



Correlation between left ventricular myocardial strain and left ventricular geometry in healthy adults: a cardiovascular magnetic resonance-feature tracking study

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Abstract

This study was aimed to investigate the correlation between left ventricular (LV) myocardial strain and LV geometry in healthy adults using cardiovascular magnetic resonance-feature tracking (CMR-FT). 124 gender-matched healthy adults who underwent healthy checkup using CMR cine imaging were retrospectively analyzed. Peak global radial, circumferential, longitudinal strain (GRS, GCS and GLS) for left ventricle were measured. LV geometry was assessed by the ratio of LV mass (LVM) and end-diastolic volume (EDV). GRS, GCS and GLS were $34.18 \pm 6.71\%$, $-22.17 \pm 2.28\%$, $-14.76 \pm 2.39\%$ for men, and $33.40 \pm 6.95\%$, $-22.49 \pm 2.27\%$, $-15.72 \pm 2.36\%$ for women. Multiple linear regression showed that LVM/EDV was associated with decreased GLS ($\beta = -0.297$, $p = 0.005$), but was not significantly associated with GRS and GCS (both $p > 0.05$). There was an increase in the magnitude of GRS, GCS and GLS with advancing age ($\beta = 0.254$, $\beta = 0.466$ and $\beta = 0.313$, all $p < 0.05$). Greater BMI was associated with decreased GRS, GCS and GLS ($\beta = -0.232$, $\beta = -0.249$ and $\beta = -0.279$, all $p < 0.05$). In conclusion, compared with GRS and GCS, GLS is more sensitive to assess LV concentric remodeling in healthy adults. GRS, GCS and GLS are all independently positively associated with age and negatively associated with BMI. Sex-based LV strain reference values for healthy Chinese adults are established.

Keywords Cardiovascular magnetic resonance-feature tracking · Left ventricular geometry · Myocardial strain

Introduction

Compared with other indirect left ventricular (LV) functional parameters, cardiovascular magnetic resonance-feature tracking (CMR-FT) is a promising technique for quantitative assessment of regional LV function and could early detect subclinical myocardial abnormalities [1, 2]. In

practice, LV myocardial strain is readily available without additional time-consuming scans or sequences using CMR-FT, highlighting its potential wide applicability. Compared with speckle-tracking echocardiography, CMR-FT is of much more accuracy and reproducibility due to higher tissue resolution and less dependence on operator's experience [3–5].

Studies have shown that LV concentric remodeling can significantly increase the risk of cardiovascular disease [6, 7]. Although there were some studies confirmed that LV geometry was closely related to myocardial strain in patients with hypertension or hypertrophic cardiomyopathy [8, 9], to the best of our knowledge, no investigation reported the correlation between LV myocardial strain and LV geometry in healthy adults. Previous studies demonstrated that both age and obesity could lead to LV concentric remodeling or hypertrophy in healthy adults [10, 11], which was associated with impaired coronary flow reserve and myocardial ischemia [12]. Therefore, we hypothesize that age or obesity related LV concentric remodeling may affect myocardial

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strain parameters. In addition, there is still considerable controversy on the correlation between age, body mass index (BMI) and LV myocardial strain in healthy population. The main purpose of this study was to investigate the correlation between LV myocardial strain and LV geometry using CMR-FT in healthy adults. Furthermore, the correlation between LV strain and other risk factors (age, BMI, etc.) was also investigated.

Materials and methods

Study population

Zhouxin medical imaging diagnostic center is a high-end medical examination institution mainly service for rich population, which was guided by Prof. Gerald M. Pohost and Kuncheng Li. As far as we know, this is the unique institution in the world that uses CMR for cardiovascular disease diagnosis. A total of 124 gender-matched healthy Chinese adults (50% men) who underwent CMR cine checkup from May 2012 to March 2018 at Zhouxin medical imaging diagnostic center were retrospectively analyzed.

The inclusion criteria are as follows: (1) subjects with normal blood pressure (systolic blood pressure < 130 mm Hg, diastolic blood pressure < 80 mm Hg, no use of antihypertensive medications); (2) subjects without overt coronary artery disease (no history of acute coronary syndrome, stable angina or coronary revascularization, or abnormal changes detected by electrocardiogram).

Exclusion criteria are as follows: (1) subjects with valvular heart disease (aortic or mitral regurgitation) or congenital heart disease detected by CMR checkup; (2) image with artifacts due to arrhythmia or poor breathing control which could not meet the measurement criteria for image analysis.

CMR scan

CMR scan were performed on 1.5 T magnetic resonance scanners (GE Signa HDxt, GE Healthcare, Waukesha, Wis) with 16-channel phased-array surface coil at 20 phases per cardiac cycle in held end expiration. Standard scout images were used to locate the orthogonal planes of the heart. Fast imaging employing steady-state acquisition (FIESTA) pulse sequences were used to acquire images in supine position. Electrocardiogram triggered contiguous parallel short axis planes (10–15 slices) were acquired throughout the left ventricle covering the base (atrioventricular valve plane) to the apex. Cine images of two long-axis views (2-chamber, 3-chamber and 4-chamber orientation) were also acquired. The scanning parameters are as follows: TR/TE = 4 ms/1.75 ms, flip angle = 60°, field of view = 310 mm × 310 mm, slice thickness = 8 mm, slice gap = 1 mm.

Left ventricular structure and function measurement

Image analysis was performed using commercial software (cvi42® version 5.6.2, Circle Cardiovascular Imaging, Canada). All the basic information about subjects (including height, weight, etc.) was hidden during image analysis. Left ventricular structure and function were measured on the short-axis cine images. The frame with the smallest blood pool in the middle of left ventricle (LV) was defined as end-systole and the largest was defined as end-diastole. The most basal section surrounding by at least 50% of the ventricular myocardium was regarded as base. The endocardial borders of the left ventricle were traced by threshold-based segmentation method. Left ventricular epicardial borders were manually traced at the same time. Trabeculations and papillary muscles were excluded from the ventricular volume but included in the myocardium. The outflow tract up to the level of the aortic valve cusps was included in left ventricular volume. End-diastolic volume (EDV), end-systolic volume (ESV), stroke volume (SV), left ventricular mass (LVM), ejection fraction (EF), cardiac output (CO) were automatically obtained by software (Fig. 1).

Myocardial strain measurement

Image analysis was performed using commercial software (cvi42® version 5.6.2, Circle Cardiovascular Imaging, Canada). The borders of left ventricular endocardium and epicardium were traced separately at end-diastole in short- and long-axis sequences (2-chamber, 3-chamber and 4-chamber views) by an experienced observer (the first author, more than 5-year experience) blinded to all individual information (including height, weight, etc.). The plane closest to the mitral valve and the myocardium is circular was defined as the most basal plane. The plane closest to the apex with blood pool was defined as the apical plane. Trabeculations and papillary muscles were excluded from the myocardium. Guided by signal in homogeneities or anatomical features, the software algorithm automatically traced image with frame-to-frame template matching throughout the entire cardiac cycle. Peak global radial strain (GRS), global circumferential strain (GCS) and global longitudinal strain (GLS) were automatically obtained, respectively (Fig. 2).

Reproducibility

20 cases were randomly selected from the study subjects to evaluate the inter- and intra-observer reproducibility of EDV, ESV, LVM, GRS, GCS and GLS. Reproducibility between observers was analyzed by two independent experienced researchers (Z.Z, QZ.M, both have more than 5-year

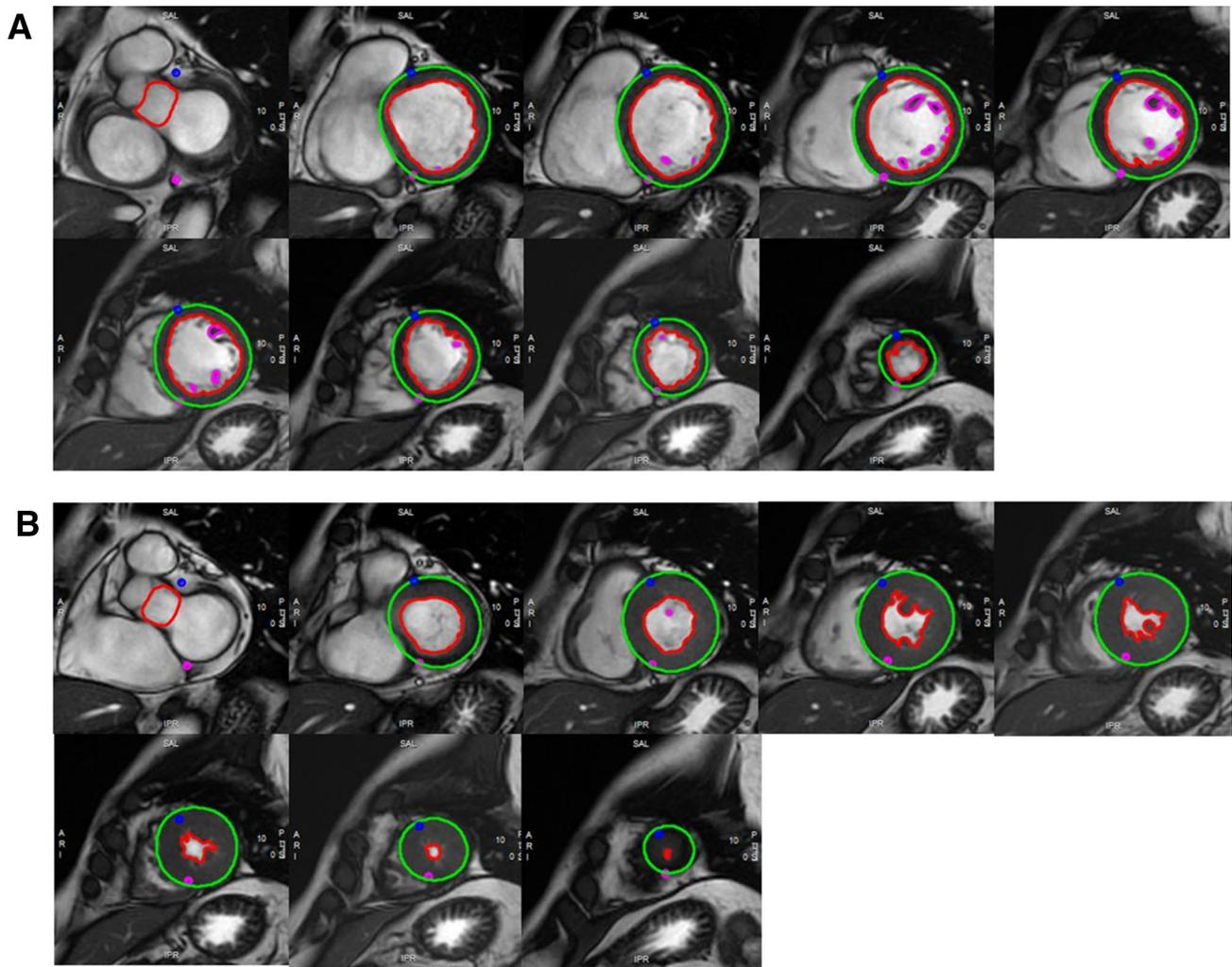


Fig. 1 Example of LV structure and function analysis on the short-axis cine images. The trace of LV endocardial and epicardial contours in the end-diastole (**a**). The trace of LV endocardial and epicardial

contours in the end-systole (**b**). Trabeculations and papillary muscles were excluded from the ventricular volume

experience), respectively. The intra-observer reproducibility was assessed by two times of measurement completed by the first author (Z.Z) and the time interval between each measurement was more than 4 weeks.

Statistics

All statistical analysis was performed with SPSS (version 19.0, IBM SPSS Inc, Chicago, IL, USA) and Graphpad prism (version 7.0, La Jolla, CA). All the data were tested for normal distribution and continuous variables with normal distribution were represented as mean \pm standard deviation. The 95% confidence intervals (CIs) for GRS, GCS and GLS were calculated. Gender differences in demographic characteristics, LV parameters (LV myocardial strains, LV volumes, LVM and LVEF etc.) were analyzed by Student's *t*-test. LV geometry was assessed by the ratio of LVM and LVEDV. Multivariable

linear regression was performed to investigate the relationship between LV strain values and LVM/EDV, age, BMI, as well as other possible risk factors (systolic blood pressure, heart rate). Furthermore, simple linear regression was used to investigate the relationship between age, BMI and LVM/EDV. Intra- and inter-observer reproducibility were assessed by intra-class correlation coefficient (ICC) and Bland–Altman analysis. Differences were regarded as statistically significant at $p < 0.05$.

Results

Demographic characteristics subjects

The demographic characteristics of the 124 healthy adults are showed in Table 1. Height, body weight, BMI and BSA were significant greater for men (all $p < 0.001$). There was

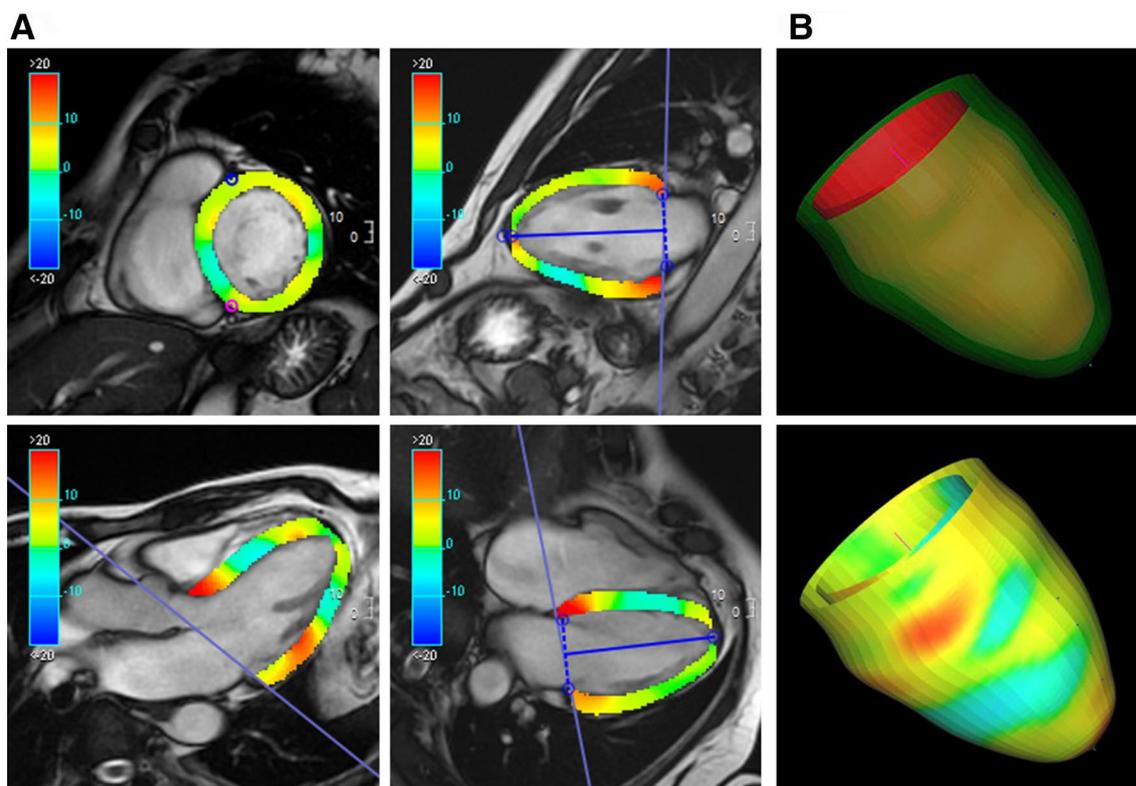


Fig. 2 Example of strain analysis with CMR-FT. Endocardial and epicardial contours are illustrated on short-axis plane and in 2-chamber, 3-chamber and 4-chamber view (a). 2D and 3D strain mapping was also demonstrated (b)

Table 1 Demographic characteristics of subjects

Variable	Total (n = 124)	Men (n = 62)	Women (n = 62)	p value
Age (years)	45.4 ± 11.22	45.48 ± 11.23	45.32 ± 11.30	0.937
Height (cm)	166.48 ± 8.08	172.23 ± 5.42	160.74 ± 5.94	< 0.001
Body weight (kg)	66.56 ± 13.02	74.64 ± 11.84	58.47 ± 8.29	< 0.001
BMI (kg/m ²)	23.88 ± 3.50	25.11 ± 3.38	22.66 ± 3.19	< 0.001
BSA (m ²)	1.75 ± 0.20	1.88 ± 0.17	1.61 ± 0.13	< 0.001
HR (beat/minute)	67.33 ± 9.32	68.55 ± 10.76	66.11 ± 7.52	0.147
SBP (mm Hg)	117.55 ± 8.70	118.84 ± 8.55	116.26 ± 8.73	< 0.099
DBP (mm Hg)	70.36 ± 5.91	70.44 ± 5.84	70.29 ± 6.02	0.892

Student's *t*-test used to test differences in parameters of demographic characteristics between men and women. Data are presented as means ± SD

BMI body mass index, *BSA* body surface area, *DBP* diastolic blood pressure, *HR* heart rate, *SBP* systolic blood pressure

Significant p values are given in bold

no significant gender difference in age, heart rate and blood pressure (all $p > 0.05$).

Left ventricular structural and functional parameters

The LV structural and functional parameters for all the subjects are showed in Table 2. EDV, ESV, SV, CO and

LVM for men were greater than women (all $p < 0.01$). There was no significant difference in EF between men and women ($p = 0.370$). After normalized by BSA, LVM for men was still greater than women ($p < 0.001$). There was no significant gender difference in normalized EDV, ESV and SV (all $p > 0.05$).

The LV myocardial strain parameters for men and women were showed in Table 3. GRS, GCS and

Table 2 Left ventricular parameters of subjects

Variable	Total (n=124)	Men (n=62)	Women (n=62)	p value
EDV (ml)	107.00 ± 17.94	115.08 ± 19.12	98.92 ± 12.26	< 0.001
ESV (ml)	31.52 ± 8.21	33.58 ± 8.97	29.45 ± 6.84	0.005
SV (ml)	75.48 ± 12.79	81.49 ± 12.61	69.46 ± 9.86	< 0.001
LVM (g)	111.87 ± 32.30	135.25 ± 26.01	88.50 ± 17.81	< 0.001
LVEF (%)	70.69 ± 5.07	71.10 ± 4.58	70.28 ± 5.52	0.370
CO (L/min)	5.06 ± 1.00	5.55 ± 1.04	4.56 ± 0.66	< 0.001
EDV/BSA (ml/m ²)	61.30 ± 8.25	61.18 ± 9.70	61.41 ± 6.55	0.877
ESV/BSA (ml/m ²)	18.12 ± 4.61	17.86 ± 4.78	18.38 ± 4.46	0.529
SV/BSA (ml/m ²)	43.19 ± 5.58	43.32 ± 6.21	43.06 ± 4.92	0.795
LVM/BSA (ml/m ²)	63.07 ± 12.66	71.45 ± 10.09	54.69 ± 8.87	< 0.001

Student’s *t*-test used to test differences in parameters of demographic characteristics between men and women. Data are presented as means ± standard deviation

BSA body surface area, CO cardiac output, EDV end-diastolic volume, ESV end-systolic volume, LVEF left ventricular ejection fraction, LVM left ventricular mass, SV stroke volume

Significant p values are given in bold

GLS for men were 34.18 ± 6.71%, - 22.17 ± 2.28%, - 14.76 ± 2.39% (95% confidence interval [CI] 21.03~47.33%), - (17.38 to 26.32)% and - (9.85 to 17.73)%, respectively). GRS, GCS and GLS for women were 33.40 ± 6.95%, - 22.49 ± 2.27%, - 15.72 ± 2.36% (95%CI 19.78–47.02%, - (18.04 to 26.94)% and - (11.09 to 20.35)%, respectively). GLS was significantly greater for women (p < 0.001) and there were no significant gender differences in GRS and GCS (both p > 0.05).

Correlation between variables and left ventricular strain

The correlation between left ventricular strain and possible related factors were showed in Table 4. Multivariable linear regression showed that LVM/EDV was associated with decreased GLS (β = -0.297, p = 0.005), but was not significantly associated with GRS and GCS both p > 0.05). Age was associated with increasing GRS, GCS and GLS (β = 0.254, β = 0.466 and β = 0.313, all p < 0.05). BMI was independently associated with decreased GRS, GCS and GLS (β = -0.232, β = -0.249 and β = -0.279, all

p < 0.05). Heart rate was independently positively associated with GCS (β = 0.212, p = 0.012). There was no significant correlation between systolic blood pressure and GRS, GCS, GLS (β = -0.007, β = -0.075 and β = 0.134, all p > 0.05).

Correlation between age, BMI and LVM/EDV

The correlation between age, BMI and LVM/EDV was showed in Fig. 3. Simple linear regression showed that LVM/EDV was positively associated with both age and BMI (r = 0.36 and r = 0.57, both p < 0.001).

Variability of left ventricular myocardial strain measurements

The intra- and inter-observer variability results were given in Table 5. All the LV parameters (volumes, mass and strain) had an intra- and inter- observer ICC > 0.85. In Bland–Altman analyses, GCS had the best intra- and inter-observer agreement among all the myocardial strain parameters.

Table 3 Left ventricular myocardial strain parameters for men and women

Variable	Men		Women		P value
	Mean ± SD	95% CI	Mean ± SD	95% CI	
GRS (%)	34.18 ± 6.71	21.03 to 47.33	33.40 ± 6.95	19.78 to 47.02	0.528
GCS (%)	- 21.85 ± 2.28	- (17.38 to 26.32)	- 22.49 ± 2.27	- (18.04 to 26.94)	0.121
GLS (%)	- 13.79 ± 2.01	- (9.85 to 17.73)	- 15.72 ± 2.36s	- (11.09 to 20.35)	< 0.001

CI confidence interval, GCS global circumferential strain, GLS global longitudinal strain, GRS global radial strain, SD standard deviation

Table 4 Multivariable linear regression of absolute myocardial strain parameters

Variable	Absolute GRS (%)		Absolute GCS (%)		Absolute GLS (%)	
	β	p value	β	p value	β	p value
LVM/EDV (g/ml)	0.014	0.901	-0.085	0.414	-0.297	0.005
Age (years)	0.254	0.010	0.466	<0.001	0.313	0.001
BMI (kg/m ²)	-0.232	0.035	-0.249	0.014	-0.279	0.006
HR (beat/min)	0.079	0.384	0.212	0.012	0.073	0.383
SBP (mm Hg)	-0.007	0.942	-0.075	0.381	0.134	0.124

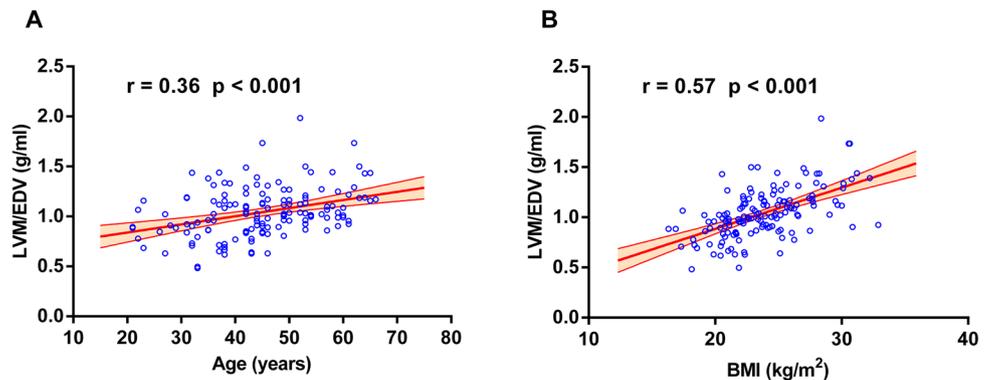
β stand for standardized coefficient of multivariable linear regression

R^2 for absolute GRS, GCS and GLS in multivariable linear regression analysis were 0.082, 0.230 and 0.216

BMI body mass index, EDV end-diastolic volume, GCS global circumferential strain, GLS global longitudinal strain, GRS global radial strain, HR heart rate, LVM left ventricular mass, SBP systolic blood pressure

Significant p values are given in bold

Fig. 3 Linear correlation shows both age (a) and BMI (b) are positively associated with LVM/EDV (both $p < 0.001$), indicating that greater age and BMI are associated with LV concentric remodeling. The shaded area represents the 95% confidence band of the regression line

**Table 5** Intra-observer and inter-observer variability

Variability	Variable	Mean bias \pm SD	Limits of agreement	ICC (95% CI)
Intra-observer				
	EDV (ml)	-2.56 \pm 3.39	-9.20 to 4.07	0.980 (0.950, 0.992)
	ESV (ml)	-1.01 \pm 1.90	-4.73 to 2.72	0.964 (0.913, 0.986)
	LVM (g)	2.72 \pm 3.64	-4.42 to 9.86	0.991 (0.977, 0.996)
	GRS (%)	0.05 \pm 2.61	-5.06 to 5.17	0.901 (0.754, 0.960)
	GCS (%)	-0.17 \pm 0.42	-0.98 to 0.65	0.975 (0.938, 0.990)
	GLS (%)	-0.02 \pm 0.96	-1.90 to 1.85	0.876 (0.693, 0.951)
Inter-observer				
	EDV (ml)	-0.34 \pm 4.75	-9.64 to 8.97	0.962 (0.907, 0.985)
	ESV (ml)	-0.57 \pm 2.12	-4.72 to 3.59	0.951 (0.881, 0.980)
	LVM (g)	3.25 \pm 6.87	-10.21 to 16.71	0.968 (0.921, 0.987)
	GRS (%)	0.13 \pm 2.65	-5.08 to 5.33	0.897 (0.745, 0.959)
	GCS (%)	-0.13 \pm 0.46	-1.04 to 0.78	0.979 (0.947, 0.992)
	GLS (%)	0.30 \pm 0.94	-1.53 to 2.14	0.880 (0.701, 0.952)

CI confidence interval, EDV end-diastolic volume, ESV end-systolic volume, GCS global circumferential strain, GLS global longitudinal strain, GRS global radial strain, ICC intraclass correlation coefficient, LVM left ventricular mass, SD standard deviation

Discussion

Through this CMR-FT study of healthy adults without hypertension and overt cardiovascular diseases, our

study highlighted that LV concentric remodeling was independently associated with decreased GLS and was not correlated with GRS and GCS, evidenced by significant negative correlation between LVM/EDV and GLS.

In addition, we also found that GRS, GCS and GLS were independently positively associated with age and were negatively associated with BMI. Moreover, our study established sex-based normal reference values of LV myocardial strain for healthy Chinese adults.

Correlation between myocardial strain and left ventricular geometry

Our study demonstrated that LV concentric remodeling was independently associated with decreasing GLS, but not GRS and GCS, to our knowledge, this was the first time reported in the healthy adults free of hypertension. Different from our findings, previous echocardiographic study on hypertensive patients indicated that concentric hypertrophy was not only associated longitudinal strain but also associated with radial and circumferential strain [8]. In addition, a previous CMR-FT study on patients with early stage hypertrophic cardiomyopathy also showed that hypertrophic cardiomyopathy could lead to a significant reduction in regional radial, circumferential and longitudinal strain [9]. Compared with the above two investigations, the subjects in our study were all healthy adults free of hypertension and overt cardiovascular disease so the degree of myocardial hypertrophy is relative mild, which may be the reason why our conclusion is different from the above studies.

Previous studies showed that left ventricular remodeling could cause myocardial ischemia, leading to myocardial cell necrosis [13, 14]. Longitudinal myocardial fibers are closest to the sub-endocardial layer, and the sub-endocardial myocardium is most sensitive to ischemia [15, 16]. In addition, studies also demonstrated that compared with GRS and GCS, GLS is more sensitive to early myocardial pathological changes [17, 18], which may account for the significant association between LV concentric remodeling and GLS.

Our study also indicated that both increasing age and BMI were associated with LV concentric remodeling (Fig. 3). However, the impact of age and BMI on GLS was opposite. The specific mechanism of the difference in the impact of age and BMI on GLS was still unclear and need further study in the future.

Correlation between myocardial strain and age and BMI

Our study demonstrated that GRS, GCS and GLS increased with age, which was consistent with the studies by Liu et al. [19, 20]. An echocardiographic study by Sun et al. showed no correlation between age and GLS [21]. A CMR-FT study on 60 healthy Chinese adults showed that with increasing

age, left ventricular GRS gradually increased, while GCS gradually decreased [22]. Another CMR-FT study on healthy Chinese adults showed that GCS gradually decreased and GRS gradually increased with age, and age was not significantly correlated with GLS [23], however, the MR scanners used were not the same magnetic field strengths, which may have a significant impact on results.

A study on 41 children showed that longitudinal strain was significantly smaller in overweight/obese children compared with control group, however, there was no significant difference in radial, circumferential strain [24]. In addition, an echocardiographic study based on 90 adolescents demonstrated that circumferential strain was larger in obese subjects but there was no significant difference in radial and longitudinal strain between obese and non-obese subjects. Our study confirmed that BMI was independently negatively associated with GRS, GCS and GLS, which was consistent with most previous studies [25–28].

Correlation between myocardial strain and other related factors

Our study showed that heart rate was positively associated with GCS and not correlated with GRS and GLS. Different from our study, an M-mode Doppler echocardiography study by Cheng et al. showed that higher resting heart rate was associated with less radial, circumferential and longitudinal strain in healthy adults [29].

A speckle tracking echocardiography showed that hypertension was only correlated with GLS, but not GRS and GCS [30]. However, Galderisi et al. indicated that hypertension was associated with decreasing GRS and GLS and not correlated with GCS [31]. Our study demonstrated that there was no correlation between systolic blood pressure and myocardial strain, which may be related to normal blood pressure of study subjects.

Ethnic differences in normal reference values for myocardial strain

Myocardial tagging is the most commonly used reference technique in the literature for strain comparison. However, to the best of our knowledge, no research has reported normal reference values for healthy Chinese adults based on tagging technique. Previous study reported that the agreement between strain measurements obtained using CMR-FT and myocardial tagging are comparable and CMR-FT could be considered as a potentially feasible and rapid alternative for tagging technique [32]. Moreira et al. showed that there was significant difference in myocardial strain among races [33]. A CMR study by Robin et al. reported the reference values of GRS, GCS and GLS were $39.8 \pm 8.3\%$, $-26.1 \pm 3.8\%$ and $-21.3 \pm 4.8\%$ for overall subjects [34]. Compared with the

study by Robin et al. the GRS, GCS and GLS obtained in our study were significantly smaller, which confirmed the significant differences in myocardial strain between races.

Reproducibility of left ventricular parameters

Previous studies showed that semi-automatic method had excellent reproducibility for LV structural and functional parameters [35], which was confirmed again in our study (all ICCs > 0.85). In addition, our study also demonstrated excellent intra- and inter-observer agreement for CMR-FT derived strain parameters (all ICCs > 0.85), which was similar to some recent studies [3, 4].

Study limitations

This study was cross-sectional study and longitudinal research was needed in the future. Living habit such as smoking and alcohol consumption were not considered in the present study. Our study only included Chinese population and therefore did not consider the influence of racial factors.

Conclusions

In conclusion, our study reveal that LV concentric remodeling is significantly associated with decreasing GLS for healthy adults, independent of age and BMI. Therefore, in clinical practice, compared with GRS and GCS, GLS is a more sensitive indicator for assessing LV concentric remodeling or hypertrophy. GRS, GCS and GLS are positively associated with age and negatively associated with BMI in healthy adults. Normal reference values of LV myocardial strain based on CMR-FT for healthy Chinese adults are provided.

Compliance with ethical standards

Conflict of interest The authors declare no conflicts of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

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