ANALYSIS OF STRAIN PARAMETERS IN PATIENTS WITH HYPERTROPHIC CARDIOMYOPATHY BY CARDIOVASCULAR MAGNETIC RESONANCE FEATURE TRACKING

Dr. Vimal Chacko Mondy

DM CARDIOVASCULAR IMAGING AND VASCULAR INTERVENTIONAL RADIOLOGY

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A THESIS SUBMITTED BY

Dr. Vimal Chacko Mondy

TO

SREE CHITRA TIRUNAL INSTITUTE FOR MEDICAL SCIENCES AND TECHNOLOGY, TRIVANDRUM.

IN PARTIAL FULFILMENT OF THE REQUIREMENTS

FOR THE AWARD OF

DM CARDIOVASCULAR IMAGING AND VASCULAR INTERVENTIONAL RADIOLOGY

2020-2022

DECLARATION BY THE STUDENT

CERTIFICATE

I, **Dr. Vimal Chacko Mondy**, hereby certify that I had personally carried out the work depicted in the thesis titled, **"Analysis of Strain parameters in patients with Hypertrophic cardiomyopathy by Cardiovascular Magnetic Resonance Feature Tracking"**.

No part of this thesis has been submitted for the award of any other degree or diploma prior to this date.

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The thesis entitled, **"Analysis of Strain parameters in patients with Hypertrophic cardiomyopathy by Cardiovascular Magnetic Resonance Feature Tracking"** was carried out under my direct supervision. No part of the thesis was submitted for the award of any degree or diploma prior to this date.

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APPROVAL OF THE THESIS

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TABLE OF CONTENTS

LIST OF FIGURES

LIST OF TABLES

LIST OF ABBREVIATIONS (Optional)

S No	Abbreviation	Full Form
1	HCM	Hypertrophic cardiomyopathy
2	LV	Left ventricular
3	LVEF	Left ventricular ejection fraction
4	STE	Speckle tracking echocardiography
5	CMR	Cardiovascular magnetic resonance
6	CMR-FT	CMR- derived myocardial feature tracking
7	bSSFP	balanced steady-state free precession
8	LVH	Left ventricular hypertrophy
9	CT	Computed tomography
10	ECG	Electrocardiogram
11	LVOTO	Left ventricular outflow tract obstruction
12	MR	Mitral regurgitation
13	SCD	Sudden cardiac death
14	ICD	Implantable cardioverter-defibrillator
15	RV	Right ventricular
16	PVM	Phase velocity mapping
17	DENSE	Displacement encoding with stimulated echoes
18	SENC	Strain-encoded
19	CSPAMM	Complementary spatial modulation of magnetization

20	SNR	Signal-to-noise ratio
21	LGE	Late gadolinium enhancement
22	VAs	Ventricular arrhythmias
23	SCS	Segmental circumferential strain
24	NSVT	Non-sustained ventricular tachycardia
25	shMOLLI	Shortened modified Look-Locker inversion recovery
26	PSIR	Phase-sensitive inversion recovery
27	PACS	Picture archiving and communication system
28	LAD-AP	Left atrial anteroposterior diameter
29	RVEF	Right ventricular ejection fraction
30	LVEDVI	Indexed left ventricular end-diastolic volume
31	LVESVI	Indexed left ventricular end-systolic volume
32	SVI	Indexed stroke volume
33	LVMI	Indexed LV myocardial mass
34	%LGE	Percentage extent of LGE
35	SWT	Segmental LV wall thickness

SYNOPSIS

ANALYSIS OF STRAIN PARAMETERS IN PATIENTS WITH HYPERTROPHIC CARDIOMYOPATHY BY CARDIOVASCULAR MAGNETIC RESONANCE FEATURE TRACKING

SYNOPSIS

BY

Dr. Vimal Chacko Mondy

for **DM Cardiovascular Imaging and Vascular Interventional Radiology** Degree

of

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SYNOPSIS

Title

Analysis of Strain parameters in Patients with Hypertrophic Cardiomyopathy by Cardiovascular Magnetic Resonance Feature Tracking

Aim and objectives

1. To analyse global myocardial mechanics using strain parameters in Hypertrophic Cardiomyopathy (HCM) by Cardiovascular Magnetic Resonance Feature Tracking (CMR-FT)
2. To evaluate the association of left ventricular strain parameters with the extent of left ventricular hypertrophy (LVH), the amount of left ventricular fibrosis, and clinical events.

Methods and Materials

A single centre cross-sectional study was performed on 81 HCM patients and 31 controls after obtaining informed consent. All subjects underwent CMR evaluation which included strain analysis using CMR-FT in addition to standard CMR protocol. The various CMR functional and morphological parameters in HCM patients were analysed and compared to controls. Native T1 values, late gadolinium enhancement, and global and segmental strain parameters were evaluated.

Results:

The peak GCS, GRS, and GLS in patients with HCM were significantly worse ($P<0.001$ for all) despite a preserved LVEF. All three global strain parameters were significantly lower ($p < 0.05$) in HCM patients with LGE compared to those without LGE and in HCM patients with LGE extent >15% compared to those with LGE extent <15%. GCS ($p = 0.007$) was determined to be a marker of NSVT on multivariate logistic regression analysis and it was an excellent test to identify HCM patients [AUC 0.98, 95% CI (0.98, 1.00), $p < 0.001$] with NSVT. HCM patients with GCS cut-off of >-12.7% on CMR were more frequently had NSVT. A significant correlation was observed between GCS and MWT ($r = 0.47$, $p < 0.001$), between GCS and %LGE ($r = 0.48$, $p < 0.001$) and between GCS and native T1 ($r = 0.76$, $p < 0.001$). The SCS in HCM patients was significantly worse compared to that in controls ($p < 0.001$). The SCS of HCM patients with NSVT was also significantly worse compared to the SCS of HCM patients without NSVT. SCS was identified as a marker for NSVT ($p < 0.001$) in patients with HCM in univariate logistic regression analysis. There was a moderate positive significant correlation between SCS and segmental LV wall thickness ($r = 0.41$, $p < 0.001$), SCS and segmental native T1 ($r = 0.42$, $p < 0.001$) and between SCS and segmental LGE ($r = 0.55$, $p < 0.001$). ROC curve analysis identified SCS [AUC 0.86, 95% CI (0.84, 0.88), $p < 0.001$] to be a very good test to identify the presence of LGE within the corresponding segment with an optimal cut-off value of >-15.85% to identify the presence of segmental LGE.

Conclusion:

CMR-FT derived strain parameters, especially GCS and SCS, can be used as surrogate markers of disease severity in HCM, with the potential to identify those patients at high risk for major adverse cardiovascular outcomes. This is particularly advantageous, considering that strain analysis using the CMR-FT technique can be performed on routinely acquired CMR cine imaging without the need for intravenous contrast administration and with high technical feasibility and reproducibility. Thus, strain parameters can be easily incorporated into routine CMR protocols, and serve as an important tool in the evaluation of pathophysiology and progression of HCM.

1 INTRODUCTION

Hypertrophic cardiomyopathy (HCM) is the most common genetic cardiomyopathy, characterized by inappropriate left ventricular (LV) hypertrophy, typically asymmetric and involving the septum. The accumulation of myocardial fibrosis, dysmorphic myocytes, and disarray of fibres are the fundamental histological substrate in the pathophysiology of this condition.(1–5) Contractile function of cardiac myocytes is impaired because of these structural abnormalities, despite apparently normal or even supernormal global systolic function based on conventional LV ejection fraction (LVEF).

LV deformation myocardial mechanics studied utilising speckle tracking echocardiography (STE) have demonstrated superior diagnostic performance than LVEF to detect regional and global myocardial dysfunction in patients with HCM and to be an independent predictor of poor cardiovascular events.(6–10) LV myocardial hypertrophy and fibrosis have been postulated to be the main factors of impaired myocardial mechanics in HCM. Cardiovascular magnetic resonance (CMR) has gained an established position in the management of HCM due to its ability to provide a detailed morphological and functional assessment of cardiac chambers and quantification of regional myocardial fibrosis within the same examination. CMR-derived myocardial feature tracking (CMR-FT), a technique analogous to STI echocardiography, derives similar quantitative deformation parameters from conventional balanced steady-state free precession (bSSFP) cine sequences with inherently better image quality(11) In recent years CMR-FT has been validated and

allowed for in-depth study of cardiomyopathies offering incremental prognostic information.(12–16) This study aims to characterize LV global mechanics in HCM using CMR-FT, and to analyse their association with the amount of LV fibrosis and the extent of LV hypertrophy (LVH).

Aims and objectives

1. To analyse global myocardial mechanics using strain parameters in HCM by CMR-FT
2. To evaluate the association of left ventricular strain parameters with the extent of LVH, the amount of left ventricular fibrosis, and clinical events.

Null hypothesis

There is no difference in the strain parameters in patients with HCM and healthy volunteers by CMR-FT and no association between left ventricular strain parameters with the extent of LVH, the amount of left ventricular fibrosis, and ventricular arrhythmias in patients with HCM.

Alternate hypothesis

There is a significant difference in the strain parameters in patients with HCM and healthy volunteers by CMR-FT with a significant correlation between left ventricular strain parameters with the extent of LVH, the amount of left ventricular fibrosis, and ventricular arrhythmias in patients with HCM.

2 LITERATURE REVIEW

Epidemiology

Hypertrophic cardiomyopathy (HCM) is the most common inherited cardiomyopathy. Variable prevalence rates have been reported ranging from 1:500 (0.2%) to 1:3,000 (0.03%) attributable to heterogeneity in study designs and cohort characteristics.(17–19) The advent of advanced in the diagnosis of cardiomyopathies, including advanced diagnostic imaging, widespread genetic testing, and a high index of suspicion and recognition of clinically apparent and gene-positive phenotype-negative disease have resulted in increased detection of this condition. The prevalence of HCM in the general population is now thought to be more common than previously estimated figures.(20) The estimated prevalence of HCM in India is 2.4 million patients, considering the modest worldwide prevalence of 1:500. However, this heterogeneous disease has been side-lined by the vast numbers of atherosclerotic cardiovascular and valvular heart disease burden in India.(21) This has resulted in suboptimal management of this potentially life-threatening condition, often with no discussion on intervention, risk stratification of sudden cardiac death, and family screening.(22)

Clinical definition

The 2020 AHA/ACC Guideline for the Diagnosis and Treatment of Patients With Hypertrophic Cardiomyopathy defines HCM as a disease state which is expressed solely in the heart, the predominant phenotype being left ventricular

hypertrophy in the absence of another cardiac, systemic, or metabolic disease capable of producing the magnitude of hypertrophy evident in a given patient and for which a disease-causing sarcomere (or sarcomere-related) variant is identified, or genetic etiology remains unresolved.(23) Diagnosis of HCM in adults can be established by imaging, 2D echocardiography, or CMR, showing a maximal end-diastolic wall thickness of ≥15 mm anywhere in the left ventricle, in the absence of another cause of hypertrophy. A diagnosis of HCM can also be made when limited hypertrophy (13–14 mm) is present in family members of a patient with HCM or conjunction with a positive genetic test.(23) The 2014 ESC Guidelines on diagnosis and management of hypertrophic cardiomyopathy also define a similar diagnostic criterion for HCM in adults - wall thickness ≥15 mm in one or more LV myocardial segments as measured by any imaging technique (echocardiography, CMR, or computed tomography (CT)), that is not explained solely by loading conditions. Additional features including family history, non-cardiac symptoms and signs, electrocardiogram (ECG) abnormalities, laboratory tests, and multi-modality cardiac imaging is required for the diagnosis of HCM in genetic and non-genetic disorders that present with lesser degrees of wall thickening (13–14 mm).(24)

Etiology

Up to 60% of adults with HCM have mutations in genes encoding cardiac sarcomere proteins with an autosomal dominant inheritance pattern.(25–27) The most common genes affected those encoding beta-myosin heavy chain (MYH7) and myosin-binding protein C (MYBPC3), whereas other genes, namely cardiac troponin I and T (TNNI3, TNNT2), tropomyosin alpha-1 chain (TPM1) and myosin light chain 3 (MYL3), are less commonly affected.(23,24) No evidence of a genetic

etiology is found in a significant number of patients with HCM, including patients with no other family members with HCM ("non-familial" HCM), suggesting that other mechanisms may be responsible for disease expression.(28) Mechanisms by which sarcomeric mutations could cause HCM phenotype include triggering myocardial changes, leading to hypertrophy and fibrosis, and a small, stiff ventricle with impaired systolic and diastolic function despite a preserved LVEF. Dynamic left ventricular outflow tract obstruction (LVOTO), mitral regurgitation (MR), diastolic dysfunction, myocardial ischemia, arrhythmias, and autonomic dysfunction are the major pathophysiologic mechanisms underlying the clinical manifestation of HCM.(23) The clinical outcome may be dominated by any one of these components or its combination.

Natural History and Clinical Course

Most patients with HCM have a normal life expectancy without significant symptoms or requiring major treatments. However, some patients especially those with pathogenic sarcomeric mutations and those with an early diagnosis have a lifelong risk of adverse events including sudden cardiac death (SCD), progressive limiting symptoms due to LVOTO or diastolic dysfunction, heart failure with associated systolic dysfunction, ventricular arrhythmia, and atrial fibrillation with risk of thromboembolic stroke. Modern cardiovascular therapies and interventions have significantly lowered HCM mortality rates to < 1.0%/year.(29,30) SCD risk stratification strategies have been developed based on non-invasive risk markers which can identify patients with the greatest risk for sudden death who benefit from implantable cardioverter-defibrillator (ICD) placement.

Sudden cardiac death risk assessment and prevention

HCM is a common cause of SCD in young people, who are at a higher risk for SCD than older patients.(31,32) Identification of major clinical risk markers and thereby stratifying patients, who may be candidates for SCD prevention with ICDs, according to the level of risk have been the focus of many studies. This strategy has substantially reduced disease-related mortality rates.(33)

The conventional non-invasive SCD risk markers used to estimate increased risk levels are based on personal and family history, non-invasive testing including echocardiography, ambulatory electrocardiographic monitoring, and CMR imaging.(23)

HCM patients with ≥1 major risk marker, in addition to clinical judgment and shared decision-making, are considered potential candidates for primary prevention ICDs.(31,32) A 5-year sudden death risk can be estimated by incorporating several disease-related features into a logistic regression equation(34), however, this risk calculator does not include contemporary SCD risk markers, including LV apical aneurysm, LGE, and systolic dysfunction (EF <50%).

Role of CMR Imaging

CMR imaging provides high spatial resolution and fully tomographic imaging of the heart, including assessment of myocardial fibrosis after intravenous administration of contrast with LGE.(35,36) CMR imaging is well suited for characterizing the various phenotypic expressions of HCM. It plays a role in the diagnosis, risk prediction, and preprocedural planning for septal reduction, and is thus considered an important complementary imaging technique in the evaluation of

patients with HCM. CMR imaging provides highly accurate LV wall thickness measurements, accurate quantification of LV and right ventricular (RV) chamber size, LV mass, and systolic function, due to its sharp contrast between the blood pool and myocardium.(37) It can also identify areas of LVH confined to certain regions of the LV wall, including the anterolateral wall, posterior septum, and apex, which is not well visualized by echocardiography.(38) Other morphologic and structural abnormalities which may impact management strategies, including LV apical aneurysms and abnormalities of the mitral valve and subvalvular apparatus that contribute to LVOTO are also identified by CMR imaging. (39,40) CMR imaging is thus an important adjunctive test to clarify the diagnosis in patients with suspected HCM and with a nondiagnostic or inconclusive echocardiographic examination. Extensive LGE (of ≥15% of the LV mass) which is the imaging correlate of myocardial fibrosis is a non-invasive marker for increased risk for potentially life-threatening ventricular tachyarrhythmias and HF progression with systolic dysfunction.(41,42) The presence of extensive LGE can aid in decision-making when the indication for ICD placement remains ambiguous after standard risk stratification.(42)

Despite the various advantages of CMR imaging, it may not be feasible in certain patients because of availability, cost, contraindications attributable to pacemakers or ICDs, severe renal insufficiency, and patient factors (pediatric age and a requirement for general anaesthesia, or sedation, claustrophobia, or body habitus). CMR imaging in uncooperative patients is also a challenge. Although extensive LGE is one of the major risk markers for SCD, there is no consensus on the optimal quantification technique.

Strain

Imaging of myocardial deformation has shown to identify cardiac dysfunction much before conventional parameters, like ejection fraction, are deranged. The architecture of the myocardium of the left ventricle is highly complex with three layers:

1. Subendocardial layer with longitudinally oriented fibres from base to apex
2. Mid-wall layer with circumferentially oriented fibres
3. Subepicardial layer with longitudinally oriented fibres from the apex to the base. (43)

The LV thus deforms along different directions in systole, resulting in longitudinal and circumferential shortening, radial thickening, and torsion.

Myocardial strain is a measure of the degree of deformation of a myocardial segment from its initial length (L0) to its maximum length (L) and is expressed as a percentage.

$$Myocardial\ strain = \frac{L - L0}{L0}$$

Strain can be defined as either Lagrangian or Eulerian strain. Most imaging modalities are based on the analysis of the Lagrangian strain (11). Three different types of strains can be calculated based on the different directions of myocardial deformation:

(1) Longitudinal strain: This is the longitudinal shortening from the base to the apex

(2) Radial strain: This is the myocardial deformation towards the centre of the LV cavity

(3) Circumferential strain: This indicates LV myocardial fibre shortening along the circular perimeter

Longitudinal and circumferential strains are expressed by negative values as it represents shortening, whereas radial strain is expressed by positive values as it indicates thickening of the myocardium.

Cardiovascular magnetic resonance techniques to assess myocardial deformation

There are several CMR techniques for the measurement of myocardial deformation. These can be divided into two broad categories:

1. Strain acquisition methods (based on tailored image acquisition)
    a. Cardiovascular magnetic resonance tagging
    b. Phase velocity mapping (PVM)
    c. Displacement encoding with stimulated echoes (DENSE)
    d. Strain-encoded (SENC)
2. Post-processing methods
    a. Feature tracking

Strain acquisition methods

Cardiovascular magnetic resonance tagging

This technique consists of a preparation phase in which magnetic labels or tag lines are orthogonally superimposed on the myocardium. Deformation of these lines

throughout the cardiac cycle is analysed(44) Complementary spatial modulation of magnetization (CSPAMM), a radiofrequency pre-pulse that saturates parallel planes in two orthogonal directions creating a grid pattern of tags, is applied. Myocardial deformation parameters are assessed by tracking the motion of these tags either visually or by using post-processing software.(44) CMR tagging is the most validated technique to assess myocardial deformation, and the imposed tags are easier to follow than the natural features used for the tissue tracking method resulting in better reproducibility (45) (46,47). Its use is limited by low spatial resolution and long post-processing time. Moreover, as the tags gradually fade due to T1 relaxation time, only the first two-thirds of the cardiac cycle can be studied.

Phase velocity mapping

Phase velocity mapping uses a bipolar gradient to encode the velocity in the phase of the signal(43). Myocardial velocity in the three directions at each pixel is calculated from which strain parameters are extracted. It has quick post-processing but is limited by lower temporal resolution compared to tagging and longer increased acquisition time.

Displacement encoding with stimulated echoes

In this technique, three radiofrequency pulses are used to generate a stimulated echo, while gradients encode displacement into the phase of an image [5]. Two-dimensional displacement for each pixel can be obtained by repeating the sequence with encoding in the orthogonal direction. This sequence has a low signal-to-noise ratio (SNR), and the encoding disappears through the cardiac cycle as with tagging. Another limitation is its poor clinical and research experience.

Strain-encoded imaging

Magnetization tags parallel to the image plane (as opposed to orthogonal in CMR tagging) along with out-of-plane phase-encoding gradients in the selected direction are used to calculate myocardial strain in this technique(48). Circumferential strain is measured from two and four-chamber views and longitudinal strain from short-axis images, but radial strain cannot be generated. This technique requires limited post-processing, but tags gradually fade (49).

Post-processing cardiovascular magnetic resonance technique to assess myocardial strain

Feature tracking

This post-processing method is based on identifying features along the boundary of the LV cavity and myocardial tissue and tracking them in the successive images of the sequence (11,50), by which the displacement of myocardial segments is measured. It can be applied to routinely acquired cine CMR images and thus does not require additional image acquisition time and can be easily applied to all CMR routine scans. It is rapid, semi-automated, and requires a short post-processing time. The endocardial and epicardial borders (excluding papillary muscles and trabeculae), the mitral valve annular plane, and the longitudinal extent of the LV at the end diastole are defined, after which CMR-FT software starts automatic border tracking. Global longitudinal strain is estimated from two long-axis SSFP cine images and circumferential and radial strains are derived from the short-axis cine images. The main limitation is due to artefacts arising from through-plane motion (51), so good tracking requires high image quality with adequate spatial and temporal

resolution(11). CMR-FT can be applied to three-dimensional regions which help to reduce artefacts from through-plane motion(11). CMR-FT is also limited by the interference of blood motion close to the endocardial boundary, and by the pixel size(11). The use of an acquisition method in clinical practice is mainly affected by dedicated acquisition times, and hence, tissue tracking is now the preferred technique to assess myocardial strain.

Circumferential and longitudinal strain values higher than −17 and −20%, respectively, are considered abnormal(52). Global strain values are more robust and reproducible compared to regional ones, of which global longitudinal and global circumferential strain are the most consistent parameters and global circumferential strain has the best interobserver agreement (52–54). Different vendors with a lack of standardization in contouring methods contribute to the variability of strain values between different studies(55).

Comparison with other imaging modalities

Speckle tracking echocardiography (STE), which is based on the same principle as that of tissue tracking, has been widely used to assess myocardial strain due to its good accuracy and wide availability(56). Small echo-dense speckles in the myocardium are tracked, thus requiring a high frame rate and image quality(57). The main limitations are poor acoustic windows for echocardiography, through-plane motion artefacts as for CMR-FT, and its limited use in patients with arrhythmias, as it is based on single-cardiac-cycle strain analysis (58).

Several studies which compared myocardial strain parameters measured with STE and CMR FT have shown a good agreement between the two techniques (59–

61). Among the measured strain parameters, the global longitudinal strain was more accurate with STE, and the global circumferential strain had a better reproducibility with CMR FT.

The feasibility of the strain analysis using tissue tracking software in computed tomography (CT) has been shown in recent studies (62), but the experience is limited and more studies are needed to validate this technique.

Strain in Hypertrophic cardiomyopathy

Several studies have shown a linear correlation between myocardial strain and the extent of late gadolinium enhancement (LGE) (50,63), and thus strain analysis could potentially be used to detect the presence of scar, without the need for intravenous contrast.

Some studies have also shown the utility of strain to predict adverse cardiovascular outcomes. In the study by Pu C et al(64), HCM patients with ventricular arrhythmias had lower GRS, GCS, and GLS, and increased %LGE compared with those without ventricular arrhythmias (VAs) ($p < 0.01$ for all). %LGE and GCS were indicators of ventricular arrhythmias in HCM patients by multivariate logistic regression analysis. HCM patients with %LGE >5.35% (AUC 0.81, 95% CI 0.70–0.91, $p < 0.001$) or GCS >-14.73% (AUC 0.79, 95% CI 0.70–0.89, $p < 0.001$) on CMR more frequently had VAs. Hinojar R et al showed that all LV strain parameters were significantly impaired in patients with all-cause mortality, hospital admission related to heart failure, lethal ventricular arrhythmias, or cardiovascular death.(65) Few studies have prospectively analysed strain parameters in patients with HCM who developed adverse outcomes. In the study by Negri F et al, GLS was

determined to be a significant independent predictor of outcome events (major adverse cardiac events including sudden cardiac death, resuscitated cardiac arrest due to ventricular fibrillation or hemodynamically unstable ventricular tachycardia, and hospitalization for heart failure) ($p = 0.01$).(66) Dohy Z et al showed that GLS and GCS were univariate predictors of all-cause mortality, heart transplantation, malignant ventricular arrhythmias, and appropriate implantable cardioverter defibrillator therapy.(67) In the study by Smith BM et al, patients with HCM with an adverse event outcome (ventricular tachycardia, implantable cardioverter-defibrillator therapy, death) had reduced GRS ($p = 0.01$) and GLS ($p = 0.046$) compared with patients with HCM without an event.(15)

Few studies have evaluated segmental circumferential strain (SCS) in patients with HCM. Xu H et al(68) in their study done in a 3T MR scanner using the CMR-FT technique processed in cvi42 software showed that segmental radial, circumferential, and longitudinal strains in hypertrophied segments of patients with HCM were lower than those in both normal controls and non-hypertrophic segments ($p < 0.05$ for all). These parameters were also shown to be decreased in non-hypertrophic segments compared with those in normal control segments ($p < 0.05$ for all). The segmental strain parameters of segments with LGE were lower than those without LGE ($p < 0.001$ for all). Segmental radial, circumferential and longitudinal strains correlated with MWT, and segmental radial strains correlated with LGE ($p < 0.001$ for all). A prospective study by Chen X et al(69), in which CMR was done in both 1.5T and 3T scanners using the CMR-FT technique processed in cvi42 software, evaluated the prognostic value of segmental strain by CMR-FT in HCM. The segmental strain of hypertrophied segments was also significantly impaired

compared with the mean segmental strain in the healthy control group. The patients who developed an adverse outcome (all-cause mortality, ICD placement due to ventricular fibrillation of tachycardia, hospitalization due to progression of heart failure) had worse segmental radial and circumferential strains.

It has also been shown that subtle functional abnormalities detected by strain analysis extend beyond the presence of LGE in patients with HCM (70). Genotype-positive, phenotype-negative individuals carrying pathogenic HCM mutations but are asymptomatic without evidence of LVH on cardiac imaging have shown alterations in myocardial strain.(71)

Lacunae in literature

Although several studies on strain parameters in HCM exist, it has yet to find a place in standard CMR protocols and routine practice in clinical decision-making and management of these patients. No studies have evaluated the role of strain in the detection of familial HCM, where genetic testing may not always be feasible. The association of strain with native T1 mapping values, which indicate interstitial fibrosis, has also not been extensively studied. Studies assessing the association of regional strain with other regional imaging markers of fibrosis in HCM are also few and far between. Moreover, no reported study evaluating strain parameters in HCM patients in the Indian population is present, to the best of our knowledge. The present study aims to fill these gaps in knowledge, thereby furthering the understanding of the pathophysiology and potentially identifying new parameters which could gain widespread utility in predicting adverse outcomes in HCM.

3 MATERIALS AND METHODS

Study type

This was a single-centre analytical cross-sectional study. Consecutive patients suspected of having HCM who were referred from cardiology clinics for CMR evaluation were included as cases. Healthy volunteers with no cardiac disease and who had normal CMR findings were included as controls. The study was performed after obtaining institutional ethics committee approval (IEC No:). Consent was obtained in English and the local language (Malayalam) from the selected subjects.

Inclusion criteria

All consecutive patients suspected of having HCM on echocardiography with age >18 years, referred for CMR evaluation from June 2020 till May 2022 will be included as cases irrespective of any gender or ethnicity bias.

Healthy volunteers with no cardiac disease and had normal CMR findings were taken as controls.

Exclusion criteria

1. Patient or relatives declining consent.
2. Patients aged under 18 years, athletes, and pregnant patients.
3. Patients who have an alternative diagnosis at the end of the CMR study.
4. Patients with a known diagnosis of metabolic/infiltrative diseases and syndromes, ischemic cardiomyopathy, previous myectomy, or alcohol septal ablation.
5. Claustrophobic patients, patients with MR incompatible metallic implants, pacemakers or cochlear implants, and other contraindications to CMR.

6. Patients with a history of renal disease and eGFR < 30mL/min/1.73 m^2 or another contraindication for intravenous gadolinium contrast.

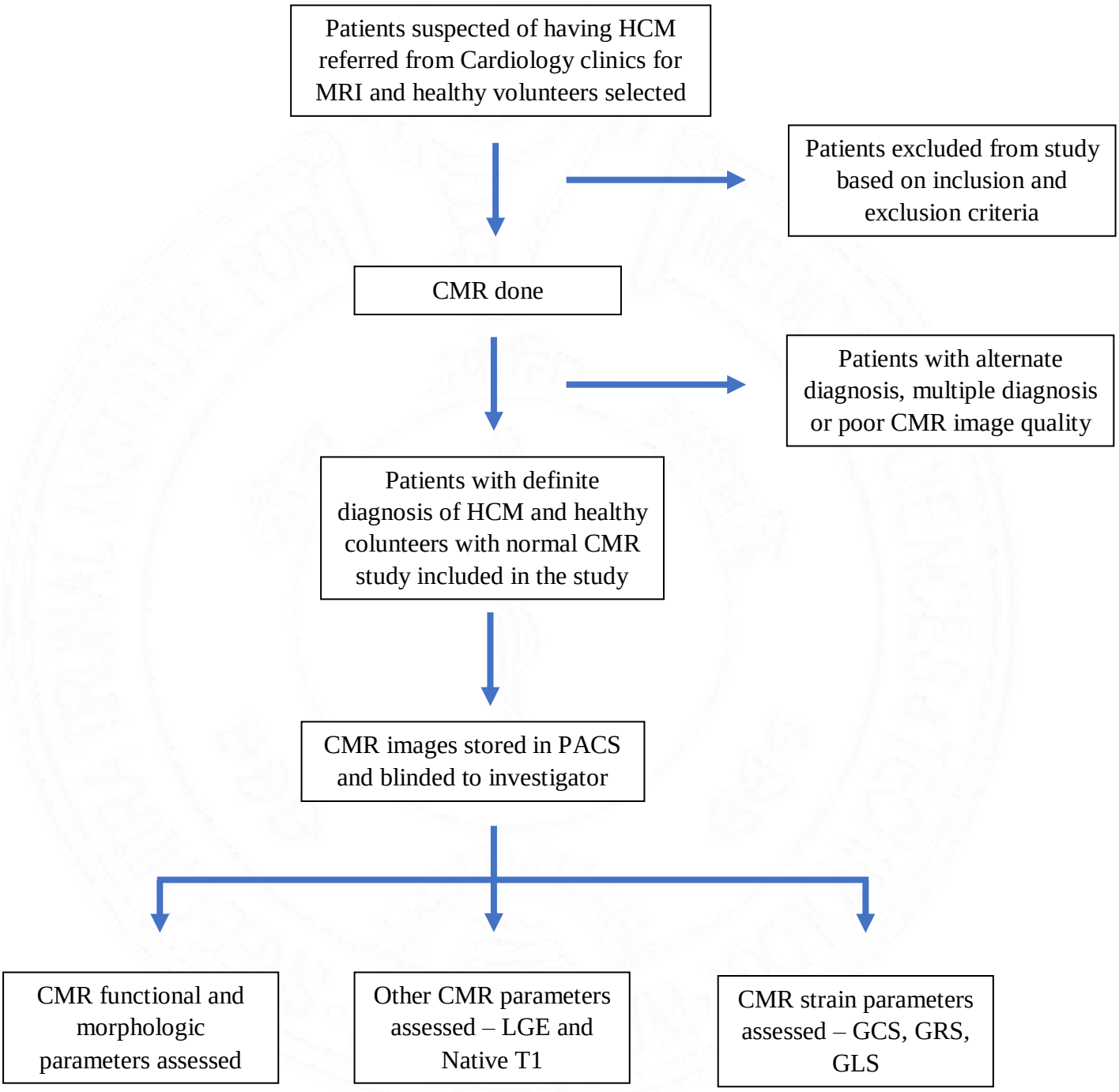

Figure 1. Flow chart of study design

Study design

This study was conducted on consecutive adult patients suspected of having HCM on echocardiography and referred for CMR evaluation from cardiology clinics. All patients underwent CMR using the protocol described below. The age, gender, primary diagnosis, symptomatology, associated comorbidities, and family history of HCM or HCM-related sudden cardiac death of the enrolled patients were recorded. All the HCM patients underwent 24 hours ambulatory Holter monitoring as part of routine protocol within a week of the MRI. Patients with ventricular arrhythmias (VAs) including non-sustained ventricular tachycardia (NSVT), defined as 3 or more consecutive beats arising below the atrioventricular node with a rate >100 beats/min and lasting <30 s, were noted.(72) Healthy volunteers with no cardiac disease and normal CMR findings were taken as controls.

CMR Protocol

CMR examinations were done on 1.5 T Siemens (MAGNETOM Avanto, Siemens Healthcare, Erlangen, Germany) equipped with a 36-element dedicated cardiac array. The standard clinical HCM CMR protocol consisted of scout images followed by functional assessment of the left ventricle using cine steady-state free precession techniques and post-contrast LGE images using phase-sensitive inversion recovery (PSIR) bSSFP sequence. Native T1 maps using the shortened modified Look-Locker inversion recovery (shMOLLI) technique, which collects only 5+1+1 samples and inversion recovery times are separated by only one R-R interval, were acquired before contrast administration. The total acquisition time was around 40

minutes. All CMR images were stored in a picture archiving and communication system (PACS).

Table 1. Parameters of CMR sequences

Parameter	Scout	Cine images bSSFP	Native T1		10 min LGE PSIR
			>700ms	<700ms	
TE	1.11ms	1.15ms	1.13ms	1.21ms	3.2ms
TR	247ms	43ms	279ms	272ms	769ms
Flip angle	80^0	57^0	35^0	35^0	25^0
FOV	400mm	340mm	360mm	360mm	340mm
Matrix size	256x128	192x192	144x256	132x192	256x256
Slice thickness	10mm	8mm	8mm	8mm	8mm
Time of inversion	-	-	-	-	Adjusted to null the myocardium
ECG gating	None	Retrospective	Prospective	Prospective	Prospective
Breath-hold	No	Yes	Yes	Yes	Yes
Spatial resolution	3x3x10mm	1.8x1.8x8mm	1.4x1.4x8mm	1.9x1.9x5mm	1.5x1.5x8mm
Interslice gap	-	2mm	NA	NA	2mm
SNR	1	0.9-1	1	1	0.9-1

Cine images

Cine images were obtained using retrospective electrocardiographic gating in short axis, four-chamber, two-chamber, and three-chamber LV outflow tract imaging planes. A total of 25 cardiac phases were acquired during one R–R interval with temporal resolution <40 ms. A bright blood imaging technique using a bSSFP

sequence was applied to obtain cine images. A short axis stack covered the heart from its base to apex, which allowed for the assessment of global and regional ventricular function, calculation of LV and RV volumes, ejection fraction, and LV mass.

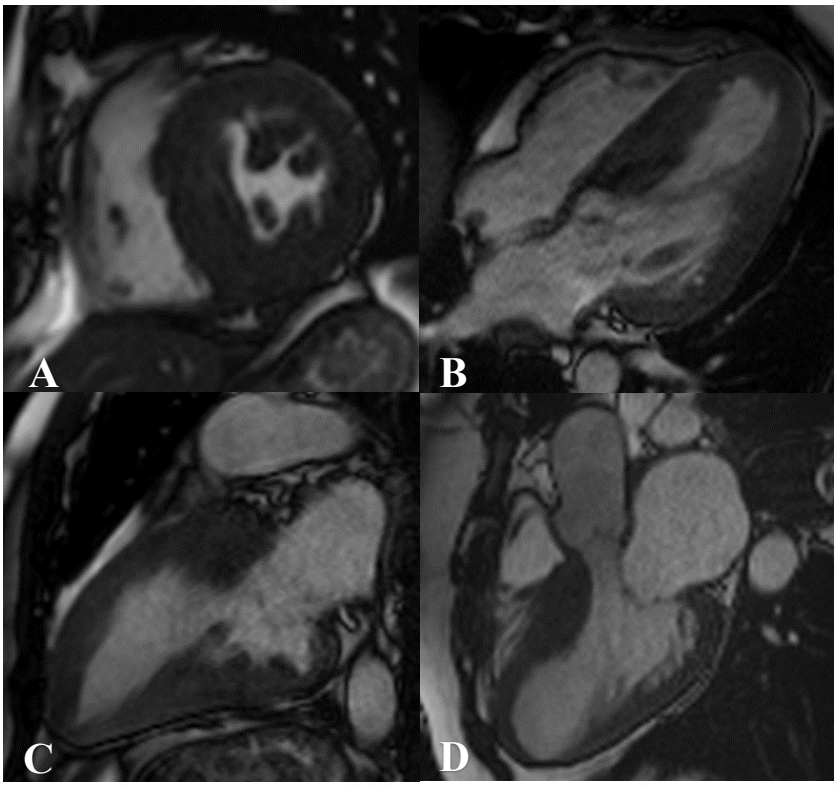

Figure 2. Cine bSSFP imaging planes - short axis (A), four-chamber (B), two-chamber (C), and three-chamber (D)

Native T1

Native T1 sequence was obtained using shMOLLI sequence before intravenous administration of contrast in three short-axis imaging planes, one each at the base, mid-ventricle, and apex of the LV.

LGE sequence

LGE images were obtained 10 minutes after administrating intravenous Gadolinium-based contrast medium (Gadotrast, Gadoterate Meglumine, Unique pharmaceuticals, India) intravenously at 0.1 mmol/kg body weight. Breath-hold segmented ECG gated PSIR bSSFP sequence performed in the same orientation as the cine images. The inversion time was adjusted to completely null normal myocardium (typically 250-400 ms).

Image analysis

For the study, CMR images were retrieved from PACS, anonymized, and stored separately in numbered folders. These images were post-processed and analysed by a reader with 3 years of experience in interpreting CMR studies. CMR data were analysed using commercially available post-processing software. Absolute and indexed LV volumes, myocardial mass, LV and RV ejection fractions, native T1, and extent of myocardial LGE, were measured using cvi42 Version 5.13.7 (Circle Cardiovascular Imaging, Calgary, Alberta, Canada) by a single experienced reader (3 years of CMR experience). Cine images were used to measure LV ejection fraction and volumes by tracing the endocardial and epicardial boundaries at the end-diastole and end-systole. Ejection fraction and myocardial mass were obtained using the semi-automated technique. Papillary muscles were excluded from the calculation of myocardial mass. The wall thickness of 17 LV myocardial segments was measured and the maximum wall thickness and well as the segment involved were noted. The left atrial anteroposterior diameter (LAD-AP) was taken as the maximum distance from the posterior wall of the left atrium to the mitral valve during the cardiac cycle, measured in a four-chamber view.

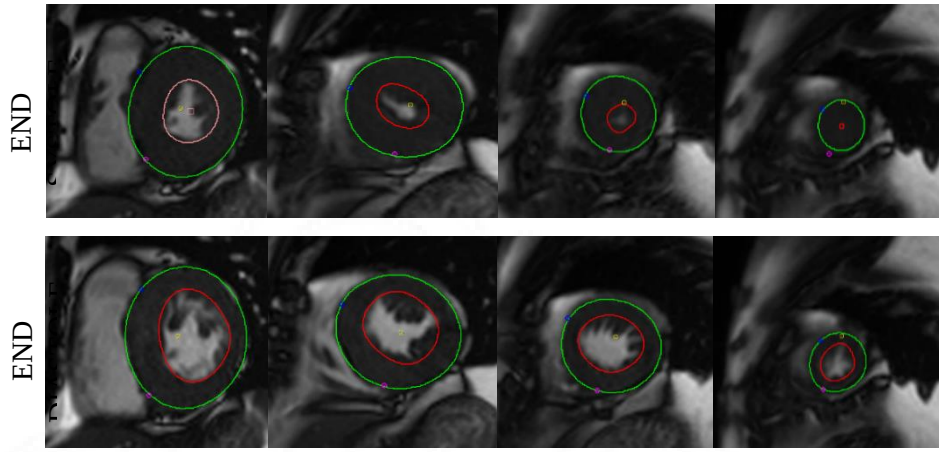

Figure 3. Endocardial and epicardial contouring in end-systole (top row) and end-diastole (bottom row) for processing cine images in cvi42 software

Native T1 sequence was loaded in the T1 mapping module of cvi42 software, epicardial and endocardial borders contoured long axis extent, and RV insertion points selected, after which the global and segmental native T1 values were automatically computed by the software.

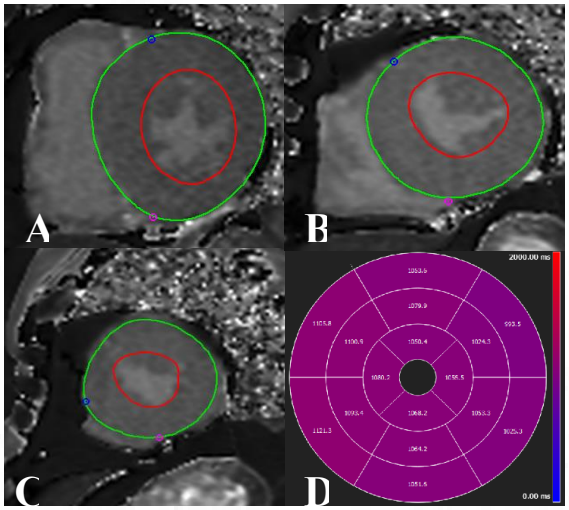

Figure 4 Processing of native T1 mapping – Epicardial and endocardial contouring in three short-axis images at the base (A), mid-ventricle (B), and apex (C). Polar map sowing segmental T1 values

LGE images were reviewed and the presence or absence of scar in the LV was noted. Further, the percentage extent of LGE in the LV as a percent of total LV mass was calculated using the mean + 5SD method. A user-defined free hand region of interest was drawn within normal nulled remote myocardium in the short axis stack of LGE PSIR images after contouring the epicardial and endocardial borders to obtain software-generated percentage extent of LGE.

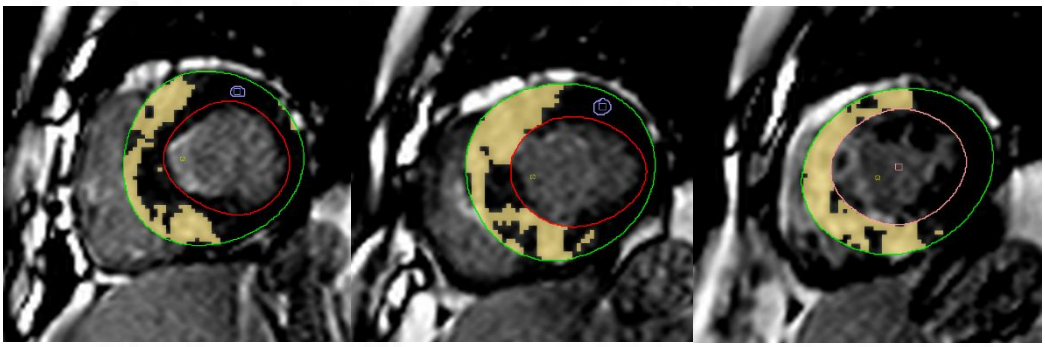

Figure 5. LGE quantification in cvi42 software – yellow highlighted areas represent LGE

All areas that were identified as enhancement by the software were cross-verified by the reader to ensure the exclusion of inversion time artefact or contamination by blood pool or pericardial fat. These were manually excluded by contour adjustment or the exclusion tool available in the software. The presence and absence of LGE in each segment were also recorded.

CMR strain analysis was done using CMR-FT (Tissue tracking strain module in cvi42). Cine images acquired in the short axis, four-chamber, two-chamber, and three chamber imaging planes were used for strain analysis. These were loaded in the module, epicardial and endocardial boundaries contoured in the end-diastolic phase, long axis extent, and RV insertion points selected, after which the global and segmental strain parameters were automatically computed by the software.

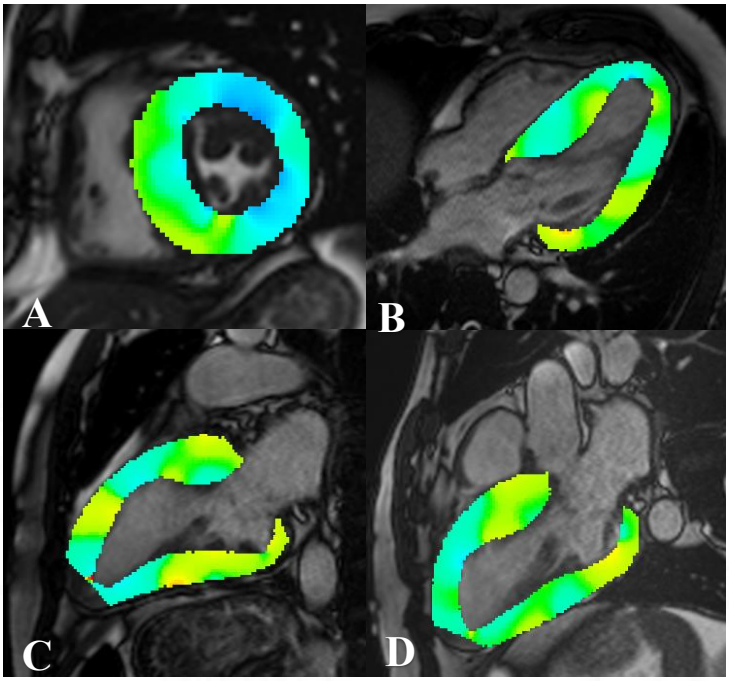

Figure 6. Strain colour maps in short axis (A), four-chamber (B), two-chamber (C), and three-chamber (D) views obtained after processing cine images in cvi42 software

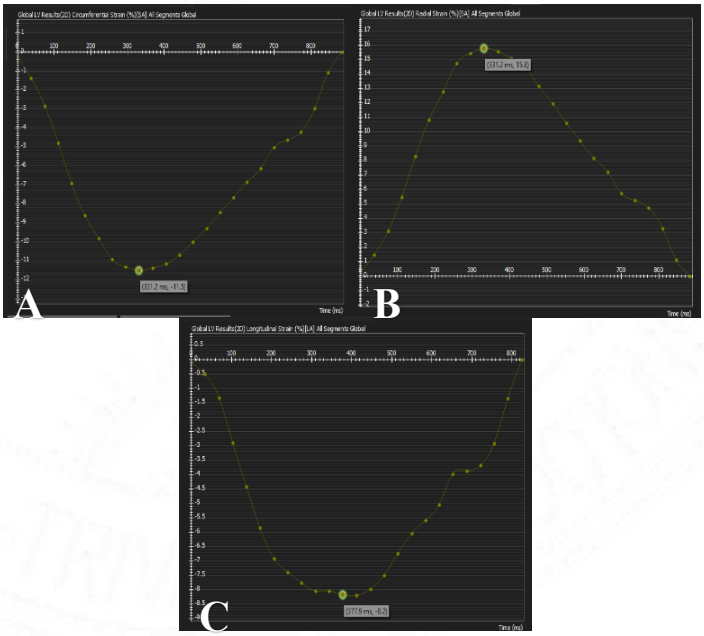

Figure 7. Global circumferential (A), radial (B), and longitudinal (C) strain graphs obtained after processing cine images in cvi42 software

Statistical analysis

The collected data were analysed using IBM SPSS Statistics for Windows (version 28.0; IBM, Armonk, NY, USA). Continuous and normally distributed variables were expressed as means ± SD, while those that did not show a normal distribution were expressed as median and interquartile ranges. Differences between a continuous normally distributed variable and a categorical variable were evaluated by an independent t-test. Categorical variables were represented as frequency (percentage) and differences assessed using the Chi-squared test or Fisher's exact test. The correlation of normally distributed variables was evaluated using Pearson correlation. Markers for non-sustained ventricular tachycardia (NSVT) in HCM were identified using univariate logistic regression. Multivariate analysis was performed using those variables which were significant ($p < 0.05$) in the univariate analysis. Two-tailed values of $p < 0.05$ were considered statistically significant.

4 RESULTS

A total of 104 patients suspected of having HCM were referred from Cardiology clinics for MRI during the study period from June 2020 to May 2022. Some patients (n = 11) were removed from the study based on inclusion and exclusion criteria. After undergoing CMR imaging, 12 patients who had an alternate diagnosis, multiple diagnoses, or poor CMR image quality were excluded. 81 patients with HCM were finally included in the study. 31 healthy volunteers with no cardiac disease and normal CMR findings were taken as controls.

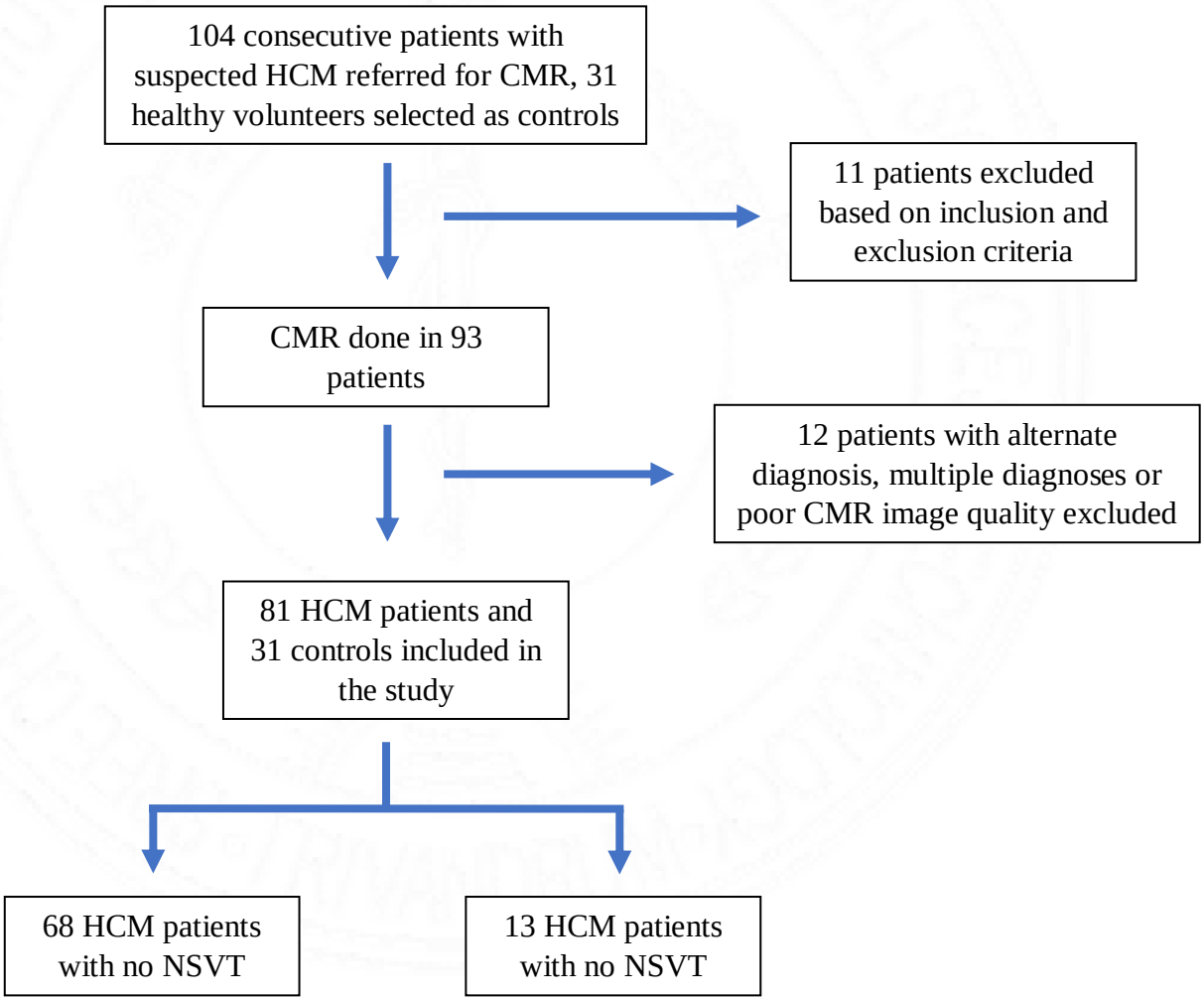

Figure 8. Flow chart showing selection of study population

Participant Characteristics

Gender distribution

Of the 81 HCM patients included in the study, 72%(n=59) were male and 28% (n=22) were female, with a male-to-female ratio of 2.7:1. Among the 31 healthy controls, 61% (n=19) were male and 39% (n=12) were female, with a male to female ratio of 1.6:1. There was no significant difference between the gender distribution between HCM patients and controls (p = 0.23).

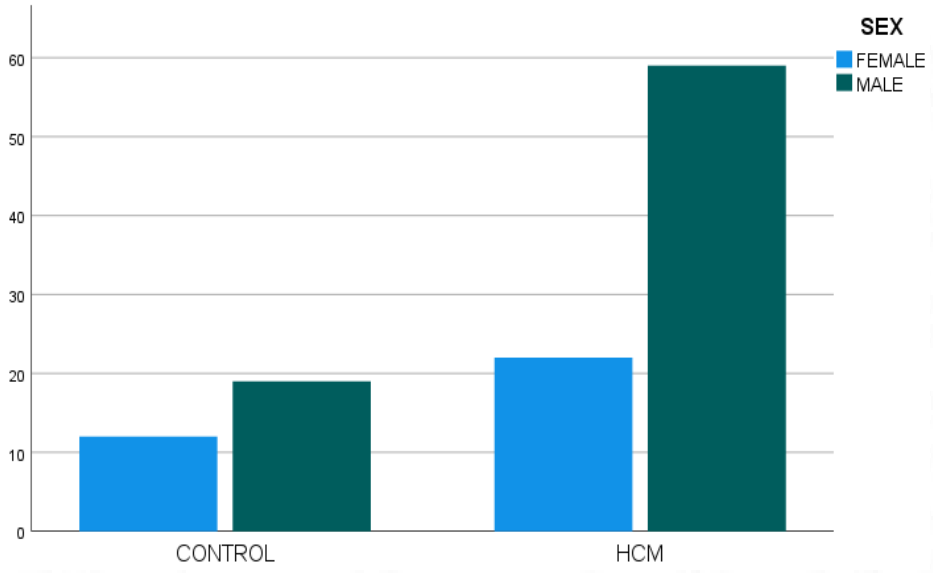

Figure 9. Gender distribution of the study population

Age distribution

Among HCM patients, the minimum and maximum ages were 18 and 79 years respectively, with a mean age of 48. Among controls, the minimum and maximum ages were 21 years and 75 years respectively with a mean age of 40 years. There was no significant difference between the ages of HCM patients and controls (p = 0.30).

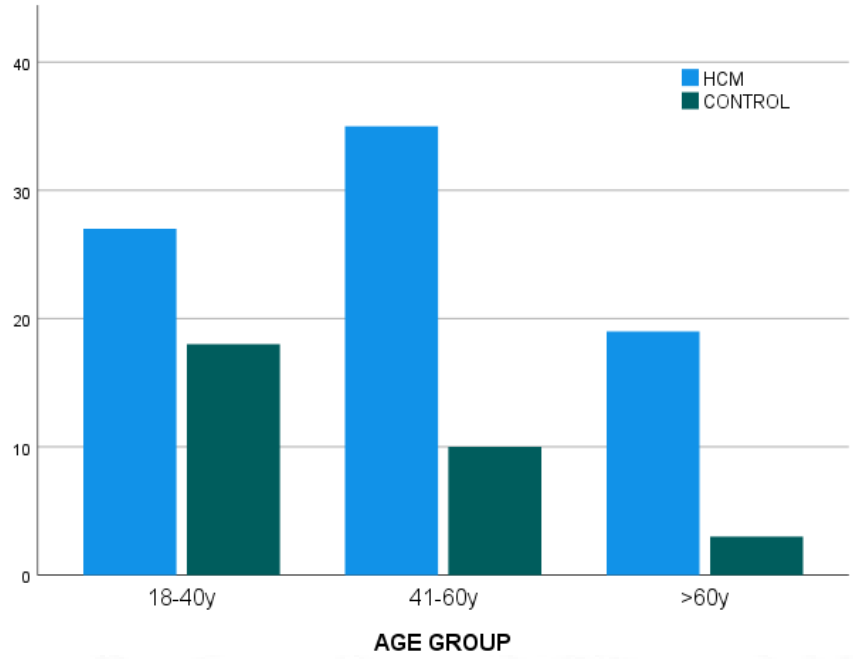

Figure 10. Age distribution of the study population

Comorbidities

The study population had the following risk factors and occurrence frequencies hypertension (35.8%), dyslipidemia (29.6%), and diabetes mellitus (25.9%). There was no significant difference in the distribution of these among HCM patients and controls.

Clinical presentation

The most common presenting symptom in HCM patients was dyspnoea on exertion seen in 70.4%, followed by palpitation in 35.8%, and syncope in 18.5%. Most patients presented with a combination of symptoms, the most common being exertional dyspnoea with palpitation.

Family history of HCM or HCM-related SCD

A family history of HCM or HCM-related SCD was present in 25.9% of HCM patients. However, no confirmatory genetic studies were available on these patients at the time of the study.

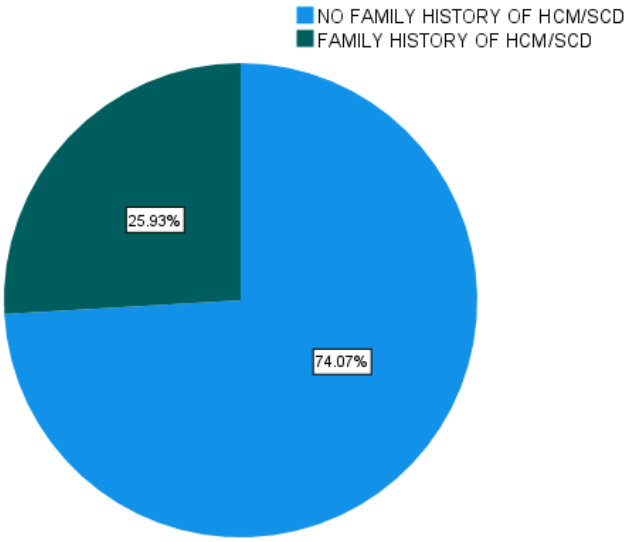

Figure 11. Family history of HCM or HCM-related SCD among HCM patients

Non-sustained Ventricular tachycardia (NSVT)

All the HCM patients underwent 24 hours of ambulatory Holter monitoring as part of the routine protocol within a week of MRI. NSVT was detected in 16.05% (n=13) of HCM patients. Among HCM patients with NSVT, 11.1% (n=9) underwent ICD placement after MRI.

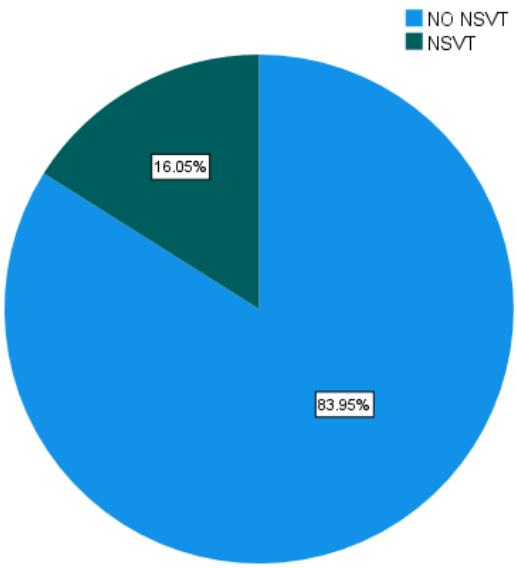

Figure 12. Non-sustained ventricular tachycardia in HCM patients

Morphological types of HCM

Among the various morphological types of HCM, the most common was asymmetric septal (n=58, 71.6%), followed by concentric (n=13, 16%), apical (n=7, 8.6%) and mid-ventricular (n=3, 3.7%).

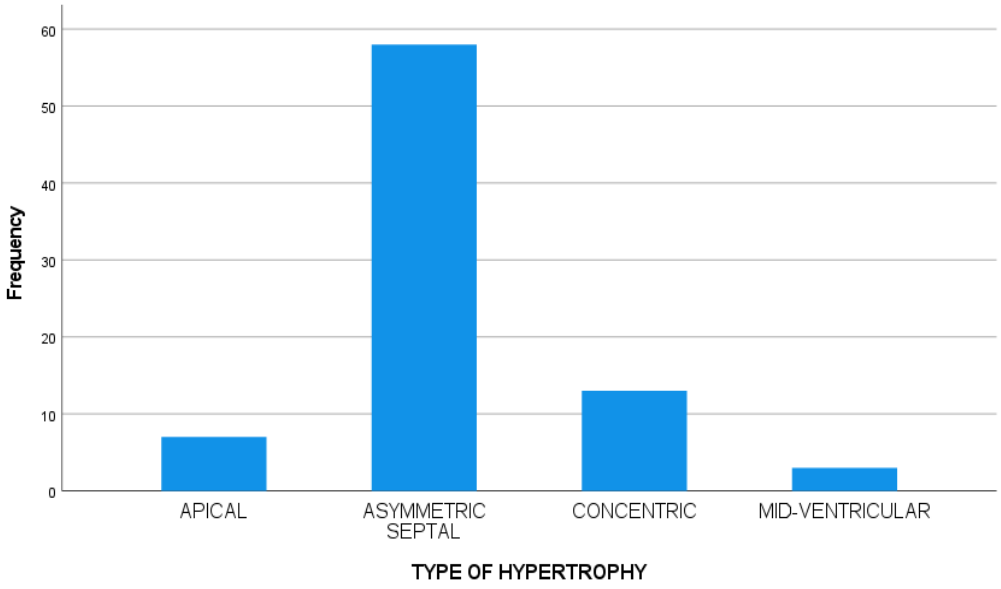

Figure 13. Frequency distribution of the various morphological variants of HCM

CMR findings

CMR functional parameters

CMR functional parameters, namely LVEF, right ventricular ejection fraction (RVEF), indexed left ventricular end-diastolic volume (LVEDVI), indexed left ventricular end-systolic volume (LVESVI), indexed stroke volume (SVI), and the indexed LV myocardial mass (LVMI), of HCM patients and controls were normally distributed. The LVEF ($p = 0.002$), LVEDVI ($p = 0.027$), SVI ($p = 0.016$), LVMI ($p < 0.001$) and RVEF ($p < 0.001$) were significantly higher in HCM patients compared with the control subjects. The LVESVI ($p = 0.468$) was lower in HCM patients with no statistically significant difference compared with the control subjects.

Table 2. CMR functional parameters of the study population

Cardiac function	Control (n = 31)	HCM (n = 81)	p-value
LVEF (%)	63.81±5.38	68.26±6.85	0.002
LVEDVI (ml/m^2)	70.11±12.2	76.7±12.2	0.027
LVESVI (ml/m^2)	26.06±8.35	24.71±8.97	0.468
SVI (ml/m^2)	43.85±9.43	48.8±9.83	0.016
LVMI (g/m^2)	42.19±9.26	85.60±23.27	<0.001
RVEF (%)	57.85±6.12	64.56±7.59	<0.001

CMR morphological data

Various morphological parameters and myocardial tissue characteristics – maximal wall thickness measured in end-diastole (MWT), left atrial anteroposterior

diameter (LAD-AP), percentage extent of LGE (%LGE) and native T1 values were analysed. The MWT and LAD-AP were significantly higher in HCM patients compared with the control subjects ($p < 0.001$ for both). LGE was present in 86.4% of HCM patients.

Table 3. CMR morphological data of the study population

Cardiac morphology	Control (n = 31)	HCM (n = 81)	p-value
MWT (mm)	7.8±3.13	22.88±4.91	<0.001
LAD-AP (mm)	44.92±3.87	59.18±8.46	<0.001
LGE present, n (%)	70 (86.4)	-	-
Native T1 (ms)	1020.35±16.08	1076.81±26.22	<0.001

CMR-FT myocardial strain

HCM patients were associated with significantly lower GCS, GRS, and GLS ($p \leq 0.001$ for all) compared to the controls.

Table 4. CMR-FT myocardial strain of the study population

Myocardial strain	Control (n = 31)	HCM (n = 81)	p-value
GCS (%)	-19.91±1.73	-15.39±2.78	<0.001
GRS (%)	32.75±3.9	24.06±4.43	<0.001
GLS (%)	-17.97±1.32	-11.04±2.29	<0.001

CMR Findings in HCM Patients with a family history of HCM or HCM-related sudden cardiac death (SCD)

There were 21 HCM patients (35%) with a family history of HCM or HCM-related SCD. HCM patients with a family history of HCM or HCM related SCD had significantly higher native T1 (p = 0.026) and worse GCS (p = 0.049). There was no statistically significant difference in LVEF, RVEF, LVEDVI, LVESVI, SVI, LVMI, MWT, LAD-AP, %LGE, GRS, or GLS between HCM patients with a family history of HCM or HCM-related SCD and those without a family history of HCM or HCM related SCD.

Table 5. CMR Findings in HCM Patients with a family history of HCM or HCM-related SCD

CMR parameters	HCM without family history (n = 60)	HCM with family history (n = 21)	p-value
LVEF (%)	68.73±6.66	66.91±7.36	0.297
LVEDVI (ml/m2)	75.38±14.06	80.53±15.42	0.163
LVESVI (ml/m2)	24.10±9.47	26.44±7.31	0.306
SVI (ml/m2)	48.04±9.74	51.23±9.95	0.202
LVMI (g/m^2)	85.55±22.30	85.76±26.45	0.972
RVEF (%)	64.89±7.45	63.61±8.09	0.511
MWT (mm)	22.26±4.90	24.68±4.59	0.052
LAD-AP (mm)	57.10±7.56	62.71±8.86	0.852
%LGE	12.39±10.69	12.13±7.80	0.919
Native T1 (ms)	1070.62±19.60	1081.90±19.85	0.026

GCS (%)	-15.29±2.07	-14.21±2.26	0.049
GRS (%)	24.12±3.87	22.76±4.57	0.191
GLS (%)	-11.28±2.24	-10.89±2.32	0.497

CMR Findings in HCM Patients with LGE

A total of 71 (87.6%) HCM patients had LGE. Patients with LGE had a tendency toward significantly higher LVMI (p = 0.007), MWT (p <0.001), native T1 (p = 0.038) and worse GCS (p = 0.004), GRS (p = 0.015) and GLS (p <0.001). There was no statistically significant difference in LVEF, LVEDVI, LVESVI, SVI, RVEF, or LAD-AP between HCM patients with LGE and those without LGE.

Table 6. CMR Findings in HCM Patients with and without LGE

CMR parameters	HCM with LGE (n = 71)	HCM without LGE (n = 10)	p-value
LVEF (%)	67.93±6.8	70.62±7.13	0.248
LVEDVI (ml/m2)	77.51±14.27	71.08±15.66	0.119
LVESVI (ml/m2)	24.85±8.36	23.69±13.09	0.704
SVI (ml/m2)	48.98±10.08	48.03±8.26	0.775
LVMI (g/m^2)	87.96±22.79	68.86±20.52	0.014
RVEF (%)	65.05±7.71	61.05±5.86	0.059
MWT (mm)	23.67±4.72	17.29±1.33	<0.001
LAD-AP (mm)	59.64±8.65	55.85±6.37	0.186
Native T1 (ms)	1075.28±20.41	1061.2±13.38	0.038

GCS (%)	-14.76±2.18	-16.82±0.78	0.004
GRS (%)	23.36±4.18	26.68±1.02	0.015
GLS (%)	-10.85±2.18	-13.54±1.11	<0.001

CMR parameters of HCM patients with and without LGE were separately compared to controls. There was a statistically significant difference in LVEF, LVMI, LAD-AP, native T1, GCS, GRS, and GLS between HCM patients with LGE and controls and between HCM patients without LGE and controls. LVEDVI, SVI, and RVEF also showed a statistically significant difference between HCM patients with LGE and controls.

Table 7. CMR Findings in Controls compared with HCM Patients with and without LGE

CMR parameters	**Controls (n = 31)**	**HCM without LGE (n=10)**	**p-value**	**Controls (n = 31)**	**HCM with LGE (n = 71)**	**p-value**
LVEF (%)	63.81±5.38	70.62±7.13	0.003	63.81±5.38	67.93±6.8	0.004
LVEDVI (ml/m2)	70.11±12.2	71.08±15.66	0.840	70.11±12.2	77.51±14.27	0.014
LVESVI (ml/m2)	26.06±8.35	23.69±13.09	0.503	26.06±8.35	24.85±8.36	0.503
SVI (ml/m2)	43.85±9.43	48.03±8.26	0.218	43.85±9.43	48.98±10.08	0.018

LVMI (g/m^2)	42.19±9.26	68.86±20.52	<0.001	42.19±9.26	87.96±22.79	<0.001
RVEF (%)	57.85±6.12	61.05±5.86	0.115	57.85±6.12	65.05±7.71	<0.001
LAD-AP (mm)	44.92±3.87	55.85±6.37	<0.001	44.92±3.87	59.64±8.65	<0.001
Native T1 (ms)	1020.35±16.08	1061.2±13.38	<0.001	1020.35±16.08	1075.28±20.41	<0.001
GCS (%)	-19.91±1.73	-16.82±0.78	<0.001	-19.91±1.73	-14.76±2.18	<0.001
GRS (%)	32.75±3.9	26.68±1.02	<0.001	32.75±3.9	23.36±4.18	<0.001
GLS (%)	-17.97±1.32	-13.54±1.11	<0.001	-17.97±1.32	-10.85±2.18	<0.001

CMR parameters in those with LGE extent >15% (n=30, 37%) were compared to those with LGE extent <15% (n=51, 63%). Patients with LGE>15% had significantly higher LVEDVI (p = 0.009), LVESVI (P = 0.002), MWT (p <0.001), LAD-AP (p = 0.003), native T1 (p = 0.003) and worse LVEF (P < 0.001), GCS (p < 0.001), GRS (p = 0.007) and GLS (p <0.001). There was no statistically significant difference in LVSVI, LVMI, or RVEF between HCM patients with LGE extent >15% and those with LGE extent <15%.

Table 8. **CMR Findings** in **HCM Patients with LGE<15% and LGE >15%**

CMR parameters	**HCM with LGE <15% (n = 51)**	**HCM with LGE >15% (n = 30)**	**p-value**
LVEF (%)	70.68±6.25	64.13±5.84	<0.001
LVEDVI (ml/m2)	73.54±13.69	82.11±14.47	0.009

LVESVI (ml/m2)	22.33±8.55	28.74±8.34	0.002
SVI (ml/m2)	49.80±8.24	47.28±12.06	0.269
LVMI (g/m^2)	85.49±30.54	92.66±23.66	0.273
RVEF (%)	65.39±7.57	63.14±7.54	0.199
MWT (mm)	21.46±4.92	25.30±3.91	<0.001
LAD-AP (mm)	57.10±7.56	62.71±8.86	0.003
Native T1 (ms)	1070.31±25.30	1087.87±24.34	0.003
GCS (%)	-15.68±1.64	-13.88±2.48	<0.001
GRS (%)	24.70±3.03	22.19±5.09	0.007
GLS (%)	-11.92±1.83	-9.92±2.36	<0.001

CMR Findings Related to NSVT in HCM Patients

HCM patients with NSVT had worse LVEF and myocardial strain parameters, higher LVEDVI, and LVESVI, and increased % LGE compared with those without NSVT ($p < 0.01$ for all). HCM patients with NSVT were also associated with higher ESVI ($p = 0.003$), SVI ($p = 0.045$), and LVMI ($p = 0.017$).

Table 9. CMR Findings HCM Patients with and without NSVT

CMR parameters	HCM with NSVT (n = 13)	HCM without NSVT (n = 68)	p-value
LVEF (%)	58.92±1.99	70.04±5.93	<0.001
LVEDVI (ml/m2)	89.85±10.72	74.2±13.81	<0.001
LVESVI (ml/m2)	31.28±5.48	23.45±8.99	0.003

SVI (ml/m2)	43.87±12.3	49.82±9.08	0.045
LVMI (g/m2)	99.56±15	82.94±23.69	0.017
RVEF (%)	61.13±7.74	65.21±7.44	0.076
MWT (mm)	28.14±1.85	21.88±4.67	0.434
LAD-AP (mm)	57.48±9.72	59.5±8.25	0.186
%LGE	21.06±9.9	10.66±9.15	<0.001
Native T1 (ms)	1102.69±17.72	1067.97±15.26	<0.001
GCS (%)	-11.27±1.01	-15.73±1.47	<0.001
GRS (%)	16.27±2.34	25.2±2.43	<0.001
GLS (%)	-7.8±1.53	-11.83±1.73	<0.001

Univariate logistic regression analysis identified LVEF (p = 0.003), LVEDVI (p = 0.002), LVESVI (p = 0.007), LVMI (p = 0.023), MWT (p < 0.001), %LGE (p = 0.002), native T1 values (p = 0.001), GCS (p < 0.001), and GLS (p = 0.01), as markers for NSVT in HCM. Multivariate logistic regression analysis was done using variables that were found to be significant in univariate logistic regression analysis, which showed GCS (p = 0.007) to be a marker of NSVT in patients with HCM having an independent association.

Table 10. Univariate and multivariate logistic regression analysis for predictors of NSVT in HCM patients

CMR parameters	**Univariate logistic regression**		**Multivariate logistic regression**	
	OR (95% CI)	**p-value**	**OR (95% CI)**	**p-value**

LVEF	0.41 (0.23-0.75)	0.003		
LVEDVI	1.08 (1.03, 1.149)	0.002		
LVESVI	1.09 (1.02, 1.17)	0.07		
SVI	0.93 (0.87-1.00)	0.051		
LVMI	1.03 (1.00, 1.06)	0.023		
RVEF	0.92 (0.85, 1.00)	0.081		
MWT	1.37 (1.14, 1.63)	<0.001		
LAD-AP	0.97 (0.89, 1.04)	0.430		
SAM	1.69 (0.50, 5.71)	0.393		
LVOTO	1.91 (0.56, 6.43)	0.297		
LGE	0.48 (0.05, 4.13)	0.507		
%LGE	1.10 (1.03, 1.18)	0.002		
Native T1	1.04 (1.02, 1.07)	0.001		
GCS (%)	5.09 (2.19, 11.83)	<0.001	9.40 (1.87, 47.25)	0.007
GRS (%)	0.58 (0.06, 4.31)	0.407		
GLS (%)	8.43 (2.43, 29.17)	0.001		

ROC curve analysis showed native T1 [AUC 0.94, 95% CI (0.89, 0.99), $p < 0.001$] and GCS [AUC 0.98, 95% CI (0.98, 1.00), $p < 0.001$] to be excellent tests to identify HCM patients with NSVT, with a higher AUC for GCS. ROC curve analysis also revealed extent of LGE [AUC 0.79, 95% CI (0.66, 0.93), $p < 0.001$] to be a good test to identify HCM patients with NSVT. Using optimal cut-off values from ROC curves, HCM patients with %LGE >14.55%, native T1 values >1080.5 or GCS >-12.7% on CMR was more frequently had NSVT.

Table 11. ROC analysis of CMR parameters to identify HCM patients with NSVT

Variable	AUC	Std. Error	p	95% Confidence Interval	
LGE extent %	0.798	0.071	<0.001	0.660	0.936
Native T1	0.946	0.025	<0.001	0.897	0.994
GCS	0.989	0.011	<0.001	0.968	1.000

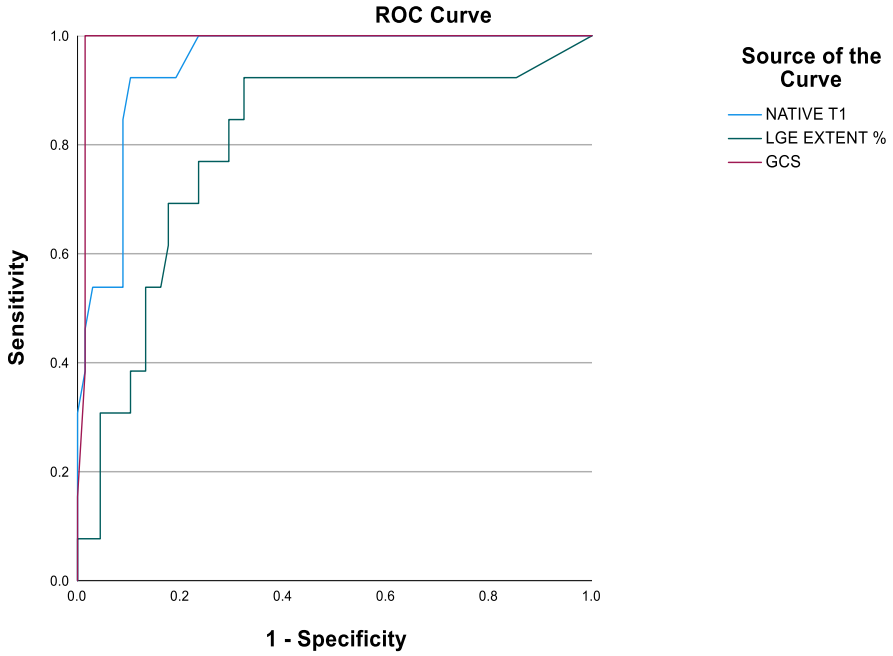

Figure 14. ROC curves to assess the ability of %LGE, native T1, and GCS in identifying HCM patients with NSVT

Correlation between GCS, MWT, %LGE, and native T1

The correlation between GCS and three variables, namely, MWT, %LGE, and native T1 were assessed. Scatter plots showed a linear relationship between GCS and

each of the three variables. Pearson correlation analysis showed a moderate positive significant correlation between GCS and MWT ($r = 0.47$, $p < 0.001$). A moderate positive significant correlation was also noted between GCS and %LGE ($r = 0.48$, $p < 0.001$). There was a strong positive significant correlation between GCS and native T1 ($r = 0.76$, $p < 0.001$).

Table 12. Correlation between GCS, MWT, %LGE, and native T1

		MWT	%LGE	Native T1
GCS	Pearson Correlation	0.47	0.47	0.76
	Sig. (2-tailed)	<.001	<.001	<.001

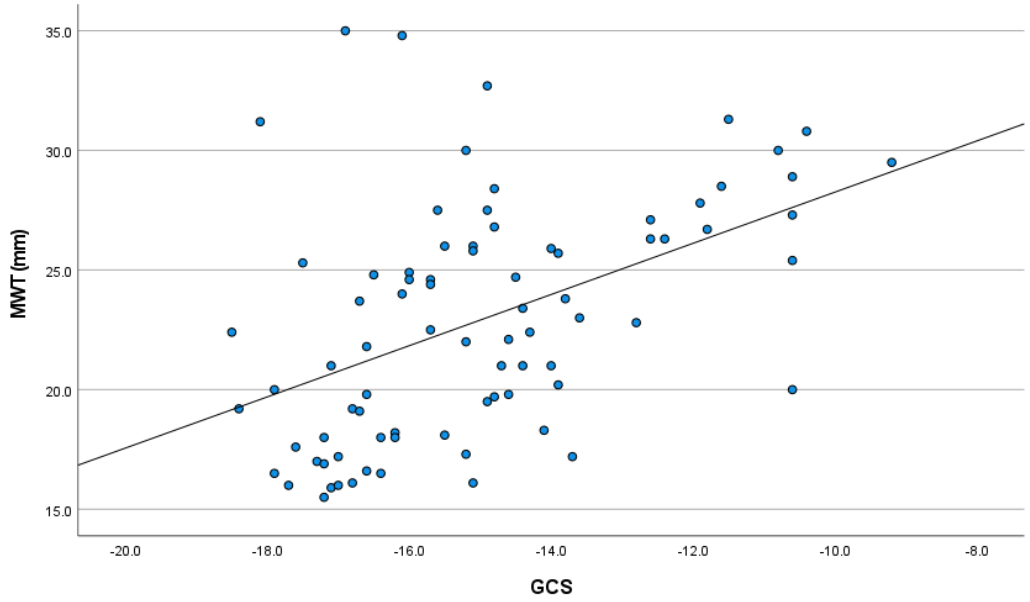

Figure 15. Scatter plot of correlation analysis between GCS and MWT

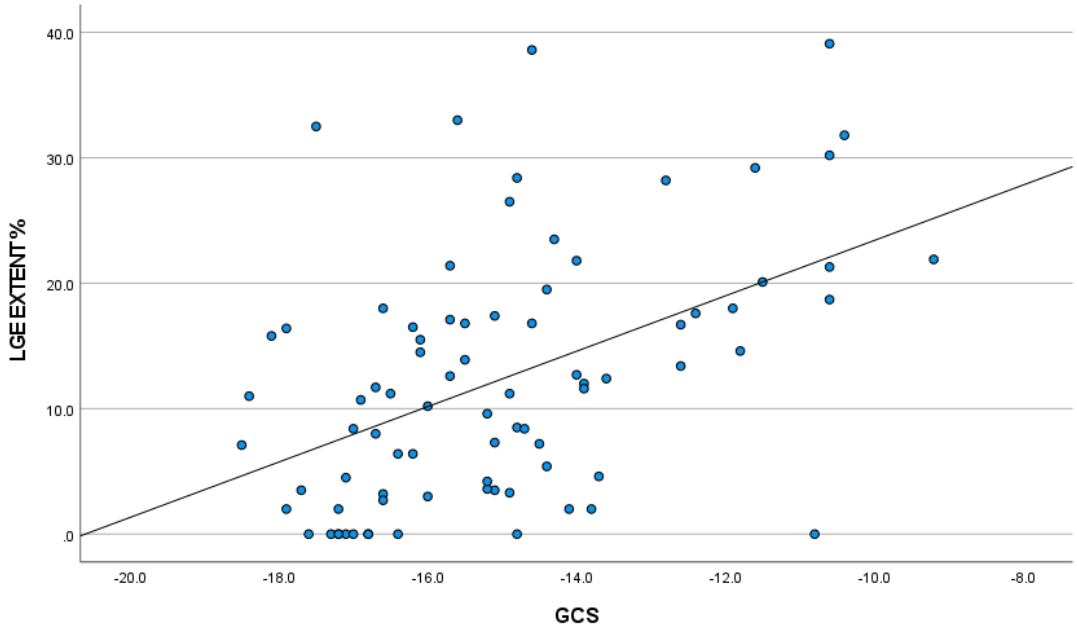

Figure 16. Scatter plot of correlation analysis between GCS and %LGE

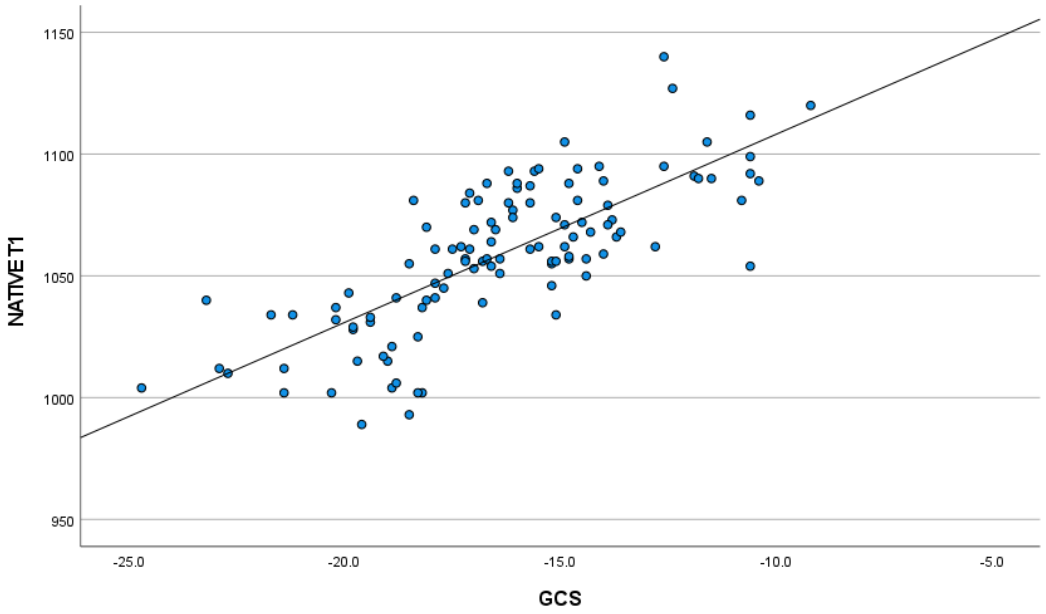

Figure 17. Scatter plot of correlation analysis between GCS and native T1

Segmental circumferential strain (SCS)

The circumferential strain in the 16 segments (segmental circumferential strain, SCS) of the LV was assessed. The mean SCS in controls was -20.75±2.86 and in patients with HCM was -16.47±4.38. The SCS in HCM patients was significantly worse than in controls ($p < 0.001$). The mean SCS of HCM patients with no NSVT was -16.24±5.32 of HCM patients with NSVT was -14.37±5.14, with a significantly worse SCS in those with NSVT ($p < 0.001$). Univariate logistic regression analysis identified SCS ($p < 0.001$), as a marker for NSVT in patients with HCM.

The correlation between SCS, segmental LV wall thickness (SWT), segmental native T1, and the presence or absence of LGE in LV myocardial segments was assessed. Scatter plots showed that there was a linear relationship between SCS and both SWT and segmental T1. There was a moderate positive significant correlation between segmental circumferential strain and segmental LV wall thickness ($r = 0.41$, $p < 0.001$). A moderate positive significant correlation between segmental circumferential strain and segmental native T1 was present ($r = 0.42$, $p < 0.001$). Segmental circumferential strain and segmental LGE also showed a moderate positive significant correlation ($r = 0.55$, $p < 0.001$).

Table 13. Correlation between SCS, SWT, segmental native T1, and segmental LGE

	SWT	**Segmental native T1**	**Segmental LGE**

SCS	Pearson Correlation	0.41	0.42	0.55
	Sig. (2-tailed)	<.001	<.001	<.001

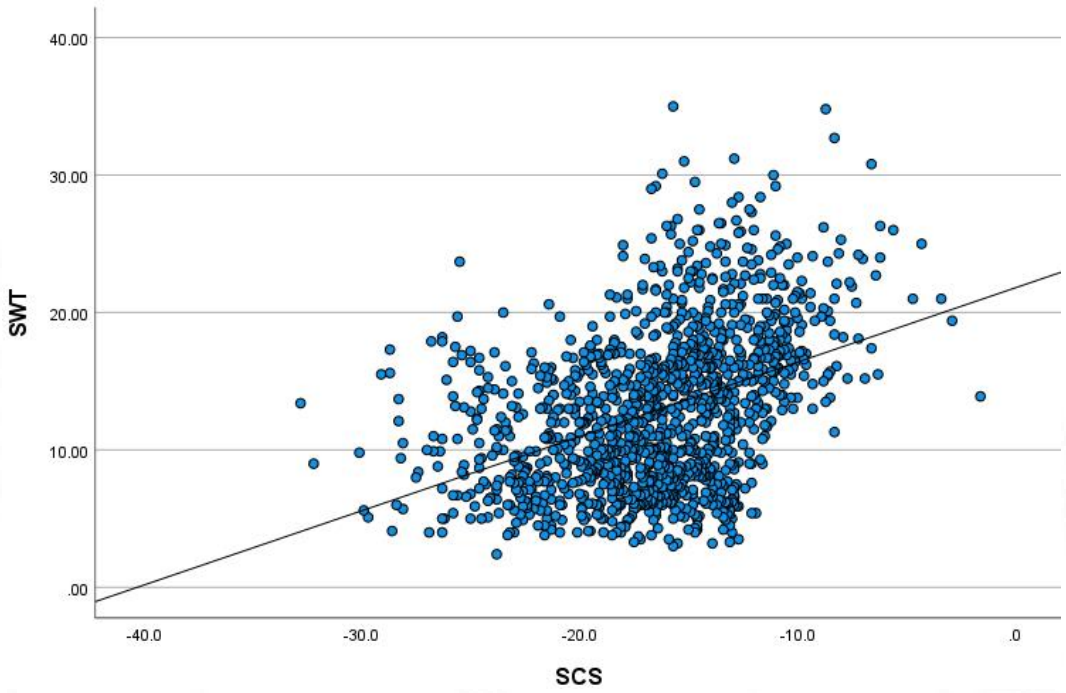

Figure 18. Scatter plot of correlation analysis between SCS and SWT

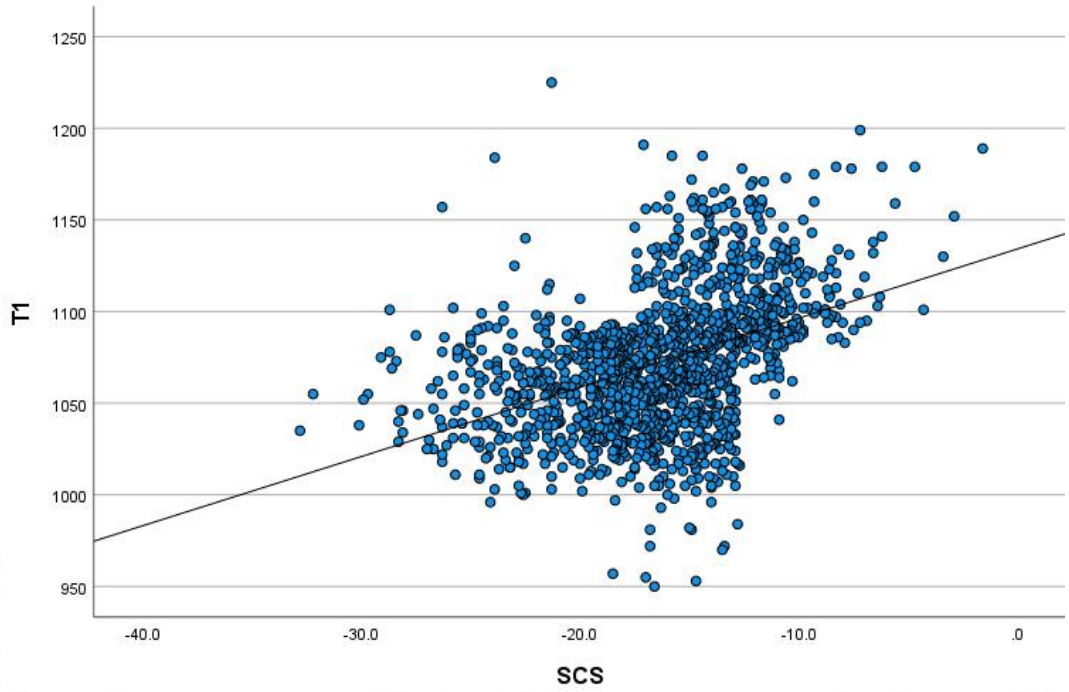

Figure 19. Scatter plot of correlation analysis between SCS and segmental T1

ROC curve analysis showed that SCS [AUC 0.86, 95% CI (0.84, 0.88), $p < 0.001$] was a very good test to identify the presence of LGE within the corresponding segment. Using optimal cut-off values from ROC curves, SCS >-15.85% was more frequently associated with the presence of segmental LGE. However, ROC curve analysis showed that SCS [AUC 0.60, 95% CI (0.56, 0.65), $p < 0.001$] was a poor test to identify HCM patients with NSVT.

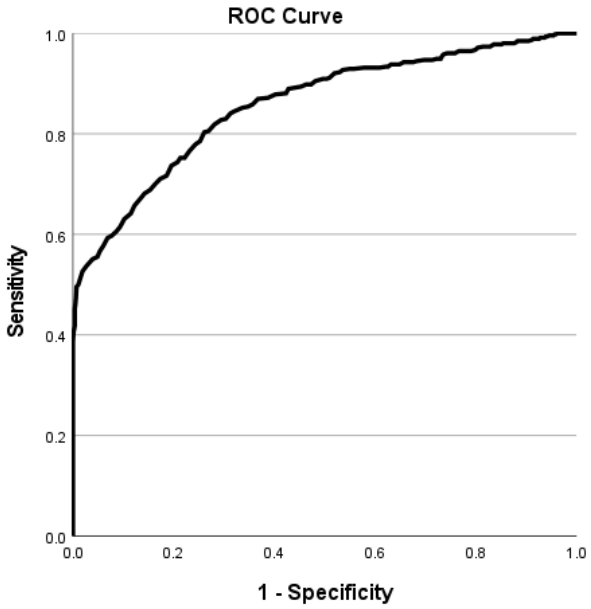

Figure 20. ROC curve to assess the ability of SCS to predict the presence of segmental LGE

Representative cases: Case 1 – Healthy control

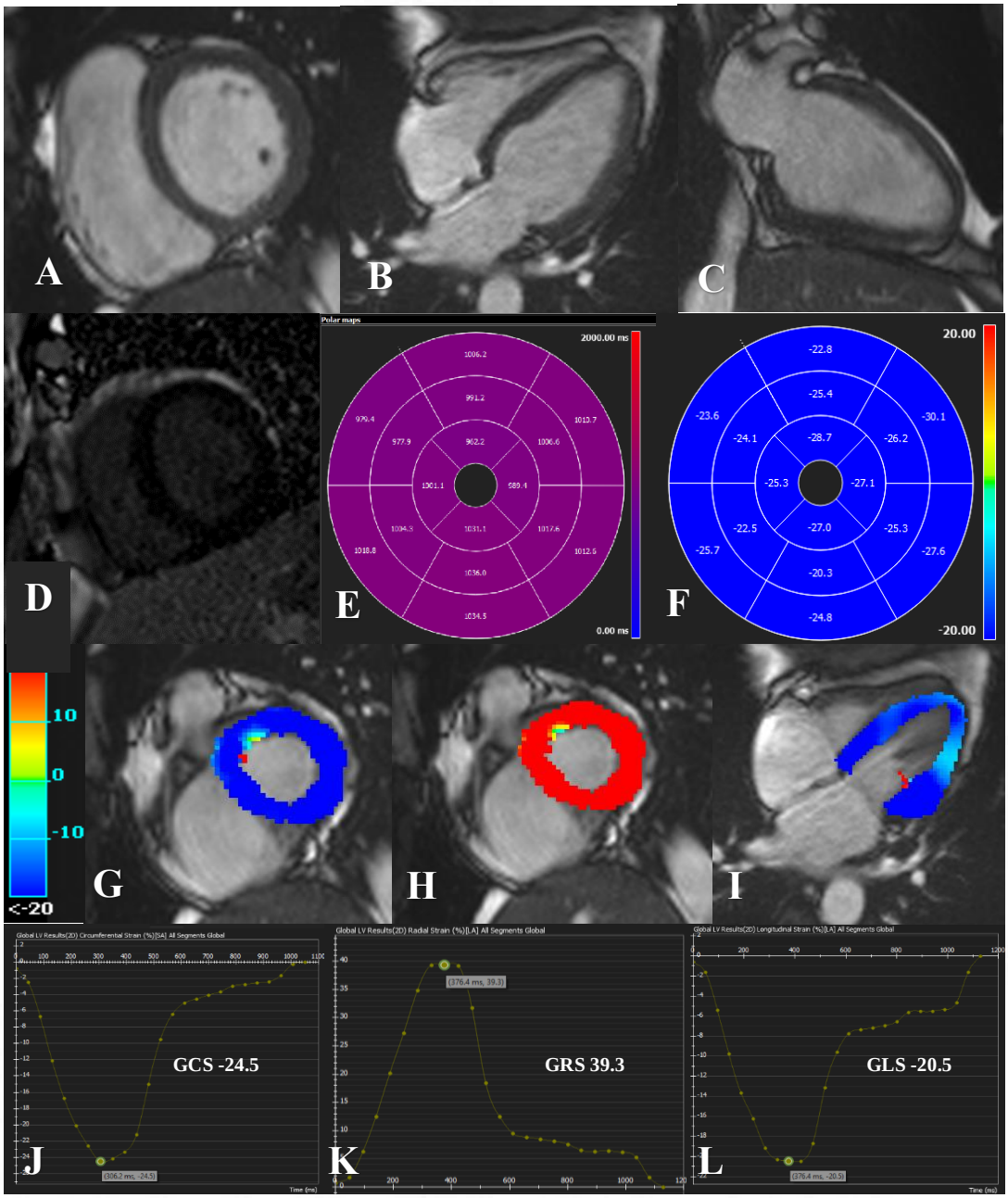

Figure 21. CMR images of a healthy volunteer. Cine short axis (A), four-chamber (B) and two-chamber (C) images show normal LV wall thickness. LGE PSIR image (D) shows no delayed enhancement. Native T1 polar map shows normal values. The polar map of Segmental circumferential strain also shows normal strain values. Colour maps of GCS (G), GRS (H), and GLS (I) with corresponding values in strain time curves show normal strain values.

Case 2 – HCM (asymmetric septal hypertrophy) patient with LGE >15% and NSVT

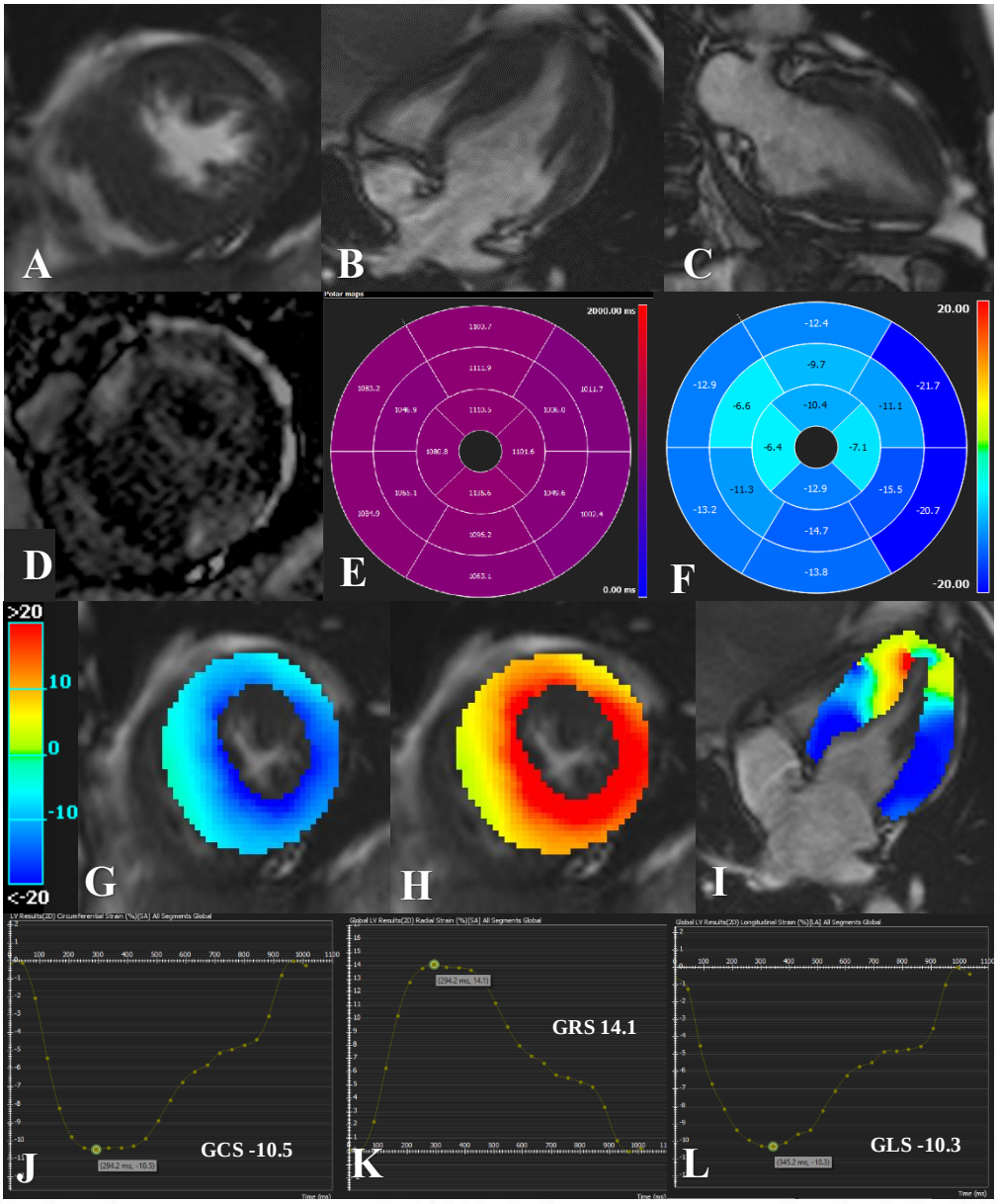

Figure 22. CMR images of an HCM (asymmetric septal hypertrophy) patient with LGE >15% and NSVT on Holter. Cine short axis (A), four-chamber (B) and two-chamber (C) images show hypertrophy of the septal segments. LGE PSIR image (D) shows extensive delayed enhancement in the septum and RV insertion points amounting to an LGE extent of 31.8%. Native T1 polar map (E) shows diffusely elevated values, predominantly involving the septum. The polar map of Segmental circumferential strain (F) also shows elevated strain values, predominantly involving the septum. Colour maps of GCS (G), GRS (H), and GLS (I) with corresponding values in strain time curves show abnormal values (-11, 16, and -5.6 respectively).

Case 3 – HCM (asymmetric septal hypertrophy) patient with LGE <15% and no NSVT

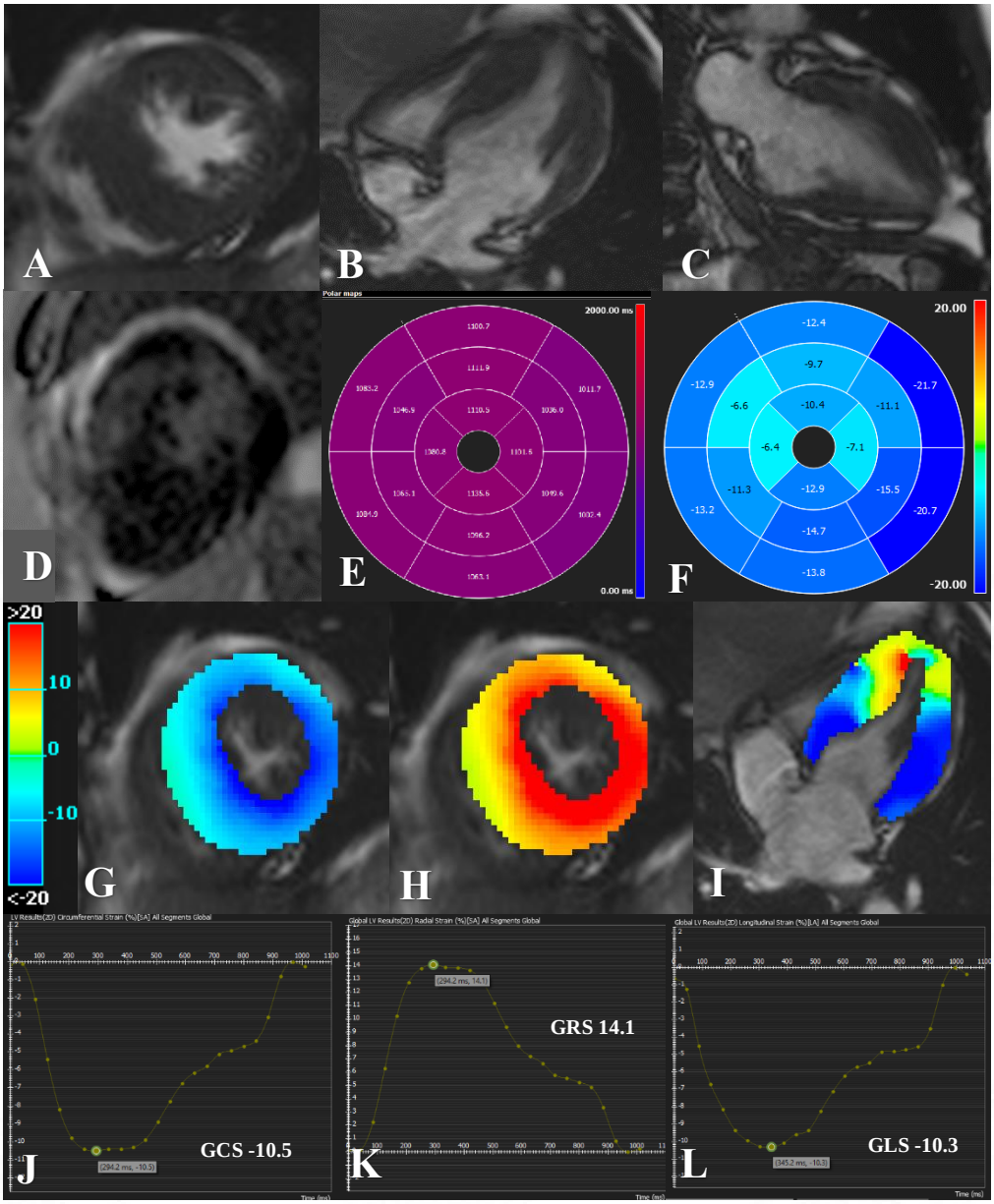

Figure 23. CMR images of an HCM (asymmetric septal hypertrophy) patient with LGE <15% who did not have NSVT on Holter. Cine short axis (A), four-chamber (B) and two-chamber (C) images show hypertrophy of the septal segments. LGE PSIR image (D) shows extensive delayed enhancement in the septum and RV insertion points amounting to an LGE extent of 13%. Native T1 polar map (E) shows diffusely elevated values, predominantly involving the septum. The polar map of Segmental circumferential strain (F) also shows elevated strain values, predominantly involving the septum. Colour maps of GCS (G), GRS (H), and GLS (I) with corresponding values in strain time curves show severely reduced strain values (-11, 16, and -5.6 respectively).

Case 4 – HCM (asymmetric septal hypertrophy) patient with no LGE but NSVT on Holter

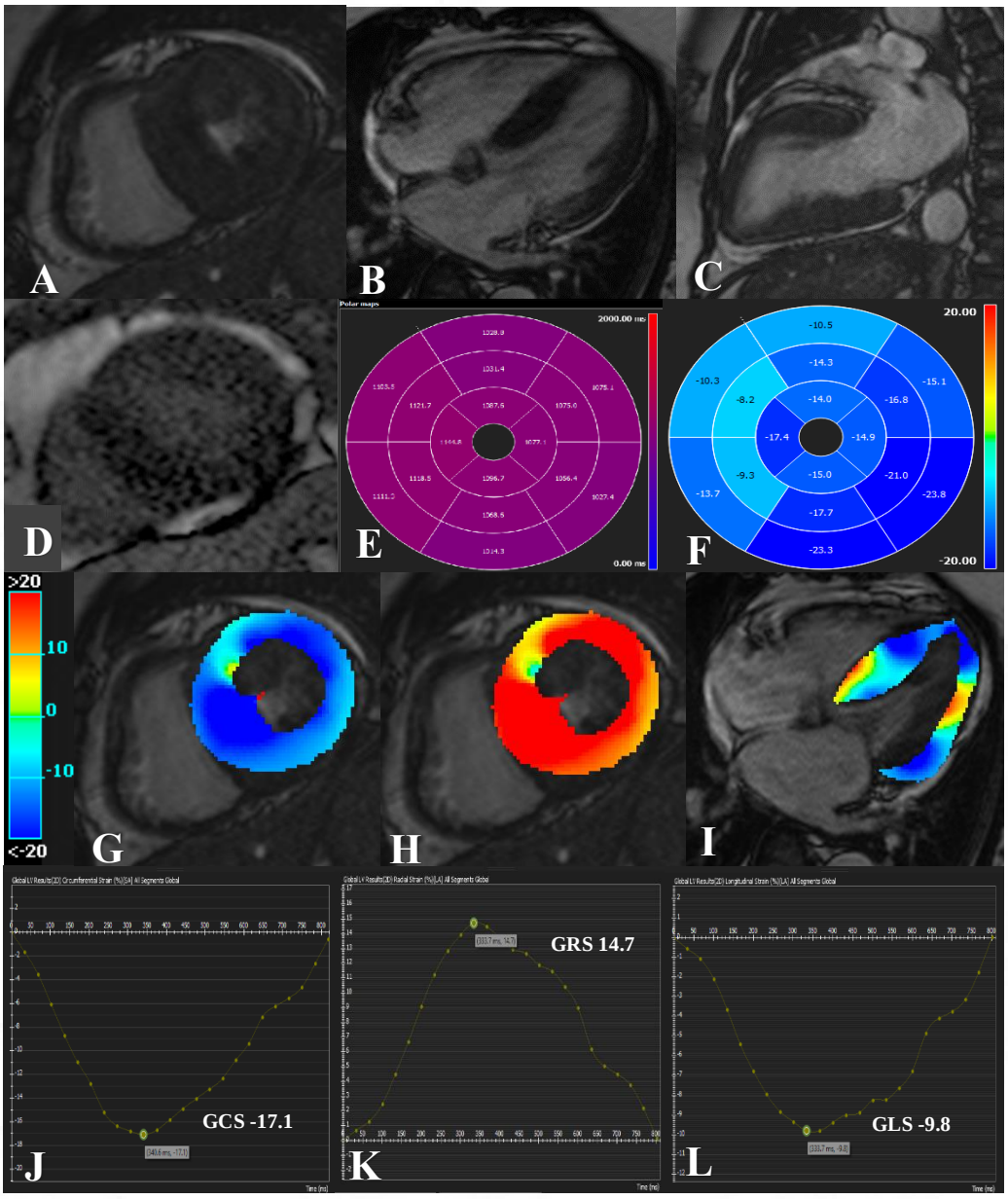

Figure 24. CMR images of an HCM (asymmetric septal hypertrophy) patient with no LGE, but had NSVT on Holter. Cine short axis (A), four-chamber (B) and two-chamber (C) images show hypertrophy of the septal segments. LGE PSIR image (D) shows no delayed enhancement. Native T1 polar map (E) shows diffusely elevated values, predominantly involving the septum. The polar map of Segmental circumferential strain (F) also shows elevated strain values, predominantly involving the septum, despite the absence of LGE. Colour maps of GCS (G), GRS (H), and GLS (I) with corresponding values in strain time curves show mildly reduced strain values (-17.1, 14.7, and -9.8 respectively).

Case 5 – HCM (asymmetric septal hypertrophy) patient with neither LGE nor NSVT

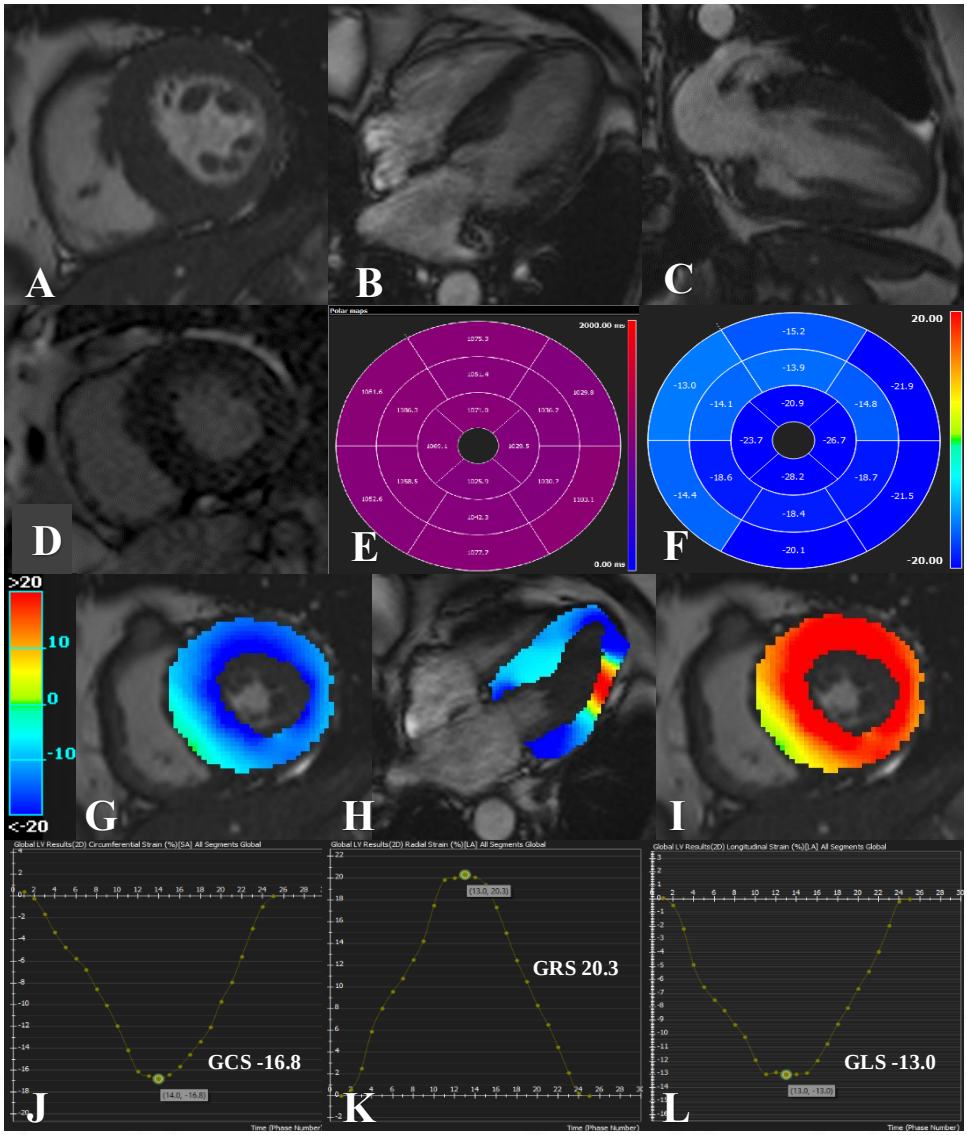

Figure 25. CMR images of an HCM (asymmetric septal hypertrophy) patient with no LGE who did not have NSVT on Holter. Cine short axis (A), four-chamber (B) and two-chamber (C) images show hypertrophy of the septal segments. LGE PSIR image (D) shows no areas of LGE. Native T1 polar map (E) shows diffusely elevated values, suggestive of interstitial fibrosis. The polar map of Segmental circumferential strain (F) also shows mildly elevated strain values, predominantly involving the septum. Colour maps of GCS (G), GRS (H), and GLS (I) with corresponding values in strain time curves show mildly reduced strain values (-16.8, 20.3, and -13 respectively).

Case 6 – HCM (concentric variant) patient with LGE>15% and NSVT

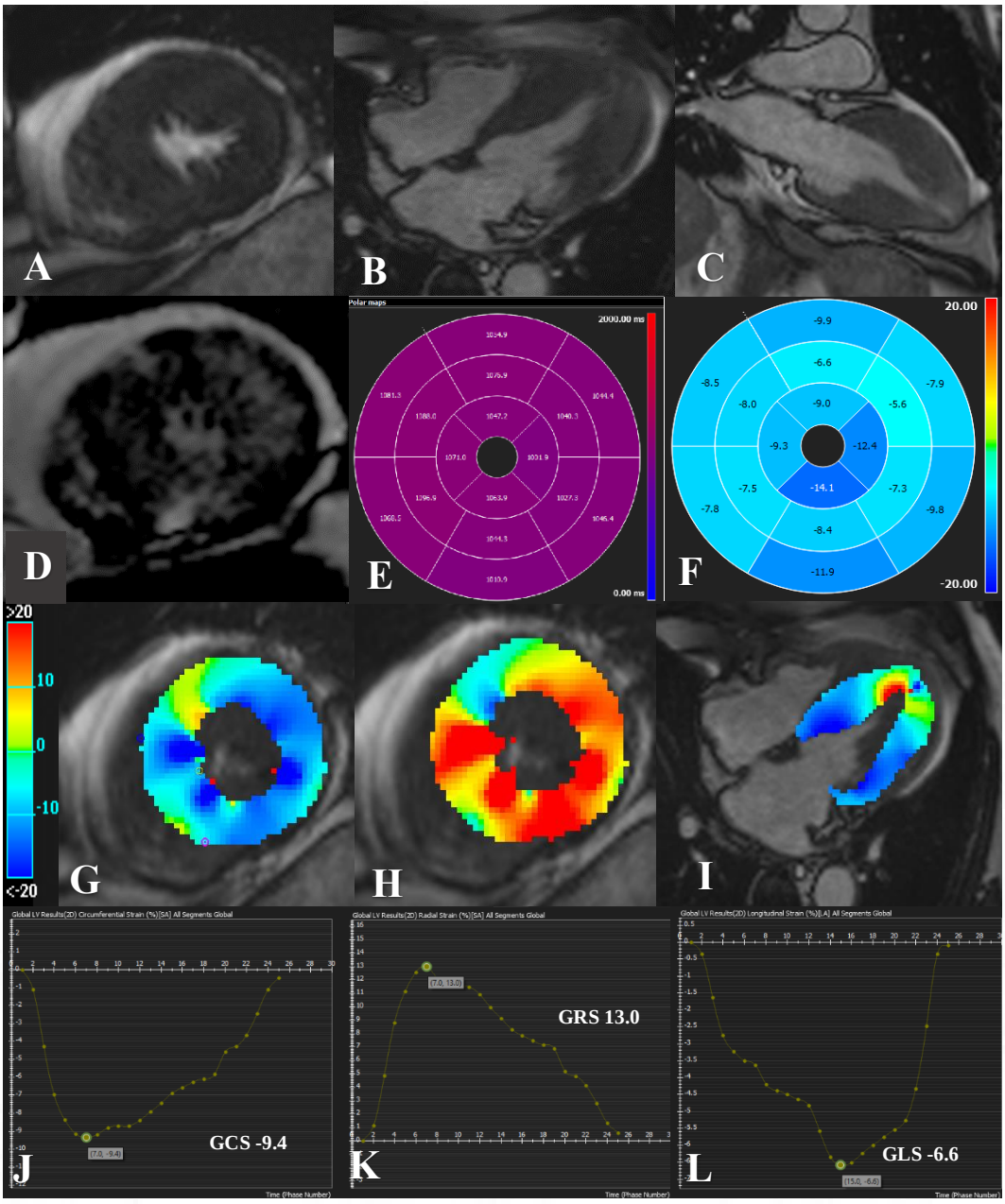

Figure 26. CMR images of an HCM (concentric variant) patient with LGE>15% who had NSVT on Holter. Cine short axis (A), four-chamber (B) and two-chamber (C) images show concentric hypertrophy of the LV myocardium. LGE PSIR image (D) shows extensive delayed enhancement in the hypertrophic myocardium and RV insertion points amounting to an LGE extent of 29.2%. Native T1 polar map (E) shows diffusely elevated values. The polar map of Segmental circumferential strain (F) also shows diffusely elevated strain values. Colour maps of GCS (G), GRS (H), and GLS (I) with corresponding values in strain time curves show severely reduced strain values (-9.4, 13, and -6.6 respectively).

Case 7 – HCM (apical variant) patient with neither LGE nor NSVT

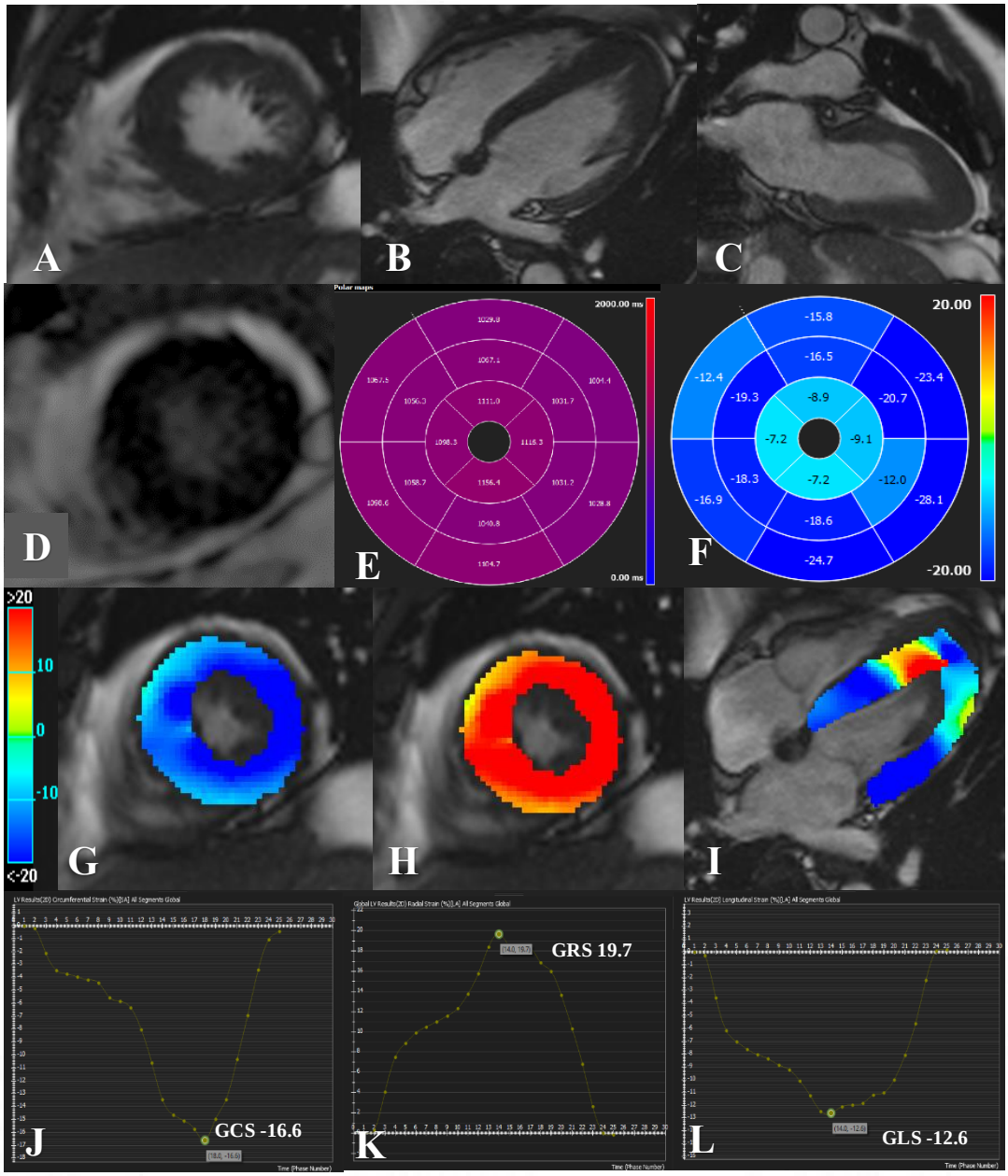

Figure 27. CMR images of an HCM (apical variant) patient with no LGE who did not have NSVT on Holter. Cine short axis (A), four-chamber (B) and two-chamber (C) images show hypertrophy of the apical segments. LGE PSIR image (D) shows no delayed enhancement. Native T1 polar map (E) shows diffusely elevated values, predominantly involving the apical segments. The polar map of Segmental circumferential strain (F) also shows elevated strain values, predominantly involving the apical segments. Colour maps of GCS (G), GRS (H), and GLS (I) with corresponding values in strain time curves show abnormal strain values (-16.8, 19.7, and -12.6 respectively).

5 DISCUSSION

This study aimed to analyse global myocardial mechanics using strain parameters in patients with HCM using CMR-FT and to evaluate the association of left ventricular strain parameters with the extent of LVH and the amount of left ventricular fibrosis. Healthy controls and patients with HCM were recruited, who subsequently underwent CMR, which included cine imaging using bSSFP, native T1 mapping, and LGE imaging. Strain parameters were obtained after processing cine images in cvi42 software which used the CMR-FT technique.

Global Strain Parameters in Healthy Volunteers

There are several studies assessing strain in healthy individuals done on MR scanners of different field strengths using different techniques and processing software. In the study by Peng J et al done in healthy volunteers, in which CMR was done in both 1.5T and 3.0T MR scanners and strain parameters were obtained using the CMR-FT technique on bSSFP cine images and processed in QStrain software, the GCS, GRS, and GLS values were reported as −24.3 ± 3.1%, 79.0 ± 19.4% and −22.4 ± 2.9% respectively.(73) Augustine D et al studied strain parameters of healthy volunteers in a 1.5T MR scanner using the CMR-FT technique on bSSFP cine images and processed in TomTec software. The GCS, GRS, and GLS values in the study were -21 ± 3, 25 ± 6, and -19 ± 3 respectively.(74) Another study evaluating CMR strain in healthy volunteers by Andre F et al in a 1.5T MR scanner using the CMR-FT technique on bSSFP cine images processed in TomTec software reported -21.3 ± 3.3% as GCS, 36.3 ± 8.7% as GRS and -21.6 ± 3.2% as GLS.(75) Liu B et al

who used the same MR scanner (1.5 T Siemens MAGNETOM Avanto, Siemens, Germany), technique (CMR-FT technique on bSSFP cine images) and software (cvi42) as the present study reported -20.9±3.6, 47.6±15.4 and -19.8±2.9 as the GCS, GRS, and GLS respectively.(76)

In the present study, the controls had mean GCS, GRS, and GLS values of -19.91±1.73, 32.75±3.9, and -17.97±1.32 respectively. These values are comparable to those reported by others, with small variations being accounted for due to the differences in the population assessed, scanners, and processing software used for strain analysis. GRS had the largest variation between different studies as it is the least reproducible because of the low imaging resolution in the radial direction as opposed to the circumferential or longitudinal directions.(77)

Global Strain Parameters in patients with HCM

The peak GCS, GRS, and GLS in patients with HCM were -15.39±2.78, 24.06±4.43, and -11.04±2.29 respectively in the present study. These values were significantly worse than the corresponding values in control subjects ($p < 0.001$ for all). The decreased GCS, GRS, and GLS were despite a preserved LVEF (68.26±6.85) in HCM patients. The hypertrophic myocardium pathology resulted in hyperejection status with normal or even higher LVEF and SVI in patients with HCM. However, the disordered arrangement of hypertrophic cardiac myocytes caused subclinical systolic and diastolic dysfunction in the early stages which are not reflected in LVEF. Myocardial strain, which is not affected by global movement and adjacent myocardium can thus detect these changes at an early stage.(52)

The global strain parameters of HCM patients have been compared to controls in other studies. The GCS, GRS, and GLS of HCM patients reported by Pu C et al(64), in their study performed using a 1.5-T scanner and CMR-FT technique in cvi42 software for strain analysis, were -19.41±3.40, 23.20 (17.25, 35.67) and −8.73 (−11.48, −6.75) respectively. All three parameters were significantly lower compared to healthy volunteers ($p < 0.05$). In a study performed using a 1.5-T scanner, CMR-FT technique in QStrain application for strain analysis, Cavus E et al(78) reported the GCS, GRS, and GLS of HCM patients to be -22.1 (-24.8, -18.3), 86.8 (65.9,115.5) and -18.9 (-22.0, -16.0) respectively. Among these, GLS and GRS were found to be significantly worse ($p < 0.001$) in HCM patients compared with controls. In the study by Li Y et al (79), who used a similar scanner (MAGNETOM Aera, Siemens Healthineers, Erlangen, Germany) and strain analysis software (cvi42), the GCS, GRS, and GLS (−20.01±3.58, 33.25±12.74 and −11.55±3.70 respectively) were significantly lower ($p < 0.05$ for all) than corresponding values in controls (−20.92±2.54, 36.58±8.70 and −14.77±2.36 respectively). The GCS (−15 ± 4.1), GRS (29 ± 9), and GLS (−13 ± 4.2) in HCM patients were also found to be significantly lower ($p < 0.001$ for all) than those in controls (−19 ± 2.8, 36 ± 9 and −19 ± 2.8 respectively) by Hinojar R et al (65), who performed CMR in 1.5-T MRI scanner and used cvi42 for strain analysis. These values are comparable to that obtained in our study, with maximum difference noted in GRS due to reasons cited above. The varying strain values across different studies can be explained by differences in the CMR scanner used for the study, scanning protocol, strain analysis software used, as well as differences in the demographics and ethnicity of the study population.

This study also showed that HCM patients with a family history of HCM or HCM-related SCD had significantly worse GCS ($p = 0.049$). Few studies have reported abnormal strain parameters in individuals with preclinical genotype positive HCM without overt phenotypic expression.(71)However, the utility of deformation parameters for detection of familial HCM, especially in resource-poor settings where genetic evaluation is seldom done, has not been evaluated. This finding of deranged GCS in patients with a family history of HCM or HCM-related SCD advocates for more stringent family screening in HCM patients with abnormal GCS.

CMR Findings in HCM Patients with LGE

The present study showed that all three global strain parameters were significantly lower ($p < 0.05$) in HCM patients with LGE compared to those without LGE. Patients with LGE also had a tendency toward significantly worse GCS ($P = 0.004$), GRS ($p = 0.015$) and GLS ($p < 0.001$). All three global strain parameters were also significantly lower ($p < 0.05$) in HCM patients with LGE extent >15% compared to those with LGE extent <15%. As the HCM disease process progresses, there is an increase in the extent of myocardial fibrosis and myocardial fibre disarray due sarcomeric protein mutation.(3) This increasing fibrosis leads to progressive worsening of myocardial function, which explains the lower strain parameters in HCM patients with more extensive LGE. This also explains why native T1, which better assesses diffuse interstitial fibrosis in HCM, was significantly higher in these patients.

Similar results have been reported in other studies. In the study by Pu C et al, patients with LGE had a tendency towards worse GRS, GCS and GLS compared to

those without LGE.(64) Satriano A et al showed that GLS ($p < 0.05$) and GCS ($p < 0.01$) within the non-enhanced myocardium were significantly reduced in HCM patients with extensive global LGE ($\geq 15\%$) compared to those without extensive global LGE.(80) All three LV strain parameters were significantly more attenuated ($p < 0.001$ for all) in patients with an extensive amount of LGE (>15%) compared to the HCM patients with <15% LGE.(65) All three global strain parameters were similarly impaired in HCM patients compared to healthy volunteers in the study by Chen X et al.(69)

CMR Findings related to NSVT in patients with HCM

In the present study, HCM patients with NSVT had significantly worse myocardial strain parameters, and increased % LGE compared with those without NSVT ($p < 0.01$ for all). Only GCS ($p = 0.007$) was identified as an independent marker for NSVT in HCM by multivariate logistic regression analysis. GCS [AUC 0.98, 95% CI (0.98, 1.00), $p < 0.001$] was determined to be an excellent test to identify HCM patients with NSVT. Using optimal cut-off values from ROC curves, HCM patients with GCS >-12.7% on CMR more frequently had NSVT.

The progression of HCM is associated with a corresponding increase in the extent of myocardial fibrosis and interstitial fibrosis which are represented by areas of high signal on LGE imaging and elevated native T1 values.(81) The rising scar burden adversely affects LV function and is also considered to be the substrate for ventricular arrhythmias. This explains the worse strain parameters, higher native T1 values and more extensive LGE in HCM patients with NSVT observed in our study.

The %LGE cut-off value of >14.55% for predicting NSVT also corresponded to findings described in other studies.(42)

In the study by Pu C et al(64), HCM patients with ventricular arrhythmias had lower GRS, GCS, and GLS, and increased %LGE compared with those without VAs ($p < 0.01$ for all). %LGE and GCS were indicators of ventricular arrhythmias in HCM patients by multivariate logistic regression analysis. These findings are consistent with those of our study. Similarly, Hinojar R et al observed that all LV strain parameters were significantly impaired in patients with adverse cardiovascular outcomes.(65) These findings have been corroborated in the prospective study by Dohy Z et al, who showed that GLS and GCS were univariate predictors of all-cause mortality, heart transplantation, and malignant ventricular arrhythmias, and appropriate implantable cardioverter defibrillator therapy.(67)

In our study, GCS was the best test to identify HCM patients with NSVT with the largest AUC among the various parameters assessed and the only independent marker of NSVT on multivariate analysis. Thus, it can be inferred that in comparison to LGE, which is the established imaging biomarker for predicting VAs in HCM, GCS performs better. Increased myocardial heterogeneity resulting from myocardial hypertrophy and fibrosis aggravates the possibility of ventricular arrhythmias. These pathological abnormalities predominantly occurred in the middle layer of the myocardium which is reflected by changes in GCS.(82) We speculated that this resulted in lower myocardial strain values, especially GCS, and can explain why among the various imaging parameters, only GCS was seen to marker for NSVT on multivariate analysis in our study. GCS can be considered as an independent

predictor for NSVT occurrence in HCM patients where LGE and native T1 values are not available or in circumstances when these cannot be performed due to patient-related risk factors.

Correlation between GCS, MWT, %LGE, and native T1

The present study showed a moderate positive significant correlation between GCS and MWT ($r = 0.47$, $p < 0.001$) and between GCS and %LGE ($r = 0.48$, $p < 0.001$). There was a strong positive significant correlation between GCS and native T1 ($r = 0.76$, $p < 0.001$). Native T1 mapping and LGE are both established CMR markers of myocardial fibrosis, which also contributes to LV dysfunction in HCM. This can explain the significant correlation between these three parameters observed in our study. Congruence of GCS with other predictors of adverse life events in HCM increases its importance in imaging. Similar findings have been reported in other studies. In the study by Pu C et al, GCS and %LGE were correlated moderately ($r = 0.51$, $p < 0.001$) and there was a weak but significant correlation between %LGE and GRS and GLS ($r = -0.38$, $p < 0.001$; $r = 0.34$, $p = 0.001$; $r = -0.31$, $p < 0.01$).(64) In the study by Hinojar R C et al, a negative correlation between all three strain parameters and the extent of LV hypertrophy was observed. The amount of LGE mass was also negatively correlated with GLS, GCS, and GRS. The study also reported that LV mass index and % LGE were independent predictors of altered LV strain parameters.(65) Li Y et al in their study reported that % LGE was inversely associated with GCS and was positively correlated with LV end-diastolic MWT ($p < 0.05$ for all). The MWT ($p = 0.001$) and GCS ($p = 0.024$) were also found to be independent determinants of the % LGE. Correlation between impaired GLS with

higher LVMI and more extensive myocardial fibrosis was also demonstrated in the study by Dohy Z et al.(67)

Segmental circumferential strain SCS

The circumferential strain in the 16 segments (segmental circumferential strain SCS) of the LV was assessed. The SCS in HCM patients (-16.47±4.38) was significantly worse compared to that in controls (-20.75±2.86) ($p < 0.001$). The mean SCS of HCM patients with NSVT (14.37±5.14) was significantly worse compared to SCS of HCM patients without NSVT (-16.24±5.32). Univariate logistic regression analysis identified SCS ($p < 0.001$), as a marker for NSVT in patients with HCM. There was a moderate positive significant correlation between SCS and segmental LV wall thickness ($r = 0.41$, $p < 0.001$), SCS and segmental native T1 ($r = 0.42$, $p < 0.001$) and between SCS and segmental LGE ($r = 0.55$, $p < 0.001$). ROC curve analysis showed that SCS [AUC 0.86, 95% CI (0.84, 0.88), $p < 0.001$] was a very good test to identify the presence of LGE within the corresponding segment. Using optimal cut-off values from ROC curves, SCS >-15.85% was more frequently associated with the presence of segmental LGE.

Regional myocardial dysfunction can occur at an early stage even when the ejection fraction is within the normal range similar to patients with heart failure with preserved ejection fraction.(83) Similarly normal or even elevated LVEF is seen in patients with early-stage HCM patients due to hypertrophic hypercontractile LV myocardium. All HCM patients in this study has normal LVEF which was significantly higher than those of controls. However, the segmental circumferential strain was decreased despite normal or increased LVEF in HCM patients, in a trend

similar to global strain values. It can thus be inferred that myocardial strain is more sensitive than LVEF in measuring subclinical dysfunction of HCM. Various morphological variants of HCM exist involving LV hypertrophy localized to different sites.(84) LGE is also more commonly seen in these hypertrophied segments.(85) Thus, in comparison to measuring global strain of the whole heart, assessment of segmental deformation analysis could prove more valuable in detecting areas of fibrosis earlier. This could explain the positive significant correlation between SCS and segmental LV wall thickness, segmental native T1, and segmental LGE observed in our study which included different variants of HCM. SCS, thus being a surrogate for localised scar, was significantly worse in HCM patients with NSVT and a marker for NSVT in univariate logistic regression analysis.

Xu H et al(68) observed that all regional strain parameters were lower in hypertrophic and non- hypertrophic segments of patients with HCM ($p < 0.05$) with lower values in segments with LGE ($p < 0.001$). These findings were similar to those seen in the present study Chen X et al(69), in their prospective study, have shown the potential of regional strain parameters to predict adverse outcomes in HCM patients.

Clinical Implications

The findings of this study suggest that myocardial strain detected by CMR-FT can provide further discrimination of the LV function and disease severity beyond LVEF and LGE, and has the potential to evaluate earlier stages of HCM with high technical feasibility. Novel therapies could thus be used to modify or potentially

reverse fibrosis detected at an earlier stage, before the development of dense scar detected on LGE.(86) GCS can predict myocardial fibrosis in HCM, which is of particular importance in those patients in whom LGE imaging quality is poor. Moreover, as strain analysis does not require the administration of intravenous gadolinium contrast, it could serve as an alternative for scar detection in those patients with significant renal impairment. The association between strain parameters and native T1, which is a marker of interstitial fibrosis, has not been extensively studied. The significant correlation of GCS and native T1 values, as well as SCS and segmental native T1, in this study, indicates that GCS can be applied clinically as a supplementary method for scar detection. In this study, GCS was found to be an independent predictor for NSVT in HCM patients in multivariate analysis. Reduced GCS may thus have the potential to identify HCM patients at risk of VAs. In addition to LGE, the extent of abnormal strain in HCM patients can enhance our understanding of disease progression and the risk of adverse cardiovascular outcomes.

Limitations

This study has a modest sample size and was conducted in a single centre. The relatively small number of patients from a single centre might limit the extrapolation of these results to other populations. This was a cross-sectional study with no long-term follow-up. Thus, the predictive values of CMR-FT to predict adverse cardiovascular outcomes like VAs cannot be addressed. The present study does not include left atrial and right ventricular strain parameters, which have also been known to affect disease outcomes in HCM. This study also did not evaluate the

intra- and inter-observer reproducibility of strain analysis. However, as CMR-FT strain analysis is highly automated, a high reproducibility is expected as described in previous studies.(64,65,69,79,87)

6 SUMMARY AND CONCLUSIONS

In our single centre, cross-sectional observational study, a total of 81 patients with HCM and 31 healthy volunteers underwent CMR, which included cine imaging using bSSFP, native T1 mapping, and LGE imaging. Strain parameters were obtained after processing cine images in cvi42 software which used the CMR-FT technique. The global myocardial mechanics using strain parameters, its association with the extent of LVH, and the amount of left ventricular fibrosis were analysed. CMR-FT strain analysis was successfully performed in all subjects included in the study, and tracking quality was found to be sufficient in all cases. The peak GCS, GRS, and GLS in patients with HCM were significantly worse ($P<0.001$ for all) despite a preserved LVEF. Moreover, all three global strain parameters were significantly lower ($P<0.05$) in HCM patients with LGE compared to those without LGE and in HCM patients with LGE extent >15% compared to those with LGE extent <15%. GCS ($P = 0.007$) was determined to be a marker of NSVT on multivariate logistic regression analysis and it was an excellent test to identify HCM patients [AUC 0.98, 95% CI (0.98, 1.00), $P < 0.001$] with NSVT on ROC curve analysis. HCM patients with GCS cut-off of >-12.7% on CMR more frequently had NSVT. A significant correlation was observed between GCS and MWT ($r = 0.47$, $p < 0.001$), between GCS and %LGE ($r = 0.48$, $p < 0.001$) and between GCS and native T1 ($r = 0.76$, $p < 0.001$). The SCS in HCM patients was significantly worse compared to that in controls ($P<0.001$). The SCS of HCM patients with NSVT was also significantly worse compared to the SCS of HCM patients without NSVT. SCS

was identified as a marker for NSVT ($P < 0.001$) in patients with HCM in univariate logistic regression analysis. There was a moderate positive significant correlation between SCS and segmental LV wall thickness ($r = 0.41$, $p < 0.001$), SCS and segmental native T1 ($r = 0.42$, $p < 0.001$) and between SCS and segmental LGE ($r = 0.55$, $p < 0.001$). ROC curve analysis showed that SCS [AUC 0.86, 95% CI (0.84, 0.88), $P < 0.001$] was a very good test to identify the presence of LGE within the corresponding segment with an optimal cut-off value of >-15.85% to identify the presence of segmental LGE.

In conclusion, CMR-FT derived strain parameters, especially GCS and SCS, could serve as surrogate markers of disease severity in HCM, with the potential to identify those patients at high risk for major adverse cardiovascular outcomes. This is particularly advantageous, considering that strain analysis using the CMR-FT technique can be performed on routinely acquired CMR cine imaging without the need for intravenous contrast administration and with high technical feasibility and reproducibility. Thus, strain parameters can be easily incorporated into routine CMR protocols, and serve as an important tool in the evaluation of pathophysiology and progression of HCM. These findings should be evaluated in large-scale prospective studies to conclusively establish their associations with adverse cardiac outcomes.

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ANNEXURES

List of publications from Thesis - NIL

CV of the Investigator

Format for CV of the Investigators

Mondy	Vimal	Chacko
Last Name	First Name	Middle Name
Date of Birth (dd/mm/yy) 14/10/1990		Sex Male
Study Site Affiliation (e.g. Principal Investigator, Co-Investigator, Coordinator): Principal Investigator		
Professional Mailing Address (Include Institution name)		Study Site Address (Include Institution name)
Senior Resident Dept. of IS & IR SCTIMST, Trivandrum Kerala -695011		Senior Resident Dept. of IS & IR SCTIMST, Trivandrum Kerala -695011
Telephone (Office):		Mobile Number: 9809916749
Telephone (Residence):		Email: vimalchackomdy@yahoo.com
Academic Qualifications (Most recent qualification first)		
Degree/Certificate	Year	Institution, Country
MD Radiodiagnosis	2019	Madras Medical College, Chennai, India
MBBS	2014	Govt. Medical College, Thrissur, India
Details of professional registration: (MCI/State Registration/Bar Council/DCI/etc including Registration Number and Year of Registration TCMC, Reg No.52495, 2015		
Current and previous positions (most recent position first)		
Month and Year	Title	Institution/Company, Country
Brief summary of relevant research experience: NIL		
Current project/s at hand: NIL		
Signature:		Date:13/05/2020 Place:Trivandrum

A	Anoop	
Last Name	First Name	Middle Name
Date of Birth (dd/mm/yy) 03/11/86		Sex Male
Study Site Affiliation (e.g. Principal Investigator, Co-Investigator, Coordinator) Co-Principal Investigator		
Professional Mailing Address (Include Institution name)		Study Site Address (Include Institution name)
Assistant professor Department of IS& IR, SCTIMST, Trivandrum Kerala- 695011		Assistant professor Department of IS& IR, SCTIMST, Trivandrum Kerala- 695011
Telephone (Office): 04712524220		Mobile Number: 8547683011
Telephone (Residence):		Email: anoop.a@sctimst.ac.in

Academic Qualifications (Most recent qualification first) PDCC. MD RadioDiagnosis, MBBS

Degree/Certificate	Year	Institution, Country
PDCC in vascular interventions and cardiac imaging	2015	Sree Chitra Tirunal Institute for Medical Sciences & Technology, Trivandrum
MD (Radio-Diagnosis) Doctor of Medicine	2014	Institute Of Post Graduate Medical Education And Research & SSKM hospital, Kolkata.
MBBS	2010	Govt. Medical College, Kozhikode, Kerala

Details of professional registration : (MCI/State Registration/Bar Council/DCI/etc including Registration Number and Year of Registration - TCMC no: 42911 of 2011

Current and previous positions (most recent position first)

Month and Year	Title	Institution/Company, Country
July 2017	Assistant Professor, IS & IR	SCTIMST
Jan 2016	Assistant Professor(Ad hoc), IS & IR	SCTIMST

Brief summary of relevant research experience:
Have got intramural and extramural funding for few unique projects and are in the process of completion

Current project/s at hand:

1) Role of non-contrast and post contrast myocardial T1 mapping in hypertrophic and dilated cardiomyopathy-IEC approved no: SCT/ IEC/856/feb2016.
2) Three-dimensional printing in congenital heart disease- Jun2018-jun2021 in SERB, Govt of India. SCT/ IEC/1076/dec2017.
3) Assesment of carotid plaque vulnerability using 3T MRI & correlation with carotid endarterectomy- TDF fund approved project, 2-year duration–October 2018-2020. SCT/ IEC/1239/aug2018.

Signature: 	Date: 27-6-19 Place: Thiruvananthapuram

Format for CV of the Investigators

Last Name- Valakada	First Name- Jineesh	Middle Name
Date of Birth (dd/mm/yy) 17/04/1987		Sex M
Study Site Affiliation (e.g. Principal Investigator, Co-Investigator, Coordinator) Co-Investigator		
Professional Mailing Address (Include Institution name)		Study Site Address (Include Institution name)
Assistant Professor Department of IS& IR, SCTIMST, Trivandrum Kerala- 695011		Department of IS& IR, SCTIMST, Trivandrum Kerala- 695011
Telephone (Office):		Mobile Number: 8447284059
Telephone (Residence):		Email: jineesh174@gmail.com
Academic Qualifications (Most recent qualification first) MD RadioDiagnosis, MBBS		
Degree/Certificate	Year	Institution, Country
Fellowship GI intervention radiology	2017	AIIMS – NEWDELHI
MD radiodiagnosis	2013	AIIMS- NEWDELHI
DNB RADIODIAGNOSIS	2014	
Details of professional registration: (MCI/State Registration/Bar Council/DCI/etc including Registration Number and Year of Registration TCMC- 44903		
Current and previous positions (most recent position first)		
Month and Year	Title	Institution/Company, Country
2018 FEB-present	Assistant professor – IS and IR	SCTIMST- TRIVANDRUM
2014-2017	Senior resident	AIIMS – NEWDELHI

Publications:.

1.Valakkada J ,Chandran R, Mishra P, Pawar DK, Maitra S,. Internal jugular vein thrombosis from rhino-cerebral mucormycosis: Be careful before cannulation. Indian J Crit Care Med Peer-Rev Off Publ Indian Soc Crit Care Med. 2014 Aug

2.Kumar V, Karunakaran A, Valakada J. Septo-optic dysplasia. Int Ophthalmol. 2017 Jan 3

3.Jineesh ,Gamanagatti S, Rangarajan K, Kumar A,. Blunt abdominal trauma: imaging and intervention. Curr Probl Diagn Radiol. 2015 Aug;44(4):321–36.

4.Abdominal lymphangiomatosis with intestinal lymphangectasia – MR lymphangiography (CDPR)

5. primary cutaneous histoplasmosis with splenic involvement

6. salphingocolic fistula – case report 2017

Current project/s at hand: 1.IVIM in hepatocellular carcinoma

2.Prophylactic ballooning in radiocephalic fistluas- RCT

Signature:	Date: Place:Trivandrum

Last Name: Gopalakrishnan	First Name: Arun	Middle Name
Date of Birth (dd/mm/yy) 14/08/1983		Sex: Male
Study Site Affiliation (e.g. Principal Investigator, Co-Investigator, Coordinator) Co-investigator		

Professional Mailing Address (Include Institution name)	Study Site Address (Include Institution name)
Department of Cardiology, SCTIMST	Department of Cardiology, SCTIMST
Telephone (Office): 04712524180	Mobile Number: 8547609631
Telephone (Residence): 04782594142	Email: arunek@sctimst.ac.in

Academic Qualifications (Most recent qualification first): DM Cardiology, MD Pediatrics, MBBS

Degree/Certificate	Year	Institution, Country
DM Cardiology	2015	SCTIMST, India
MD Pediatrics	2011	JIPMER, India
MBBS	2008	Govt. MCH, TVM, India

Details of professional registration : (MCI/State Registration/Bar Council/DCI/etc including Registration Number and Year of Registration: 37394, Travancore Cochin Medical Council, Dated 17th January 2008

Current and previous positions (most recent position first)

Month and Year	Title	Institution/Company, Country
Jan – Aug 2016	Asst Prof (Adhoc) Cardiology	SCTIMST
Sep 2016 to date	Asst Prof Cardiology	SCTIMST

Brief summary of relevant research experience:
52 journal publications. 5 completed projects

Current project/s at hand: 3 extramural funded projects, 2 intramural funded projects, 3 non funded projects
Kerala Acute Heart Failure Registry
Evaluation of intermediate term cardiac and neurodevelopmental outcomes of children undergoing corrective arterial switch operation for complete transposition of great arteries.
Estimation study for reduction in transport of referral cases to tertiary hospitals by use of mobile enabled telemedicine system in remote hospitals.

Signature: 	Date: 04 – 05 – 2020 Place: Thiruvananthapuram

Appendices

APPENDIX A – ETHICS COMMITTEE APPROVAL

Technical Advisory Committee (Clinical Studies)

SREE CHITRA TIRUNAL INSTITUTE FOR MEDICAL SCIENCES & TECHNOLOGY
THIRUVANANTHAPURAM – 695011, INDIA

TAC Registration No: SCT-/S/2020/1112 **Date: 27.07.2020**

Project title: ANALYSIS OF STRAIN PARAMETERS IN PATIENTS WITH HYPERTROPHIC CARDIOMYOPATHY BY CARDIOVASCULAR MAGNETIC RESONANCE FEATURE TRACKING

Principal Investigator:	
Dr Vimal Chacko Mondy, Senior Resident, Department of IS & IR, SCTIMST	Degree: MBBS, MD
Co-Principal Investigator(s):	
Dr. Anoop A, Assistant Professor, Department of IS and IR, SCTIMST	Degree: MBBS, MD, PDCC
Dr. Jineesh V, Assistant Professor, Department of IS and IR, SCTIMST	Degree: MBBS, MD, DNB, PDCC
Co- Investigator(s):	
Dr Arun Gopalakrishnan, Assistant Professor, Department of Cardiology, SCTIMST	Degree: MBBS, MD, DM

Members who participated in the TAC meeting on 20/06/2020
Dr Harikrishnan S (Chairman)
Dr Manikandan S
Dr Narayanan Namboodiri
Dr Jayadevan E R
Dr Sylaja P N
Dr Ramshekhar N Menon
Dr Unnikrishnan K P
Dr Syam K
Dr Sanjay G
Dr Deepti A N
Dr Sabarinath Menon
Dr Jayanand Sudhir B
Dr Srinivas G (Member Secretary)

Dr Sabarinath Menon, Dr Ramshekhar N Menon, Dr Sylaja P N, Dr Deepti A N, Dr Manikandan S, Dr Narayanan Namboodiri, Dr Srinivas G, Dr Sanjay G, Dr Harikrishnan S, Dr Unnikrishnan K P, Dr Syam K and Dr Jayadevan E R stayed away from the proceedings when the projects in which they are involved as investigator were discussed (#1072,1087, 1089, 1092, 1093, 1095, 1096, 1097, 1098, 1099, 1100, 1101, 1103, 1107, 1108, 1111, 1113, 1114, 1116, 1118, 1119, 1120, 1121, 1122, 1123, 1127, 1129, 1130)

Risk Classification of the project (Minimum/ Moderate/ High): Minimum
Requirement of DSMB: No
Recommended members of DSMB: Not applicable

Recommendations of TAC:
Recommended for consideration of IEC in the light of the responses received from the investigator
The PI may note that there can be no additions / alterations in the documents approved by TAC when they are submitted to the IEC.

MEMBER SECRETARY
TAC (Clinical Studies)
SCTIMST

Dr Srinivas G

Note for IEC
Copy of the investigator's responses to questions/suggestions from TAC is attached (Appendix-1).

Page 1 of 2

PROFORMA

Title: Analysis of Strain parameters in patients with Hypertrophic cardiomyopathy by Cardiovascular Magnetic Resonance Feature Tracking

1. Patient ID:
2. Age:
3. Sex:
4. Clinical details:
    a) Syncope
    b) Family history of SCD/HCM:
    c) NSVT
    d) NYHA class:
5. Other Factors:
    a) Smoker Yes / No
    b) Diabetes Mellitus Yes / No
    c) Hypertension Yes / No
    d) Dyslipidemia Yes / No
6. Cardiac MRI findings:
    a) Type of hypertrophy: Apical, global, septal, mid-ventricular
    b) Left ventricular End diastolic volume (LV-EDV) index, ml/m^2
    c) Left ventricular Ejection Fraction LVEF %
    d) Right ventricular Ejection Fraction RVEF %
    e) LV Mass Index (mg/m^2)
    f) LV Segment with maximum wall thickness
    g) Maximal left ventricular wall thickness (LVWT) (mm)
    h) Left atrial (LA) volume index, ml/m^2
    i) LGE
        1. Present/Absent
        2. LGE extension:
            i. 1–5%, n (%)
            ii. 6–10%, n (%)
            iii. 11–15%, n (%)
            iv. 16–20%, n (%)

v. >20%, n (%)

j) Segmental Native T1 values

k) LV Feature Tracking

1. Global longitudinal strain GLS, %
2. Global circumferential strain GCS, %

Global radial strain GRS, %

INFORMATION SHEET

TITLE OF THE STUDY: Analysis of Strain parameters in patients with Hypertrophic cardiomyopathy by Cardiovascular Magnetic Resonance Feature Tracking.

Name of Institute where study undertaken: Sree Chitra Tirunal Institute of Medical Sciences & Technology

Study number: ----------

Participant's name: ----------

Date of Birth / Age(in years): ---------- son/daughter of----------

You have been informed that there is a marked hypertrophy of a part of your heart, which is believed to be the cause of your symptoms (like syncope, palpitation, arrhythmia). As part of diagnosis and treatment planning of your condition, Cardiac MRI is planned. That investigation is being routinely done in other patients also with a similar indication or other appropriate indications.

You are being requested to participate in a study to analyse strain parameters using Cardiac MRI. Participating in this study, in which only data from the investigations you have undergone for your diagnosis and treatment planning will be used, will in no way influence treatment decisions.

What is cardiac MRI and does it have any harmful effects?

Cardiac MRI is an advanced imaging technique which uses radio waves and a powerful magnet linked to a computer are used to make detailed pictures of heart. These images can show the difference between normal and abnormal tissue with anatomy and function. Post processing will be done using dedicated software. There is no risk of radiation exposure. This test is vital in diagnosis of your condition, its treatment planning and for follow up subsequently.

If you take part what will you have to do?

For this study, we'll be using some of the data like history, ECG and other clinical details, Imaging details (Cardiac MRI), treatment technique, outcome of the procedure, delayed follow up clinical and radiological regarding your disease and treatment which you undergo in this hospital.

No additional cost will be incurred /no additional drugs will be used and there are no additional risks as a part of the research.

Analysis of these data may or may not be useful for you, but this is likely to give more understanding of this disease and treatment, for the benefit of future generations. You understand that strict confidentiality will be maintained.

Can you withdraw from this study after it starts?

Your participation in this study is entirely voluntary and you are also free to decide to withdraw permission to participate in this study. If you do so, this will not affect your usual treatment at this hospital in any way.

What will happen if you develop any study related injury?

This study only analyzes the results of your investigation and treatment details and thus we do not expect any injury to happen to you, but if you do develop any side effects or problems due to the study, these will be treated at this institute by the experienced team of medical professionals. We are unable to provide any monetary compensation, however.

Will you have to pay for the study?

The study will only analyse the results of the investigations which you will undergo in natural process of your treatment at this institute and no extra cost will be borne by you for this particular study.

What happens after the study is over?

You may or may not benefit from this study, however it may benefit other patients with similar illness.

Will your personal details be kept confidential?

The results of this study may be published in a medical journal, but you will not be identified by name in any publication or presentation of results. However, your medical notes may be reviewed by people associated with the study, without your additional permission, should you decide to participate in this study.

If you have any further questions, please ask Dr Vimal Chacko Mondy (Tel: 9809916749) or email: vimalchackomdy@sctimst.ac.in or contact IEC member secretary (tel: 0471-2524263)

CONSENT FORM

TITLE OF THE STUDY: Analysis of Strain parameters in patients with Hypertrophic cardiomyopathy by Cardiovascular Magnetic Resonance Feature Tracking.

Study number:……..

Participant's name: …… Date of Birth / Age (in years): ……..

I_____

_____, Son/daughter of

_____(Please tick boxes)

- Declare that I have read the above information provide to me regarding the study: "Analysis of clinical and angiographic outcome predictors in high risk carotid stenting" and have clarified any doubts that I had. [ ]

- I also understand that my participation in this study is entirely voluntary and that I am free to withdraw permission to continue to participate at any time without affecting my usual treatment or my legal rights. [ ]

- I also understand that study investigators will be using some of the data like history and other clinical details, Imaging details (Cardiac MRI) delayed follow up clinical and radiological regarding the disease and treatment which I undergo in hospital. [ ]

- I also understand that no additional cost will be incurred /no additional drugs will be used and there are no additional risks as a part of the research. [ ]

- I understand that the study staff and institutional ethics committee members will not need my permission to look at my health records even if I withdraw from the trial. I agree to this access. []

- I understand that my identity will not be revealed in any information released to third parties or published. [ ]

- I voluntarily agree to take part in this study. [ ]

- I received a copy of this signed consent form. [ ]

Name:

Signature:

Date:

Name of witness:

Relation to participant:

Date:

(Person Obtaining Consent) I attest that the requirements for informed consent for the medical research project described in this form have been satisfied. I have discussed the research project with the participant and explained to him or her in nontechnical terms all of the information contained in this informed consent form, including any risks and adverse reactions that may reasonably be expected to occur. I further certify that I encouraged the participant to ask questions and that all questions asked were answered.

_____ _____

Name and Signature of Person Obtaining

Consent Principal Investigator.

For any clarifications regarding the study's ethics clearance you may contact the Member Secretary of the SCTIMST-IEC. The phone number is: 0471-2524263 and the email id is iec.mem.sec@sctimst.ac.in

കാര്യവിവരണപത്രം

പഠനശീർഷകം: കാർഡിയോവാസ്കുലാർ മാഗ്നെറ്റിക് ഫീച്ചർ ട്രാക്കിംഗ് ഉപയോഗിച്ച് ഹൈപ്പർട്രോഫിക് കാർഡിയോമയോപ്പതി ഉള്ള രോഗികളിൽ സ്ട്രെയിൻ ചിത്രീകരണ ഘടകങ്ങളുടെ വിശകലനം.

പഠനം നടത്തുന്ന സ്ഥാപനം: ശ്രീ ചിത്ര തിരുനാൾ ഇൻസ്റ്റിറ്റ്യൂട്ട് ഫോർ മെഡിക്കൽ സയൻസസ് ആൻറ് ടെക്നോളജി (SCTIMST)

പഠന നമ്പർ:

പങ്കാളിയുടെ പേര്:

ജനന തിയതി / വയസ്സ് (വർഷത്തിൽ):

പുത്രൻ / പുത്രി:

താങ്കളുടെ രോഗലക്ഷണങ്ങളുടെ (ബോധക്ഷയം, കിതപ്പ്, ഹൃദയമിടിപ്പിന്റെ താളവ്യത്യാസം) കാരണമെന്ന് വിശ്വസിക്കപ്പെടുന്ന പ്രകടമായി ഹൈപ്പർട്രോഫി ഹൃദയത്തിലൊരു ഭാഗത്തുണ്ടെന്നു താങ്കളെ അറിയിച്ചിട്ടുണ്ട്. താങ്കളുടെ അവസ്ഥയുടെ രോഗനിർണയത്തിനും ചികിത്സ ആസൂത്രണം ചെയ്യാനുമായി ഹൃദയത്തിന്റെ എംആർഐ ഉദ്ദേശിക്കുന്നു. സമാനമായ സൂചനകളോ മറ്റു അനുയോജ്യമായ സൂചനകളോ ഉള്ള മറ്റു രോഗികളിലും ഈ പരിശോധന പതിവായി ചെയ്യാറുണ്ട്.

താങ്കൾ രോഗനിർണയത്തിനായി വിധേയമായ പരിശോധനകളുടെയും ആസൂത്രണം ചെയ്ത ചികിത്സയുടെയും വിവരങ്ങൾ മാത്രമാണ് ഉപയോഗിക്കുന്നത് എന്നതിനാൽ ഒരുവിധത്തിലും താങ്കളുടെ ചികിത്സാതീരുമാനങ്ങളെ പഠനം സ്വാധീനിക്കില്ല.

എന്താണ് കാർഡിയാക് എംആർഐ അഥവാ ഇത് ചെയ്യുന്നത് വഴി എന്തെങ്കിലും പ്രത്യാഘാതങ്ങൾ ഉണ്ടോ?

കാർഡിയാക് എംആർഐ ഒരു നൂതന സാങ്കേതിക വിദ്യ വഴി ഹൃദയ പേശികളുടെ പ്രവർത്തനതകരാറുകൾ കണ്ടുപിടിക്കുന്ന സാങ്കേതികവിദ്യയാണ്. അതിശക്തമായ കാന്തിക മണ്ഡലം ഉപയോഗിച്ചുകൊണ്ട് കംപ്യൂട്ടറിന്റെ സഹായത്തോടുകൂടി ഹൃദയത്തിന്റെ ശരിയായ ഘടനയുടെ വ്യക്തമായ പ്രവർത്തനം പകർത്തിയെടുക്കുന്ന ഒരു സ്കാനിംഗ് രീതിയാണ് കാർഡിയാക് എംആർഐ. കമ്പ്യൂട്ടർ സോഫ്റ്റ്വെയർ സഹായത്തോടുകൂടി പകർത്തിയെടുക്കുന്ന ഈ ചിത്രങ്ങൾ ഹൃദയത്തിന്റെ സ്വാഭാവികവും അസ്വാഭാവികവുമായ സിരകളുടെയും ശരീരഘടനയുടെയും പ്രവർത്തനം മനസ്സിലാക്കാൻ കഴിയുന്നു. മറ്റു സ്കാനിങ്ങുകൾ പോലെ ശരീരത്തിന് ഈ സ്കാനിംഗ് കൊണ്ട് യാതൊരു ദോഷവുമില്ല. ഈ പരിശോധന താങ്കളുടെ ശരിയായ അസുഖം കണ്ടുപിടിക്കുന്നതിനും അതിനു ശേഷം ചികിത്സ തുടങ്ങുന്നതിനും തുടർചികിത്സ തീരുമാനിക്കാനും അത്യന്താപേക്ഷിതമാണ്.

ഇതിൽ പങ്കെടുത്താൽ താങ്കൾ എന്താണ് ചെയേണ്ടത്?

ഈ പഠനത്തിൽ താങ്കൾ പങ്കാളിയായാൽ ആശുപത്രിയിൽ താങ്കളുടെ രോഗത്തിന്റെ രേഖകൾ ഇസിജി, മറ്റു ചികിത്സാസംബന്ധമായ വിവരങ്ങൾ, സ്കാനിംഗ് ഫിലിമുകൾ (കാർഡിയാക് എംആർഐ) ചികിത്സാ രീതികൾ ചികിത്സക്കു ശേഷമുള്ള റിപ്പോർട്ട്, തുടർചികിത്സ സംബന്ധിച്ചുള്ള താങ്കളുടെ അസുഖത്തിന്റെ രേഖകളുടേയും ചികിത്സയുടെയും വിവരങ്ങൾ നൽകേണ്ടതായി വന്നേക്കാം.

ഈ പഠന പ്രവർത്തനത്തിൽ പങ്കാളിയാകുന്നതു വഴി താങ്കൾക്ക് അധിക പണമൊന്നും അടക്കേണ്ടതില്ല. അതുപോലെ അധികം മരുന്ന് ഉപയോഗിക്കുകയോ മറ്റു അപകടമോ ഉണ്ടായിരിക്കുന്നതല്ല.

ഈ പഠനപ്രവർത്തനത്തിന്റെ ഭാഗമായി ശേഖരിക്കപ്പെടുന്ന വിവരങ്ങൾ ചിലപ്പോൾ താങ്കൾക്ക് പിന്നീട് ഉപകാരപ്പെട്ടേക്കാം. അതുപോലെ ഈ വിവരങ്ങൾ വരും തലമുറക്ക് കൂടുതലായി ഈ അസുഖത്തിനും ചികിത്സക്കും ഉപകാരപ്പെട്ടേക്കാം. തങ്ങൾ നൽകുന്ന ഈ വിവരങ്ങൾ തീർച്ചയായും വളരെ രഹസ്യമായി സൂക്ഷിക്കുന്നതായിരിക്കുമെന്ന് നിങ്ങൾ മനസ്സിലാക്കുക.

ഈ പഠനപ്രവർത്തനത്തിൽ പങ്കെടുത്താൽ ഇതിൽ നിന്നും പിന്മാറാൻ സാധിക്കുമോ?

ഈ പഠനപ്രവർത്തനത്തിൽ താങ്കളുടെ പങ്കാളിത്തം പൂർണമായും സ്വമേധയാലും നിയന്ത്രിതവുമാണ്. ഇതിൽനിന്ന് എപ്പോൾ വേണമെങ്കിലും താങ്കളുടെ സമ്മതം പിൻവലിക്കാനാകുന്നതുമാണ്. അഥവാ അങ്ങനെ ചെയ്താലും ഈ ആശുപത്രിയിൽ താങ്കൾക്ക് സാധാരണ ഗതിയിൽ ലഭിക്കുന്ന ചികിത്സക്ക് യാതൊരു രീതിയിലുള്ള തടസ്സങ്ങളും ഉണ്ടാവുകയില്ല.

ഈ പഠനത്തിന്റെ ഭാഗമായി എന്തെങ്കിലും അപകടം സംഭവിക്കുകയാണെങ്കിൽ എന്ത് സംഭവിക്കും?

ഈ പഠന പ്രവർത്തനം താങ്കളുടെ പരിശോധന റിപ്പോർട്ടുകളും ചികിത്സാ വിവരങ്ങളും വിശകലനം ചെയുക മാത്രമാണ് ചെയുന്നത്. ഇതുമൂലം തങ്ങൾക്ക് യാതൊരു തരത്തിലുള്ള അപകടമോ ബുദ്ധിമുട്ടോ ഉണ്ടാവാനുള്ള സാധ്യത തീരെയില്ല. അഥവാ ഇതിന്റെ ഭാഗമായി ഏതെങ്കിലും ബുദ്ധിമുട്ട് ഉണ്ടാവുകയാണെങ്കിൽ അത് ഈ ആശുപത്രിയിലെ അനുഭവജ്ഞരായ ഡോക്ടർമാർ ചികിത്സിക്കുന്നതായിരിക്കും. ഇതിന്റെ ഭാഗമായി സാമ്പത്തികപരമായ യാതൊരു നഷ്ടപരിഹാരങ്ങളും നൽകുന്നതല്ല.

താങ്കൾ ഈ പഠനത്തിനായി പണം അടക്കേണ്ടതുണ്ടോ?

ഈ പഠനത്തിനായി സാധാരണ താങ്കൾ ഈ ആശുപത്രിയിൽ ചെയ്യുന്ന വൈദ്യപരിശോധനയുടെ റിപ്പോർട്ടുകൾ മാത്രമാണ് പരിശോധിക്കുന്നത്. ഇതിനായി താങ്കൾ അധിക പണമൊന്നും അടക്കേണ്ടതായി വരുന്നില്ല.

ഈ പഠനം കഴിഞ്ഞാൽ എന്താണ് സംഭവിക്കുക?

ഈ പഠനത്തിൽ താങ്കൾ പങ്കാളിയാവുന്നതു വഴി ചിലപ്പോൾ ഇതിന്റെ ഗുണം നിങ്ങൾക്ക് കിട്ടിയെന്നോ കിട്ടിയില്ലെന്നോ വരാം. എന്നിരുന്നാലും ഇതുപോലെ സമാനമായ അസുഖമുള്ള രോഗികൾക്ക് ഇതിന്റെ ഗുണം ചിലപ്പോൾ കിട്ടിയെന്നു വരാം.

താങ്കളുടെ വ്യക്തിപരമായ വിവരങ്ങൾ രഹസ്യമായി സൂക്ഷിക്കുമോ?

താങ്കൾ ഈ പഠനത്തിന്റെ പങ്കാളിയായാൽ ഈ പഠനത്തിലൂടെ ശേഖരിച്ച വിവരങ്ങൾ വൈദ്യ പ്രസിദ്ധീകരങ്ങളിൽ ഉൾപ്പെടുത്തുന്നതാണ്. എന്നാൽ പേര് വിവരങ്ങൾ ഒന്നും തന്നെ ഉൾപ്പെടുത്തുന്നതല്ല. എന്നിരുന്നാലും താങ്കളുടെ ചികിത്സാരേഖകൾ പഠനത്തിലേർപ്പെട്ടിരിക്കുന്ന ആളുകൾ താങ്കളുടെ അനുവാദമില്ലാതെ തന്നെ വിലയിരുത്തുന്നതായിരിക്കും.

തുടർന്നുള്ള അന്വേഷണങ്ങൾക്കും കൂടുതൽ വിവരങ്ങൾക്കും ബന്ധപ്പെടുക

ഡോ. വിമൽ ചാക്കോ മോണ്ടി

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സമ്മതപത്രം

പഠനത്തിന്റെ പേര്: കാർഡിയോവാസ്കുലാർ മാഗ്നെറ്റിക് ഫീച്ചർ ട്രാക്കിംഗ് ഉപയോഗിച്ച് ഹൈപ്പർട്രോഫിക് കാർഡിയോമയോപ്പതി ഉള്ള രോഗികളിൽ സ്ട്രെയിൻ ചിത്രീകരണ ഘടകങ്ങളുടെ വിശകലനം.

പങ്കെടുക്കുന്ന ആളിന്റെ പേര്:

ജനനതിയതി:

ഞാൻ ..... മകൻ / മകൾ

(താഴെ കൊടിത്തിരിക്കുന്ന ബോക്സ് ടിക്ക് ചെയ്യുക)

മുകളിൽ പറഞ്ഞിരിക്കുന്ന പഠനത്തെപ്പറ്റി ഞാൻ വിവരങ്ങൾ വായിച്ചു മനസിലാക്കുകയും എനിക്കുണ്ടായ എല്ലാ സംശയങ്ങളും നിവാരണം നടത്തിയിട്ടുണ്ട് എന്ന് ഞാൻ സമ്മതിക്കുന്നു [ ]

ഈ പഠനത്തിൽ പങ്കെടുക്കാനുള്ള എന്റെ തീരുമാനം നിയമപരമായ എല്ലാ അവകാശങ്ങളോടും കൂടി തന്നെ എന്റെ ചികിത്സയെ ബാധിക്കാതെ ഏതു സമയത്തും എsâ സമ്മതം പിൻവലിക്കാവുന്നതാണെന്നും ഞാൻ മനസ്സിലാക്കുന്നു [ ]

ഞാൻ പഠനത്തിൽനിന്നും പിന്മാറിയാലും എന്റെ അസുഖവിവരങ്ങൾ പഠനത്തിലേർപ്പെട്ടിരിക്കുന്ന സ്റ്റാഫുകൾക്കും, സ്ഥാപനത്തിന്റെ എത്തിക്സ് കമ്മിറ്റിക്കും എന്റെ അധികാരമില്ലാതെ തന്നെ പരിശോധിക്കാനുള്ള അധികാരമുണ്ടായിരിക്കുമെന്നു ഞാൻ മനസ്സിലാക്കുന്നു [ ]

എന്റെ വ്യക്തിപരമായ കാര്യങ്ങൾ മറ്റൊരാൾക്കും കൈമാറ്റം ചെയ്യപെടുകയില്ല എന്നും ഞാൻ മനസ്സിലാകുന്നു [ ]

ഈ പഠനപ്രവർത്തനം കഴിയുമ്പോൾ എന്റെ വ്യക്തിപരമായ കാര്യങ്ങൾ പ്രസിദ്ധീകരണങ്ങളിലോ മറ്റൊരാളിലേക്കോ കൈമാറില്ലെന്ന് ഞാൻ മനസിലാക്കുന്നു [ ]

ഞാൻ ഈ പഠനത്തിൽ സ്വമേധയാൽ പങ്കാളിയാകുന്നു [ ]

ഒപ്പിട്ട ഈ സമ്മതപത്രത്തിന്റെ ഒരു കോപ്പി ഞാൻ കൈപ്പറ്റിയിരിക്കുന്നു [ ]

പേര്:

ഒപ്പ്:

തിയതി:

സാക്ഷിയുടെ പേര്:

പങ്കെടുക്കുന്ന ആളുമായുള്ള ബന്ധം:

തിയതി:

വൈദ്യഗവേഷണ പഠനത്തിന്റെ ആവശ്യകതയെപ്പറ്റി അറിയിച്ചുകൊണ്ടുള്ള ഈ സമ്മതപത്രത്തെ തൃപ്തികരമാണെന്ന് ഞാൻ വിലയിരുത്തുന്നു. ഈ സമ്മതപത്രത്തിലുൾപ്പെട്ടിരിക്കുന്ന കാര്യങ്ങൾ പങ്കെടുക്കുന്ന വ്യക്തിയോട് വിശദീകരിച്ചിട്ടുണ്ട്. അപകടങ്ങളെപ്പറ്റിയും പ്രത്യാഘാതങ്ങളെപ്പറ്റിയും ഞാൻ വിശദമായി പ്രതിപാദിച്ചിട്ടുണ്ടുണ്ട്. തുടർന്നും പങ്കെടുക്കുന്ന വ്യക്തിയെ ചോദ്യങ്ങളും സംശയങ്ങളും ചോദിക്കാൻ പ്രേരിപ്പിക്കുകയും അവയ്ക്കെല്ലാം ഉത്തരം നൽകുകയും ചെയ്തിട്ടുണ്ട്.

സമ്മതപത്രം ഒപ്പിട്ടുവാങ്ങിയ ആളുടെ പേരും ഒപ്പും.

APPENDIX C - PUBLICATIONS

APPENDIX D – PLAGIARISM CHECK REPORT

RE-2022-44054-plag-report

ORIGINALITY REPORT

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