European Radiology (2022) 32:2594–2603
https://doi.org/10.1007/s00330-021-08346-2

CARDIAC

Correlation between left ventricular fractal dimension and impaired strain assessed by cardiac MRI feature tracking in patients with left ventricular noncompaction and normal left ventricular ejection fraction

Shiqin Yu[1] · Xiuyu Chen[1] · Kai Yang[1] · Jiaxin Wang[1] · Kankan Zhao[2] · Wenhao Dong[1] · Weipeng Yan[1] · Guohai Su[3] · Shihua Zhao[1]

Received: 14 June 2021 / Revised: 23 August 2021 / Accepted: 24 September 2021 / Published online: 15 November 2021

Abstract

Objectives To investigate the correlation between the extent of excessive trabeculation assessed by fractal dimension (FD) and myocardial contractility assessed by cardiac MRI feature tracking in patients with left ventricular noncompaction (LVNC) and normal left ventricular ejection fraction (LVEF).

Methods Forty-one LVNC patients with normal LVEF (≥ 50%) and 41 healthy controls were retrospectively included. All patients fulfilled three available diagnostic criteria on MRI. Cardiac MRI feature tracking was performed on cine images to determine left ventricular (LV) peak strains in three directions: global radial strain (GRS), global circumferential strain (GCS), and global longitudinal strain (GLS). The complexity of excessive trabeculation was quantified by fractal analysis on short-axis cine stacks.

Results Compared with controls, patients with LVNC had impaired GRS, GCS, and GLS (all $p < 0.05$). The global, maximal, and regional FD values of the LVNC population were all significantly higher than those of the controls (all $p < 0.05$). Global FD was positively correlated with the end-diastolic volume index, end-systolic volume index, and stroke volume index ($r = 0.483$, 0.505, and 0.335, respectively, all $p < 0.05$), but negatively correlated with GRS and GCS ($r = -0.458$ and 0.508, respectively, both $p < 0.001$). Moreover, apical FD was also weakly associated with LVEF and GLS ($r = -0.249$ and 0.252, respectively, both $p < 0.05$).

Conclusion In patients with LVNC, LV systolic dysfunction was detected early by cardiac MRI feature tracking despite the presence of normal LVEF and was associated with excessive trabecular complexity assessed by FD.

Key Points

- *Left ventricular global strain was already impaired in patients with extremely prominent excessive trabeculation but normal left ventricular ejection fraction.*
- *An increased fractal dimension was associated with impaired deformation in left ventricular noncompaction.*

Keywords Isolated noncompaction of the ventricular myocardium · Left ventricle · Magnetic resonance imaging · Strain · Fractals

✉ Guohai Su
gttstg@163.com

✉ Shihua Zhao
cjrzhaoshihua2009@163.com

[1] MR Center, Fuwai Hospital, Stata Key Laboratory of Cardiovascular Disease, National Center for Cardiovascular Diseases of China, Chinese Academy of Medical Sciences and Peking Union Medical College, No. 167, Beilishi Road, Xicheng District, Beijing 100037, China

[2] Paul C. Lauterbur Research Center for Biomedical Imaging, Shenzhen Institutes of Advanced Technology, Chinese Academy of Sciences, SZ University Town, Shenzhen 518055, China

[3] Department of Cardiology, Jinan Central Hospital, Shandong First Medical University and Shandong Academy of Medical Sciences, No. 105 Jiefang Road, Jinan 250013, Shandong, China

Abbreviations

AUC	Area under the curve
CI	Cardiac index
EDVi	End-diastolic volume index
ESVi	End-systolic volume index
FD	Fractal dimension
GCS	Global circumferential strain
GLS	Global longitudinal strain
GRS	Global radial strain
IQR	Interquartile range
LV	Left ventricular
LVEF	Left ventricular ejection fraction
LVNC	Left ventricular noncompaction
SVi	Stroke volume index

Introduction

Left ventricular noncompaction (LVNC) is characterized by a two-layered structure with excessive trabeculation and deep intertrabecular recesses (noncompacted layer), as well as thinning of the compacted myocardium. A series of malignant courses has been described, including heart failure, ventricular arrhythmia, and stroke [1]. However, the investigation and management of LVNC are under debate due to undefined gold standard diagnostic criteria. Increasing evidence indicates that the so-called LVNC is a myocardial phenotype but is not always a cardiomyopathy [2–4]. Individuals meeting current methods and thresholds of diagnosis could have cardiomyopathy or left ventricular (LV) pathologic remodelling but could also have LV physiologic and reversible remodelling or even normal hearts [5, 6]. Patients with extremely prominent excessive trabeculation but without reduced left ventricular ejection fraction (LVEF) are common in our clinical experience, and it is unclear whether they have a pathologic condition.

The noncompacted to compacted ratio (NC/C) is the most commonly used diagnostic index in both clinical and research applications. However, this method tends to overdiagnose LVNC [7]. Moreover, using the NC/C ratio to quantify the extent of excessive trabeculation is arbitrary, and it is difficult to evaluate the complex three-dimensional architecture. Recently, fractal analysis, a novel mathematical method, was proposed for the objective evaluation of both global and regional trabecular complexity in different groups of populations and had high reproducibility [8–11]. This approach characterizes geometric patterns of the region of interest by quantifying the space-filling capacity. Computed from the outline of LV trabeculae and endocardium on routine short-axis cine stacks by cardiac MRI, fractal dimension (FD) is an index comprehensively quantifying the trabecular complexity in the whole ventricle. In a few investigations, FD was suggested to have a potential role in the evaluation of the degree of excessive trabeculation as well as differential diagnosis and prognostic prediction in cardiovascular diseases [8, 11–13].

Abnormal LV apical rotation and LV deformation have been identified by speckle tracking echocardiography in LVNC [14–16]. However, the correlation between the degree of excessive trabeculation and abnormal myocardial deformation in LVNC remains uncertain. Cardiac MRI could improve visualizing trabeculation with high spatial resolution. Moreover, cardiac MRI feature tracking strain analysis has been demonstrated to be an effective method to detect early and subtle contractile abnormalities [17, 18]. Therefore, the present study aimed to investigate myocardial contractility in patients with severe excessive trabeculation but normal LVEF through feature tracking strain analysis, and to evaluate the relationship between excessive trabecular extent (measured by FD) and cardiac function.

Methods

Study population

The present retrospective study was approved by the review board of a local hospital. We included 41 consecutive patients with a clinical diagnosis of LVNC from September 2019 to December 2020, and 41 healthy subjects without evidence of clinically significant cardiovascular disease were included as controls. Our hospital is the national center for cardiovascular diseases, and the included patients were all Chinese (Han nationality). The patients were evaluated because they had cardiovascular symptoms, abnormal electrocardiogram findings, or a family history of LVNC in first-degree relatives. Patients who met the diagnostic criterion for LVNC by echocardiography were scheduled for further cardiac MRI examinations. We concentrated on patients with extremely prominent and regular trabeculation that could not be explained by adaptation; therefore, the inclusion criteria for LVNC subjects were as follows: (1) the presence of noncompacted and compacted LV myocardium with a two-layered appearance, with at least involvement of the LV apex; (2) end-diastolic NC/C ratio > 2.3 on long-axis views [19] and ≥ 3 on short-axis views [20]; (3) noncompacted mass > 20% of the global LV mass [21]; (4) LVEF ≥ 50%; and (5) no pathologic (pressure/volume load, e.g., hypertension) or physiologic (e.g., pregnancy and vigorous physical activity) remodelling factors leading to excessive trabeculation.

Cardiac MRI protocol

Electrocardiography-triggered and respiratory-gated cardiac MRI was performed on a 3.0-T scanner (Ingenia, Philips Medical Systems) using front and back surface coils. Cine

images were acquired using a balanced steady-state free precession (b-SSFP) sequence. The typical imaging parameters were as follows: field of view = 320*320 mm ~ 350*350 mm, matrix = 172*209 ~ 196*215, repetition time (TR) = 2.9 ms, echo time (TE) = 1.5 ms, flip angle = 45°, temporal resolution = 30 ~ 55 ms, and slice thickness = 8 mm. Ten to fifteen minutes after an intravenous administration of gadolinium-DTPA (Magnevist, Bayer) at a dose of 0.2 mmol/kg, late gadolinium enhancement images were obtained using a segmented phase-sensitive inversion recovery sequence at end diastole. The typical imaging parameters were as follows: field of view = 310*310 ~ 360*360 mm, matrix = 200*160 ~ 224*212, TR = 6.0 ms, TE = 2.8 ms, flip angle = 25°, slice thickness = 8 mm, and TI = 300 to 350 ms.

Cardiac MRI analysis

LV volume, compacted myocardial thickness, percentage of excessive trabecular mass, and myocardial strain were quantified by commercial software CVI42 (Circle Cardiovascular Imaging, Inc.). Endocardial and epicardial contours of LV myocardium on short-axis cine were manually outlined at end diastole and end systole to calculate stroke volume index (SVi), end-diastolic volume index (EDVi), end-systolic volume index (ESVi), and cardiac index (CI), in which papillary muscles and trabeculae were included in the LV volume. To measure compacted myocardial thickness, the myocardium in every slice of the short-axis cine stacks was equally divided into 50 chords automatically at end diastole, and segmental thickness was recorded by the average value of the corresponding chords using the American Heart Association segment model [22]. Trabecular mass was calculated by global LV mass minus compacted LV mass at end diastole. To assess global LV mass, the endocardial contour was drawn at the edge of the trabecula. Feature-tracking analyses were performed on short-axis cine stacks and three long-axis cine images (LV two-chamber, three-chamber, and four-chamber) to compute peak strain parameters, including global radial strain (GRS), global circumferential strain (GCS), and global longitudinal strain (GLS). Manually delineated LV contours at end diastole were used to track borders throughout the cardiac cycle automatically. All the boundary points of every slice and phase were checked, and the contours were adjusted if necessary. Note that the LV apex (segment 17) was excluded from the above analyses.

Fractal analysis was performed by a semiautomated in-house tool (FracAnalyse) [23] in MATLAB (MathWorks Inc.) that has been validated in several studies [10, 11, 13]. A region of interest was allocated outside of the LV endocardial border on short-axis cine stacks at end-diastole (Fig. 1). Image segmentation was performed to extract endocardial contours. The FD value is the slope of a least-squares linear regression fit, which was generated by the logarithm of the number of boxes containing the endocardial contour with a range of box sizes. Global FD was the average FD value of each slice encompassing the entire left ventricle. Maximal FD was the maximal value of all LV stacks. Regional FD (basal, medial, and apical) values were the average values of the corresponding slices. Ten of the patients were randomly selected to test the reproducibility of FD. Two investigators with 4 and 6 years of experience in cardiac MRI evaluated this set of patients independently to analyze interobserver agreement, and one

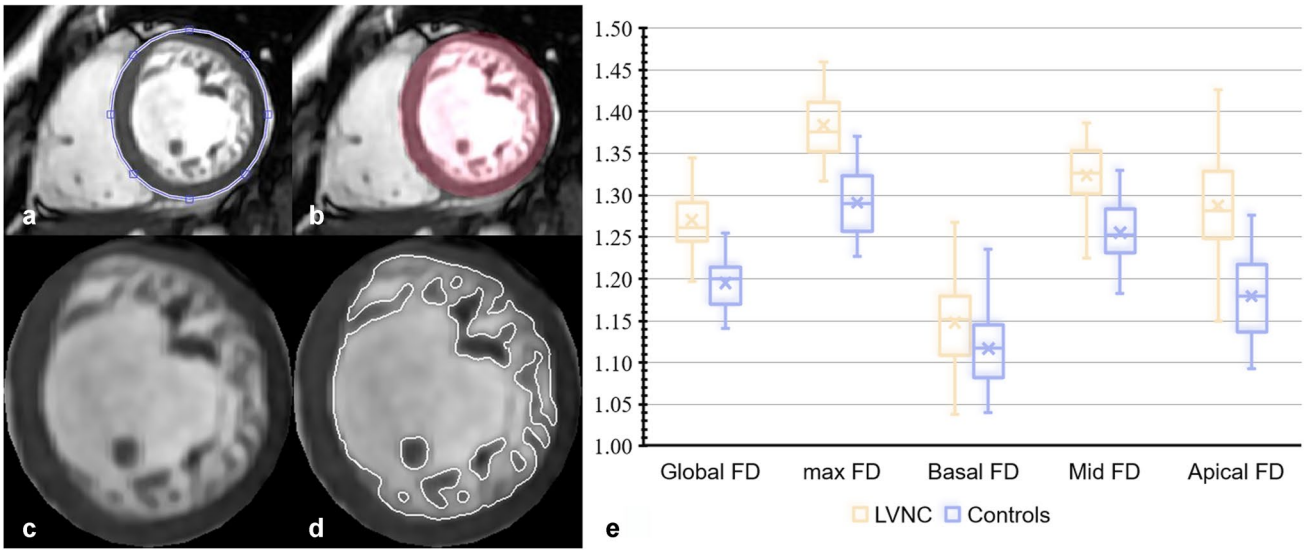

Fig. 1 Fractal analysis. **a** Region of interest (ROI) allocation; **b** ROI confirmation; **c** ROI segmentation; **d** outline identification; **e** global and regional fractal dimension (FD) values of patients with left ventricular noncompaction (LVNC) and healthy controls

of the investigators repeated the assessment 1 month later to assess intraobserver agreement.

Statistical analysis

According to the normality of each variable, continuous variables are expressed as the mean ± standard deviation or median values with interquartile range (IQR), and differences between groups were analyzed with the *t*-test or Mann–Whitney *U* test. Categorical variables are given as counts with percentages, and the chi-square test or Fisher's exact test was performed for comparison. Pearson's correlation was performed to investigate the association between trabecular complexity and cardiac function parameters. The intraclass correlation coefficient was used to evaluate the reproducibility of FD. Receiver operating characteristic curve analysis was used to assess differential diagnostic efficiency and determine cut-off values. The above analyses were conducted with IBM SPSS Statistics 23.0 and MedCalc 16.8.4. A two-tailed $p < 0.05$ was considered statistically significant.

Results

Baseline demographics

The mean age of the study population was 37 ± 16 years, and no difference was observed in baseline characteristics between patients with LVNC and healthy controls (Table 1). Electrocardiogram abnormalities were common in patients with LVNC (88%, 36 of 41). Ventricular premature beat was the most frequent, and 10% of patients presented with nonsustained ventricular tachycardia (≥ 3 beats, terminating spontaneously). The most common clinical symptom was palpitation followed by chest pain and chest distress.

Table 1 Baseline characteristics of the study population

Characteristics	LVNC (*n* = 41)	Controls (*n* = 41)	*p* value
Age, years	37 ± 16	37 ± 16	0.994
Male, *n* (%)	20 (49)	20 (49)	1
BMI, kg/m^2	22.58 ± 2.59	22.60 ± 3.11	0.970
BSA, m^2	1.72 ± 0.15	1.68 ± 0.22	0.337
Hyperlipidemia, *n* (%)	2 (5)	6 (15)	0.264
Diabetes mellitus, *n* (%)	1 (2)	1 (2)	1
Family history of cardiomyopathy, *n* (%)	4 (10)	0 (0)	0.116
Clinical symptoms, *n* (%)		-	-
Palpitation	17 (41)		
Chest pain	9 (22)		
Syncope	3 (7)		
Chest distress	9 (22)		
Asymptomatic	8 (20)		
NYHA class, *n* (%)		-	-
I	38 (93)		
II	3 (7)		
ECG examination, *n* (%)		-	-
Nonsustained ventricular tachycardia	4 (10)		
Ventricular premature beat	17 (41)		
Left bundle branch block	1 (2)		
Sinus bradycardia	9 (22)		
ST-T change	16 (39)		
Abnormal Q wave	1 (2)		
Atrial fibrillation	2 (5)		
Transient atrial tachycardia	3 (7)		
Prolonged QT interval	1 (2)		
Normal	5 (12)		

LVNC, left ventricular noncompaction; *BMI*, body mass index; *BSA*, body surface area; *ECG*, electrocardiogram

Table 2 Cardiac MRI parameters of the study population

Parameters	LVNC ($n=41$)	Controls ($n=41$)	p value
LVEF, %	59.02 ± 5.48	60.95 ± 4.47	0.086
SVi, ml/m^2	53.18 ± 9.13	29.07 ± 5.25	< 0.001
EDVi, ml/m^2	90.13 ± 13.17	74.49 ± 10.85	< 0.001
ESVi, ml/m^2	36.95 ± 7.56	29.07 ± 5.25	< 0.001
CI, l/min/m^2	3.64 ± 0.75	3.31 ± 0.61	0.032
Mass index, g/m^2	34.35 ± 7.57	35.85 ± 9.01	0.413
GRS, %	31.06 (27.36, 33.84)	35.92 (31.27, 41.21)	< 0.001
GCS, %	− 18.11 ± 2.67	− 20.24 ± 2.16	< 0.001
GLS, %	− 15.20 ± 2.25	− 16.28 ± 2.36	0.037
Global FD	1.270 ± 0.036	1.195 ± 0.030	< 0.001
Maximal FD	1.384 ± 0.043	1.291 ± 0.037	< 0.001
Basal FD	1.148 ± 0.056	1.117 ± 0.044	0.006
Medial FD	1.324 ± 0.038	1.255 ± 0.037	< 0.001
Apical FD	1.287 ± 0.066	1.180 ± 0.053	< 0.001
NC/C ratio (LAX)	4.28 (3.37, 5.01)	-	-
NC/C ratio (SAX)	4.89 (4.38, 6.40)	-	-
TM, % of LV	40.85 ± 9.06	-	-

LVEF, left ventricular ejection fraction; *SVi*, stroke volume index; *EDVi*, end-diastolic volume index; *ESVi*, end-systolic volume index; *CI*, cardiac index; *GRS*, global radial strain; *GCS*, global circumferential strain; *GLS*, global longitudinal strain; *FD*, fractal dimension; *NC/C ratio*, noncompacted to compacted ratio; *LAX*, long-axis view; *SAX*, short-axis view; *TM*, trabeculated mass; *LV*, left ventricle

Conventional cardiac MRI parameters

An overview of the assessed cardiac MRI parameters is presented in Table 2. The median NC/C ratios for patients with LVNC were 4.28 and 4.89 on long-axis and short-axis views, respectively. The excessive trabecular mass was 40.85 ± 9.06% of the global LV mass. Figure 2 shows compacted myocardial thickness according to AHA 16 segments, and segments 11–16 were significantly thinner in patients with LVNC than in controls (segment 11, 3.57 ± 0.88 mm vs. 4.28 ± 1.17 mm; segment 12, 3.56 ± 0.92 mm vs. 4.22 ± 1.10 mm; segment 13, 2.94 ± 0.78 mm vs. 3.65 ± 0.97 mm; segment 14, 3.37 ± 0.76 mm vs. 4.20 ± 0.93 mm; segment 15, 2.95 ± 0.73 mm vs. 3.68 ± 0.86 mm; segment 16, 2.51 ± 0.71 mm vs. 3.47 ± 0.95 mm; all $p < 0.05$). In terms of LVEF, no significant difference was observed between the two groups ($p = 0.086$); however, SVi, EDVi, ESVi, and CI were all significantly increased in the LVNC group (53.18 ± 9.13 ml/m^2 vs. 29.07 ± 5.25 ml/m^2, 90.13 ± 13.17 ml/m^2 vs. 74.49 ± 10.85 ml/m^2, 36.95 ± 7.56 ml/m^2 vs. 29.07 ± 5.25 ml/m^2, 3.64 ± 0.75 l/min/m^2 vs. 3.31 ± 0.61 l/min/m^2, respectively, all $p < 0.05$). The late gadolinium enhancement sequence was performed in thirty of the patients, and only one of them presented with linear enhancement in the mid-wall of the septum.

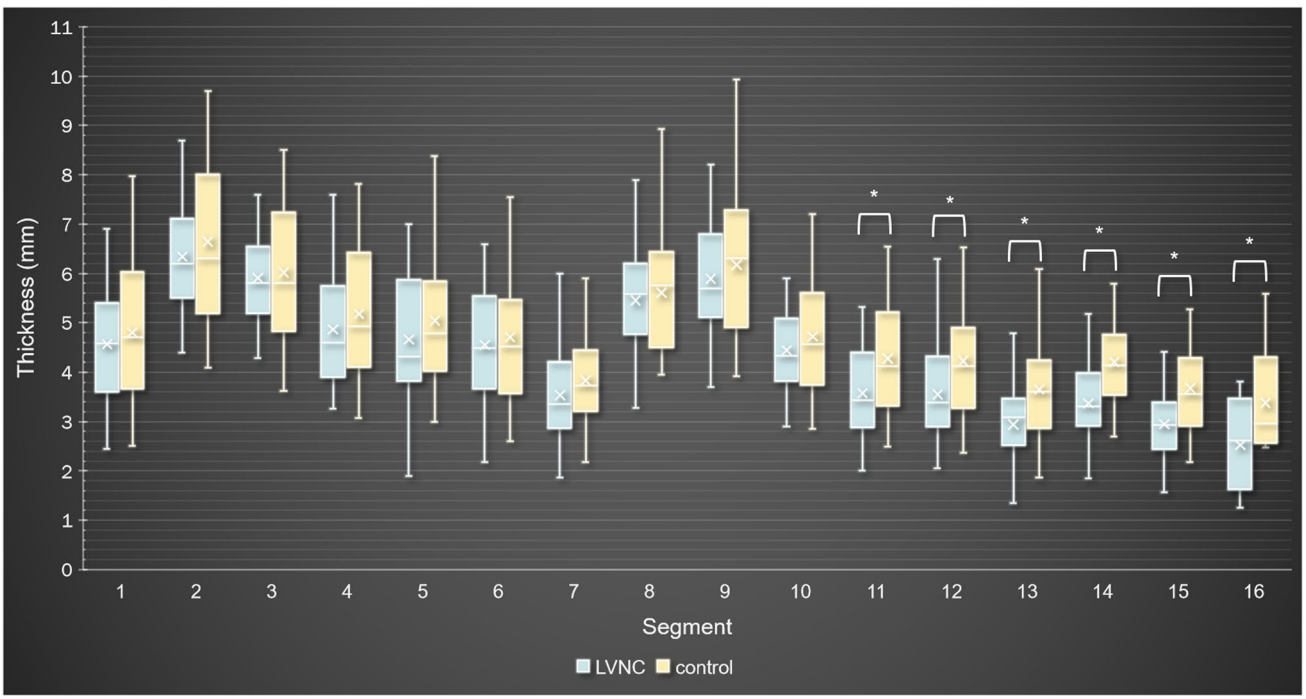

Fig. 2 Segmental compacted myocardial thickness of the left ventricle in patients with left ventricular noncompaction (LVNC) and controls. *$p < 0.05$ in the comparison between patients with LVNC and controls

Cardiac MRI fractal and strain analysis

The global, maximal, and regional FD values of the LVNC population were all significantly higher than those of the controls (Table 2). The medial segments had the highest FD in both groups, while the apical FD was prominently higher in patients with LVNC than in healthy subjects (1.287 ± 0.066 vs. 1.180 ± 0.053, $p < 0.001$). All the strain parameters were impaired in patients with LVNC compared with those in controls (median GRS, 31.06%, IQR 27.36–33.84% vs. 35.92%, IQR 31.27–41.21%; mean GCS, $-18.11\% \pm 2.67$ vs. $-20.24\% \pm 2.16$; mean GLS, $-15.20\% \pm 2.25$ vs. $-16.28\% \pm 2.36$; all $p \leq 0.05$). A series of representative cases, including healthy controls and patients with different degrees of excessive trabeculation, are shown in Fig. 3. As the extent of trabeculation increased, the global FD increased and global strain parameters worsened. Among LV strain and FD parameters, maximal FD was demonstrated to be the best discriminator (area under the curve [AUC]: 0.959) between patients with LVNC and healthy subjects, with a cut-off value of 1.329 (Fig. 4, Supplemental Table S1).

Association between FD and myocardial function

Table 3 shows that global, maximal, medial, and apical FD were all positively correlated with EDVi, ESVi, and SVi (r ranged from 0.277 to 0.505, all $p < 0.05$) but negatively correlated with GRS ($r = -0.458, -0.353, -0.265$, and -0.466, respectively, all $p < 0.05$) and GCS ($r = 0.508$, 0.398, 0.286, and 0.513, respectively, all $p < 0.05$). Apical FD was also weakly associated with LVEF and GLS ($r = -0.249$ and 0.252, respectively, both $p < 0.05$).

Intraobserver and interobserver variability for FD

The reproducibility of global and regional FD was excellent (Table 4). The intraclass correlation coefficients ranged from 0.941 to 0.987 for intraobserver agreement and ranged from 0.821 to 0.970 for interobserver agreement.

Discussion

The present study investigated cardiac MRI characteristics of patients with severe excessive trabeculation but without reduced LVEF. The main findings were as follows: (1) Compared with controls, LV global strain in all three directions was already impaired in patients with LVNC, despite normal LVEF; and (2) LV trabecular complexity measured by FD was associated with impaired strains.

The published studies concentrating on LVNC were controversial and challenging to make valuable progress without a gold diagnostic standard [24]. The patients who met the current diagnostic criteria ranged from those with cardiomyopathy and remodelling to those with normal

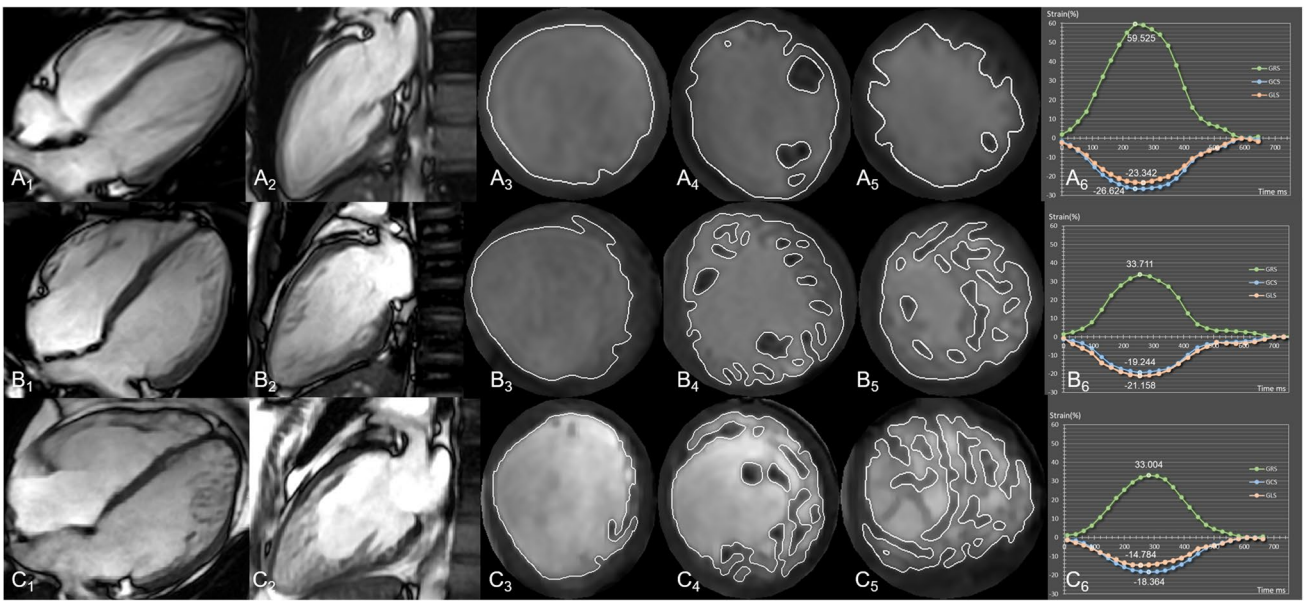

Fig. 3 Representative examples of 2-chamber and 4-chamber cine images at end diastole ($A_{1\text{-}2}$, $B_{1\text{-}2}$, $C_{1\text{-}2}$); basal, medial, and apical fractal analysis ($A_{3\text{-}5}$, fractal dimension [FD] values: 1.054, 1.206, 1.156; $B_{3\text{-}5}$, FD values: 1.094, 1.407, 1.448; $C_{3\text{-}5}$, FD values: 1.116, 1.403, 1.511); global radial strain (GRS), global circumferential strain (GCS), and global longitudinal strain (GLS) (A_6, B_6, C_6): cluster A is a healthy control (female, 39 years) and clusters B and C are patients with different degrees of excessive trabeculation (male, 15 years; female, 29 years, respectively)

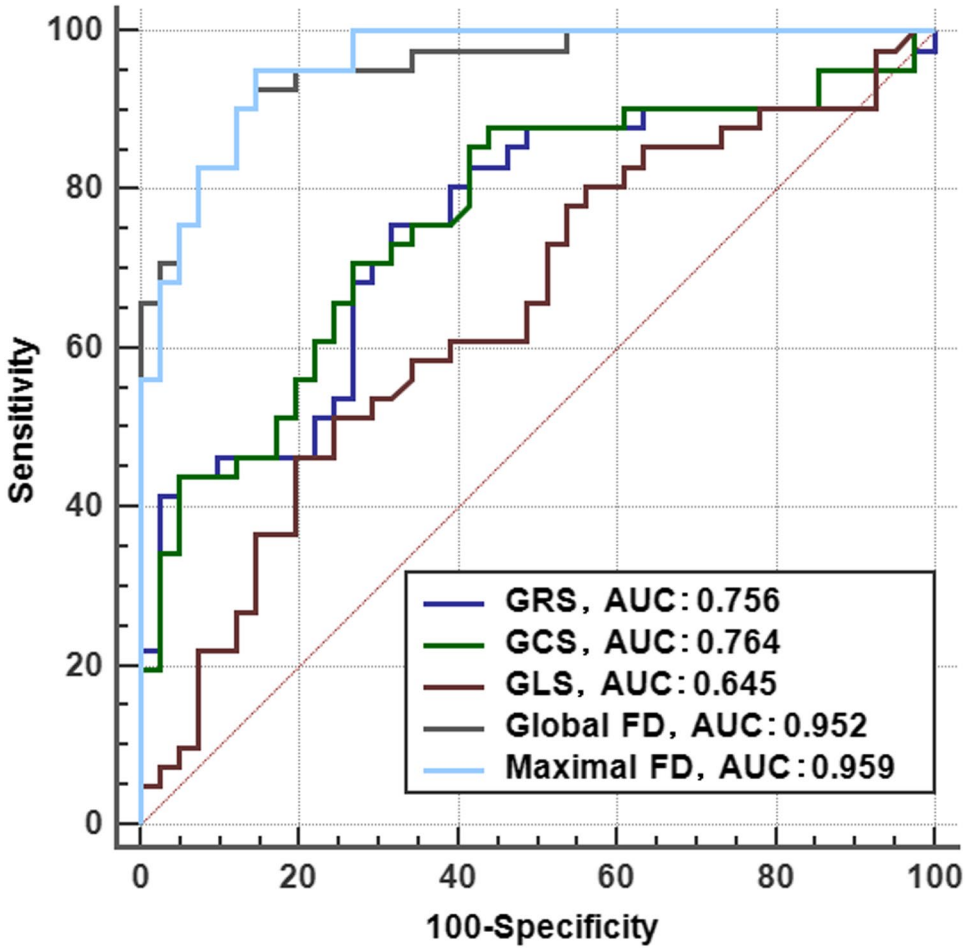

Fig. 4 Receiver operating characteristic curve analysis for discriminating patients with left ventricular noncompaction from controls. FD, fractal dimension; GRS, global radial strain; GCS, global circumferential strain; GLS, global longitudinal strain; AUC, area under the curve

Table 3 Association between FD and myocardial function

Parameters		LVEF	CI	EDVi	ESVi	SVi	GRS	GCS	GLS
Global FD	*r*	−0.240	0.145	0.483	0.505	0.335	−0.458	0.508	0.195
	p value	0.030	0.193	<0.001	<0.001	0.002	<0.001	<0.001	0.079
Maximal FD	*r*	−0.191	0.179	0.388	0.396	0.277	−0.353	0.398	0.191
	p value	0.086	0.108	<0.001	<0.001	0.012	0.001	<0.001	0.085
Basal FD	*r*	−0.060	−0.119	0.156	0.165	0.107	−0.195	0.218	−0.169
	p value	0.591	0.287	0.161	0.138	0.340	0.079	0.049	0.129
Medial FD	*r*	−0.098	0.123	0.373	0.340	0.300	−0.265	0.286	0.068
	p value	0.380	0.271	0.001	0.002	0.006	0.016	0.009	0.543
Apical FD	*r*	−0.249	0.163	0.456	0.485	0.310	−0.466	0.513	0.252
	p value	0.024	0.143	<0.001	<0.001	0.005	<0.001	<0.001	0.023

FD, fractal dimension; *LVEF*, left ventricular ejection fraction; *CI*, cardiac index; *EDVi*, end-diastolic volume index; *ESVi*, end-systolic volume index; *SVi*, stroke volume index; *GRS*, global radial strain; *GCS*, global circumferential strain; *GLS*, global longitudinal strain

variations. This study focused on patients with LVNC fulfilling three diagnostic criteria with normal LVEF, in which the increased trabeculation was extremely prominent and regular and could not be explained by adaptation. The median NC/C ratios for the present patients were 4.28 and 4.89 on long-axis and short-axis views, respectively. This result is considerable since the mean NC/C ratio of the segments analyzed in healthy participants was 1.96 ± 0.66 in the Multi-Ethnic Study of Atherosclerosis (MESA) [25]. Similarly, the excessive trabecular mass was 40.85 ± 9.06% of the global LV mass in the present patients, while the cut-off value was only 20% in the Jacquier criterion for LVNC diagnosis [21].

Table 4 Inter- and intraobserver variability of fractal dimension measurements

Parameters	Interobserver		Intraobserver	
	ICC	95% CI	ICC	95% CI
Global FD	0.958	0.870 to 0.987	0.987	0.959 to 0.996
Maximal FD	0.970	0.904 to 0.991	0.974	0.919 to 0.992
Basal FD	0.821	0.505 to 0.942	0.945	0.831 to 0.983
Medial FD	0.916	0.757 to 0.973	0.941	0.822 to 0.981
Apical FD	0.922	0.729 to 0.977	0.954	0.860 to 0.986

FD, fractal dimension; *ICC*, intraclass correlation coefficient; *CI*, confidence interval

As van Waning et al. demonstrated, noncompaction cardiomyopathy with a likely pathogenic variant was more likely to have a higher degree of excessive trabeculation and more often met ≥ 4 MRI diagnostic criteria than without a pathogenic variant [26]. Hence, we speculated that the prominent excessive trabeculation in the present patients might be explained by pathogenic variants. In our clinical experience, the trabeculae of patients who had specific remodelling factors were usually thick and disordered, which seems to be a process of irregular hypertrophy. In contrast, the trabeculae of LVNC patients were fine-grained and regular. More importantly, the degree of trabeculation in LVNC patients was much more serious than in those with compensatory remodelling. In accordance with a previous study, Zheng et al. demonstrated that LVNC patients had significantly higher FD values than dilated cardiomyopathy patients [12].

Although the present patients had normal LVEF, cardiac MRI feature tracking detected early LV systolic dysfunction. In a recent investigation of the strain characteristics of LVNC, reduced strain was observed in patients with LVNC, even when compared with healthy controls who met one or more LVNC diagnostic criteria [27]. The decrease in deformation could indicate an early stage for cardiac dysfunction. An investigation involving two age groups of LVNC patients with comparable extents of trabeculation and late gadolinium enhancement showed that the LV strain parameters were impaired in both groups. However, the LVEF of the young adult group was significantly reduced, while the child/adolescent group presented a similar LVEF to the healthy control group [28]. From this result, we speculate that reduced strain at an early age might progress to reduced LVEF in the long term. In other words, LVNC with normal LVEF cannot exclude a disease process. Moreover, by developing a geometrical model, Paun et al. identified a trade-off among ventricle size, stroke volume, and strain in trabeculated ventricles. Dilatated ventricle, increased stroke volume, or reduced deformation could be observed in the trabeculated ventricle when the other two mentioned indices remained the same. This could be a possible explanation for excessive trabeculation in athletes, pregnant women, and patients with dilated cardiomyopathy [29]. In line with the previous findings, increased EDVi, ESVi, and SVi and reduced strain were observed in the present patients with normal LVEF.

Fractal analysis, objectively describing the complexity of trabeculation both in general and regionally, was performed for better quantification and diagnosis in LVNC. We investigated and displayed the FD values in detail for patients with LVNC and controls, including global, maximal, and segmental (basal, medial, and apical) data. Excessive trabeculation was most notable in the apical myocardium, with considerable FD differences between patients and controls, which was consistent with previous studies [8, 12]. Moreover, the location of thinning compacted myocardial segments (segments 11–16) was consistent with that of the most pronounced excessive trabeculation, which might support the presence of cardiomyopathy. In addition to being a potential index for measuring excessive trabeculation, FD could also be helpful for diagnosis. Dreisbach et al. demonstrated that GCS had an independent discriminant value beyond MRI diagnostic criteria [27]. However, our study showed that global FD (AUC: 0.952) performed much better than strain parameters (AUC: 0.645 ~ 0.764) for discriminating between patients and controls. Captur et al. also reported that global FD had a high accuracy for LVNC diagnosis (AUC: 0.893) [8]. Moreover, a study demonstrated that fractal analysis could discriminate LVNC from dilated cardiomyopathy, with maximal apical FD showing a sensitivity of 77% and a specificity of 88% (AUC = 0.881) and global FD showing a sensitivity of 89% and a specificity of 76% (AUC = 0.895) [12].

Moreover, the present research illustrated the association between global/regional FD and cardiac function. The higher the degree of excessive trabeculation, the larger the left ventricle and the more impaired the strains. Compared with participants (previously free of cardiovascular disease) from MESA in NC/C ratio quintile 5 (NC/C ranged from 2.46 to 5.41), the present patients had greater EDVi and ESVi values (EDVi: 90.13 ± 13.17 ml/m^2 vs. 68.3 ± 13.2 ml/m^2; ESVi: 36.95 ± 7.56 ml/m^2 vs. 26.3 ± 8.0 ml/m^2) [25] and higher apical FD values (mean apical FD of the present patients [BMI: 22.58 ± 2.59 kg/m^2]: 1.287 ± 0.066; maximal apical FD of the MESA participants with a BMI < 25 kg/m^2: 1.244 ± 0.02) [30]. Among the strain parameters, GCS showed the strongest correlation with the degree of excessive trabeculation, particularly in apical segments. Only apical FD was slightly associated with GLS. An analysis conducted in healthy subjects observed findings consistent with the above results in our study: FD was positively related to volumetric parameters and negatively related to strain values [10]. Therefore, prominently increased trabeculation should not be ignored, and surveillance should be performed during follow-up.

This study has several limitations, as follows: first, genetic information could not be obtained in this retrospective analysis; second, the sample size was relatively small but comparable

with previous studies, and prospective studies with large sample sizes and long-term follow-up are warranted; third, myocardial displacement of the adjacent slice could influence the strain assessment, and inter-vendor variability also exists among post-processing software. Moreover, the interpretation of FD value should be considered cautiously for patients of different races, ages, sexes, and BMIs. Thus, the cut-off value has limited application.

Conclusion

Patients with LVNC and normal LVEF had impaired deformation and increased FD values compared with controls. Left ventricle trabecular complexity measured by FD was associated with impaired strain.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s00330-021-08346-2.

Funding This study was co-funded by the National Natural Science Foundation of China (No. 81930044, No. 81620108015).

Declarations

Guarantor The scientific guarantor of this publication is Shihua Zhao.

Conflict of interest The authors of this manuscript declare no relationships with any companies, whose products or services may be related to the subject matter of the article.

Statistics and biometry No complex statistical methods were necessary for this paper.

Informed consent Written informed consent was waived by the Institutional Review Board.

Ethical approval Institutional Review Board approval was obtained.

Methodology

- retrospective
- performed at one institution

References

1. Kayvanpour E, Sedaghat-Hamedani F, Gi WT et al (2019) Clinical and genetic insights into non-compaction: a meta-analysis and systematic review on 7598 individuals. Clin Res Cardiol 108(11):1297–1308
2. Anderson RH, Jensen B, Mohun TJ et al (2017) Key questions relating to left ventricular noncompaction cardiomyopathy: is the emperor still wearing any clothes? Can J Cardiol 33(6):747–757
3. Oechslin E, Jenni R (2018) Left ventricular noncompaction: from physiologic remodeling to noncompaction cardiomyopathy. J Am Coll Cardiol 71(7):723–726
4. Oechslin E, Jenni R, Klaassen S (2021) Left ventricular noncompaction is a myocardial phenotype: cardiomyopathy-yes or no? Can J Cardiol 37(3):366–369
5. Gati S, Rajani R, Carr-White GS, Chambers JB (2014) Adult left ventricular noncompaction: reappraisal of current diagnostic imaging modalities. JACC Cardiovasc Imaging 7(12):1266–1275
6. D'Silva A, Jensen B (2021) Left ventricular non-compaction cardiomyopathy: how many needles in the haystack? Heart 107(16):1344–1352
7. Weir-McCall JR, Yeap PM, Papagiorcopulo C et al (2016) Left ventricular noncompaction: anatomical phenotype or distinct cardiomyopathy? J Am Coll Cardiol 68(20):2157–2165
8. Captur G, Muthurangu V, Cook C et al (2013) Quantification of left ventricular trabeculae using fractal analysis. J Cardiovasc Magn Reson 15:36
9. Captur G, Lopes LR, Patel V et al (2014) Abnormal cardiac formation in hypertrophic cardiomyopathy: fractal analysis of trabeculae and preclinical gene expression. Circ Cardiovasc Genet 7(3):241–248
10. Cai J, Bryant JA, Le TT et al (2017) Fractal analysis of left ventricular trabeculations is associated with impaired myocardial deformation in healthy Chinese. J Cardiovasc Magn Reson 19(1):102
11. Dawes TJW, Cai J, Quinlan M et al (2018) Fractal analysis of right ventricular trabeculae in pulmonary hypertension. Radiology 288(2):386–395
12. Zheng T, Ma X, Li S et al (2019) Value of cardiac magnetic resonance fractal analysis combined with myocardial strain in discriminating isolated left ventricular noncompaction and dilated cardiomyopathy. J Magn Reson Imaging 50(1):153–163
13. Wang J, Li Y, Yang F et al (2021) Fractal analysis: prognostic value of left ventricular trabecular complexity cardiovascular MRI in participants with hypertrophic cardiomyopathy. Radiology 298(1):71–79
14. van Dalen BM, Caliskan K, Soliman OI et al (2008) Left ventricular solid body rotation in non-compaction cardiomyopathy: a potential new objective and quantitative functional diagnostic criterion? Eur J Heart Fail 10(11):1088–1093
15. Bellavia D, Michelena HI, Martinez M et al (2010) Speckle myocardial imaging modalities for early detection of myocardial impairment in isolated left ventricular non-compaction. Heart 96(6):440–447
16. van Dalen BM, Caliskan K, Soliman OI et al (2011) Diagnostic value of rigid body rotation in noncompaction cardiomyopathy. J Am Soc Echocardiogr 24(5):548–555
17. Chen X, Li L, Cheng H et al (2019) Early left ventricular involvement detected by cardiovascular magnetic resonance feature tracking in arrhythmogenic right ventricular cardiomyopathy: the effects of left ventricular late gadolinium enhancement and right ventricular dysfunction. J Am Heart Assoc 8(17):e012989
18. Kraigher-Krainer E, Shah AM, Gupta DK et al (2014) Impaired systolic function by strain imaging in heart failure with preserved ejection fraction. J Am Coll Cardiol 63(5):447–456
19. Petersen SE, Selvanayagam JB, Wiesmann F et al (2005) Left ventricular non-compaction: insights from cardiovascular magnetic resonance imaging. J Am Coll Cardiol 46(1):101–105
20. Grothoff M, Pachowsky M, Hoffmann J et al (2012) Value of cardiovascular MR in diagnosing left ventricular non-compaction cardiomyopathy and in discriminating between other cardiomyopathies. Eur Radiol 22(12):2699–2709
21. Jacquier A, Thuny F, Jop B et al (2010) Measurement of trabeculated left ventricular mass using cardiac magnetic resonance imaging in the diagnosis of left ventricular non-compaction. Eur Heart J 31(9):1098–1104

22. Cerqueira MD, Weissman NJ, Dilsizian V et al (2002) 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 105(4):539–542
23. Cai J (2017) UK-Digital-Heart-Project/fracAnalyse: fracAnalyse v1.2. https://github.com/UK-Digital-Heart-Project/fracAnalyse
24. Ross SB, Jones K, Blanch B et al (2020) A systematic review and meta-analysis of the prevalence of left ventricular non-compaction in adults. Eur Heart J 41(14):1428–1436
25. Zemrak F, Ahlman MA, Captur G et al (2014) The relationship of left ventricular trabeculation to ventricular function and structure over a 9.5-year follow-up: the MESA study. J Am Coll Cardiol 64(19):1971–1980
26. van Waning JI, Caliskan K, Chelu RG et al (2021) Diagnostic cardiovascular magnetic resonance imaging criteria in noncompaction cardiomyopathy and the yield of genetic testing. Can J Cardiol 37(3):433–442
27. Dreisbach JG, Mathur S, Houbois CP et al (2020) Cardiovascular magnetic resonance based diagnosis of left ventricular non-compaction cardiomyopathy: impact of cine bSSFP strain analysis. J Cardiovasc Magn Reson 22(1):9
28. Nucifora G, Sree Raman K, Muser D et al (2017) Cardiac magnetic resonance evaluation of left ventricular functional, morphological, and structural features in children and adolescents vs. young adults with isolated left ventricular non-compaction. Int J Cardiol 246:68–73
29. Paun B, Bijnens B, Butakoff C (2018) Relationship between the left ventricular size and the amount of trabeculations. Int J Numer Method Biomed Eng 34(3). https://doi.org/10.1002/cnm.2939
30. Captur G, Zemrak F, Muthurangu V et al (2015) Fractal analysis of myocardial trabeculations in 2547 study participants: Multi-Ethnic Study of Atherosclerosis. Radiology 277(3):707–715