR}\) (R = -0.40, p < 0.01) (Figure 6B).

**LV MASS TO VOLUME RATIO, ECV, AND CIRCUMFERENTIAL STRAIN.** Left ventricular mass to volume ratio correlated significantly with ECV (R = 0.337, p = 0.006) and native T1 (R = 0.341, p = 0.006). Circumferential strain and strain rate correlated significantly with LV mass to volume ratio (R = 0.733, p < 0.0001 and R = -0.642, p < 0.0001, respectively).

**DISCUSSION**

In this study, T1 mapping by CMR showed greater diffuse fibrosis as measured by ECV in subjects with HTN LVH compared with HTN non-LVH and control subjects versus controls (0.29 ± 0.03 vs. 0.26 ± 0.02, p < 0.01) and HTN non-LVH subjects (0.29 ± 0.03 vs. 0.27 ± 0.02, p = 0.05) (Table 2, Figure 1). There were no differences in ECV (p = 0.6) between HTN non-LVH and control subjects. Similar findings were seen with partition coefficient (λ) (Table 2) (Online Appendix).

**TABLE 2** ECV, Partition Coefficient, and Native T1 Values in HTN LVH Subjects Versus Non-LVH and Controls

<table>
<thead>
<tr>
<th></th>
<th>Normotensive Controls (n = 22)</th>
<th>Hypertensive Non-LVH (n = 23)</th>
<th>Hypertensive LVH (n = 20)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Extracellular volume</td>
<td>0.26 ± 0.02</td>
<td>0.27 ± 0.02</td>
<td>0.29 ± 0.03†</td>
</tr>
<tr>
<td>Native T1 (ms)</td>
<td>967.4 ± 35.0</td>
<td>974.0 ± 33.6</td>
<td>996.0 ± 32.5†</td>
</tr>
<tr>
<td>Partition coefficient (λ)</td>
<td>0.43 ± 0.03</td>
<td>0.45 ± 0.03</td>
<td>0.48 ± 0.04‡</td>
</tr>
</tbody>
</table>

Values are mean ± SD. *p < 0.05 vs. non-LVH groups; †p < 0.05 vs. controls. ECV = extracellular volume; HTN = hypertensive; LVH = left ventricular hypertrophy.
Higher ECV values were associated with reduced peak systolic circumferential strain and early diastolic circumferential strain rate across all subjects. Furthermore, native T1 levels were found to be longer in HTN LVH subjects compared with normotensive controls. Similarly, increased native T1 was associated with reductions in peak circumferential systolic strain and early diastolic strain rate. Left ventricular mass to volume ratio also correlated with strain and strain rate with increased mass to volume ratio associated with increased ECV, increased native T1, and reduced circumferential strain and strain rate.

ECV and native T1 have different sensitivity to the underlying changes in the intracellular and extracellular spaces within the myocardium. Native T1 is a function of the relaxation of water in both the intracellular and extracellular spaces.
extracellular and intracellular compartments and may reflect both changes in cellular hypertrophy or extracellular fibrosis. As there is fast water exchange between these compartments, without giving contrast the contribution of the intracellular and extracellular compartments cannot be separated. Because gadolinium contrast agents accumulate only in the extracellular space, the post-contrast T1 shortening is still affected by water exchange with the intracellular cellular space, the post-contrast T1 shortening is primarily due to a shortening of T1 relaxation time in the extracellular space (although the measured T1 is still affected by water exchange with the intracellular compartment) (20). The ECV is calculated from a combination of native and post-contrast measurements and reflects the volume fraction of extracellular space on a pixel-wise basis. Thus, native T1 and ECV are sensitive to different compartments within the myocardium and may each reflect different aspects of the pathological changes of hypertensive heart disease.

**MYOCARDIAL FIBROSIS IN HYPERTENSION.** Myocardial fibrosis is a common end point of many cellular and noncellular pathological processes in hypertensive heart disease. The pathogenesis of hypertensive heart disease involves remodeling of the myocardium with fibrosis of the muscle and perivascular space, medial hypertrophy of intramyocardial coronary vasculature, and cardiomyocyte hypertrophy (21). The mechanisms responsible for the development, progression, and pattern of LVH are incompletely defined but include the severity and duration of hypertension, effects of growth factors, cytokines and neurohormones, and genetic predisposition (22). Myocardial fibrosis predisposes patients to diastolic and systolic dysfunction, myocardial ischemia, and atrial and ventricular arrhythmias (23). A strong correlation has been noted between increased myocardial collagen content and left ventricular diastolic dysfunction by echocardiography (24). This study also showed that treatment with losartan reduced the collagen content and left ventricular stiffness. This suggests that diffuse fibrosis seen in hypertensive patients is reversible in response to certain antihypertensive therapies. Reduction in diffuse fibrosis can result in improvement of diastolic function, systolic function, and perhaps outcomes. Thus, measurement of diffuse fibrosis levels could serve as a therapeutic target to

<table>
<thead>
<tr>
<th>TABLE 3 Strain and Strain Rate Among the 3 Groups</th>
<th>Normotensive Controls</th>
<th>Hypertensive Non-LVH</th>
<th>Hypertensive LVH</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peak base circumferential strain</td>
<td>−0.17 ± 0.03</td>
<td>−0.15 ± 0.03</td>
<td>−0.12 ± 0.03*</td>
</tr>
<tr>
<td>Peak mid-circumferential strain</td>
<td>−0.17 ± 0.03</td>
<td>−0.17 ± 0.03</td>
<td>−0.12 ± 0.03*</td>
</tr>
<tr>
<td>Peak average circumferential strain</td>
<td>−0.17 ± 0.02</td>
<td>−0.16 ± 0.03</td>
<td>−0.12 ± 0.02*</td>
</tr>
<tr>
<td>Base εSR (s⁻¹)</td>
<td>0.81 ± 0.17</td>
<td>0.68 ± 0.17</td>
<td>0.48 ± 0.27*</td>
</tr>
<tr>
<td>Mid εSR (s⁻¹)</td>
<td>0.83 ± 0.19</td>
<td>0.72 ± 0.23</td>
<td>0.43 ± 0.22*</td>
</tr>
<tr>
<td>Average εSR (s⁻¹)</td>
<td>0.82 ± 0.16</td>
<td>0.71 ± 0.18</td>
<td>0.49 ± 0.26*</td>
</tr>
</tbody>
</table>

Values are mean ± SD. *p < 0.05 vs. non-LVH groups and controls. εSR = early diastolic circumferential strain rate; LVH = left ventricular hypertrophy.

**FIGURE 5** Correlation Between ECV and Circumferential Strain and Strain Rate

(A) Peak circumferential strain versus ECV. Pearson’s correlation shows a linear association between ECV and peak circumferential strain (Pearson’s correlation coefficient of 0.26, p = 0.05). (B) Average early diastolic circumferential strain rate versus ECV. Pearson’s correlation shows a linear association between ECV and peak circumferential strain rate (Pearson’s correlation coefficient of −0.34, p = 0.01). Ave εSR = average early diastolic circumferential strain rate; other abbreviations as in Figure 2.
measure the efficacy of antihypertensive and other therapies.

Initial animal studies in mice with hypertensive heart disease have shown that measurement of ECV as quantified by CMR T1 measurements can detect extracellular matrix expansion due to underlying interstitial fibrosis (20). Our study likewise uses the measurement of ECV of gadolinium as a surrogate marker for underlying diffuse fibrosis among the study groups.

This is the first study to measure the level of diffuse fibrosis using ECV in HTN LVH subjects compared with HTN non-LVH subtypes using a noninvasive imaging method. HTN LVH subjects in this study had greater diffuse fibrosis as measured by ECV. The presence of diffuse fibrosis may be an underlying mechanism contributing to the increased cardiovascular risk in HTN LVH subjects, and therapies that modify diffuse fibrosis may affect the risk. The link between diffuse fibrosis and increased cardiovascular risk was examined in a recent study (25) of heart failure patients with preserved EF and found that shortened post-contrast T1 times, a marker of diffuse fibrosis, was associated with increased cardiac events.

Although there is greater diffuse fibrosis in HTN LVH subjects, the association between ECV and LVMI is nonlinear suggesting that there may be differential stimulation of fibrosis and myocyte hypertrophy in these patients. The HTN non-LVH subjects had better controlled blood pressures, and their LV mass was not significantly higher than that of control subjects.

Fibrosis in these subjects was similar to that of controls, and the lack of fibrosis may be related to the lower risk of cardiovascular events for this group.

**NATIVE T1.** Native T1 of HTN LVH subjects in this study were significantly higher than that of HTN non-LVH or control subjects. Native T1 as discussed in the preceding text is affected by both intracellular myocardial tissue and the extracellular space. The extracellular fibrosis and myocardial cell hypertrophy seen in HTN LVH patients contribute to elevated native T1 levels. The measurement of native T1 as a potential predictor of increased cardiovascular events in LVH may have added value in that it does not require contrast administration, which may otherwise be contraindicated in those with stage 4 or 5 chronic kidney disease.

**DIFFUSE FIBROSIS AND SYSTOLIC STRAIN.** Earlier studies have shown reduced peak longitudinal and radial systolic strain in hypertensive patients using echocardiography and correlated the reduction in strain with increased collagen synthesis and reduced collagen degradation (26). Studies using CMR myocardial tagging have shown reduction in both circumferential and longitudinal strain in HTN patients with LVH (27). In this study, HTN LVH subjects were found to have significantly reduced peak systolic circumferential strain and eSR. We have also shown a positive correlation among the peak systolic circumferential strain, average eSR, and increasing levels of diffuse fibrosis as measured by ECV and native T1 levels, consistent with the expected
relationship between myocardial function and fibrosis. Reduced systolic strain has been previously described in heart failure patients with preserved EF, many of whom have HTN LVH and similar characteristics (28). A possible mechanism linking ECV to reduced systolic strain in such patients may be increased extracellular matrix deposition leading to increased LV stiffness, resulting in reduced end-diastolic muscle fiber length and, by Frank-Starling’s law, reduced cardiac muscle contraction and LV systolic strain. Indeed, prior studies have also shown that diffuse fibrosis has been linked with worsening systolic/diastolic function and adverse LV remodeling (23). However, further studies are needed to verify this hypothesis.

**STUDY LIMITATIONS.** The study is limited by a relatively small sample size; however, this is the largest study to date evaluating ECV in hypertensive heart disease and LVH. Given the small sample size of this study, the effect of variables such as age, gender, diabetes, hypertension duration, or antihypertensive medications such as renin-angiotensin inhibitors on ECV and native T1 could not be evaluated. Although the severity of LVH by CMR was relatively mild in this study, it was associated with increased levels of ECV and higher native T1, suggesting significantly greater diffuse fibrosis in the HTN LVH group compared with the other groups. There are differing methods of T1 mapping, and although consensus guidelines have recently been published regarding use of T1 mapping, further research is needed before establishing a standardized method of T1 mapping for clinical use (29). The method that we used in this study was previously compared with that of the standard MOLLI technique and produced similar results (15). Also, the applicability of results to an individual subject is less certain given the higher variability of T1 relaxation times and thus ECV when only measured in a single subject. The use of multiple points for the calculation of partition coefficient and ECV in our study is advantageous because it allows us to check the assumption of linearity at different time points to verify the equilibrium assumption and enables an assessment of the uncertainty in determining $\lambda$. The use of only 2 time points (1 pre- and 1 post-contrast) does not permit the measure of uncertainty of the fit and may be more sensitive to measurement outliers. Two of our control subjects as mentioned in the preceding text had elevated ECV levels, and it is unclear whether these results are due to normal variation or due to undetermined pathologies.

**FUTURE DIRECTIONS.** There are limited data on the prognostic value of diffuse fibrosis as measured by ECV in hypertensive subjects. Additionally, the prognostic value of native T1 levels has yet to be studied in this study population. Although diffuse fibrosis in HTN LVH subjects may be an underlying mechanism that explains the increased cardiovascular morbidity and mortality seen in these subjects, further studies are needed to conclusively link the presence of diffuse fibrosis with hard outcomes in these patients. Currently, only 1 study has evaluated the prognostic capability of T1 mapping in predicting cardiovascular events in a similar study population (25).

**CONCLUSIONS**

The present study shows that HTN LVH patients have greater diffuse fibrosis and reduced circumferential strain and circumferential strain rate compared with HTN non-LVH and control subjects. Although diffuse fibrosis is linearly related to worsening circumferential strain, variations in ECV among patients with LVH may provide insight into the differential expression of fibrosis and myocyte hypertrophy among patients with hypertensive heart disease. Measurement of ECV and native T1 levels may serve as a useful novel target to monitor the efficacy of therapies for HTN patients.

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**REFERENCES**


KEY WORDS cardiac magnetic resonance, extracellular volume, hypertension, hypertensive heart disease, left ventricular hypertrophy, myocardial fibrosis, T1 mapping

APPENDIX For supplemental tables and figures, please see the online version of this article.