T1 Mapping and Extracellular Volume in Cardiomyopathy Showing Left Ventricular Hypertrophy: Differentiation Between Hypertrophic Cardiomyopathy and Hypertensive Heart Disease

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International Journal of General Medicine

ORIGINAL RESEARCH

T1 Mapping and Extracellular Volume in Cardiomyopathy Showing Left Ventricular Hypertrophy: Differentiation Between Hypertrophic Cardiomyopathy and Hypertensive Heart Disease

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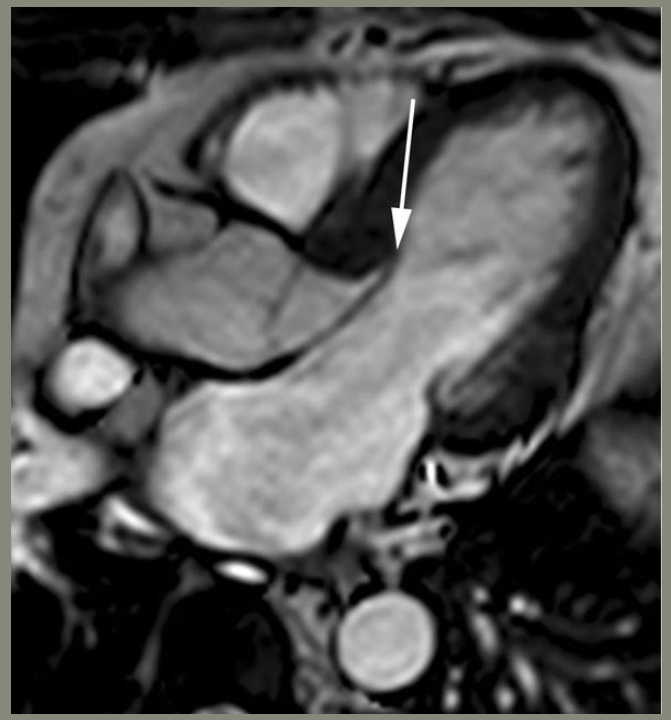
Introduction

Introduction

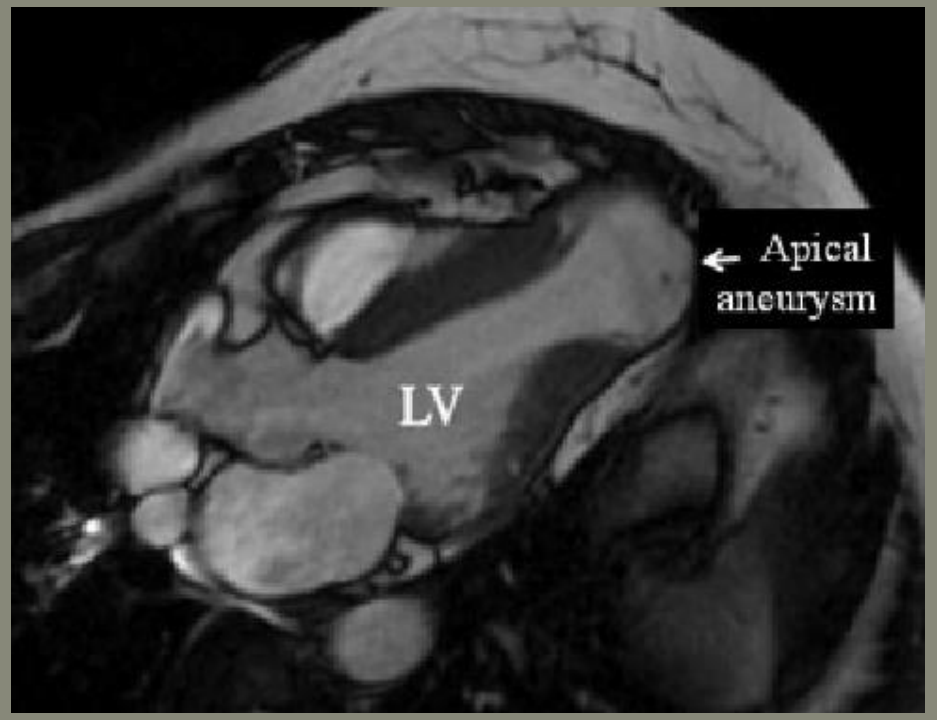
- Left ventricular hypertrophy (LVH) is a common clinical manifestations with many causes.
- It can be difficult to identify the aetiology of diffuse LVH, and particularly to distinguish between hypertrophic cardiomyopathy (HCM) and hypertensive heart disease (HHD).

Hypertrophic Cardiomyopathy (HCM)

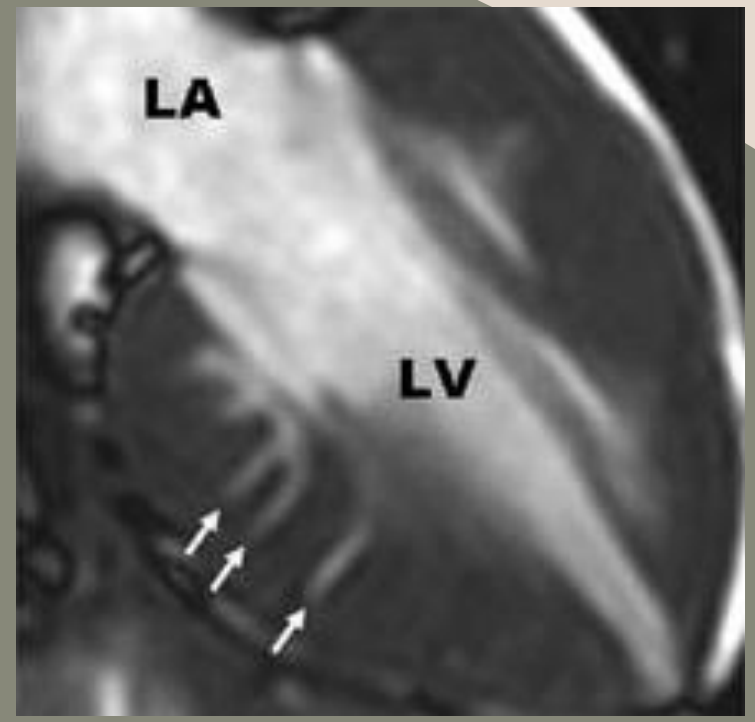
- A relatively common genetic disorder.
- Most frequently characterized by asymmetric hypertrophy of the left ventricle.
- The pathological basis is genetically driven hypertrophy of the cardiomyocytes.
- Specific features:
  - Asymmetrical hypertrophy
  - Dynamic LV outflow tract obstruction
  - Elongated mitral valve leaflets
  - Aberrant papillary muscle configuration
  - Apical aneurysms
  - Myocardial crypts
- Outflow tract obstruction is common in patients with HCM.



Elongated mitral valve



Apical aneurysm



Myocardial crypts

Hypertrophic Cardiomyopathy (HCM)

- Currently, the diagnosis of HCM is based on the finding of maximal LV wall thickness ≥ 15 mm in the absence of increased LV wall stress.
- Myocardial fibrosis in HCM mainly manifested as:
  - collagen hyperplasia
  - disarray of fibers and fascicles
  - myocardial cell disorder and necrosis

Hypertensive Heart Disease (HHD)

- May be involved in the development of hypertension in the first place, as well as being a consequence of raised systemic pressure.
- An adaptive response of cardiomyocytes to long term stress overload.
- Manifested by cardiomyocyte hypertrophy and interstitial fibrosis.

- The degree of myocardial fibrosis in HCM is significantly more serious than that associated with hypertension.
- Late gadolinium enhancement (LGE) of cardiac MR is currently the gold standard for non-invasive evaluation of localized myocardial fibrosis.
- However, LGE-CMR cannot quantitatively evaluate LVH, and cannot effectively distinguish the diffuse type of LVH.
- T1 mapping is capable of measuring T1 values in any region of the myocardium → which allow the myocardial extracellular volume (ECV) fraction can be measured
  - ➢ Can quantitatively represent the degree of interstitial fibrosis.

Materials & Methods

Study Population

- Retrospective study.
- Performed at Cardiology Department of Beijing Chaoyang Hospital from Jan 2017 to Nov 2018.
- All individuals undergoing transthoracic echocardiogram evaluation for LVH were enrolled.
- Subjects with any contraindication to CMR were excluded.
- Patients who were diagnosed with HCM by CMR were included.

Inclusion Criteria

HCM:

- Maximal LVWT of ≥ 15 mm in adults without family history of HCM
- Maximal LVWT ≥ 13 mm in adults with family history of HCM
- No other cardiac or systemic diseases that could result in similar LVH
- LVWT < 15 mm but clear lack of apical tapering and high suspicion of apical HCM with family history

HHD:

- Patients undergoing treatment for primary HPT
- LVH in the basal septal and inferolateral segments – defined as maximal LVWT > 12 mm with no evidence of dilated LV cavity on echo

Exclusion Criteria

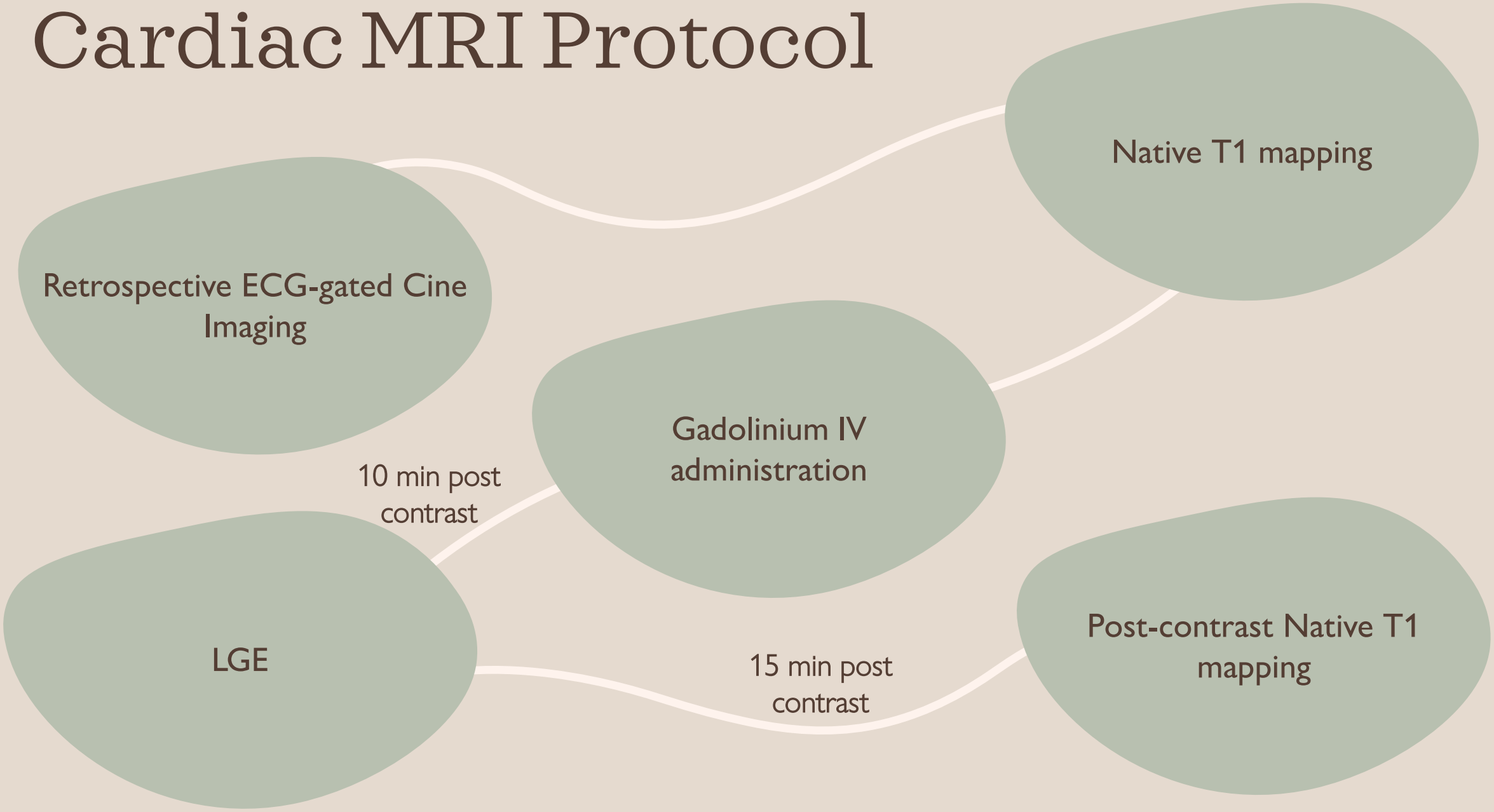
- Patient who underwent CMR without an extracellular contrast agent or who did not have hematocrit measured within 7 days of CMR study
- Patients with segments in the T1 mapping with poor motion correction
- Patients with acute heart failure
- Patient that fulfilled HCM criteria were excluded if also had arterial hypertension

- Total of 102 patients enrolled in this study.
- Compared with 29 healthy volunteers, with similar age and gender distribution
  - Had no evidence of heart disease on physical examination, 12-lead ECG, and echocardiography.
  - Not taking any medications.

Cardiac MRI Acquisition

- Performed at 3T scanner (Prisma, Siemens, Healthcare, Erlangen, Germany).
- Using an anterior-phased array body coil (18-element) and posterior phased-array spine coil (24-element) within 1 week of the patient undergoing transthoracic echocardiogram.
- A 4-lead vectorcardiogram used for cardiac gating.
- Breath-holding process carefully explained to the subjects.
- Abdominal belt was wrapped tightly.

Cardiac MRI Protocol



Cardiac MRI Protocol

- Retrospective ECG gating cine imaging was performed using a segmented balanced steady-state free precession sequence in continuous short-axis views.
- Involving the entire LV from base to apex.
- Imaging parameters for cine images:
  - Repetition time (45.64 ms)
  - Flip angle (80˚)
  - Field-of-view (340 mm)
  - SENSE factor 2
  - Echo time (1.43 ms)
  - Section thickness (8 mm)
  - Matrix size (256 x 169)
  - 25 cardiac phases/ R-R interval on ECG

Cardiac MRI Protocol

- After the cine images acquisition, native T1 data obtained from three short-axis images (basal, center, apical) of the LV using a modified look-locker inversion recovery (MOLLI) sequence.
- Imaging parameters for T1 data:
  - Repetition time (315.96 ms)
  - Echo time (1.12 ms)
  - Flip angle (35˚)
  - Section thickness (8 mm)
  - Field-of-view (360 mm)
  - Matrix size (256 x 169)

Cardiac MRI Protocol

- Then gadolinium-based contrast medium administered intravenously.
  - Gadopentetate dimeglumine, 0.1 mmol/kg body weight
- LGE images obtained in short-axis locations from the base to apex of the LV, by using 3D inversion recovery T1 turbo field-echo sequence, 10 mins after contrasts administration.
- Imaging parameters for LGE:
  - Repetition time (700 ms)
  - Inversion time (300-500 ms)
  - Section thickness (8 mm)
  - Matrix size (256 x 192)
  - Echo time (1.96 ms)
  - Flip angle (20˚)
  - Field-of-view (350 mm)
  - SENSE factor 2

Cardiac MRI Protocol

- 15 mins after contrast administration, post-contrast T1 data obtained using similar image sequence as for obtaining native T1 data.

Image Analysis

- Carried out using dedicated cardiac MRI software (syngo.via, Siemens Healthcare) by one of the author of this paper (radiologist with 4 years MRI experience), and the findings were reviewed by another author (radiologist with 30 years of MRI experience).
- LV borders were manually traced – papillary muscles were excluded from LV mass.
- Maximal end-diastolic wall thickness (EDWT) of the septum manually measured.
- T1 maps obtained using syngo.via – T1 values quantified in 16 segments in each of the three LV slices (basal, center and apical).
- 3 ROI placed within each segment to avoid the signals from the blood pool and artifacts
  - placed independent of the results from LGE imaging.
  - Size approximately 0.1-0.2 cm2, and at same 5 pixels were included.
  - The T1 values calculated as average of the 3 ROIs.

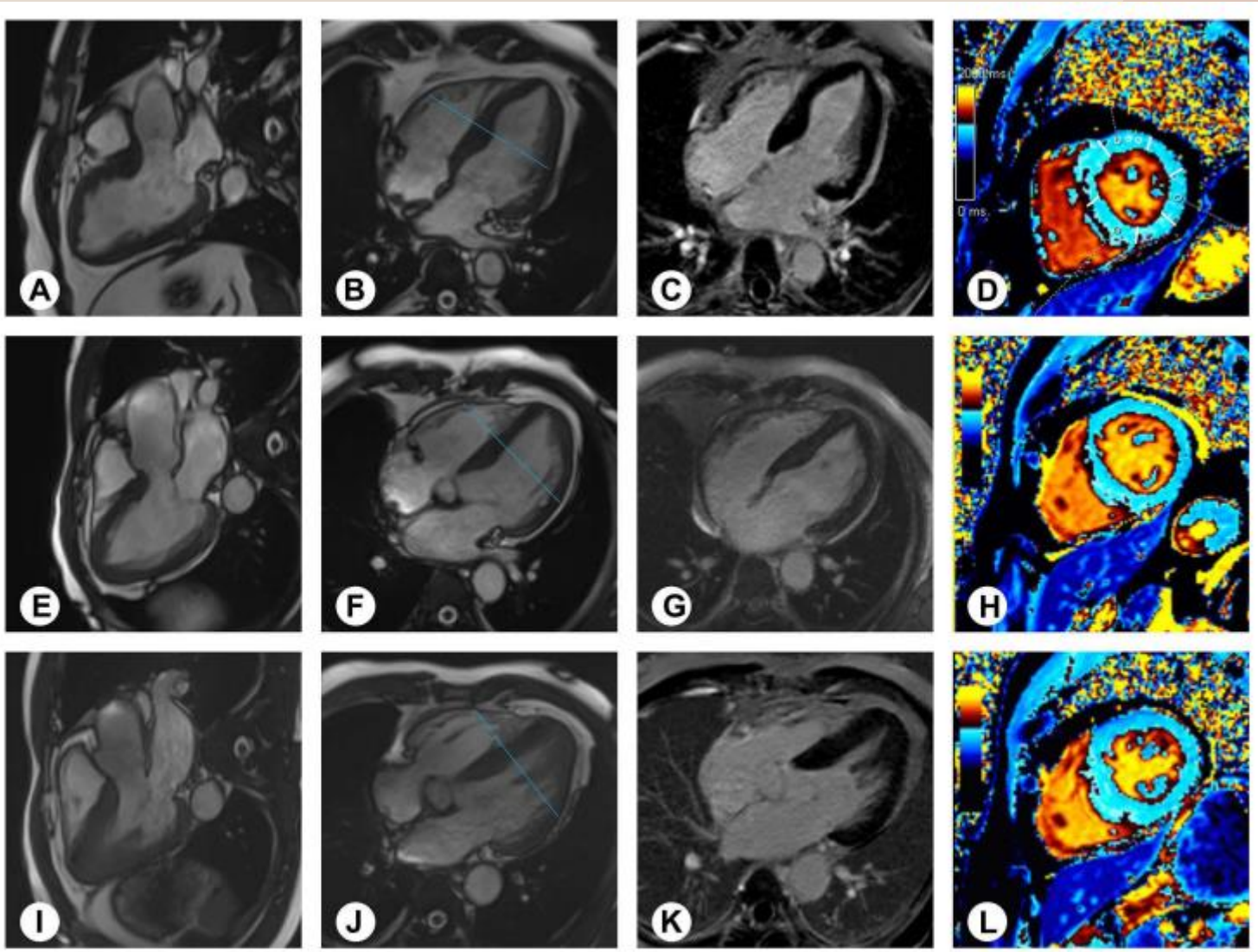


Figure 1 Images of a 47-year-old man with HHD (**A–D**). Images of a 59-year-old man with HCM (**E–H**), and follow-up after 3 year (**I–L**). Cine-magnetic resonance imaging in the three-chamber (**A** and **E**) and four-chamber (**B** and **F**) view showing similar looking hypertrophy of the interventricular septum in HHD and HCM, and the maximum septal wall thickness was 16 mm. And late gadolinium enhancement (**C** and **G**) was not found at the myocardium. At follow-up, theHCM myocardium became more hypertrophy, and clear lack of apical tapering. Native T1 maps in the LV center-chamber short-axis (**D, H, L**) showed with different average value: HHD=1195ms; HCM=1218ms; follow-up HCM=1285ms. Gray scale range: 0–2000 ms. The blue line in (**B, F, J**) represented the level at which the short axis mapping image is positioned on the long axis image.

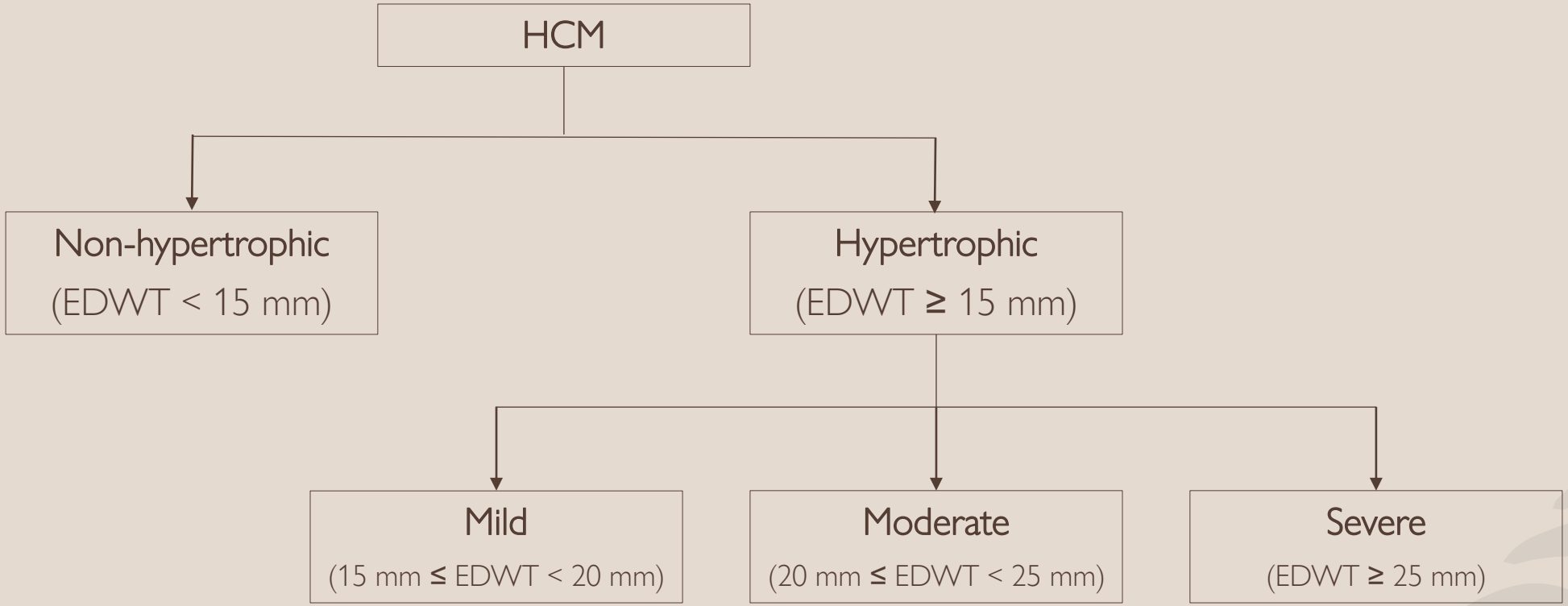

HCM
Non-hypertrophic
(EDWT < 15 mm)
Hypertrophic
(EDWT ≥ 15 mm)
Mild
(15 mm ≤ EDWT < 20 mm)
Moderate
(20 mm ≤ EDWT < 25 mm)
Severe
(EDWT ≥ 25 mm)

Image Analysis

- The average T1 values of the 3 LV slices were used to compare the HCM, HHD and healthy controls.
- The mean T1 was used to determine global T1.
- The haematocrit-corrected ECV fraction calculated.
- Estimation of the ECV measured using this formula:

$$ECV = (1 - haematocrt)\frac{1/T1_{myocardial\,post} - 1/T1_{myocardial\,pre}}{1/T1_{blood\,post} - 1/T1_{blood\,pre}}$$

- LGE evaluated by agreement between 2 radiologists experienced in reading CMR.
- Evaluation of LGE performed independent of the evaluation of T1 values.

Statistical Analysis

- The mean and SD were recorded for continuous variables.
- Frequency and percentage were recorded for categorical variables.
- For each variable, a normality test was performed.
- Continuous variables were compared using the *t*-test or the nonparametric Mann-Whitney *U*-test.
- Receiver operating characteristic (ROC) curves generated, and the areas under the curves (AUCs) were calculated and compared.
- The ROC of native T1 and ECV were compared for basal, center, apex and mean native T1 and ECV.

Results

BASELINE CHARACTERISTICS

Table 1 Baseline Characteristics of Healthy Controls, HHD, and HCM Patients

	Normal (n=29)	HHD (n=35)	HCM (n=38)	*P*
Age, y	42.9±19.5	48.5±16.3	52.1±13.9	0.085
Male, %(n)	41.4(12)	88.6(31)	65.8(25)	<0.001
Heart rate, bpm	69.7±24.1	90.5±16.6$^{\#}$	71.7±13.4*	<0.001
Systolic BP, mmHg	129.7±14.2	149.2±24.3$^{\#}$	131.2±16.4*	<0.01
Diastolic BP, mmHg	72.4±18.3	88.9±20.7$^{\#}$	76.6±12.0*	<0.01
Smokers, %(n)	23.8(5)	50(15)	34.8(8)	0.155
Diabetes, %(n)	6.9(2)	11.4(4)	21.1(8)	0.221
Hematocrit, L/L	40.1±3.1	42.9±4.5$^{\#}$	40.9±4.5	0.037
LVEF, %	67.9±9.7	57.7±17.8	68.3±9.8	0.003
LVEDV mL	46.2±6.6	52.9±10.3$^{\#}$	45.5±4.5*	<0.01
LVESV, mL	26.6 ± 6.4	36.6±12.2$^{\#}$	26.6±6.4*	<0.001
NT-proBNP, mmol/L	45.7±63.1	1787.5±2364.9$^{\#}$	995.3±1209.0§	<0.001
Outflow tract obstruction, %(n)	0(0)	0(0)	50(18)	<0.001

Notes: Values are the mean ± SD. *$P < 0.05$ HHD vs HCM; $^{\#}P < 0.05$ HHD vs control; $^{\S}P < 0.05$ HCM vs control.

Abbreviations: HHD, hypertensive heart disease; HCM, hypertrophic cardiomyopathy; BP, blood pressure; LVEF, left ventricular ejection fraction; LVEDV, left ventricular end-diastolic volume; LVESV, left ventricular end-systolic volume; NT-proBNP, N-terminal prohormone of brain natriuretic peptide.

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LGE

Table 2 Functional Measures Based on Cardiovascular Magnetic Resonance Imaging Measurements

	Control (N = 29)	HHD (N = 35)	HCM (N = 38)	*P*
LGE				
Present, % (n)	0 (0)	34.6 (9)	84.8 (28)	0.001
RV insertion points, % (n)	0 (0)	7.7 (2)	21.2 (7)	0.02
T1 mapping				
Basal native T1 (ms)	1229.3 ± 47.1	1257.1 ± 85.0	1291.5 ± 53.6*§	0.001
Central native T1 (ms)	1228.4 ± 42.7	1277.8 ± 70.5#	1290.0 ± 64.3§	<0.001
Apex native T1 (ms)	1250.6 ± 61.2	1258.2 ± 66.8	1299.5 ± 65.7*§	0.005
Native T1 (ms)	1236.1 ± 42.6	1264.3 ± 67.7	1293.6 ± 53.8*§	<0.001
ECV (%)	26.8 ± 5.8	27.1 ± 6.7	34.9 ± 9.8*§	0.001
Outflow tract obstruction, % (n)	0 (0)	0 (0)	50 (18)	

Notes: Values are mean ± SD. *P < 0.05 HHD vs HCM; # P < 0.05 HHD vs control; §P < 0.05 HCM vs control.

Abbreviations: HHD, hypertensive heart disease; HCM, hypertrophic cardiomyopathy; ECV, extracellular volume; LGE, late gadolinium enhancement; RV, right ventricular.

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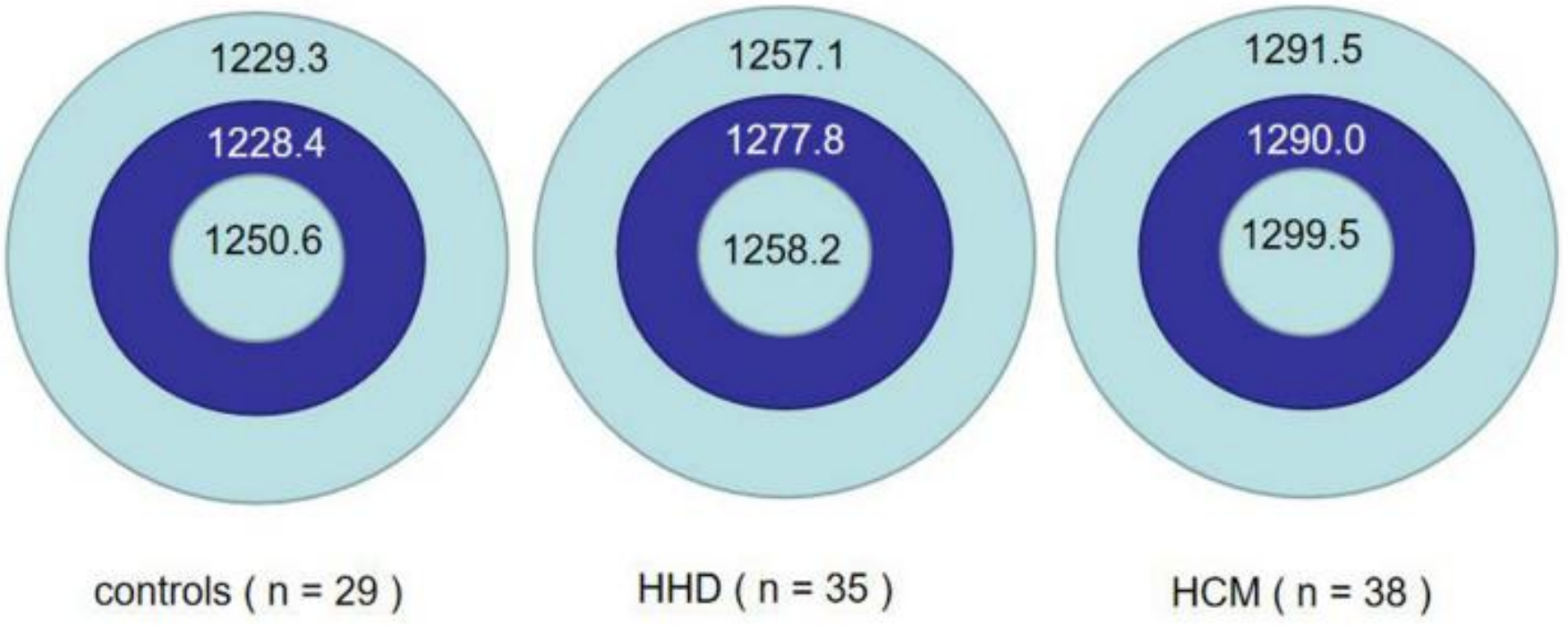

Figure 2 The mapping data. The health controls, HHD and HCM native T1 values in the basal, center, apex slice and average native T1 values.

LGE Pattern

	HCM	HHD
Location	Anteroseptal and inferoseptal segments	Septal to inferior regions at mid-ventricular level
Pattern	Mid-wall patchy or epicardial patchy patterns	Mid-wall linear, mid-wall or epicardial patchy patterns

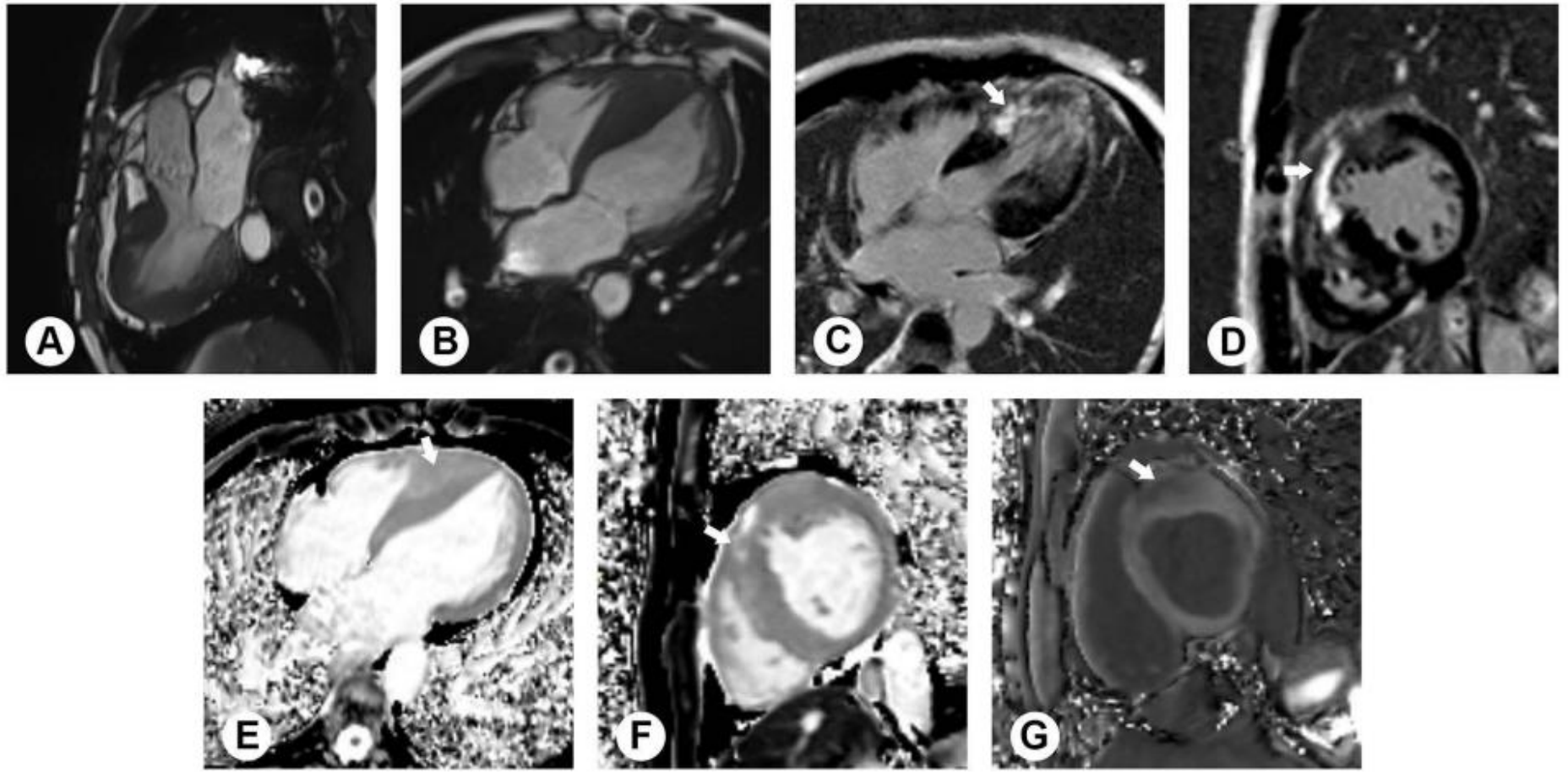

Figure 3 Images of a 34-year-old man with hypertrophic cardiomyopathy. Cine-magnetic resonance imaging in the three-chamber (**A**) and four-chamber (**B**) view showing hypertrophy of the interventricular septum and apex. The maximum septal wall thickness was 27 mm, and the left ventricular ejection fraction was 50% in this patient. Extensive myocardial late gadolinium enhancement (**C** and **D**) was found at the mid-wall layer from the anterior region to the inferior septum (arrows), with apex involvement, which was hyperintense as compared to the blood. Native T1 maps in the LV mid-chamber short-axis and four-chamber view (**E** and **F**) showed patchy areas of increased T1 relaxation (arrows) in the septum, which was more marked in hypertrophic segments. Post-contrast T1 map (**G**) showed patchy areas of decreased T1 relaxation (arrows) in the septum. Gray scale range: 0–2000 ms.

NATIVE T1 VALUES

Table 3 Native T1 Values in Different Degrees Hypertrophic Myocardial Segments of HCM and HHD Patients

Parameters		No-Hypertrophic Segment	Mild Hypertrophic Segment	Moderate Hypertrophic Segment	Severe Hypertrophic Segment
HCM	N	474	96	21	17
	Native T1 (ms)	1287.32±85.41	1310.80±67.38	1339.44±101.39	1394.55±66.99
HHD	N	518	37	6	0
	Native T1 (ms)	1269.04±86.88	1291.62±92.04	1345.18±66.99	–
P value		0.000	0.644	0.900	–

Notes: Continuous variables are expressed as mean ± standard deviation; P value: statistical significance between HCM and HHD segments using Mann–Whitney *U*-test.
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ROC & AUCS

Table 4 Cut-off Values from Receiver-Operating Characteristic Curve Analysis

Parameter	Cut-Off Value	AUC (95% CI)	P value	Specificity (%) (95% CI)	Sensitivity (%) (95% CI)
Basal native T1	1282	0.733 (0.612–0.854)	0.001	63.16 (46.0–78.2)	89.66 (72.6–97.8)
Central native T1	1236	0.704 (0.575–0.834)	0.004	86.84 (71.9–95.6)	72.41 (52.8–87.3)
Apex native T1	1267	0.693 (0.568–0.818)	0.007	65.79 (48.6–80.4)	75.86 (56.5–89.7)
Mean native T1	1282	0.726 (0.604–0.848)	P <0.001	63.16 (46.0–78.2)	89.66 (72.6–97.8)
ECV	28.8	0.772 (0.689–0.904)	0.000	85.00 (59.0–91.7)	62.07 (43.4–87.4)

Abbreviations: AUC, area under the curve; CI, confidence interval; ECV, extracellular volume.

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Abbreviations: AUC, area under the curve; CI, confidence interval; ECV, extracellular volume.

Discussion

- LVH is associated with increased morbidity and mortality related to MI, heart failure and stroke
  - Continuous graded relationship between LV mass and development of cardiovascular disease.
- Difficulties in discrimination of hypertrophic aetiologies interfere with appropriate diagnosis, risk assessment and clinical management.

LGE

- This study demonstrates some differences in LGE patterns between HHD and HCM.
- The frequency and number of LGE segments were higher in HCM than in HHD.
- Nevertheless, these differences were not specific, and could not accurately distinguish HHD and HCM.

Native T1

- Decreased in fat infiltration and iron overload.
- Increased in fibrosis, oedema and amyloidosis.
- Native T1 values gradually increases with the severity of the hypertrophy in the hypertrophic segments of HCM and HHD.
- For diffuse myocardial changes, a single basal and a single center-ventricular short-axis slice may provide adequate diagnostic information.

T1 Mapping and ECV in Discriminators of LVH Aetiologies

- Native T1 and ECV were significantly higher in patients with HCM compared to HHD.
  - In healthy individuals, ECV values 25.3 ± 3.5 % (on 1.5T MRI).
  - Besides amyloidosis, increased ECV is most often due to excessive collagen deposition – hence a more robust measure of the myocardial fibrosis.
  - Low ECV values occur in thrombus and fat/lipomatous metaplasia.
- From this study, ECV demonstrated the best diagnostic efficacy – due to different pathology.
  - ➢ Cardiac myocytes of the LV are enlarged in HHD.
  - ➢ Myocardial fibrosis is the key pathogenic process in HCM.

Conclusion

Conclusion

- The frequency and number of LGE segments were higher in HCM than in HHD.
- Differences also seen in location and morphology of the LGE in HCM and HHD.
- Native T1 and ECV were significantly higher in patients with HCM than in patients with HHD.
- Native T1 values and ECV can both contribute clinically relevant evidence for discrimination between HCM and HHD.
  - ECV had better diagnostic efficacy for distinguishing between these LVH aetiologies.

thank you