Myocardial Characterization in Patients with Nonischemic Dilated Cardiomyopathy Combined with Ventricular Arrhythmias: Insights from Cardiovascular Magnetic Resonance Feature Tracking

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Abstract

This study investigated the feasibility of using cardiovascular magnetic resonance feature tracking (CMR-FT) for analysis of left ventricular (LV) strain and strain rate in patients with non-ischemic dilated cardiomyopathy (NIDCM) combined with ventricular arrhythmias (VAs). And evaluated the correlation between the LV global strain and left ventricular ejection (LVEF). We performed a retrospective study in a cohort of 34 consecutive patients with NIDCM combined with VAs who underwent CMR examination in our hospital between January 2016 and December 2019. Global and segmental peak values of LV longitudinal, circumferential, radial strain, and systolic strain rate were analyzed. Pearson analysis was calculated to assess the correlation of LV global deformation and LVEF as well as the correlation of between LV global deformation. Compared with the healthy controls, the global peak radial strain (GPRS), global peak circumferential strain (GPCS), and global peak longitudinal strain (GPLS) were significantly reduced in patients with NIDCM combined with VAs ($P < 0.001$, respectively). Additionally, Pearson analysis showed GPCS negatively correlated with LVEF ($r = -0.946$, $P < 0.001$), GPLS negatively correlated with LVEF ($r = -0.860$, $P < 0.001$), and GPRS positively correlated with LVEF ($r = 0.920$, $P < 0.001$). CMR-FT is a feasible and promising technique for assessing LV myocardial deformation of patients with NIDCM combined with VAs. And, GPCS was better negatively correlated with LVEF and higher reproducibility of intra-class correlation coefficient (ICC), which can help to guide clinical treatment and have great implication on clinical decision.

Introduction

Non-ischemic dilated cardiomyopathy (NIDCM) is a myocardial disorder characterized by the presence of left ventricular (LV) or biventricular dilatation and systolic dysfunction in the absence of coronary artery disease or abnormal loading conditions proportionate to the degree of LV impairment[1–3]. In the process development of NIDCM, it may or may not develop overt heart failure (HF). Although modern management of HF increased the survival rates of NIDCM and has resulted in long periods of clinical stability, the 5-year mortality rate remains as high as 20% [4]. Moreover, in clinical practice, patients with dilated cardiomyopathy are prone to arrhythmias, and the cause of mortality in these patients is either end-organ dysfunction due to pump failure or arrhythmia-related death [5]. Several studies that analyzed the ventricular arrhythmias (VAs) substrate found that myocardial fibrosis plays an important role in the genesis of VAs in patients with NIDCM [6–8]. Therefore, patients with NIDCM combined VAs should be continuously re-assessed, particularly in the presence of abrupt worsening of left ventricle (LV) function or an increased ventricular arrhythmic burden.

At present, novel cardiovascular magnetic resonance (CMR) techniques are rapidly emerging as useful and unique tools for a comprehensive cardiac evaluation of dilated cardiomyopathy, including evaluation of chamber size quantification, ventricular function and mass, myocardial wall thicknesses, segmental function, myocardial fibrosis, myocardial edema, and tissue characterization [9–11]. Myocardial strain allows quantitative measurement of global but also regional myocardial function and deformation offering additional information beyond ejection fraction[12, 13]. Moreover, CMR-FT has high spatial, temporal resolution and nearly incompressible biventricular model, which is more accurate than speckle-tracking echocardiography [14–16].

However, the feasibility of CMR-based feature tracking strain analysis in patients with NIDCM combined with VAs has not been investigated. Therefore, the purpose of the current study was to observe the left ventricular myocardial strain for patients with NIDCM combined with VAs and study the correlation between the LV global strain values and LVEF, and relationship between pair-wise LV global strain values.

Methods

Patient population

We performed a retrospective study in a cohort of 96 consecutive suspected patients with NIDCM in our hospital between January 2016 and December 2019. **Inclusion criteria were:** (1) the definition and diagnosis of patients with NIDCM was made according to the CMR current recommendations [17], (2) all patients diagnosed with NIDCM underwent 24-hour Holter electrocardiography examinations, (3) all NIDCM patients with VAs which CMR-FT analysis could be performed were included. **Exclusion criteria were:** (1) coronary artery disease with $>50\%$ stenosis on elective angiography, (2) NIDCM patients without ventricular arrhythmias based on 24-hour Holter electrocardiography examinations, (3) NIDCM patients with ventricular arrhythmias had performed radiofrequency ablation, (4) systemic disease, (5) hypertensive heart disease, (6) valvular disease, (7) congenital heart disease, (8) combined myocardial infarction, and (9) inappropriate image.

Control group

As a control, 25 healthy volunteers who met the following inclusion criteria were recruited from our hospital: (i) no symptoms or prior history of cardiovascular disease; (ii) no prior diagnosis of hyperlipidaemia, hypertension or diabetes mellitus; (iii) normal physical examination and electrocardiogram; (iv) no contraindications to CMR. (v) CMR-FT analysis could be performed in all subjects.

This study was approved by the Ethics Committee of Guizhou Provincial People's Hospital (No. 2020-384) and it complies with the ethical principles of the Declaration of Helsinki (2000 EDITION). All enrolled healthy volunteers provided written informed consent prior to investigation. However, written informed consent for patients with NIDCM were waived by the Ethics Committee of Guizhou Provincial People's Hospital because this study on NIDCM patients was retrospective.

Twenty-four-hour Holter electrocardiography (ECG) monitoring

Three-channel 24-hour Holter ECG recordings were obtained in all patients in the absence of class I or class III antiarrhythmic drugs. The Holter recordings were analyzed by computer (Shenzhen Bosheng, China) with manual overread performed by an experienced doctor. All Holter readouts were confirmed by the independent senior observers blinded to clinical data.

Cardiac magnetic resonance (CMR) imaging

CMR imaging was performed using a 1.5-Tesla (Aera, Siemens, Germany), 1.5-Tesla (Verio, Siemens, Germany) and a standardized imaging protocol [18]. Balanced steady-state free precession sequence (SSFP) sequences with breath-hold were performed to obtain cine CMR images, comprising a stack of contiguous parallel short-axis slices covering the entire LV from base to apex and three LV long-axis slice (2-, 3-, and 4-chamber views) images. Cine images in the short axis (SA) planes were acquired at 1.5 Tesla using a balanced, SSFP sequence (repetition time/echo time/flip angle [TR/TE/FA] 2.4/1.2/50–75 degrees, matrix 192×256, resolution 1.9×1.9×8 mm³, field of view 289 mm×356 mm, temporal resolution ≤40 ms). In-plane axial resolution ranged from 1.39–1.5 mm per dimension. Delayed enhancement images were acquired at end-diastole during breath-holding using a segmented inversion-recovery gradient-echo turbo fast low angle shot sequence obtained 8–10 min after injection of 0.2 mmol/kg of gadopentetate dimeglumine (Magnevist, Bayer) contrast medium. 18-channel phased-array chest coil was used for all data acquisition.

CMR feature-tracking analysis

CMR-FT analysis was performed with dedicated software (CVI42 v5.11, Circle Cardiovascular Imaging, Calgary, Canada). SAX and LAX cine images were uploaded into the software which reconstructed a 3D model and derived peak radial, circumferential and longitudinal strain [19]. CMR-FT post-processing software was used to analyze the LV strain, short-axis view, and 2- and 4-ch views of the ventricle, which were divided according to the American Heart Association (AHA) 17-segment model [20]. The apical cap (segment 17) was not considered for analysis. Global and regional LV strain and systolic strain rate measurements were analyzed and feature tracking allows quantification of global and regional longitudinal, circumferential and radial strain and strain rates. The quality of tracking was visually verified and manually adjusted if necessary. Inter-observer reproducibility was measured using a randomly selected sample of 20 cases by two independent observers.

In addition, LV end-diastolic volume (LVEDV), end-systolic volume (LVESV), stroke volume (LVSV), ejection fraction (LVEF) and LV mass were measured via standardized protocols using semi-automated commercial software (CVI42) [18,21]. And, the late gadolinium enhancement (LGE) mass and LV LGE percent (defined as the LGE mass divided by normal myocardial mass) were also quantitatively analyzed by commercially available software (CVI42). The LGE was defined by using a signal intensity threshold level of 5 standard deviations (SDs) above a remote myocardial region that was used as a reference on the same section.

Statistical analysis

Statistical analysis was performed with commercially available statistical software (IBM SPSS Statistics 20.0, Chicago, Illinois). Qualitative or quantitative variables were expressed as mean ± standard deviation (SD), percentages, or median (interquartile range) as appropriate. All data were controlled for a normal distribution by the Kolmogorov–Smirnov test before analyzing the differences between two groups data. For continuous variables, differences between two groups were compared using Unpaired Students' t-test or

Mann–Whitney U test. The distribution of qualitative variables was analyzed by chi-square test or Fisher's exact test. The association between the LVEF and LV strain parameters was assessed using Pearson correlation in all patients. And, the correlation between the LV strain parameters was observed using Pearson correlation in all patients. A two-tailed $P < 0.05$ was considered statistically significant. The intraobserver and interobserver variability for LV strain values were studied in a group of 20 randomly selected subjects by one observer, repeated twice, and by two observers who were unaware of each other's measurements.

Results

Baseline characteristics of the study participants

Of the 96 consecutive suspected patients with NIDCM initially enrolled in the study, 62 subjects were excluded according to inclusion and exclusion criteria. Thus, in total, 34 patients diagnosed with NIDCM combined with VAs (67% were males, mean age was 46 ± 14 years) and 25 healthy controls were finally included. And, CMR-FT analysis could be performed in all subjects. No patients had LGE with an ischemic pattern.

There was no statistical difference between the NIDCM combined VAs group and the control group in terms of sex and body surface area (BSA) ($P > 0.05$, for each), whereas age had difference between NIDCM patients and controls ($P < 0.05$). Baseline characteristics in the NIDCM combined VAs group and the control group are presented in Table 1.

Table 1
Baseline characteristics of patients with NIDCM and controls

Variable	DCM(n = 34)	Controls(n = 25)	t/ χ^2 /Z	P value
Age (years)	46 $\pm$ 14	29 $\pm$ 6	-5.57	< 0.001
Sex (male)	23(67%)	15(60%)	1.23	0.436
BSA (m ²)	1.76(1.49,1.83)	1.70(1.59,1.80)	-0.26	0.793
Clinical Symptom	Palpitation, chest distress	—	—	—
Holter n (%)				
PVCs	18(53%)	—	—	—
NSVT	15(44%)	—	—	—
SVT	1(3%)	—	—	—
LVEF (%)	22.23 $\pm$ 7.86	63.21 $\pm$ 5.13	22.72	< 0.001
EDV (mL)	287.45 $\pm$ 85.26	114.19 $\pm$ 22.48	-9.89	< 0.001
ESV (mL)	223.63 $\pm$ 85.01	45.99 $\pm$ 12.47	-10.34	< 0.001
SV (mL)	50.37 $\pm$ 15.35	82.31 $\pm$ 11.56	8.73	< 0.001
CO (L/min)	3.62 $\pm$ 0.87	5.26 $\pm$ 0.82	7.32	< 0.001
CI (L/min/m ²)	2.70(1.98,3.49)	4.27(3.38,4.42)	-4.65	< 0.001
LVEDVI(mL/m ²)	172.39 $\pm$ 45.10	69.84 $\pm$ 15.33	-10.89	< 0.001
LVESVI(mL/m ²)	132.82 $\pm$ 46.03	27.59 $\pm$ 7.44	-11.29	< 0.001
SVI(mL/m ²)	39.62 $\pm$ 16.07	42.09 $\pm$ 10.39	0.674	0.503
LGE positive, n (%)	29 (85%)	—	—	—
LGE mass (g)	12.16 $\pm$ 3.87	—	—	—
LGE percent (%)	11.73 $\pm$ 3.42	—	—	—
Results are reported as mean $\pm$ SD, percentages, or median (interquartile range) as appropriate. BSA, body surface area; LVEF, left ventricular ejection; EDV, end-diastolic volume; ESV, end-systolic volume; SV, Stroke volume; CO, cardiac output; CI, Cardiac index; LVEDVI, indexed-left ventricular end diastolic volume; LVESVI, indexed-left ventricular end systolic volume; SVI, indexed-stroke volume; PVCs, Premature ventricular contractions; NSVT, nonsustained ventricular tachycardia; SVT, sustained ventricular tachycardia; LGE, the late gadolinium enhancement				

Cardiac Function Parameters

LGE was present in 29 (85%) of NIDCM patients with a mean global LGE mass of 12.16 $\pm$ 3.87. The LVEF, LVEDV, LVESV, SV, CO, CI, LVEDVI and LVESVI were significantly lower in the patients with NIDCM combined VAs than in the controls (P < 0.001 for all), whereas SVI had no differences between NIDCM patients and controls (P > 0.05). Patient cardiac function parameters data is summarized in Table 1.

24-hour Holter Findings

A total of 34 patients with NIDCM combined VAs were diagnosed after underwent 24 Holter electrocardiogram examinations. The 24-hour Holter documented 15 patients (44%) with nonsustained ventricular tachycardia, 11 patients (32%) with frequent premature ventricular beats (ie, > 1,000 over 24 hours of Holter monitoring), 7 patients (21%) with frequent premature ventricular beats (ie, < 1,000 over 24 hours of Holter monitoring), and 1 patient (3%) with sustained ventricular tachycardia.

CMR Global And Segmental Strain Analysis

At the LV global strains level, patients with NIDCM combined VAs demonstrated significantly impaired LV GPRS, GPCS, GPLS GPRSR, GPCSR and GPLSR compared to healthy controls ($P < 0.001$ for all) in Table 2. For segmental strain level, we found that patients with NIDCM with VAs had significantly lower PLS, PLSR, PCS, PCSR, PRS, and PRSR values at most segments to different degrees, compared with the control group ($P < 0.001$ for each); whereas the only exception was the PRS at the middle anterior lateral segment, PLS at the apical anterior lateral, apical septal and middle anterior lateral segments, and PRSR at the middle septal inferior and middle anterior segments, where no significant difference could be identified ($P > 0.05$) (Table 3, and 4). And, a representative example of the derivation of strain in patient with NIDCM combined VAs in Fig. 1.

Table 2
Global strain of NIDCM combined with VAs and controls

Variable	NIDCM(n = 34)	Controls(n = 25)	t/Z	P value
GPRS	8.21 ± 2.78	41.69 ± 5.38	31.16	< 0.001
GPCS	-5.99 ± 3.73	-21.75 ± 2.54	-18.22	< 0.001
GPLS	-7.06 ± 2.25	-15.54 ± 1.23	-17.04	< 0.001
GPRSR	0.69 ± 0.39	1.91 ± 0.48	10.80	< 0.001
GPCSR	-0.37(- 0.54, - 0.17)	-1.37(- 1.52, - 1.28)	-6.48	< 0.001
GPLSR	-0.23 ± 0.18	-0.74 ± 0.15	-11.39	< 0.001
Results are reported as mean ± SD or median (interquartile range) as appropriate. NIDCM, nonischemic dilated cardiomyopathy; GPRS, global peak radial strain; GPRSR, global peak systolic radial strain rate; GPCS, global peak circumferential strain; GPRSR, global peak systolic circumferential strain rate; GPLS, global peak longitudinal strain; GPLSR, global peak systolic longitudinal strain rate				

Table 3
Segmental values of strain in patients with NIDCM combined with VAs and controls

Variable	PRS		P	PCS		P	PLS		P
segment	Controls	NIDCM		Controls	NIDCM		Controls	NIDCM	
Basal									
anterior	47.75 ± 6.09	5.79 ± 3.40	< 0.001	-16.26 ± 2.35	-5.73 ± 2.55	< 0.001	-17.34(-18.91, -16.42)	-7.40(-8.36, -6.28)	< 0.001
Anterior septal	56.98 ± 6.86	9.05 ± 4.63	< 0.001	-19.78(-22.06, -17.83)	-6.14(-7.23, -4.99)	< 0.001	-17.28(-18.67, -14.53)	-6.37(-7.16, -5.02)	< 0.001
interior septal	50.34(46.68,55.13)	8.27(7.46,11.32)	< 0.001	-16.38 ± 4.44	-7.07 ± 3.51	< 0.001	-9.83(-14.37, -7.61)	-5.22(-6.46, -4.19)	< 0.001
interior	43.77 ± 4.94	10.84 ± 3.35	< 0.001	-9.80 ± 4.99	-5.75 ± 2.93	< 0.001	-19.10 ± 4.33	-5.90 ± 2.11	< 0.001
inferior lateral	50.14(46.22,58.36)	5.28(4.13,8.23)	< 0.001	-6.24(-9.99, -5.26)	-5.15(-6.17, -4.13)	0.002	-16.11(-18.78, -14.33)	-6.97(-8.11, -5.29)	< 0.001
anterior lateral	57.25(54.76,63.17)	5.33(3.61,8.31)	< 0.001	-10.22(-15.45, -7.91)	-4.34(-6.09, -4.14)	< 0.001	-15.53(-17.46, -14.39)	-7.91(-8.81, -4.53)	< 0.001
Middle									
anterior	47.32(41.89,52.18)	6.12(4.37,7.19)	< 0.001	-18.75(-20.17, -15.56)	-6.61(-8.03, -5.41)	< 0.001	-4.55(-8.76, -3.36)	-2.12(-3.21, -1.05)	< 0.001
anterior septal	42.47(39.36,46.73)	5.15(3.99,9.37)	< 0.001	-23.57(-26.27, -21.16)	-6.48(-9.08, -4.98)	< 0.001	-6.31(-8.29, -4.17)	-5.22(-6.33, -3.09)	0.025
inferoseptal	38.77 ± 5.52	9.19 ± 3.27	< 0.001	-19.43 ± 2.13	-6.80 ± 1.94	< 0.001	-9.05 ± 4.52	-3.26 ± 1.76	< 0.001
inferior	42.79 ± 4.89	7.39 ± 2.88	< 0.001	-15.92(-17.25, -13.78)	-6.76(-8.10, -5.72)	< 0.001	-12.68(-16.53, -8.64)	-4.85(-6.33, -3.27)	< 0.001
inferior lateral	51.22(47.18,56.77)	7.08(5.01,8.83)	< 0.001	-15.27(-18.88, -10.90)	-5.79(-7.15, -4.66)	< 0.001	-16.55(-18.13, -13.80)	-5.54(-6.62, -3.69)	< 0.001
anterior lateral	49.69 ± 6.45	13.76 ± 3.38	< 0.001	-12.34(-14.23, -8.29)	-6.14(-7.34, -5.14)	< 0.001	-6.53(-8.02, -5.03)	-6.14(-7.40, -4.92)	0.362
Apical									
anterior	49.77 ± 10.12	14.33 ± 4.61	< 0.001	-17.24(-19.45, -14.71)	-5.02(-6.08, -4.09)	< 0.001	-3.07(-6.33, -1.51)	-3.22(-4.51, -1.14)	0.334
PRS, segmental peak radial strain; PCS, segmental peak circumferential strain; PLS, segmental peak longitudinal strain									

Variable segment	PRS		P	PCS		P	PLS		P
	Controls	NIDCM		Controls	NIDCM		Controls	NIDCM	
septal	52.27 ± 6.59	12.68 ± 4.62	< 0.001	-18.09(-22.35, -15.64)	-6.56(-7.30, -5.78)	< 0.001	-4.33(-6.57, -3.43)	-3.95(-4.67, -1.16)	0.096
inferior	10.29 ± 3.63	9.37 ± 4.85	0.153	-20.11(-24.81, -18.22)	-8.39(-9.59, -6.69)	< 0.001	-5.41(-7.39, -3.35)	-2.04(-4.21, -0.94)	< 0.001
lateral	14.99 ± 5.85	13.42 ± 4.89	0.524	-25.84(-27.14, -22.34)	-8.24(-9.18, -7.28)	< 0.001	-6.69 ± 2.49	-3.30 ± 2.59	< 0.001
PRS, segmental peak radial strain; PCS, segmental peak circumferential strain; PLS, segmental peak longitudinal strain									

Table 4
Segmental values of strain rate in patients with NIDCM combined VAs and controls

Variable	PRSR		P	PCSR		P	PLSR		P
segment	Controls	NIDCM		Controls	NIDCM		Controls	NIDCM	
Basal									
anterior	2.47(2.12,3.12)	1.16(0.82,1.45)	< 0.001	-1.90(-2.36, -1.25)	-0.64(-1.10, -0.30)	< 0.001	-1.34(-1.69, -0.93)	-0.97(-1.17, -0.59)	0.003
Anterior septal	3.39 ± 0.41	1.26 ± 0.92	< 0.001	-1.75 ± 0.59	-0.68 ± 0.54	< 0.001	-1.09 ± 0.33	-0.76 ± 0.49	0.006
interior septal	2.07(1.47,2.41)	1.26(0.86,1.75)	< 0.001	-1.23(-1.71, -0.90)	-0.55(-0.84, -0.37)	< 0.001	-1.24 ± 0.58	-0.86 ± 0.45	0.008
interior	2.15 ± 0.62	1.51 ± 0.82	< 0.001	-1.19 ± 0.68	-0.66 ± 0.51	< 0.001	-1.10 ± 0.53	-0.74 ± 0.57	0.017
inferior lateral	3.36 ± 1.06	1.67 ± 0.71	< 0.001	-1.66(-1.84, -1.25)	-0.56(-0.96, -0.36)	< 0.001	-1.17 ± 0.34	-0.77 ± 0.54	0.002
anterior lateral	3.91 ± 1.14	1.81 ± 1.01	< 0.001	-1.65 ± 0.42	-0.80 ± 0.50	< 0.001	-1.20 ± 0.49	-0.80 ± 0.50	0.003
Middle									
anterior	3.09 ± 1.04	1.98 ± 1.14	0.004	-1.69 ± 0.25	-0.87 ± 0.63	< 0.001	-1.08(-1.33, -0.81)	-0.88(-1.17, -0.51)	0.034
anterior septal	2.15(1.79,3.04)	1.16(0.64,1.60)	< 0.001	-1.36 ± 0.55	-0.63 ± 0.71	< 0.001	-1.06(-1.29, -0.90)	-0.64(-1.02, -0.28)	< 0.001
inferoseptal	1.75(1.36,2.07)	0.76(0.51,1.13)	< 0.001	-1.50 ± 0.34	-0.79 ± 0.53	< 0.001	-1.15 ± 0.34	-0.72 ± 0.39	< 0.001
inferior	1.82 ± 0.76	0.91 ± 0.63	< 0.001	-1.37 ± 0.42	-0.85 ± 0.48	< 0.001	-1.16 ± 0.36	-0.77 ± 0.50	0.002
inferior lateral	2.56(1.98,3.28)	0.99(0.57,1.20)	< 0.001	-1.82 ± 0.43	-0.88 ± 0.67	< 0.001	-1.46 ± 0.57	-0.92 ± 0.35	< 0.001
anterior lateral	2.91 ± 0.77	1.30 ± 0.80	< 0.001	-1.62 ± 0.43	-0.79 ± 0.58	< 0.001	-1.06(-1.25, -0.66)	-0.58(-0.95, -0.34)	0.004
Apical									
anterior	2.29 ± 0.61	1.08 ± 0.49	< 0.001	-1.32(-1.78, -1.17)	-0.92(-1.25, -0.46)	< 0.001	-0.96 ± 0.45	-0.50 ± 0.52	0.001
septal	2.14 ± 0.34	1.08 ± 0.47	0.001	-1.34 ± 0.30	-0.78 ± 0.37	< 0.001	-1.14 ± 0.38	-1.05 ± 0.46	0.003

PRSR, segmental peak systolic radial strain rate; PRCR, segmental peak systolic circumferential strain rate; PLSR, segmental peak systolic longitudinal strain rate

Variable segment	PRSR		P	PCSR		P	PLSR		P
	Controls	NIDCM		Controls	NIDCM		Controls	NIDCM	
inferior	3.89 ± 1.05	1.11 ± 0.65	< 0.001	-1.51(-1.77, -1.39)	-0.76(-1.09, -0.46)	< 0.001	-1.28 ± 0.34	-0.78 ± 0.42	< 0.001
lateral	3.23(2.62,4.26)	1.20(0.77,1.68)	< 0.001	-1.55(-1.83, -1.23)	-0.86(-1.13, -0.58)	< 0.001	-1.24 ± 0.39	-0.76 ± 0.46	< 0.001
PRSR, segmental peak systolic radial strain rate; PCSR, segmental peak systolic circumferential strain rate; PLSR, segmental peak systolic longitudinal strain rate									

Correlation Between The Lv Global Strain Values And Lvef

GPCS negatively correlated with LVEF ($r=-0.946$, $P < 0.001$), GPLS negatively correlated with LVEF ($r=-0.860$, $P < 0.001$), and GPRS positively correlated with LVEF ($r = 0.920$, $P < 0.001$), as shown in Fig. 2A-C. And, GPCSR negatively correlated with LVEF ($r=-0.840$, $P < 0.001$), GPLSR negatively correlated with LVEF ($r=-0.767$, $P < 0.001$), and GPRSR positively correlated with LVEF ($r = 0.742$, $P < 0.001$), as shown in Fig. 2D-F.

Correlation Between With Pair-wise Comparison Lv Global Strain Values

With pair-wise comparison, we identified both GPCS and GPLS were negative correlated with GPRS, while the GPCS and GPLS were positively correlated with each other (Fig. 3A–C (GPCS vs. GPRS: $r=-0.896$, $P < 0.001$; GPRS vs. GPLS, $r=-0.906$, $P < 0.001$; GPCS vs. GPLS, $r = 0.834$, $P < 0.001$). Additionally, we also proved a negative correlation between the GPCSR and GPRSR as well as between the GPRSR and GPLSR, while the GPCSR and GPLSR were positively correlated with each other (Fig. 3D–F (GPCSR vs. GPRSR: $r=-0.757$, $P < 0.001$; GPRSR vs. GPLSR, $r=-0.804$, $P < 0.001$; GPCSR vs. GPLSR, $r = 0.818$, $P < 0.001$).

Intra-observer And Inter-observer Variability

Intra-observer and inter-observer reproducibility analysis for LV global strains parameters was tested and presented in Tables 5.

Tables 5 Intra- and inter-observer reproducibility for left ventricle global strain

Parameters	Intra-observer agreement		Inter-observer agreement	
	ICC [95%CI]	Mean difference ± SD	ICC [95%CI]	Mean difference ± SD
GPRS (%)	0.93 (0.80 – 0.97)	13.04 ± 10.28	0.90 (0.89 – 0.96)	1.43 ± 1.32
GPCS (%)	0.96(0.89 – 0.98)	4.67 ± 5.03	0.96 (0.90 – 0.98)	2.09 ± 1.54
GPLS (%)	0.92 (0.78 – 0.97)	10.67 ± 8.36	0.93 (0.83 – 0.99)	3.98 ± 3.11
GPRSR(1/s)	0.89(0.75 – 0.95)	4.82 ± 5.02	0.89 (0.78 – 0.96)	1.49 ± 1.34
GPCSR(1/s)	0.95(0.91 – 0.99)	6.40 ± 4.79	0.92 (0.79 – 0.97)	0.78 ± 0.53
GPLSR(1/s)	0.93(0.80 – 0.97)	8.33 ± 11.23	0.91(0.85 – 0.96)	3.86 ± 3.02
GPRS, global peak radial strain; GPRSR, global peak systolic radial strain rate; GPCS, global peak circumferential strain; GPRSR, global peak systolic circumferential strain rate; GPLS, global peak longitudinal strain; GPLSR, global peak systolic longitudinal strain rate				

Discussion

To the best of our knowledge, the present study is the first to assess the feasibility and performance in patients with NIDCM combined with VAs using CMR-FT methods. Firstly, we found that LV deformation analysis can differentiate patients NIDCM with VAs from controls using CMR-FT. Secondly, we proved that the LV global strain values had a linear correlation with LVEF. Moreover, we performed pair-wise comparison among the LV global strain values, which showed linear correlations among one another. These findings which to detect early deregulated LV function in patients with NIDCM with VAs have great implication on clinical decision, which might help improve clinical outcomes.

CMR-FT has been proposed as an alternative method to quantify the myocardial strain calculated by post processing the conventional cine magnetic resonance imaging [16, 22]. Yu et al [23] performed that LV myocardial strain in patients with dilated cardiomyopathy can be sensitively detected by CMR-FT. Similar to the study by Yu et al., we research showed that GPRS, GPCS, and GPLS were significantly reduced in patients with NIDCM combined with VAs, suggesting global LV myocardial deformation impairment in all directions. Additionally, in this study, our research also evaluated the LV strains rate of NIDCM patients with VAs using CMR-FT. Here, we revealed that NIDCM patients with VAs was associated with a significant impairment of myocardial deformation rate in all directions, indicating that LV function relies on coordinated wall motion from all directions.

Consistent with previous research by Yu, et al., in this study, we observed that the degree of damage was not same in each direction. However, surprisingly, in contrast to other work [23], our research found that GPCS, rather than GPRS changed more than GPRS and GPLS, indicating that patients with NIDCM combined with VAs had more serious damage in the circumferential direction of the LV. Some differences in patients' characteristics could explain this discordance. For example, our research objects for patients with NIDCM combined with VAs while Yu's subjects were only just DCM. Because in this study, we showed that late gadolinium enhancement (LGE) was present in 29 (85%) of largely patients with NIDCM combined with VAs. In addition, previous studies have shown that LGE is the substrate for the occurrence of VAs [24], and VAs mainly occur in the areas of myocardial fibrosis of the dilated myocardium of NIDCM. Furthermore, several other studies proved that classical NIDCM showed the LGE positivity in nonischemic patterns with involvement of areas subjected to increased tension, such as the interventricular septal mid-wall at the site of insertion of ventricular fibers [25, 26]; it is mostly influenced by circumferentially oriented muscle fibers in the mid-wall. Since NIDCM shows typical mid-wall fibrosis on CMR, it more affects the myocardial circumferential strain, which leads to a decrease in GPCS in patients with NIDCM combined with VAs. All of these changes can lower the middle-wall or epicardial oxygen demand and increase the middle-wall and epicardial blood flow, finally leading to reduced peak strains (GPCS, GPRS, and GPLS) in patients with NIDCM combined with VAs.

Additionally, for the segmental myocardial strains, our research demonstrated that the PCS, PRS, PLS, PCSR, PRSR, and PLSR were significantly decreased in most LV myocardial segments, but the intensities of different strains were widely different from one another. This is concomitant with the truth that NIDCM is characterized as diffuse progression over all the whole heart; however, the degree of impairment was heterogeneous.

The LVEF is used as an important marker with which to assess LV function. Regarding the correlation between the LV global strain values and LVEF for patients with NIDCM, only a few studies have been published [23, 27]. They found that the LV myocardial strains were significantly associated with the LVEF. Similar to previous studies [23, 27], in this study, we proved that the LV myocardial strains and myocardial strains rate were significantly associated with the LVEF. The reason may be as follows. Myocardial strain measures the degree of deformation of a myocardial segment from its initial length (usually in end-diastole) to its maximum length (usually in end-systole) and is expressed as a percentage. Thus, the strain determines the fractional change in the one-dimensional length from end-diastole to end-systole [28], and the LVEF reflects the fractional change in the three-dimensional volume; therefore, these two measures are in parallel, which may lead to the significant correlation between the myocardial strain and the LVEF. Moreover, in this study, we showed that GPCS was better negatively correlated with LVEF ($r=-0.946$, $P < 0.001$), and proved that the higher reproducibility intraobserver and interobserver ICC were respectively 0.96 and 0.96 for GPCS measurements, indicating GPCS was a feasible feature tracking parameter in detecting patients with NIDCM combined with VAs. Because the GPCS was not affected by poor tracking of the subannular region, unlike GPLS. For this reason, it was considered the most robust parameter in CMR-FT studies of myocardial strain.

Furthermore, regarding the correlations among the LV global strain values for patients with NIDCM, only a few studies have been published [23, 29]. Maciver. et al. investigated that the GPCS had a linear correlation with the GPLS by three-dimensional speckle tracking echocardiography [29]. And, Yu, et al showed linear correlations among GPRS, GPCS, and GPLS one another [23]. In this present research, we carried out pair-wise contrast among the GPRS, GPCS, and GPLS, which demonstrated linear correlations among

one another. Moreover, we showed pair-wise comparison among the GPRSR, GPCSR, and GPLSR, which proved linear correlations among one another (Fig. 3). These consequences suggested that the generation of LV global myocardial strain and strain rate were based on integrated rather than isolated.

Limitations

Firstly, this was a single-center observational study with a limited number of patients with NIDCM combined VAs. Records were retrospectively collected and diagnosed for NIDCM combined with VAs. Secondly, lots of different factors may influence the quantification of LV strain, including image acquisition, algorithms and even CVI software versions [30]. The strains values supplied by our study are algorithms and software specific, they can't be simply used under other circumstances.

Conclusions

In conclusion, LV global strains assessed by CMR-FT imaging could identify patients with NIDCM combined VAs and healthy volunteers. And, GPCS was better negatively correlated with LVEF and higher reproducibility of intra-class correlation coefficient (ICC), suggesting it was the feasible feature tracking parameter in detecting patients with NIDCM combined with VAs. These findings have important implications for the design of future studies evaluating the role of VAs risk stratification in patients with NIDCM combined VAs.

Declarations

Conflict of interest

The authors declare that they have no conflicts of interest.

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Figures

Figure 1

Representative example of the derivation of strain using cvi42 software in a 44-year-old male patient with NIDCM combined VAs. The result of LV tissue-tracking of cine SSFP images in the short axi, 2-chamber, and 4-chamber view. Picture A1–3 Myocardial strain tissue-tracking are illustrated on short-axis plane, in 4-chamber, and 2-chamber view. Picture B1–3: Myocardial pseudo-color map shows the strain values in the axi, 4- chamber, and 2- chamber view. Picture C1–3: Strain of each segment on the bull's eye diagram of AHA for the peak radial strain (%), peak circumferential strain (%), and peak longitudinal strain (%), Picture D1–3: AHA segmentation

strain curve values for the radial strain (%), circumferential strain (%), and peak longitudinal strain (%). Red represents positive values, while blue represents negative; deeper colors indicate higher values

Figure 2

Pearson analysis suggested that GPCS negatively correlated with LVEF (A), GPLS negatively correlated with LVEF (B), and GPRS positively correlated with LVEF (C); And Pearson analysis also showed that GPCSR negatively correlated with LVEF (D), GPLSR negatively correlated with LVEF (E), and GPRSR positively correlated with LVEF (F)

Figure 3

Pearson analysis suggested that GPCS negatively correlated with GPRS (A), GPRS negatively correlated with GPLS (B), and GPCS positively correlated with GPLS (C); Pearson analysis also showed that GPCSR negatively correlated with GPRSR (D), GPRSR negatively correlated with GPLSR (E), and GPCSR positively correlated with GPLSR (F)