

Assessment of Diffuse and Focal Myocardial Fibrosis in Hypertrophic Cardiomyopathy Using Native T1 Mapping, Extracellular Volume, and Late Gadolinium Enhancement

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Abstract:

Background: Hypertrophic cardiomyopathy (HCM) harbors both focal scar and diffuse interstitial fibrosis, which influence risk stratification. Conventional late gadolinium enhancement (LGE) detects macroscopic scar, whereas T1 mapping and extracellular volume (ECV) quantify diffuse fibrosis. This study evaluated the relationship between LGE, T1 mapping, and ECV in HCM. **Methods:** In this cross-sectional analysis, 50 HCM patients underwent 1.5 T cardiac MRI including cine imaging, native and post-contrast T1 mapping, and phase-sensitive LGE sequences. ECV was computed from pre- and post-contrast T1 values adjusted for hematocrit. Segmental native T1, ECV, and LGE presence were recorded across 17 myocardial regions. Associations were tested by Fisher's exact and logistic regression. **Results:** Cohort mean age was 42 ± 12 years (60% male); 56% had LV outflow tract obstruction. Global native T1 ranged 1004–1076 ms and mean ECV 26.7–31.9%. Only the basal anterolateral segment showed a significant LGE–ECV association ($p = 0.024$). Native T1 predicted fibrosis in 13 of 16 segments (OR per ms increase 1.013–1.038, $p < 0.01$), with strongest effect in the mid inferoseptal wall. **Conclusion:** Native T1 mapping and ECV quantification detect diffuse interstitial fibrosis in HCM, complementing LGE's identification of focal scar. They reveal subclinical fibrosis even without LGE, improving risk stratification and supporting more personalized management, with potential value for routine CMR protocols and prognosis.

Keywords: Hypertrophic Cardiomyopathy; T1 Mapping; Extracellular Volume; Late Gadolinium Enhancement; Myocardial Fibrosis.

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Introduction

Hypertrophic cardiomyopathy (HCM) is a common inherited heart disease that affects about 1 in every 200 to 500 people. Although, many HCM patients are asymptomatic and can have normal lives, there is a noticeable risk of sudden cardiac death (SCD) in these patients ⁽¹⁾. Clinical experience has demonstrated the risk of SCD associated with HCM could be significantly reduced with the administration of implantable cardioverter-defibrillators (ICDs); however, despite their proven efficacy, these devices are associated with multiple problems including bleeding, infection, lead dislodgement or malfunction, and inappropriate shocks. Thus, a precise selection criterion should be utilized when choosing HCM patients indicated for ICDs ⁽²⁾.

The ECS guidelines recommended using a risk calculator to estimate the chance of SCD in 5 years, while the ACS/AHA guidelines recommended using a Use 7 key warning signs (biomarkers). One of the seven biomarkers is the late gadolinium enhancement (LGE), which is used in the cardiac MRI technique (CMR) to visualize the fibrosis present in the heart ⁽³⁾.

LGE is a CMR technique that uses a special dye called gadolinium to detect scar tissue (fibrosis) in the heart muscle. HCM is generally associated with thickened cardiac muscles that can further develop into many fibrous tissue and scarring, which eventually can disrupt the electrical activity of the heart, leading to arrhythmias ⁽⁴⁾. It was hypothesized that LGE could help in assessing the severity of HCM via its ability to detect the amount and location of fibrosis in the heart, as it has been proven that more LGE means higher risk of sudden cardiac death, so it's a valuable tool in deciding if a patient might need an ICD. However, LGE was relatively limited due to its inability to detect small or diffuse fibrosis ⁽⁵⁾.

T1 mapping is a newer cardiac MRI technique that gives a quantitative value (a number) for how the heart muscle looks at the microscopic level. Native T1 values are higher in areas with fibrosis, even if not clearly seen on LGE, thus this technique could accurately detect subtle or widespread fibrosis earlier than LGE can ⁽⁶⁾.

The previous two techniques (LGE and T1 mapping) can complement each other when combined to ultimately calculate the value of Extracellular Volume (ECV) Fraction. Therefore, we conducted this cross-sectional study to discuss the clinical application of CMR T1 relaxation in assessing diffuse myocardial fibrosis in HCM patients.

Methodology

This observational cross-sectional study was conducted to evaluate the utility of native and post-contrast cardiac magnetic resonance (CMR) T₁ mapping for non-invasive assessment of diffuse myocardial fibrosis in patients with hypertrophic cardiomyopathy (HCM). 50 patients who underwent CMR between January 2019 and December 2021 were identified from Benha University, Radiology department's PACS database.

The study protocol was approved by the Ethics Committee of Benha University, and informed consent was obtained from all participants prior to their enrollment in the study. Participant confidentiality was strictly maintained throughout the research process. All collected data were securely stored and used solely for scientific purposes, accessible only to the investigators and supervisors directly involved in the study.

Eligibility Criteria

Participants were included if they were patients aged ≥ 8 years with clear, high-quality CMR images including native and post-contrast T1 mapping sequences, demonstrating an HCM phenotype on imaging-defined as unexplained left ventricular hypertrophy. Patients were

excluded if their CMR studies were compromised by poor image quality (due to arrhythmia, motion artifacts, or incomplete sequences) or if they had known alternative cardiac conditions, such as ischemic heart disease, dilated or restrictive cardiomyopathy, or prior myocardial infarction. Patients were also excluded if they were contraindicated to receive gadolinium.

Study Procedure

All Patients were subjected to the following:

A. History and Examination:

- **Complete history taking:** (Complete medical history, family history and social history) was recorded.
- **Clinical data:** presenting symptoms (chest pain, dyspnea, syncope), history of HCM or family screening.

B. CMR Data:

All cardiac MRI scans were performed at Department using a 1.5 Tesla Siemens scanner with ECG gating and breath-hold instructions to minimize motion artifacts. The imaging protocol included cine SSFP sequences for assessing cardiac function, native T1 mapping using a MOLLI sequence, and post-contrast T1 mapping acquired 15 minutes after gadolinium administration. Late gadolinium enhancement (LGE) was performed with phase-sensitive inversion recovery (PSIR) to highlight myocardial fibrosis. Image analysis, including T1 values, ECV calculation, and segmental assessment, was carried out on the PACS system by experienced radiologists, ensuring consistency and high-quality data interpretation.

For each patient, the following data were recorded:

Native T1 values were obtained from mid-ventricular short-axis MOLLI sequences within the normal machine range of 950–1069 ms, while post-contrast T1 values were acquired 15 minutes after administration of 0.2 mmol/kg gadolinium contrast, and extracellular volume (ECV) percentage was calculated by integrating

pre- and post-contrast T1 values with correction for hematocrit. Cardiac structural and functional metrics assessed included maximal left ventricular (LV) wall thickness, segmental hypertrophy patterns, left and right ventricular volumes and ejection fractions, LV mass, and the presence of left ventricular outflow tract (LVOT) obstruction. In addition, late gadolinium enhancement (LGE) patterns were analyzed and correlated with ECV expansion across all 17 myocardial segments.

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Statistical analysis

Statistical analysis was conducted by SPSS v28 (IBM Inc., Armonk, NY, USA). Quantitative variables were reported as mean and standard deviation (SD). Qualitative variables were reported as frequency and percentage (%). Pearson or spearman correlation was done to evaluate the scale of correlation between two quantitative variables. (SPSS Inc., Chicago, Illinois, USA)

Results

This cross-sectional study involved fifty patients diagnosed with HCM. There were 30(60%) males, and 20(40%) females show (**figure 1**), also LVOTO were present in 28(56%) and absent in 22(44%) (**figure 2**).

A full summary description of the results of native T1 mapping within each segment are in (**Table 1**). The mid Inferoseptal segment is the highest segment with native T1 value equal to 1076 ± 45.6 msec (mean $\pm$ SD) and the apical Anterior segment has the lowest native T1 value equal to 1004 ± 91.5 msec (mean $\pm$ SD).

In (**Table 2**) there is a quantitative summary description of the results of extracellular volume percentage (ECV) for each cardiac segment. The basal anteroseptal and mid anteroseptal segments are the highest segments with ECV values equal to 30.5 (18.6, 54.2) median (Minimum, Maximum), 30.5 ± 6.08 (mean $\pm$ SD), respectively. and the

mid Inferolateral segment has the lowest ECV value equal to 25.9 (16.2, 49.5) median (Minimum, Maximum).

We evaluated the association between the ECV and LGE for each cardiac segment. Considering $\geq 30\%$ is the threshold of expansion. The small sample size and two binary variable made fisher exact test is the more suitable than chi-square test to assess these relations. For the basal anterior segment see (Table 3), the

enhancement of LGE was associated with expanded ECV in 12 (44.4%) patients and no expansion in 15 (55.6%) patients, on the other hand, the non-enhancement of LGE was associated with expanded ECV in 4 (17.4%) patients and no expansion in 19 (82.6%). This result is not statistically significant ($P = 0.067$) and shows no significant association, however, there might be a trend to association.

Table 1: Summary of cardiac CMR functions

CMR Functions	Mean	SD	Median	Minimum	Maximum
LV EF	16.8	7.14	18.5	1	28
LV EDV	125	31.4	121	46	199
LV ESV	29.9	17.4	24.5	10	103
LV SV	95.2	22.5	95.5	36	151
LV EDVI	64.5	13.8	61.5	33	115
LV ESVI	15.4	8.16	13	6	46
LV SVI	49.2	10.1	50	26	78
LV Mass	255	98.2	243	82	472
Mass Indexed	131	49.9	118	48	262
RV EF	71.3	9.7	73	35	87
RV EDV	121	29.1	118	42	195
RV ESV	36.4	18.6	32.5	6.2	112
RV SV	85.9	18.8	85	36	139
RV EDVI	62.8	12.8	61	30	98
RV ESVI	18.8	9.45	18	4	64
RV SVI	44.2	8.43	45	26	64
COP	5.92	1.38	5.7	3	9.2
HR	65.3	11.6	66	43	94
Maximum Thickness	25.8	5.47	25	15	38

SD: standard deviation, RV: Right ventricle, LV: left ventricle, EF: ejection fraction, EDV: end-diastolic volume, ESV: end-systolic volume, SV: stroke volume, EDVI: EDV indexed, ESVI: ESV indexed, SVI: SV indexed, COP: Cardiac Output, HR: Heart Rate

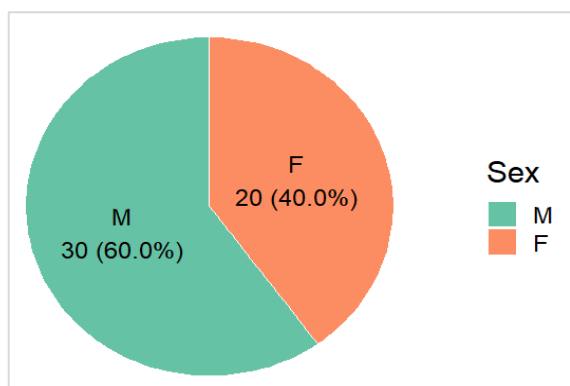


Figure 1: Sex distribution.

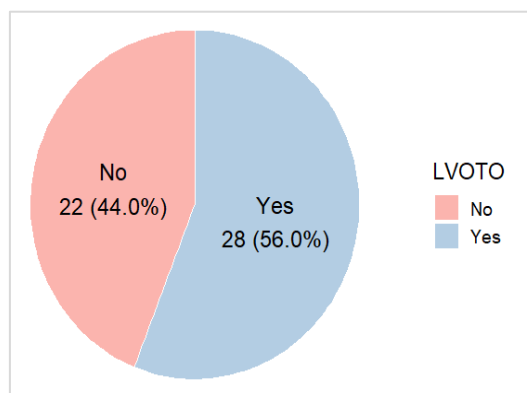


Figure 2: LVOTO distribution.

Table 2: Summary of Native T1 Mapping for each cardiac segment

Native T1 Mapping of cardiac segments	Mean	SD	Median	Minimum	Maximum
T1 basal anterior (msec)	1040	139	1055	130	1160
T1 basal anteroseptal (msec)	1058	137.1	1070	160	1167
T1 basal Inferoseptal (msec)	1067	41.2	1068	991	1144
T1 basal Inferior (msec)	1066	47.4	1065	940	1163
T1 basal Inferolateral (msec)	1075	76.8	1061	920	1325
T1 basal Anterolateral (msec)	1043	61.4	1037	834	1175
T1 mid Anterior (msec)	1043	49.6	1040	914	1151
T1 mid Anteroseptal (msec)	1066	47.4	1060	989	1201
T1 mid Inferoseptal (msec)	1076	45.6	1084	988	1190
T1 mid Inferior (msec)	1062	50.7	1067	951	1178
T1 mid Inferolateral (msec)	1044	73.4	1033	947	1316
T1 mid Anterolateral (msec)	1027	79.9	1029	819	1352
T1 apical Anterior (msec)	1004	91.5	1016	775	1228
T1 apical septal (msec)	1048	68.6	1052	902	1180
T1 apical inferior (msec)	1048	61.1	1045	919	1159
T1 apical lateral (msec)	1015	80.9	1018	776	1150

SD = standard deviation

Table 3: Quantitative summary description of ECV

ECV of cardiac segments	Mean	SD	Median	Minimum	Maximum
ECV basal anterior	28.3	4.69	28.3	17	40.7
ECV basal anteroseptal	31.9	6.53	30.5	18.6	54.2
ECV basal Inferoseptal	30.4	6.08	30	17.6	53.9
ECV basal Inferior	29.7	4.39	28.4	18.5	39.5
ECV basal Inferolateral	28.9	4.95	28.1	20.9	46.1
ECV basal Anterolateral	26.7	4.37	25.7	18.6	39.3
ECV mid Anterior	29	5.38	27.9	18.4	43.5
ECV mid anteroseptal	30.5	6.08	29.6	19.3	47.7
ECV mid Inferoseptal	30.8	6.65	29.6	19.5	54.2
ECV mid Inferior	29.2	6.2	27.9	21.2	48.8
ECV mid Inferolateral	28.1	5.78	25.9	16.2	49.5
ECV mid Anterolateral	27.5	4.77	26.6	17.6	44.1
ECV apical Anterior	29.5	6.29	28.8	14.8	56.2
ECV apical septal	30	4.93	29.7	21.4	44
ECV apical inferior	30.1	7.66	28.3	20.2	60.4
ECV apical lateral	29.7	5.98	28	21.3	55.3

SD = standard deviation, ECV; extra-cellular volume

The methodical analysis of sixteen standardized myocardial segments showed that the expanded extracellular volume (ECV 30 %) was related to late gadolinium enhancement (LGE) in the basal anterolateral segment only. The LGE was significantly more common in patients

with large ECV 60 % and 11.1 % in patients with and without enlarged extracellular space, respectively ($p = 0.024$). There were less dramatic, although still significant, changes in the prevalence of LGE with ECV expansion in basal anterior (44.4 % versus 17.4 %, $p = 0.067$)

and basal inferior (70 % versus 32.5 %, $p = 0.067$) regions. Such a trend was not present in any other basal, mid or apical segment with the p -values of 0.082, 0.081, 0.095, 0.769 respectively. The current results, therefore, indicate that there is a poor and irregular correlation between diffuse fibrosis and focal enhancement in the greater part of the myocardium, with a stronger correlation being left to the basal anterolateral wall. (**Table 4**)

In (**Figure 3**), we described the distribution of the possibilities of patients with associations between the obstruction and the fibrosis at each cardiac segment.

There were four categories: 1) no obstruction and no fibrosis, 2) obstruction and no fibrosis, 3) no obstruction with no fibrosis, 4) obstruction with fibrosis. Most patients had obstruction with no fibrosis and the lowest numbers of patients had no obstruction but with fibrosis. These are just observations, but the results are not statistically significant as shown in.

Table 5 demonstrates the logistic regression analysis between ECV and native T1 in the patients and shows that the mid inferoseptal segment had the highest significant odds ratio between the 13 statistically significant segments.

Table 4: Association between ECV and LVE at different segments

Segment	Enhancing with Expanded $\geq 30\%$	Enhancing without Expanded $< 30\%$	Non-Enhancing with Expanded $\geq 30\%$	Non-Enhancing without Expanded $< 30\%$	p-value
Basal anterior	12 (44.4%)	15 (55.6%)	4 (17.4%)	19 (82.6%)	0.067
Basal anteroseptal	19 (63.3%)	11 (36.7%)	10 (50%)	10 (50%)	0.393
Basal inferoseptal	16 (53.3%)	14 (46.7%)	10 (50%)	10 (50%)	1
Basal inferior	7 (70%)	3 (30%)	13 (32.5%)	27 (67.5%)	0.067
Basal inferolateral	3 (60%)	2 (40%)	9 (20%)	36 (80%)	0.082
Basal anterolateral	3 (60%)	2 (40%)	5 (11.1%)	40 (88.9%)	0.024*
Mid anterior	7 (43.8%)	9 (56.2%)	11 (32.4%)	23 (67.6%)	0.532
Mid anteroseptal	12 (52.2%)	11 (47.8%)	12 (44.4%)	15 (55.6%)	0.777
Mid inferoseptal	12 (48%)	13 (52%)	11 (44%)	14 (56%)	1
Mid inferior	7 (38.9%)	11 (61.1%)	9 (28.1%)	23 (71.9%)	0.532
Mid inferolateral	3 (27.3%)	8 (72.7%)	9 (23.1%)	30 (76.9%)	1
Mid anterolateral	4 (50%)	4 (50%)	9 (21.4%)	33 (78.6%)	0.181
Apical anterior	4 (57.1%)	3 (42.9%)	16 (37.2%)	27 (62.8%)	0.416
Apical septal	5 (45.5%)	6 (54.5%)	17 (43.6%)	22 (56.4%)	1
Apical inferior	4 (36.4%)	7 (63.6%)	14 (35.9%)	25 (64.1%)	1
Apical lateral	1 (20%)	4 (80%)	16 (35.6%)	29 (64.4%)	0.65

ECV = extracellular volume fraction; LGE = late gadolinium enhancement. "Expanded" denotes $ECV \geq 30\%$; "Not expanded" denotes $ECV < 30\%$. p -values derived from Fisher's exact test; values ≤ 0.05 indicate statistical significance. Percentages refer to the row-specific proportion within each segment.

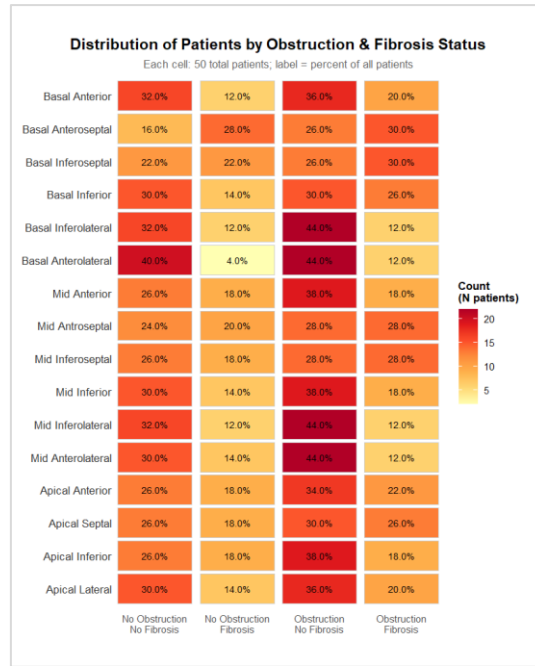


Figure 3: Heat map between LVOTO and fibrosis ($ECV \geq 30$) at each cardiac segment.

Table 5: Summary of logistic regression between ECV and native T1

cardiac segments	Odds Ratio	95% CI	P-value
Basal Anterior	0.999	(0.993-1.004)	0.5690
Basal Anteroseptal	1	(0.995-1.005)	0.9430
Basal infer septal	1.025	(1.010-1.044)	0.0033
Basal Inferior	1.028	(1.012-1.049)	0.0019
Basal Inferolateral	1.019	(1.008-1.036)	0.0058
Basal Anterolateral	1.016	(1.002-1.032)	0.0341
Mid Anterior	1.006	(0.994-1.020)	0.3160
Mid Anteroseptal	1.028	(1.012-1.050)	0.0032
Mid Infer septal	1.038	(1.019-1.064)	0.0007
Mid Inferior	1.028	(1.012-1.050)	0.0021
Mid Inferolateral	1.025	(1.011-1.046)	0.0033
Mid Anterolateral	1.018	(1.006-1.034)	0.0148
Apical Anterior	1.013	(1.005-1.024)	0.0067
Apical Septal	1.014	(1.005-1.027)	0.0085
Apical Inferior	1.03	(1.015-1.049)	0.0004
Apical Lateral	1.01	(1.001-1.020)	0.0456

Non-significant: $P > 0.05$, Significant: $P \leq 0.05$

Case Presentation

Case [1]

History:

An 85-years old male patient, diagnosed as HCM, Echocardiography showed $EF=60\%$, asymmetrical hypertrophy of septal and inferior walls patient, diagnosed as

HCM, Echocardiography

showed $EF=60\%$, asymmetrical hypertrophy of septal and inferior walls

CMRI findings:

- Shows asymmetrical wall hypertrophy at anterior septal and inferior walls with maximum wall thickness seen at the basal anteroseptal segment measuring about 25mm.

- Preserved systolic function EF=57 %.
- Hypokinesia of the hypertrophied septal walls.
- End-diastolic LV mass =211gm.
- Indexed LV mass = 123 gm/m².
- There is no mid cavity obliteration.
- Mild chordal SAM.
- Peak systolic velocity at the LVOT is 2 m/sec.

Delayed gadolinium enhancement:

- Focal patchy enhancement is seen at mid insertion points as well as subendocardial enhancement of the basal segment of the septum No microvascular obstruction (MVO) is noted or ventricular thrombus

Case [2]

History: A 21-year-old male known to have HCM.

CMRI findings:

- Asymmetrical left ventricular hypertrophy involving basal and midventricular septal wall with maximal thickness of basal antroseptal and mid-ventricular inferoseptal wall measuring 24 mm.
- Average LV volumes with preserved systolic function with EF 80%.
- **No Mid cavity** obliteration is noted.
- **SAM** of anterior mitral leaflet with severe mitral valve regurgitation , eccentric posteriorly directed jet
- **LVOT** obstruction with peak systolic (velocity 2.5 cm/sec underestimation by cardiac MRI is noted).
- No wall motion abnormality.

***Left ventricle**

mass 293 gm.

****LV**

mass index is 152 gm/m².

Delayed gadolinium enhancement:

- Inferior insertion point fibrosis
- Scar quantification 10% by EWA method

Case 3

History:

- An 18-year-old male patient diagnosed as non-obstructive HCM with significant family history.

CMRI findings:

- Asymmetrical left ventricular hypertrophy involving the basal and mid antroseptal wall the maximum thickness =20 mm.
- Preserved systolic function with EF 74%.
- No resting wall motion abnormality.
- No evidence of systolic anterior motion (SAM) neither LVOT obstruction maximum LVOT velocity at rest (1.5m/sec).
- Left ventricle mass=153 gm. LV mass index= 83 gm /m²

Early and delayed gadolinium enhancement:

- Sandy myocardial patches are seen involving the basal and mid-ventricular septal walls.
- Non-significant fibrosis of insertion points
- No ventricular thrombus is noted or MVO.

Case [4]

History:

A 32-year-old male patient, known to have Hypertrophic obstructive cardiomyopathy referred for assessment of burden of myocardial fibrosis.

CMRI findings:

Asymmetrical

LV myocardial hypertrophy which involving:

- Basal anterior and septal walls, all mid ventricular segments, and apical inferior and lateral walls.
- Maximum wall thickness = 38 mm, seen at the anterior basal wall.
- Indexed LV wall mass measured about 159 gm/m²
- ❖ Resting wall motion abnormalities is seen as hypokinesia of most of hypertrophied segments with preserved systolic function, EF = 73%.
- ❖ **SAM** of anterior mitral leaflet and the corresponding chordae
- ❖ Flow acceleration jet at the LVOT with maximum systolic velocity **across LVOT = 3m/sec.**

Early and delayed gadolinium enhancement:

- No microvascular obstruction (MVO) is noted or ventricular thrombi.
- Patchy myocardial enhancement involving hypertrophied segments mainly basal anterior mid septal wall and mid inferior wall

Case 5

History:

An 8-year-old male child patient recently diagnosed as Hypertrophic cardiomyopathy, he had significant positive family history, and he referred for assessment of ventricular volumes, functions and assessment of fibrosis.

CMRI findings:

- Asymmetrically hypertrophied myocardium involving
- Basal and mid antero-infero septal walls, anterior wall
- Mid inferolateral and inferior walls.
- All apical segments apart from lateral wall
- Maximum thickness = 33 mm at basal and mid-ventricular septal walls.
- LV mass 266 gm (Indexed 258 gm/m²).
- Preserved systolic function with EF 79%.
- Systolic anterior motion (SAM) of the anterior mitral leaflet and corresponding chorda with maximum velocity at rest of LVOT=2.5 m/sec.
- Mid-cavitary obliteration during systole (kissing septum).
- **Mild hypokinesia of hypertrophied segments.**

Early and delayed gadolinium enhancement:

- Sandy like scattered mid-myocardial fibrosis involving almost all hypertrophied segments.
- No ventricular thrombus is noted or MVO.

Case [6]

History:

- **A 63-year-old female, known with HCM. Diabetic and hypertensive, diagnosed as HCM.**

CMRI findings:

- Shows non-uniform hypertrophied myocardial segments, detected at the antero-septal segment at the basal level, measuring 1.8 cm (with ratio of antero-septal to infero-lateral segment 1.8 and 0.7 cm, ratio=2.5).
- Focal hypertrophy in basal anterior segment =15 mm, and mid inferoseptal segment =15 mm is noted
- The rest of LV walls thickness ranging from 7.0 to 11 mm
- There is no mid cavity obliteration.
- Mild chordal **SAM** is noted with peak systolic velocity at the LVOT is 2.5 m/sec.
- Good systolic function with calculated EF=75%.
- No resting wall motion abnormalities is noted.

Delayed gadolinium enhancement: No LGE.

Discussion

This was a cross-sectional study conducted on 50 patients diagnosed with HCM, 30 males (60%) and 20 females (40%), while Left Ventricular Outflow Tract Obstruction (LVOTO) was present in 28 (56%) and absent in 22 (44%).

In according with our baseline demographics, Ho et al.⁽⁷⁾ performed a cross-sectional CMR study on 77 patients with HCM, and 11 healthy controls. 32% were female, demonstrating a slight male predominance similar to many HCM cohorts.

Similarly, Brouwer et al.⁽⁸⁾ enrolled 20 HCM patients (80% male) against 14 age and sex matched healthy controls (57% male).

Dass et al.⁽⁹⁾ was a cross sectional CMR study that enrolled a total of 28 patients with HCM, of whom 18 were male (64 %) and 10 female (36 %), alongside 12 healthy controls. Furthermore, LVOTO

was present in 14 patients (50%) and absent in 14 patients (50%).

Additionally, Li et al.⁽¹⁰⁾ was a prospective prognostic CMR study that enrolled 263 consecutive patients with HCM, referred for contrast-enhanced CMR between September 2013 and December 2017. After excluding 20 patients for missing or poor-quality T1 mapping, 243 patients remained (125 males 51.4 %) and (118 females 48.6 %). Obstructive HCM (LV outflow tract obstruction) was present in 110 patients (45.3 %) and absent in 133 (54.7 %).

Similarly, Wang et al.⁽¹¹⁾ was a single center prospective CMR cohort study that enrolled 885 consecutive adult patients with HCM, undergoing contrast enhanced MRI between September 2013 and December 2021. After excluding 137 for inadequate image quality or missing data, 748 participants remained; 454 males [60.7 %] and 294 females [39.3 %]. Left ventricular outflow tract obstruction (LVOTO) was present in 308 patients (41.2 %) and absent in 440 (58.8 %).

Our analysis of the cardiac function-related parameters with CMR revealed that the patients had Severely reduced LV function (median EF ~18.5%) with marked hypertrophy (max thickness ~26 mm). On the other hand, the other parameters including EDV, ESV, SV, LV mass, RVEF, COP and HR did not differ significantly from the normal range.

This is consistent with Brouwer et al,⁽⁸⁾ which reported that the LV mass was elevated in HCM patients (83 ± 37 g/m²) with maximal wall thickness of 18 ± 3 mm; however, despite the hypertrophy global LV function remained preserved, reflecting in the process typical phenotype of manifest HCM.

In accordance with our findings, Dass et al.⁽⁹⁾ demonstrated that left ventricular mass index was elevated in HCM (85 ± 33 g/m²), with an elevated EDV index of 62 ± 21 mL/m² and an ESV index of 17 ± 6 mL/m². On the other hand, evaluation of LVEF revealed that the

HCM cohort in this study demonstrated a preserved ejection fraction (LVEF 74 ± 5 %).

Xu et al.⁽¹²⁾ reported that LV mass index was elevated at 63.8 ± 22.8 g/m², while the indexed LV volumes were within normal limits.

Our analysis utilizing the technique of Native T1 Mapping demonstrated that elevated T1 values (Mean segmental T1 1004–1076 ms, SD 41–92 ms) indicating diffuse interstitial changes, with the highest focal elevation in infero-septal wall (1076 ± 45.6 ms) and the lowest at apical anterior wall (1004 ± 91.5 ms).

In accordance, Ho et al.⁽⁷⁾ reported that the pre-contrast native T1 times averaged approximately 1087 ± 81 ms across the 16 myocardial segments in the HCM group, compared with lower values in controls.

In Dass et al.⁽⁹⁾ it was revealed by native T1 mapping that HCM patients had a global mean myocardial T1 relaxation time of 1209 ± 28 ms, which was elevated compared to healthy controls (1178 ± 13 ms; $P < 0.05$).

Li et al.⁽¹⁰⁾ demonstrated that native T1 mapping gave a global myocardial relaxation time of 1281 ± 69.3 ms across the cohort with patients who subsequently experienced adverse events having higher baseline native T1 (1316.6 ± 112.5 ms) compared with those without events (1278.4 ± 64.6 ms).

Similarly, Qin et al.⁽¹³⁾ reported Global native T1 mapping values were significantly elevated in HCM patients compared to controls ($1,308.0 \pm 55.5$ ms vs. $1,240.0 \pm 29.8$ ms; $P < 0.001$), with segmental analysis showing that maximal native T1 reached $1,393.4 \pm 140.4$ ms and minimum native T1 averaged $1,231.5 \pm 70.9$ ms in HCM.

Wang et al.⁽¹¹⁾ demonstrated that the native T1 mapping yielded a global myocardial T1 relaxation time of 1332.9 ± 72.0 ms across the cohort, reflecting diffuse myocardial tissue characteristics but without segmental breakdown.

Interestingly, Brouwer et al.⁽⁸⁾ revealed that by using a MOLLI sequence at mid ventricular level, native T1 mapping did not demonstrate significant differences between HCM patients (LGE negative regions) and healthy controls, indicating similar tissue characteristics where focal scar was absent.

In our findings, the ECV distribution values confirmed diffuse fibrosis (Mean 26.7–31.9%), with a particular focus on the basal antero-septal wall ($31.9 \pm 6.53\%$), while the lowest was the infero-lateral wall ($28.1 \pm 5.78\%$).

In Brouwer et al.,⁽⁸⁾ it was demonstrated that ECV myocardium averaged 0.26 ± 0.03 in HCM patients and 0.26 ± 0.02 in controls ($P=0.83$) with subgroup analysis showing no difference between LGE positive (0.27 ± 0.03) and LGE negative patients (0.25 ± 0.03), nor between either group or controls.

Li et al.⁽¹⁰⁾ reported that Mean extracellular volume fraction across all 243 patients was $30.0 \pm 6.0\%$, however, segmental or regional ECV values were not separately reported.

In accordance, Qin et al.⁽¹³⁾ reported that ECV was significantly higher in HCM patients than in controls ($29.6 \pm 6.0\%$ vs. $25.4 \pm 2.0\%$; $P < 0.001$), with segmental ECV values ranging from a minimum of $24.2 \pm 3.5\%$ to a maximum of $36.4 \pm 9.6\%$ and increased global ECV ($>29.4\%$) presenting in 81 patients (39.9%).

In contrast, Wang et al.⁽¹¹⁾ reported that ECV for the entire group was $29.5 \pm 4.7\%$, indicating a modest degree of diffuse interstitial expansion.

ECV in Xu et al.⁽¹²⁾ was elevated in the HCM cohort, with a mean ECV of $24.5 \pm 2.8\%$, a minimum segmental ECV of $22.2 \pm 2.9\%$, and a maximum segmental ECV of $27.3 \pm 2.8\%$ and segmental analysis mirrored T1 distribution, showing focal ECV increases in the same hypertrophied regions.

Furthermore, our analysis reported that the association between LGE and ECV was

statistically significant only in the detection of fibrosis at the Basal anterolateral wall, where LGE⁺ had 60% fibrosis vs. 11.1% when LGE ($P = 0.024$). Other segments including the basal anterior, inferior, inferolateral walls showed only trends of associations ($P \approx 0.067$ – 0.082), but it failed to reach statistical significance, indicating weak or no concordance, suggesting complementary roles.

Brouwer et al.⁽⁸⁾ reported that within LGE positive patients, regions stratified by signal intensity (SI $< 20\%$, 20 – 50% , $> 50\%$ of maximal SI) exhibited stepwise ECV increases: 0.27 ± 0.03 (SI $< 20\%$), 0.35 ± 0.06 (SI 20 – 50%), and 0.45 ± 0.11 (SI $> 50\%$), with all pairwise comparisons statistically significant. This confirms that T1 derived ECV corresponds well to the gradations of focal fibrosis seen on LGE.

Additionally, Dass et al.⁽⁹⁾ demonstrated that the relationship between LGE and T1 values was statistically significant when assessed across myocardial segments, with a moderate correlation ($r = 0.35$, $P < 0.0001$); however, because ECV was not measured, no direct comparison between LGE and ECV could be made.

In consistent with our findings, Qin et al.⁽¹³⁾ reported that significant correlations were observed between LGE extent and both global native T1 ($r = 0.448$; $P < 0.001$) and ECV ($r = 0.684$; $P < 0.001$). Moreover, LGE/LV mass $\geq 15\%$ was also significantly correlated with global native T1 ($r_s = 0.538$) and global ECV ($r_s = 0.608$), indicating concordance between diffuse and focal fibrosis measures.

We conducted regression analysis to detect associations between fibrosis (ECV $\geq 30\%$) and LVOTO, however no segment showed a statistically significant association, indicating in the process that hemodynamic obstruction is independent of measured diffuse fibrosis by ECV.

This is consistent with Brouwer et al.,⁽⁸⁾ that reported that Segmental ECV analysis in LGE negative myocardium revealed no

significant segment to segment differences in HCM (ANOVA $P=0.63$) or between HCM segments and controls.

Additionally, Li et al.⁽¹⁰⁾ demonstrated that LVOTO showed no significant correlation with global native T1 ($r=-0.002$, $P=0.980$) and only weak correlation with global ECV ($r=-0.151$, $P=0.032$). Furthermore, LVOT pressure gradient was not identified as a significant predictor in Cox regression models, suggesting that hemodynamic obstruction is not independently associated with diffuse fibrosis.

Another study conducted by tondi et al.,⁽¹⁴⁾ revealed that dividing HCM patients by presence of increased extracellular volume ($r\text{-ECV} \geq 29\%$) found no significant differences between groups in terms of LVOTO ($p > 0.05$), suggesting diffuse fibrosis measured by ECV is not associated with LVOTO severity.

Ultimately, our analysis demonstrated that Native T1 is a robust predictor of fibrosis in 13 of 16 segments (all but basal anterior, basal anteroseptal, mid anterior), with strongest effect in mid infero-septal (OR 1.038).

Dass et al.,⁽⁹⁾ concluded in their study that segmental T1 elevation reliably distinguished fibrotic (LGE⁺) from nonfibrotic regions⁽⁹⁾.

Similarly, Li et al.,⁽¹⁰⁾ reported that elevated native T1 was associated with higher event rates, the study did not perform segmental logistic regression to determine odds ratios for native T1 as a predictor of underlying myocardial fibrosis.

Moreover, Qin et al.,⁽¹³⁾ demonstrated that Native T1 mapping was found to be a strong and independent predictor of adverse outcomes. In multivariate Cox regression, global native T1 was associated with a higher risk of major adverse cardiovascular events (HR = 1.446, 95 % CI: 1.195–1.749, $P < 0.001$). Specifically, in patients classified as low-risk by both ESC and ACC/AHA guidelines, native T1 retained

independent predictive power (HR = 1.532, $P < 0.001$).

In accordance, Kato et al.,⁽¹⁵⁾ found significant elevation of native T1 time in 15 of 16 myocardial segments in HCM patients compared to controls, with regional heterogeneity, with elevated native T1 was present even in LGE-negative segments, indicating diffuse fibrosis not captured by LGE.

The findings of this study confirm the increasingly central role of high-resolution cardiac magnetic resonance (HRMR) technologies in risk stratification and clinical management of patients with HCM. LGE has been a major imaging criterion in the identification of focal myocardial fibrosis, which has helped in determining the subjects at increased risk of SCD as well as the indication of implantable ICDs⁽¹⁶⁾.

However, the inherent low sensitivity of LGE, especially of diffuse or microscopic fibrosis, highlights the need of more comprehensive evaluation tools. The native T1 mapping and ECV quantification provides a more detailed evaluation of the myocardial tissue composition, which can identify early or diffuse fibrotic alterations that could be missed by LGE⁽¹⁷⁾.

This feature is particularly relevant to patients with low or intermediate risk by traditional criteria but with a high fibrotic load. Our data along with the results of the modern studies show that high native T1 and high ECV values are always associated with fibrosis and poor cardiovascular outcomes. The lack of correlation between diffuse fibrosis and LVOTO also indicates the different pathophysiological processes⁽¹⁸⁾.

Therefore, the use of T1-based imaging in the regular assessment of HCM may help to better individualize risk assessment and optimize ICD implantation approaches, which would lead to better patient outcomes and reduce the number of unnecessary device-related complications⁽¹⁹⁾.

Conclusion

Native T1 mapping and extracellular volume reliably detect diffuse fibrosis in hypertrophic cardiomyopathy and correlate segmentally with late gadolinium enhancement, highlighting their complementary roles for comprehensive myocardial tissue characterization.

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