POLISH
JOURNAL *of* RADIOLOGY

Original paper

Feature-tracking cardiac magnetic resonance method: a valuable marker of replacement fibrosis in hypertrophic cardiomyopathy

Nahid Rezaeian[1,A,B,C,D,E,F], Leila Hosseini[2,B,E], Negar Omidi[3,C,D,E], Mahya Khaki[1,B], Homa Najafi[1,B], Kianoosh Kasani[1,B], Mostafa Mousavizadeh[1,C], Yasaman Khalili[1,C], Mohammad Mehdi Hemmati Komasi[4,B], Yaser Toloueitabar[1,E], Sanaz Asadian[1,C,D,E,F]

[1]Rajaie Cardiovascular Medical and Research Centre, Iran University of Medical Sciences, Tehran, Iran
[2]North Khorasan University of Medical Sciences, Bojnurd, Iran
[3]Tehran Heart Centre (THC), Tehran University of Medical Sciences, Tehran, Iran
[4]Iran University of Medical Sciences, Tehran, Iran

Abstract

Purpose: Left ventricular (LV) replacement fibrosis is a marker of adverse cardiac events in hypertrophic cardiomyopathy (HCM). We aimed to assess the efficacy of the feature-tracking cardiac magnetic resonance (FT-CMR) in the detection of LV replacement fibrosis.

Material and methods: Fifty-one patients with HCM (51% female, mean age = 21 ± 5.2 years) and significant myocardial hypertrophy, who underwent CMR between February 2018 and December 2019 were enrolled. Functional and 3D FT-CMR parameters were measured. LV global longitudinal strain, global radial strain (GRS), and global circumferential strain (GCS) were recorded. The percentage of enhanced myocardial mass was calculated. Univariate and multivariate regression analyses were performed to determine the predictors of fibrosis. A *p*-value of less than 0.05 was considered significant.

Results: The mean enhanced mass percentage was 15.2 ± 10.53%. Among LV volumetric parameters, end-systolic and end-diastolic volume indices predicted fibrosis (fitness [F] = 8.11 and $p = 0.006$ vs. $F = 6.6$ and $p = 0.012$, correspondingly). The univariate linear regression demonstrated that GCS and GRS predicted total enhanced mass (%) ($F = 12.29$ and $p = 0.001$ vs. $F = 7.92$ and $p = 0.007$, respectively). After the inclusion of all volumetric and deformation parameters, the multivariate analysis identified the model of a combination of LV end-diastolic volume index (LV EDVI) and LV GCS as a robust predictor of the fibrosis percentage ($F = 8.86$ and $p = 0.005$).

Conclusions: Non-contrast CMR parameters including LV GCS and LV EDVI are valuable markers of replacement fibrosis in HCM patients with notable myocardial hypertrophy.

Key words: cardiovascular magnetic resonance, feature tracking, hypertrophic cardiomyopathy, late gadolinium enhancement, replacement fibrosis.

Introduction

Hypertrophic cardiomyopathy (HCM) is characterized by the presence of left ventricular (LV) hypertrophy in the absence of any aetiologies that result in such hypertrophy, including systemic and cardiac diseases, whether they feature sarcomeric-related mutations or whether they remain unresolved [1]. Myocardial fibrosis occurs in HCM and contributes to arrhythmias and even sudden cardiac death [2]. Fibrosis consists of combined interstitial and replacement types, with the characteristic cardiac magnetic resonance (CMR) pattern being patchy fibrosis in ventricular insertion points in late gadolinium enhancement (LGE) images [3,4].

The burden of fibrosis detected by LGE could not only predict sudden cardiac death and total mortality but also determine the need for an implantable cardiac defibrillator for primary prevention [5,6]. According to a study by Bruder *et al.*, myocardial fibrosis and scar were associated with a hazard ratio of about 5.47 for total mortality in asymptomatic patients during a 3-year follow-up [7].

Advanced feature-tracking cardiac magnetic resonance (FT-CMR) imaging has contributed to the diagnostic and prognostic evaluation of a diverse range of cardiac disorders in recent years. Different studies have concluded that LV myocardial strain, as measured via the FT-CMR technique, is a sensitive predictor of preclinical LV dysfunction [8,9].

Although the importance of myocardial fibrosis detected by CMR in the diagnosis and prognostication of HCM is well-established, only a few studies have thus far focused on the role of LV FT-CMR values in the prediction of myocardial fibrosis [2,10,11].

Accordingly, in the present study, we aimed to assess whether FT-CMR could reveal the presence of underlying myocardial fibrosis.

Material and methods

Study population

This retrospective cross-sectional research was conducted on 51 selected patients (51% female, mean age = 21 ± 5.2 years) with established HCM, who were referred to our tertiary cardiovascular centre between February 2018 and December 2019. All the patients had significantly increased LV mass index (≥ 110 g/m^2 in males and ≥ 95 g/m^2 in females) [12,13]. The exclusion criteria comprised more-than-mild valvular disease, evidence of obstructive coronary artery disease or myocardial infarction, and the presence of cardiac implantable electronic devices. All the patients underwent transthoracic echocardiography within 1 week before or after CMR examinations.

Cardiac magnetic resonance diagnostic criteria

HCM was defined as the presence of asymmetrical LV hypertrophy with maximal LV end-diastolic wall thickness of 15 mm or more in the absence of other conditions of LV hypertrophy. The threshold for diagnosis was decreased in the presence of a positive family history or a genetic test of HCM (≥ 13 mm) [1,14]. The presence of patchy mid-wall fibrosis in anterior and posterior right ventricular (RV) insertion points and regions of maximum LV wall thickness was an ancillary diagnostic marker of HCM [15].

Cardiac magnetic resonance imaging technique

CMR was performed with a 1.5-Tesla scanner (Siemens Avanto, Erlangen, Germany) featuring an 8-element cardiac-phased array receiver surface coil. Functional cine ECG-gated sequences were obtained with the patient having a breath-hold. Multiple views, consisting of the 2-, 3-, and 4-chamber views as well as the short-axis images, were obtained (field of view = 300 mm, imaging matrix = 156 × 192, slice thickness = 8 mm, without interslice gaps for short-axis images; repetition time/echo time = 31/1.2 ms).

All the CMR sequences were examined by an expert cardiologist. Additionally, an expert radiologist re-evaluated all the patients' data.

Feature-tracking cardiac magnetic resonance

Following the definition of LV endocardial and epicardial borders manually in the end-diastolic phase in the 2-, 3-, and 4-chamber views as well as all the slices of the short-axis views, 3D deformation parameters were analysed off-line utilizing CVI 42 software (Circle CVi, Calgary, Canada) (Figure 1). Image brightness was changed manually to achieve the highest contrast between the endocardium and the blood pool. The strain percentage represented the amount of myocardial fibre change from the end-diastolic frame to the end-systolic frame.

Longitudinal and circumferential values were depicted as negative numbers, given the shortening in muscle length from the end-diastolic view to the end-systolic view, while radial strain was described as a positive value due to myocardial thickening in the cardiac cycle. Regional systolic strain and systolic rates together with diastolic strain rates were determined in 6 basal and mid-ventricular segments, as well as 4 apical segments, in accordance with the myocardial classification of the American College of Cardiology/American Heart Association (ACC-AHA) [16]. For convenience, all the strain indices were depicted as an absolute value.

Late gadolinium enhancement

Ten minutes after the intravenous injection of 0.15 mmol/kg of the gadoterate meglumine (Dotarem) contrast agent, LGE sequences were obtained in a stack of short-axis and multiple long-axis projections to cover the entire LV myocardium. The inversion time of the normal myocardial region was determined via the scout sequence. The extent of myocardial fibrosis was assessed in the short-axis slices after the endocardial and epicardial borders of the LV were defined in all the stacks from the base to the apex of the heart. Within each slice, the normal myocardial region was traced, and all areas with the signal intensity of 5 standard deviations (SDs) above the standard values were determined [17,18]. Papillary muscles were considered in the blood pool and were not included in the myocardial mass calculations. Subsequently, the enhancement volume and the mass percentage were quantified as the proportion of the volume and mass of the myocardial region with fibrosis divided by the total LV mass, respectively [19] (Figure 2). Assessment of regional
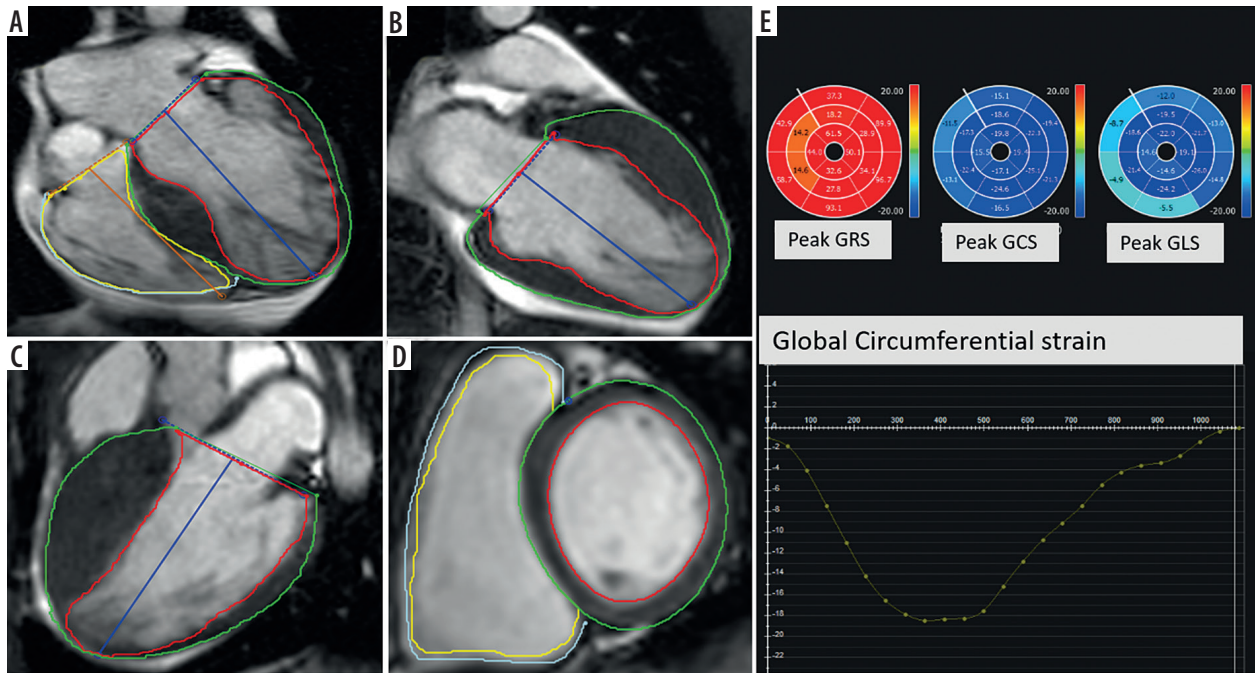
Figure 1. A-D) Four-, two-, and three-chamber as well as short-axis cine functional images with defined endocardial and epicardial borders for strain analysis by feature-tracking cardiac magnetic resonance method in a case of hypertrophic cardiomyopathy. **E)** Bull's eye plots and strain curve which depicts peak circumferential strain
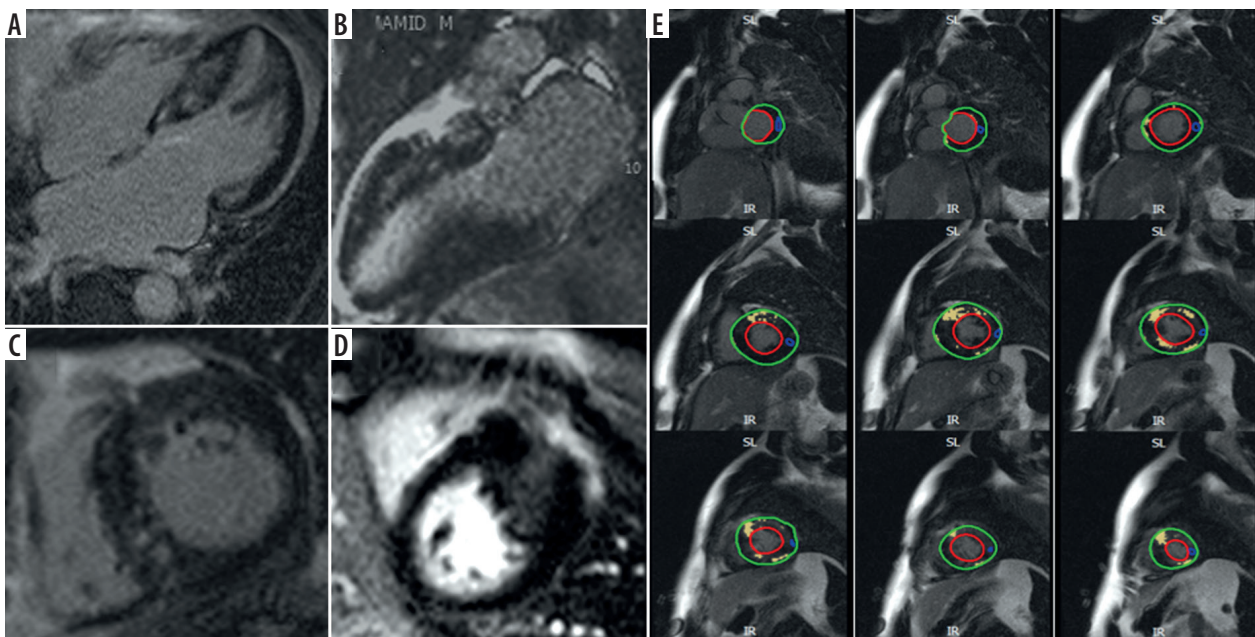

Figure 2. A-D) Four-, two-, and short-axis late gadolinium enhancement (LGE) sequence in a patient with hypertrophic cardiomyopathy depicts extensive patchy predominantly mid-wall fibrosis. **E)** Stack of short-axis LGE slices with endocardial and epicardial borders drawn. The small blue reference region of interest is marked to determine regions of fibrosis by the 5-standard deviation method

myocardial fibrosis was performed for each AHA myocardial segment at LV basal and mid-levels. Segmental myocardial fibrosis was defined as the presence of LGE in at least 50% of the volume of that segment based on visual assessment.

Echocardiography

The echocardiographic reports were evaluated, and the patients were divided into obstructive and nonobstructive types, based on LV outflow tract gradients of 30 mmHg or more calculated at rest.

Statistical analysis

The categorical variables were displayed as frequencies and percentages, while the continuous variables were reported as the mean ± the SD or as the median with the interquartile range depending on the normality of distribution.

The correlation between the variables was tested using the Pearson and Spearman correlation coefficients, as appropriate. The differences between the 2 groups were assessed using a 2-sample t-test or the Wilcoxon rank-sum test depending on parametric or nonparametric data for the continuous variables. Additionally, the χ^2 test was applied for the categorical variables. The relationships between strain parameters and LGE characteristics were evaluated using correlation and linear regression analyses. The Akaike information criterion (AIC) model selection was employed to distinguish between a set of possible models describing the relationship between global strain measurements and total enhanced mass measures. The best-fit model, carrying 97% of the cumulative model weight, encompassed every parameter with no interaction effects.

In addition to the univariate logistic regression, a parsimonious logistic regression model was developed through a backward selection of each of the regional strain, global strain, and strain rate variables; they were selected based on the clinical relevance or significance of their univariate associations ($p < 0.2$) to determine the predictors of LGE measured by the amount of the enhanced cardiac mass. The Hosmer-Lemeshow goodness-of-fit test was drawn upon to summarize the discrepancy between the observed values and the values expected under the model in question. A p-value of less than 0.05 was considered statistically significant. The data were analysed using Stata software (StataCorp, 2015. Stata Statistical Software: Release 14. College Station, TX: StataCorp LP).

Results

The final analysis was conducted on 51 patients with established HCM. The mean age of the participants was 21.0 ± 5.2 years, and women comprised 51% ($n = 26$) of the study population. The mean $\pm$ SD for LV mass index was 121.53 ± 9.56 in males and 105.00 ± 8.64 in females. Most of the patients (58.8%, 30/51) were diagnosed with nonobstructive HCM, while 41.2% (21/51) had obstructive HCM. The systolic function of the LV was preserved in all the participants, with a median and interquartile range of the LV ejection fraction of 58% and 53-61, respectively. The mean enhanced mass was $15.2 \pm 10.5\%$ of the total LV mass. Table 1 demonstrates the demographic data of the study population.

All global longitudinal strain (GLS), global radial strain (GRS), and global circumferential strain (GCS) values were comparable between the 2 groups of obstructive and nonobstructive HCM ($p = 0.4$, $p = 0.3$, and $p = 0.1$, correspondingly).

The univariate linear regression analysis established that both left ventricular end-systolic volume index (LV ESVI) (fitness [F] [1, 49] = 8.11 and $p = 0.006$) and left ventricular end-diastolic volume index (LV EDVI) (F [1, 49] = 6.6 and $p = 0.012$) statistically significantly predicted enhanced mass. The prediction ability of both LV indices remained significant after adjustments were made for LV outflow tract obstruction.

The univariate linear regression, performed to evaluate the predictive role of deformation parameters for total enhanced mass, demonstrated that GCS and GRS statistically significantly predicted total enhanced mass (%) (F =12.29 and $p = 0.001$ vs. F = 7.92 and $p = 0.007$, respectively) (Table 2).

Table 1. Demographic data of the study population

Factor	
Total number of patients	51
Gender	
Male	49% (25/51)
Female	51% (26/51)
Mean age ±SD (years)	21 ± 5.2
Non-obstructive HCM	58.8% (30/51)
Obstructive HCM	41.2% (21/51)
Median of the LVEF (IQR)	58% (53-61)
Mean enhanced mass ratio ± SD	15.2% ± 10.53

HCM – hypertrophic cardiomyopathy, LVEF – left ventricular ejection fraction, IQR – interquartile range

Table 2. Univariate regression of global strains predicting total enhanced mass

Parameter	Coefficient (95% CI)	Adjusted R^2	Fitness	p-value
GCS	3.49 (1.48-5.50)	0.1831	12.29	0.001
GCS R systolic	17.20 (−7.96 to 42.37)	0.0178	1.89	0.175
GCS R diastolic	−4.44 (−20.67 to 11.77)	−0.0144	0.30	0.584
GRS	−0.75 (−1.28 to −0.21)	0.1216	7.92	0.007
GRS R systolic	−0.33 (−1.32 to 0.66)	−0.0115	0.44	0.508
GRS R diastolic	1.29 (−3.59 to 6.18)	−0.0148	0.28	0.596
GLS	0.61 (−1.32 to 2.54)	0.0121	0.40	0.527
GLS R systolic	0.31 (−3.83 to 4.46)	−0.0203	0.02	0.878
GLS R diastolic	0.58 (−0.25 to 1.42)	0.0189	1.94	0.169

GCS – global circumferential strain, R – rate, GRS – global radial strain, GLS – global longitudinal strain

Multiple regressions were run to predict the total enhanced mass of the LV from the GCS, GLS, and GRS values in Model I (Table 3). The inclusion of all the global strain values in a single model statistically significantly predicted the outcome variable (i.e. the ratio of enhanced LV mass) ($p = 0.004$); nonetheless, we computed multiple goodness-of-fit measures for each multiple regression model. As is presented in Table 3, GCS uniquely predicted total enhanced mass better than the combination of the other global strain values, with the greatest measures of AIC, AIC for small sample size (AICC), and Bayesian information criterion (BIC). After the inclusion of LV EDVI, the cardiac index, LV ejection fraction, and LV ESVI in Model III, LV GCS and LV EDVI together predicted total enhanced mass better than the other independent variables.

A univariate logistic regression analysis was also carried out to assess which regional strain or strain rate values could predict fibrosis in the same segment. The results are shown in Table 4.

Discussion

In the current investigation, we assessed the role of non-contrast CMR parameters in the prediction of the amount of LV replacement fibrosis in patients with HCM and significantly increased LV mass index. The salient findings of our study are as follows:

1) Among all the global deformation parameters, including LV strain and strain rates, GCS was the single robust predictor of the amount of replacement fibrosis in our patients with HCM. Furthermore, GRS was another powerful predictor of fibrosis.

2) LV EDVI and LV ESVI potently predicted LV fibrosis. The combination of LV GCS and LV EDVI was the most powerful predictor of fibrosis, and this combination was more potent than each parameter alone.

3) Segmental strain values predicted the presence of LV regional fibrosis in approximately half of the LV segments.

4) No significant difference was found in global LV strain values between our 2 groups of obstructive and nonobstructive HCM.

Strikingly, our investigation revealed LV GCS, followed by GRS, as the most robust predictor of LGE. Bogarapu *et al.* evaluated 29 paediatric patients with HCM who underwent CMR. Patients with myocardial fibrosis demonstrated a reduction in LV GLS, GCS, and GRS, as well as the strain rate, especially in regions with evidence of fibrosis [2]. A finding of our research was that GCS was the best predictor of LV fibrosis. It is well-known that myocardial fibrosis mainly involves the mid-myocardial layer in patients with HCM and has a lesser tendency to involve the subendocardial or subepicardial myocardium. LV GCS is predominantly reproduced by mid-myocardial (mesocardial) fibres. As a result, we assume that the de-

Table 3. Multivariate regression models of global strains predicting total enhanced mass

		Adjusted R^2	AIC	AICC	BIC	Fitness (df)	*p*-value
Model 1	GCS	0.1830	476.60	477.11	480.47	12.20 (1.49)	0.001
	GCS GLS	0.1972	476.66	477.53	482.45	7.14 (2.48)	0.001
	GCS GLS GRS	0.1892	478.09	479.42	485.82	4.89 (3.47)	0.004
Model 2	GCS	0.1830	476.60	477.11	480.47	12.20 (1.49)	0.001
	GCS GCS R systolic	0.1686	478.44	479.31	484.24	6.07 (2.48)	0.004
	GCS GCS R systolic GCS R diastolic	0.1516	480.40	481.73	488.13	3.98 (3.47)	0.013
Model 3	GCS LV EDVI	0.2392	437.91	474.78	479.71	8.86 (2.48)	0.005
	GCS GLS GRS LV CI LV EF LV ESVI LV EDVI	0.2638	475.51	478.12	478.11	3.99 (6.44)	0.002

AIC – Akaike information criterion, BIC – Bayesian information criterion, AICC – AIC for small sample size, GLS – global longitudinal strain, GCS – global circumferential strain, GRS – global radial strain, R – rate, LV – left ventricular, EDVI – end-diastolic volume index, CI – cardiac index, EF – ejection fraction, ESVI – end-systolic volume index

Table 4. Univariate regression of regional left ventricular strain values predicting fibrosis in each segment

Segment	Regional strain	OR	CI	*p*-value
Basal anterior	RCS	1.1839	0.9837-1.4248	0.063
	RCS R systole	2.6083	0.7746-3.1391	0.043
	RRS R diastole	0.8278	0.6331-1.0824	0.159
Mid anterior	RRS R diastole	1.3865	0.9896-1.9428	0.017
	RRS	0.9726	0.9384-1.0080	0.084
	RLS R diastole	0.2766	0.0647-1.1821	0.037
	RLS R systole	3.8377	0.6036-2.3966	0.113
Apical anterior	RRS	0.9744	0.9481-1.0015	0.035
	RRS R systole	0.7829	0.6045-1.0140	0.040
	RRS R diastole	1.4326	1.0442-1.9655	0.008
Apical septal	RLS	0.9300	0.8370-1.0333	0.169
	RLS R diastole	2.5148	0.7692-8.2210	0.108
Basal infero-septal	RLS R diastole	1.8605	0.7772-4.4541	0.130
	RCS	1.0932	0.9740-1.2271	0.112
	RCS R systole	2.2671	0.6563-7.8314	0.142
	RRS	0.9787	0.9523-1.0058	0.089
Basal inferior	RRS	0.9800	0.9586-1.0019	0.041
Mid inferior	RRS	0.9331	0.8821-0.9871	0.005
	RCS	1.1085	1.0012-1.2012	0.039
	RLS	1.1989	1.0422-1.3792	0.002
Apical lateral	RLS R systole	0.3443	0.0783-1.5131	0.102

RCS – regional circumferential strain, R – rate, RRS – regional radial strain, RLS – regional longitudinal strain

rangement of mesocardial myocytes by replacement fibrosis may affect circumferential strain earlier than radial or longitudinal strain. In another landmark study by Vigneault *et al.*, FT-CMR could reveal subtle myocardial dysfunction in patients suffering from HCM with sarcomeric mutations. The authors remarkably demonstrated that the difference in endocardial/epicardial LV circumferential strain was higher both in cases of overt HCM and in HCM carriers [19]. This finding underscores the diagnostic value of deformation parameters, particularly circumferential strain, in the preclinical stage of HCM.

In the current investigation, we properly applied the signal threshold versus reference mean method for quantification of fibrosis on the LGE sequence. Regions with signal intensity 5-SD above the mean of reference myocardium were considered as areas of fibrosis. Based on previous studies, the threshold of more than 3-SD is associated with the highest accuracy with acceptable reproducibility. Moreover, it is mentioned that the 5-SD method provides the most congruity with visual assessment for estimation of the fibrosis extent [17,18].

Previous research has revealed an association between strain parameters and the presence of LV fibrosis. Popovic *et al.* demonstrated that all strain values were reduced in their patients with HCM despite the absence of myocar-

dial fibrosis, while their subgroup with myocardial fibrosis had notably decreased LV GLS [20]. Another investigation showed that in patients with a history of myocardial infarction, deformation indices derived via speckle-tracking echocardiography were capable of differentiating normal and remote regions from infarcted segments [21]. This finding reinforces the valuable role of strain indices in the assessment of various pathological conditions that result in myocardial replacement fibrosis.

In the present research, we assessed the distribution of LGE in LV segments according to the AHA recommendation and demonstrated that in some myocardial segments, regional strain values predicted the presence of myocardial fibrosis [1]. Serri *et al.* reported that global strain was markedly decreased and basal longitudinal septal strain was significantly diminished compared with the other segments in their patients with asymmetrical HCM [22]. In a recent study on 26 HCM patients the results of logistic regression analysis reported regional circumferential strain as a strong predictor of segmental LGE. The authors concluded that FT-CMR, especially regional circumferential strain, reliably shows fibrosis-containing segments [23].

In a study on patients aged below 20 years, Smith *et al.* concluded that segments with LGE correlated with a decrease in GLS, GCS, and GRS and reported that LV fibrosis

was a strong predictor of adverse cardiovascular events [24]. Interestingly, we found that in some myocardial segments, there was no association between regional strain and fibrosis, which may have been due to technical problems in the calculation of myocardial strain or the fact that there is no one-by-one association between the reduction in the LV regional strain value and the presence of segmental fibrosis. Moreover, we suppose that it might have been better to include segmental myocardial thickness as a contributing variable in the calculated strain value.

Our study revealed the ability of LV volume indices, including EDVI and ESVI, to predict concurrent myocardial fibrosis and HCM. Moreover, adding LV EDVI to LV GCS strengthened the power of the regression model, which implies that a combination of these parameters could help estimate underlying LV myocardial fibrosis. This finding, nevertheless, requires further elaboration in future studies.

In a study by She *et al.* on 44 obstructive and 108 nonobstructive HCM patients, maximum LV wall thickness and the subtraction of peak radial strain potently differentiated the 2 groups of patients [25]. We found that neither the burden of myocardial fibrosis nor global strain was statistically significantly different between obstructive and nonobstructive HCM as determined in rest echocardiography. What needs highlighting in this regard is that we drew upon echocardiography reports for the assessment of LV outflow tract obstruction in our retrospective study. Such disparities in findings warrant further research with the aid of stress tests in this challenging field.

The strength of strain analysis in routine CMR lies in the fact that it confers additional information regarding the presence of replacement myocardial fibrosis in patients with HCM. We posit that FT-CMR–derived myocardial strain values could be added to the present risk calculators in HCM. Indubitably, however, further investigations are needed to shed more light on this notion.

The value of strain images is further highlighted in scenarios where patients whose susceptibility to renal insufficiency precludes the administration of gadolinium contrast agents and where the post-contrast image quality is unacceptable.

In this research, a notable limitation is that we did not apply the results of advanced CMR mapping techniques. Moreover, our study population consisted of only a medium-sized group of selected subjects from a single tertiary centre, who had notably increased LV mass index and a higher percentage of LGE enhancement in the CMR examination as expected. It is also worthy of note that the evaluation of prognosis is another issue of great significance that necessitates further large-scale multicentric investigations.

Conclusions

We conclude that in patients with HCM and significantly increased LV mass index, LV replacement fibrosis can be predicted by a reduction in LV GCS and an increase in LV EDVI. These unique CMR parameters may be useful to identify myocardial fibrosis in patients with HCM without the use of contrast agents.

Acknowledgments

Conflict of interest

The authors report no conflict of interest.

References

1. Ommen SR, Mital S, Burke MA, et al. 2020 AHA/ACC guideline for the diagnosis and treatment of patients with hypertrophic cardiomyopathy: a report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. Circulation 2020; 142: e558-e631.

2. Bogarapu S, Puchalski MD, Everitt MD, et al. Novel cardiac magnetic resonance feature tracking (CMR-FT) analysis for detection of myocardial fibrosis in pediatric hypertrophic cardiomyopathy. Pediatr Cardiol 2016; 37: 663-673.

3. Pennell DJ. Cardiovascular magnetic resonance. Circulation 2010; 121: 692-705.

4. Reichek N, Gupta D. Hypertrophic cardiomyopathy: cardiac magnetic resonance imaging changes the paradigm. J Am Coll Cardiol 2008; 52: 567-568.

5. Green JJ, Berger JS, Kramer CM, Salerno M. Prognostic value of late gadolinium enhancement in clinical outcomes for hypertrophic cardiomyopathy. JACC Cardiovasc Imaging 2012; 5: 370-377.

6. Maron MS. Clinical utility of cardiovascular magnetic resonance in hypertrophic cardiomyopathy. J Cardiovasc Magn Res 2012; 14: 13.

7. Bruder O, Wagner A, Jensen CJ, et al. Myocardial scar visualized by cardiovascular magnetic resonance imaging predicts major adverse events in patients with hypertrophic cardiomyopathy. J Am Coll Cardiol 2010; 56: 875-887.

8. Jafari F, Safaei AM, Hosseini L, et al. The role of cardiac magnetic resonance imaging in the detection and monitoring of cardiotoxicity in patients with breast cancer after treatment: a comprehensive review. Heart Fail Rev 2021; 26: 679-697.

9. Rezaeian N, Mohtasham MA, Khaleel AJ, et al. Comparison of global strain values of myocardium in beta-thalassemia major patients with iron load using specific feature tracking in cardiac magnetic resonance imaging. Int J Cardiovasc Imaging 2020; 36: 1343-1349.

10. Chan RH, Maron BJ, Olivotto I, et al. Prognostic value of quantitative contrast-enhanced cardiovascular magnetic resonance for

the evaluation of sudden death risk in patients with hypertrophic cardiomyopathy. Circulation 2014; 130: 484-495.

11. Hen Y, Iguchi N, Utanohara Y, et al. Prognostic value of late gadolinium enhancement on cardiac magnetic resonance imaging in Japanese hypertrophic cardiomyopathy patients. Circ J 2014; 78: 929-937.

12. Petersen SE, Khanji MY, Plein S, et al. European Association of Cardiovascular Imaging expert consensus paper: a comprehensive review of cardiovascular magnetic resonance normal values of cardiac chamber size and aortic root in adults and recommendations for grading severity. Eur Heart J Cardiovasc Imaging 2019; 20: 1321-1331.

13. Kinno M, Waller A, Gardin J. Approaches to echocardiographic assessment of left ventricular mass what does echocardiography add. Am J Cardiol 2016.

14. Elliott PM, Anastasakis A, Borger MA, et al. 2014 ESC Guidelines on diagnosis and management of hypertrophic cardiomyopathy: the Task Force for the Diagnosis and Management of Hypertrophic Cardiomyopathy of the European Society of Cardiology (ESC). Eur Heart J 2014; 35: 2733-2779.

15. Śpiewak M, Kłopotowski M, Ojrzyńska N, et al. Impact of cardiac magnetic resonance on the diagnosis of hypertrophic cardiomyopathy – a 10-year experience with over 1000 patients. Eur Radiol 2021; 31: 1194-1205.

16. Cerqueira MD, Weissman NJ, Dilsizian V, et al.; American Heart Association Writing Group on Myocardial Segmentation and Registration for Cardiac Imaging. Standardized myocardial segmentation and nomenclature for tomographic imaging of the heart: a statement for healthcare professionals from the Cardiac Imaging Committee of the Council on Clinical Cardiology of the American Heart Association. Circulation 2002; 105: 539-542.

17. Mikami Y, Kolman L, Joncas SX, et al. Accuracy and reproducibility of semi-automated late gadolinium enhancement quantification techniques in patients with hypertrophic cardiomyopathy. J Cardiovasc Magn Reson 2014; 16: 85.

18. Liu D, Ma X, Liu J, et al. Quantitative analysis of late gadolinium enhancement in hypertrophic cardiomyopathy: comparison of diagnostic performance in myocardial fibrosis between gadobutrol and gadopentetate dimeglumine. Int J Cardiovasc Imaging 2017; 33: 1191-1200.

19. Vigneault DM, Yang E, Jensen PJ, et al. Left ventricular strain is abnormal in preclinical and overt hypertrophic cardiomyopathy: cardiac MR feature tracking. Radiology 2019; 290: 640-648.

20. Popović ZB, Kwon DH, Mishra M, et al. Association between regional ventricular function and myocardial fibrosis in hypertrophic cardiomyopathy assessed by speckle tracking echocardiography and delayed hyperenhancement magnetic resonance imaging. J Am Soc Echocardiogr 2008; 21: 1299-1305.

21. Voigt JU, Arnold MF, Karlsson M, et al. Assessment of regional longitudinal myocardial strain rate derived from Doppler myocardial imaging indexes in normal and infarcted myocardium. J Am Soc Echocardiogr 2000; 13: 588-598.

22. Serri K, Reant P, Lafitte M, et al. Global and regional myocardial function quantification by two-dimensional strain: application in hypertrophic cardiomyopathy. J Am Coll Cardiol 2006; 47: 1175-1181.

23. Sharifian M, Rezaeian N, Asadian S, et al. Efficacy of novel non-contrast cardiac magnetic resonance methods in indicating fibrosis in hypertrophic cardiomyopathy. Cardiol Res Pract 2021; 2021: 9931136.

24. Smith BM, Dorfman AL, Yu S, et al. Clinical significance of late gadolinium enhancement in patients < 20 years of age with hypertrophic cardiomyopathy. Am J Cardiol 2014; 113: 1234-1239.

25. She JQ, Guo JJ, Yu YF, et al. Left ventricular outflow tract obstruction in hypertrophic cardiomyopathy: the utility of myocardial strain based on cardiac MR tissue tracking. J Magn Reson Imaging 2021; 53: 51-60.