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Higher hemoglobin levels are associated with impaired left ventricular global strains in metabolic syndrome: a 3.0 T CMR feature tracking study

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Abstract

Background Metabolic syndrome (MetS) is a known contributor to increased cardiovascular risk and all-cause mortality. Recent literatures suggested that higher hemoglobin (Hb) levels were associated with Mets, left ventricular (LV) dysfunction and adverse events in general population. This study aimed to assess the associations between Hb levels and LV global strains in patients with MetS.

Methods A retrospective analysis included 254 patients with MetS and 78 sex-, age-, and Hb-matched controls. The MetS patients were stratified into five groups based on Hb levels: anemia, low-normal Hb, moderate-normal Hb, high-normal Hb, and high Hb. LV global radial, circumferential, and longitudinal strains (LVGRS, LVGCS, and LVGLS, respectively) were measured using the cardiac magnetic resonance feature tracking technique. Associations between Hb levels and LV global strains were evaluated using multiple linear regression, restricted cubic spline (RCS), and subgroup analyses.

Results After full adjustment, the LV global strains from three directions in the high Hb groups (LVGRS: $\beta = -4.943$, 95% CI − 7.673 to − 2.213; LVGCS: $\beta = -2.341$, 95% CI − 3.608 to − 1.074; LVGLS: $\beta = -2.797$, 95% CI − 4.049 to − 1.546, all $p < 0.05$) were significantly reduced than those in their respective moderate-normal Hb groups. Full adjusted RCS plots revealed inverted L-shaped associations between Hb levels and LV global strains, with significant reductions observed above 143 g/L (all p for nonlinearity < 0.05). Subgroup analyses indicated that the associations were more pronounced in MetS patients with obesity (LVGRS: $\beta = -0.005$ [95% CI − 0.087 to 0.097] versus −0.087 [95% CI − 0.145 to − 0.030]; LVGCS: $\beta = -0.006$ [95% CI − 0.045 to 0.034] versus −0.048 [95% CI − 0.075 to − 0.021]; LVGLS: $\beta = -0.011$ [95% CI − 0.053 to 0.032] versus −0.063 [95% CI − 0.089 to − 0.036] for non-obese and obese patients; all p for interaction < 0.05).

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Conclusions Higher Hb levels are significantly associated with more severe LV dysfunction in MetS patients, particularly in those with obesity. Targeted monitoring and management of higher Hb levels in MetS patients may help mitigate further deterioration of cardiac function.

Keywords Cardiac magnetic resonance, Hemoglobin levels, Left ventricular strain, Metabolic syndrome, Obesity

Introduction

Metabolic syndrome (MetS) is a constellation of cardiovascular risk factors, including abdominal obesity, elevated blood pressure, impaired fasting glucose, and dyslipidemia [1]. Globally, MetS affects approximately 25% of the population, with its prevalence rising in both developed and developing countries, imposing substantial economic burdens [2–4]. MetS has been linked to a 1.32-fold higher risk of major cardiovascular events, a 1.64-fold higher risk of cardiovascular mortality, and a 1.45-fold higher risk of all-cause mortality [5]. Previous studies have reported that higher hemoglobin (Hb) levels were associated with MetS, and serve as the independent risk factor for adverse metabolic outcomes and increased mortality in the general population [6, 7]. Moreover, Tapio et al. [8] found that higher Hb levels are associated with poorer left ventricular (LV) function in the general population. We speculate that higher Hb levels may linked to impaired LV function in MetS, leading to adverse outcomes. However, the impact of Hb levels on LV function in MetS patients remains unclear.

Previous studies exploring LV function in MetS patients have largely been based on speckle-tracking echocardiography [9–12]. Cardiac magnetic resonance (CMR) offers high spatial and temporal resolution and superior soft tissue contrast, making it a powerful non-invasive tool for comprehensive cardiac assessment, including morphology, function, flow, and tissue characterization [13]. While LV ejection fraction (LVEF) is the clinical standard for assessing LV function, it may fail to detect subtle dysfunction in conditions such as LV hypertrophy, small LV cavities, or regional myocardial abnormalities [14, 15]. Myocardial strain analysis using CMR feature tracking is a more sensitive technique, capable of quantifying myocardial fiber deformation and providing superior insights into LV function [15, 16]. This study aimed to investigate the association between Hb levels and LV global strains in patients with MetS using the CMR feature tracking technique.

Methods

Study population

This study was approved by the Biomedical Research Ethics Committee of our hospital (No. 2019 – 756), and informed consent was waived due to its retrospective design. We included MetS patients and matched controls who underwent CMR examinations between January 2011 and August 2024. MetS was defined according to the 2009 criteria of the International Diabetes Federation Task Force on Epidemiology and Prevention [1]. Diagnosis required at least three of the following five criteria: (a) elevated waist circumference (population- and country-specific thresholds), (b) elevated triglycerides (≥ 150 mg/dL [1.7 mmol/L] or specific treatment), (c) reduced high-density lipoprotein cholesterol (< 40 mg/dL [1.0 mmol/L] in men or < 50 mg/dL [1.3 mmol/L] in women or specific treatment), (d) elevated blood pressure (systolic ≥ 130 mmHg and/or diastolic ≥ 85 mmHg or antihypertensive treatment), and (e) elevated fasting glucose (≥ 100 mg/dL [5.6 mmol/L] or previously diagnosed type 2 diabetes mellitus [T2DM]). For patients without waist circumference data, body mass index (BMI) > 25 kg/m² was used as an alternative threshold [17, 18]. Exclusion criteria for MetS patients included (a) congenital heart diseases, (b) severe valvular heart disease, (c) primary or secondary myocardiopathy, (d) myocarditis, (e) myocardial infarction, (f) severe renal failure (estimated glomerular filtration rate [eGFR] < 30 mL/min), (g) incomplete clinical records, and (h) poor-quality CMR images (defined as LV global strains cannot be obtained with severe artifacts due to respiratory movement or arrhythmias). A detailed enrollment flowchart for MetS patients is presented in Fig. 1. Matched controls adhered to additional exclusion criteria outlined in the Additional File 1. MetS patients were stratified into five Hb level groups [19, 20]: (a) anemia group (< 120 g/L in women; <130 g/L in men), (b) low-normal Hb group (120–129 g/L in women; 130–139 g/L in men), (c) moderate-normal Hb group (130–139 g/L in women; 140–149 g/L in men), (d) high-normal Hb group (140–149 g/L in women; 150–159 g/L in men), and (e) high Hb group (≥ 150 g/L in women; ≥160 g/L in men). We collected baseline clinical and laboratory data, including sex, age, BMI, heart rate, and medication use among MetS patients. Our Hb measurements and LV assessments were conducted within one week of patient admission.

CMR examination protocol and image analysis

All CMR examinations were conducted using 3.0-T scanners (MAGNETOM Skyra and MAGNETOM Trio Tim; Siemens Medical Solutions, Erlangen, Germany) in the supine position during breath-hold intervals, employing standard electrocardiogram-triggering devices. A steady-state free precession sequence was utilized to obtain CMR cine images from the base to the apex, including short-axis views and LV two-, three-, and four-chamber

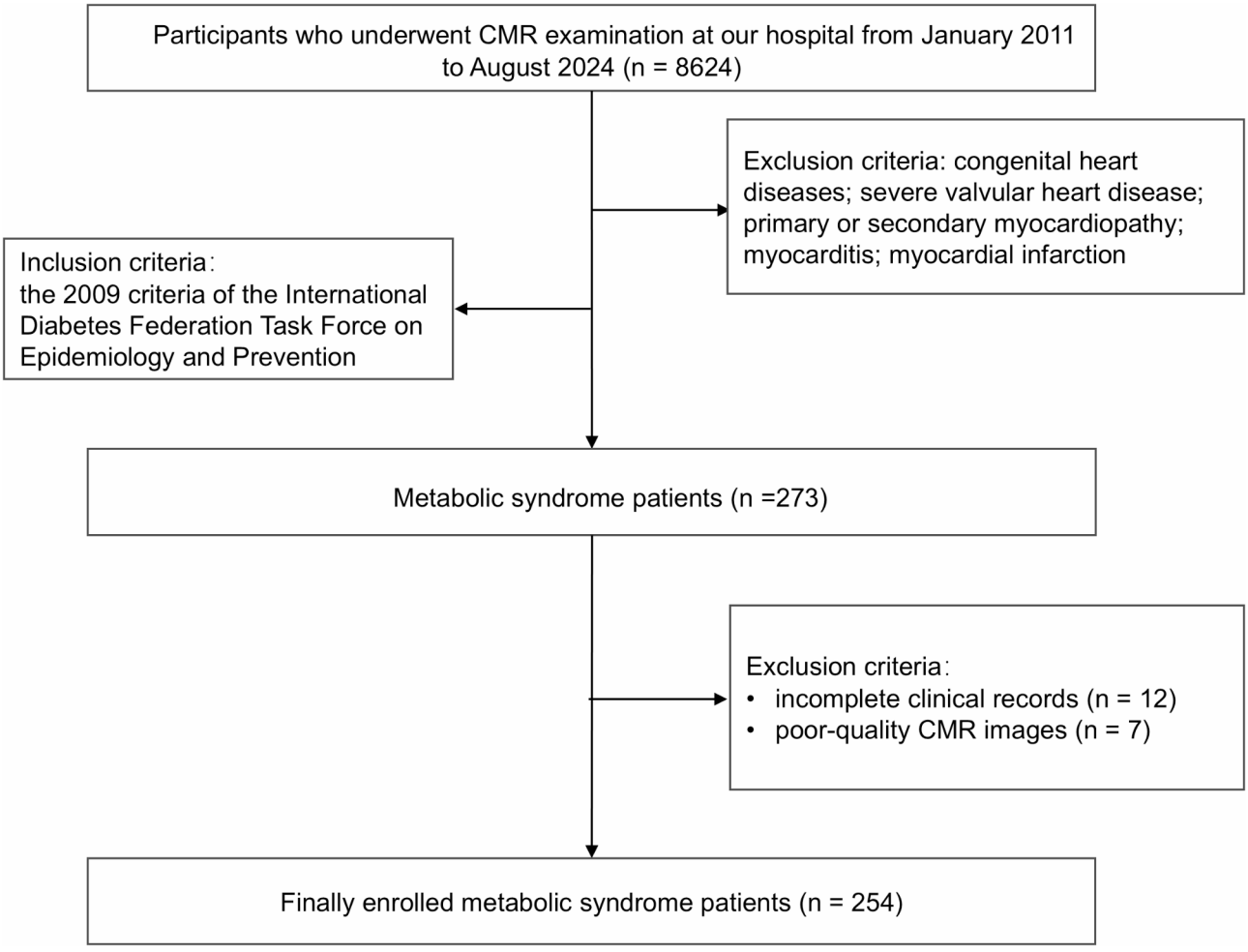

Fig. 1 Flowchart of the patient collection. CMR, cardiac magnetic resonance

long-axis views. Imaging parameters were as follows: repetition time = 3.4/2.8 ms, echo time = 1.22/1.20 ms, slice thickness = 8.0 mm, field of view = 234 × 280/250 × 300 mm^2, matrix size = 208 × 139/192 × 162 pixels, and flip angle = 39°/50°.

LV functional and global strains parameters were measured using commercial software (cvi42, v.6.0.2; Circle Cardiovascular Imaging, Inc., Calgary, Alberta, Canada), which automatically identifies and delineates the LV endocardium and epicardium at the end-systolic and end-diastolic phases on short-axis views. A radiologist with 3 year of experience (L.X.), blinded to clinical data, subsequently corrected the contours from base to apex. After these adjustments, LV functional parameters, including LV end-diastolic volume index (LVEDVI), LV end-systolic volume index (LVESVI), LV stroke volume index (LVSVI), LVEF and LV mass index (LVMI), were obtained. The papillary muscles and trabeculae were included in the LV cavity and excluded from the LVMI. LV global strain parameters, including LV global radial strain (LVGRS), LV global circumferential strain (LVGCS), and LV global longitudinal strain (LVGLS), were measured from short-axis and LV two-, three-, and four-chamber long-axis views by manually adjusting the automatically generated endocardial and epicardial contours at end-diastole. Due to heart contractility, LVGRS is positive, whereas LVGCS and LVGLS are negative [15]. To avoid confusion with negative directions, we report the absolute values for LVGCS and LVGLS in all analyses, except when comparing group differences.

Reproducibility

The LV epicardial and endocardial borders were re-delineated in 10 random controls and 30 MetS patients by the same radiologist (L.X.) 1 month after the initial delineation to assess intra-observer variability. Additionally, another radiologist (Y.S.Q.), with 7 year of experience and blinded to LX's results, reassessed the images to evaluate inter-observer variability. Both radiologists were blinded to clinical data.

Statistical analysis

The distribution of continuous data was tested using histograms, Q-Q plots, and the Shapiro–Wilk test. Continuous variables are presented as mean ± *SD* or medians with interquartile ranges (IQRs), whereas categorical variables are presented as frequencies (percentages). The independent *t* test, Mann–Whitney *U* test, one-way analysis of variance, Kruskal–Wallis test, chi-square test, and Fisher's exact test were applied as appropriate to compare group differences. Multiple linear regression models were used to evaluate the associations between Hb levels and LV global strains in MetS. The moderate-normal Hb group served as the reference group. Three regression models were constructed: Model 1 was adjusted for sex, age; Model 2 was adjusted for BMI, triglyceride, eGFR, smoking, heart rate, anti-diabetes drug based on Model 1; Model 3 was adjusted for LVEDVI and LVMI based on Model 2. The median Hb level of each group was used for the trend test. To investigate potential nonlinear relationships, restricted cubic spline (RCS) plots with three nodes, based on the Akaike information criterion, were employed. Subgroup analyses were conducted based on sex, age, obesity, eGFR, smoking, and anti-diabetes drug. Obesity was defined as BMI ≥ 28 kg/m^2 [21]. Intraclass correlation coefficients (ICCs) were calculated to assess intra-observer and inter-observer variability. Statistical analyses were performed using SPSS version 26 (IBM Corp., Armonk, New York), R software version 4.4.1 (http://www.r-project.org), and Prism software version 10.1.2 (324; GraphPad Software, Inc., San Diego, California). For details regarding the software packages and scripts used for the RCS plots and Forest plots, please see the Additional File 1. A two-tailed *p* value of < 0.05 was considered statistically significant.

Results

Baseline clinical data

A total of 254 MetS patients and 78 sex-, age-, and Hb-matched controls were included. Compared with control group, MetS patients had higher BMIs, elevated blood pressure, higher triglycerides, lower high-density lipoprotein and lower eGFR (all $p < 0.05$; refer to Additional File 1, Table S1). The number of MetS patients across the anemia to high Hb groups was 46, 44, 65, 51, and 48, respectively. Table 1 summarizes baseline clinical data across five different Hb levels in MetS patients. we observed significant differences in age, sex, BMI, diastolic blood pressures, and the prevalence of T2DM (all $p < 0.05$).

The impact of MetS on LV function and deformation

Figure 2 presents the measurements of LV strains in all three directions using the CMR feature tracking technique. Compared with the control group, MetS patients had larger LVEDVI, larger LVESVI, higher LVMI, and lower LVEF (all $p < 0.05$; refer to Additional File 1, Table S2). Additionally, statistical significance was also found in impaired strains parameters: LVGRS: 23.51 ± 8.40% versus 30.44 ± 6.83%; LVGCS: −14.96 ± 4.03% versus −18.04 ± 2.82%; LVGLS: −13.87 ± 4.12% versus −17.25 ± 2.04% (all $p < 0.05$; Additional File 1, Table S2).

Associations between Hb levels and LV global strains in MetS

Multiple comparisons among MetS patients

Among the five Hb groups in MetS patients (Table 2), statistical significance was found in LVESVI, LVSVI, LVMI, LVEF, LVGRS, LVGCS, and LVGLS (all $p < 0.05$). Post hoc correction revealed MetS patients in high Hb group had significantly impaired LVGLS than the other four groups (all $p < 0.05$; Table 2). Similar results were observed for LVGRS and LVGCS, except when compared to high-normal group (all $p < 0.05$; Table 2).

Multiple linear regression

The results of multiple linear regression assessing the associations between Hb levels and LV global strains in MetS patients are presented in Table 3. After adjusting for sex, age, BMI, triglyceride, eGFR, smoking, heart rate, anti-diabetes drug, LVEDVI, and LVMI, the LV global strains from three directions in the high Hb groups (LVGRS:β = −4.943, 95% CI − 7.673 to − 2.213; LVGCS:β = −2.341, 95% CI − 3.608 to − 1.074; LVGLS:β = −2.797, 95% CI − 4.049 to − 1.546, all $p < 0.05$) were significantly reduced than those in their respective moderate-normal Hb groups. Trend analysis revealed a linear decline in LVGCS and LVGLS as Hb levels increased, after adjusting for all covariates (p for trend = 0.022 and < 0.001, respectively). However, no significant linear trend was observed between Hb levels and LVGRS (p for trend = 0.090).

RCS plots based on multiple linear regression

The RCS plots, adjusted for all covariates (Fig. 3), indicated significant inverted L-shaped associations with an inflection point at 143 g/L for Hb levels and LV global strains in MetS patients. Specifically, LVGRS: p for overall = 0.014, p for nonlinearity = 0.037; LVGCS: p for overall = 0.003, p for nonlinearity = 0.046; LVGLS: p for overall < 0.001, p for nonlinearity = 0.019. As Hb levels increased, LV global strains plateaued until reaching the inflection point, after which a gradual decline was observed. Based on this inflection point, MetS patients were categorized into higher and lower Hb groups. Higher Hb levels were significantly associated with reduced LV global strains in MetS patients (all $p < 0.05$; Fig. 4).

Table 1 Baseline clinical data among 5 different hemoglobin levels in MetS patients

	Anemia group (< 120 g/L in female; < 130 g/L in male) (*n* = 46)	Low-normal Hb group (120–129 g/L in female; 130–139 g/L in male) (*n* = 44)	Moderate-normal Hb group (130–139 g/L in female; 140–149 g/L in male) (*n* = 65)	High-normal Hb group (140–149 g/L in female; 150–159 g/L in male) (*n* = 51)	High Hb group (≥ 150 g/L in female; ≥ 160 g/L in male) (*n* = 48)	*P* value
Demographics						
Male, n (%)	23 (50.00) *	26 (59.09) *	42 (64.62)	41 (80.39)	42 (87.50)	< 0.001
Age (years)	56 ± 15*	55 ± 11*	52 ± 12*	49 ± 13	44 ± 14	< 0.001
BMI (kg/m^2)	26.50 ± 4.37*	26.34 ± 3.19*	27.26 ± 2.66*	27.64 ± 2.96	29.17 ± 4.28	0.001
Heart rate (bpm)	85 ± 17	80 ± 16	83 ± 16	87 ± 25	90 ± 20	0.121
SBP (mmHg)	135 ± 20	135 ± 18	133 ± 20	138 ± 22	139 ± 20	0.653
DBP (mmHg)	83 ± 19*	83 ± 11*	84 ± 14*	90 ± 16	93 ± 15	0.001
T2DM	21 (45.65) *	25 (56.82) *	23 (35.38) *	13 (25.49)	12 (25.00)	0.005
HTN	33 (71.74)	34 (77.27)	45 (69.23)	34 (66.67)	36 (75.00)	0.780
Smoking	17 (36.96)	14 (31.82)	36 (80.00)	17 (33.33)	19 (39.58)	0.069
Laboratory data						
TG (mmol/L)	1.82 (1.20–2.44)	1.97(1.45–2.88)	1.98(1.55–3.46)	2.07(1.59–2.51)	2.07(1.49–2.85)	0.616
TC (mmol/L)	3.86 ± 1.28	4.17 ± 1.10	4.21 ± 1.06	4.37 ± 1.21	4.35 ± 1.13	0.211
HDL (mmol/L)	0.90 ± 0.28	1.04 ± 0.26	1.03 ± 0.29	0.99 ± 0.21	0.95 ± 0.22	0.066
LDL (mmol/L)	2.10 ± 1.02	2.39 ± 0.84	2.39 ± 0.84	2.60 ± 1.05	2.56 ± 0.79	0.065
eGFR (mL/min/1.73m^2)	79.92 ± 30.13	89.00 ± 18.79	90.28 ± 22.64	90.69 ± 18.44	94.16 ± 25.28	0.050
Creatinine (umol/L)	89.22 ± 39.04	77.27 ± 21.73	82.43 ± 28.76	83.50 ± 21.05	86.33 ± 26.65	0.335
Medication						
Anti-diabetes drug	14 (30.43)	19 (43.18)	15 (23.08)	8 (15.69)	8 (16.67)	0.013
Insulin	5 (10.87)	4 (9.09)	8 (12.31)	3 (5.88)	2 (4.17)	0.550
Biguanides	9 (19.57)	16 (36.36)	6 (9.23)	3 (5.88)	7 (14.58)	< 0.001
α-GI	7 (15.22)	9 (20.45)	7 (10.77)	3 (5.88)	3 (6.25)	0.133
Sulfonylureas	4 (8.70)	6 (13.64)	4 (6.15)	4 (7.84)	4 (8.33)	0.761
SGLT2 inhibitors	1 (2.17)	0 (0.00)	2 (3.08)	1 (1.96)	1 (2.08)	0.962
Anti-hypertensive drug	28 (60.87)	25 (56.82)	37 (56.92)	28 (54.90)	26 (54.17)	0.972
ACEI/ARB	14 (30.43)	18 (40.91)	19 (29.23)	16 (31.37)	14 (29.17)	0.722
β-blocker	8 (17.39)	8 (18.18)	16 (24.62)	11 (21.57)	14 (29.17)	0.631
CCB	21 (45.65)	13 (29.55)	26 (40.00)	24 (47.06)	18 (37.50)	0.435
Diuretic	4 (8.70)	5 (11.36)	10 (15.38)	11 (21.57)	12 (25.00)	0.172
ATA	11 (23.91)	6 (13.64)	13 (20.00)	8 (15.69)	7 (14.58)	0.660
Satins	6 (13.04)	5 (11.36)	12 (18.46)	8 (15.69)	7 (14.58)	0.873

Data are presented as the mean ± SD or median (Q1, Q3).

ACEI/ARB angiotensin converting enzyme inhibitor/angiotensin II receptor antagonist; *α-GI* α-glucosidase inhibitors; *ATA* anti-thrombotic agents: BMI, body mass index; *CCB* calcium channel clockers; *DBP* diastolic blood pressure; *eGFR* estimated glomerular filtration rate; *Hb* hemoglobin; *HDL* high-density lipoprotein; *HTN* hypertension; *LDL* low-density lipoprotein; *SBP* systolic blood pressure; *SGLT2* sodium-dependent glucose transporters 2; *MetS* metabolic syndrome; *T2DM* type 2 diabetes mellitus; *TC* total cholesterol; *TG* triglycerides.

**P* less than 0.05 versus High Hb group

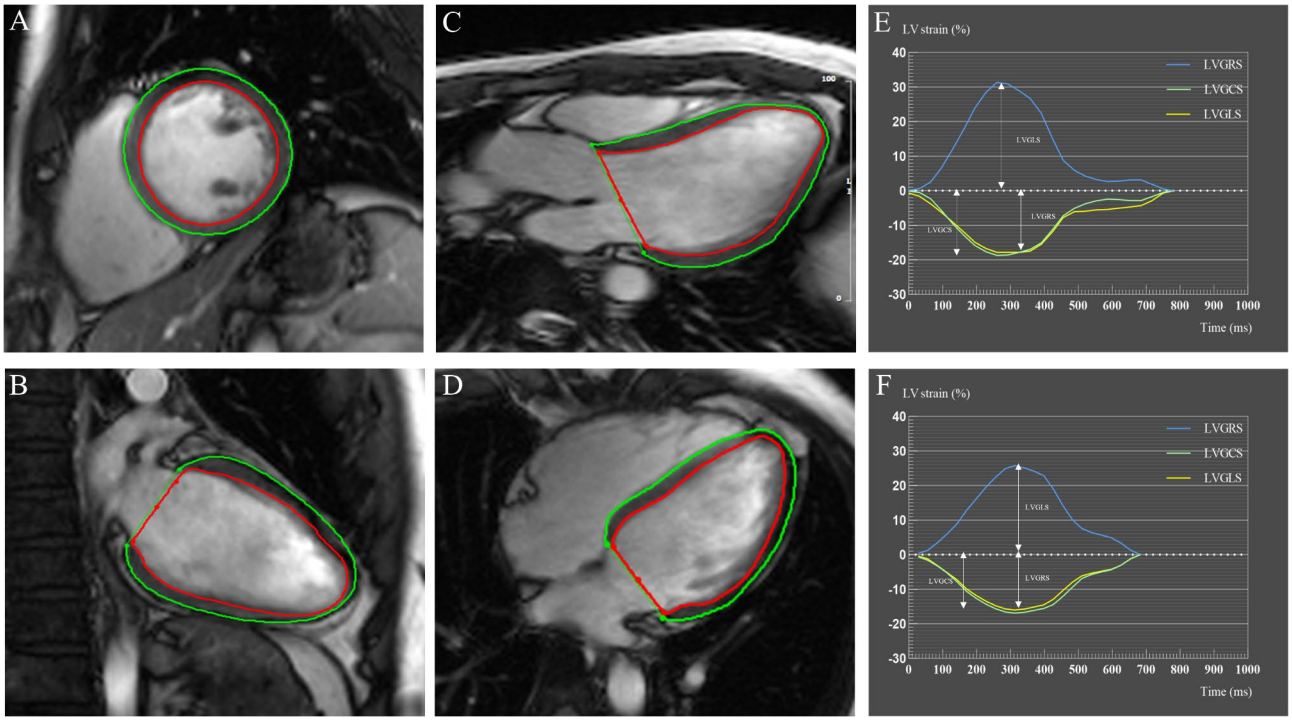

Fig. 2 Measurement of left ventricular global strains. Left ventricular strains were obtained though delineating the endocardium and epicardium at end diastole on the short axis view (A) and LV 2-, 3-, 4-chamber long axis views (B-D, respectively). E: CMR- derived the global strain curves from a control participant; F: CMR- derived the global strain curves from a patient with MetS. CMR, cardiac magnetic resonance; LVGCS, left ventricular global circumferential strain;LVGLS, left ventricular global longitudinal strain; LVGRS, left ventricular global radial strain

Table 2 Left ventricular function and global strains among 5 different hemoglobin levels in MetS patients

	Anemia group (< 120 g/L in female; < 130 g/L in male) (*n* = 46)	Low-normal Hb group (120–129 g/L in female; 130–139 g/L in male) (*n* = 44)	Moderate-normal Hb group (130–139 g/L in female; 140–149 g/L in male) (*n* = 65)	High-normal Hb group (140–149 g/L in female; 150–159 g/L in male) (*n* = 51)	High Hb group (≥ 150 g/L in female; ≥ 160 g/L in male) (*n* = 48)	*P* value
Function parameters						
LVEDVI (mL)	79.20 ± 25.62	72.33 ± 16.61	76.52 ± 21.17	76.97 ± 25.67	85.25 ± 31.20	0.143
LVESVI (mL)	30.14 (26.27–39.30)	29.21(23.55–38.19) *	29.53 (24.06–38.57)	31.72 (24.56–40.66)	37.17 (28.37–61.32)	0.044
LVSVI (mL)	41.98 ± 9.21*	39.22 ± 9.46	40.08 ± 10.69	38.30 ± 9.09	35.32 ± 11.18	0.023
LVEF (%)	55.05 ± 9.97*	55.58 ± 12.03*	54.55 ± 13.90*	52.74 ± 12.41	45.05 ± 16.58	< 0.001
LVMI (g)	54.10 ± 16.28*	55.49 ± 16.01	56.09 ± 16.43	57.06 ± 16.85	64.76 ± 20.59	0.025
Strain parameters						
LVGRS, (%)	24.15 ± 6.43*	24.15 ± 7.83*	25.66 ± 8.86*	23.69 ± 8.34	19.23 ± 8.79	0.001
LVGCS, (%)	− 15.42 ± 2.73*	− 15.35 ± 3.60*	− 15.87 ± 4.09*	− 15.06 ± 4.04	− 12.82 ± 4.69	0.001
LVGLS, (%)	− 14.81 ± 3.42*	− 14.54 ± 3.73*	− 14.85 ± 3.91*	− 13.79 ± 3.73*	− 11.11 ± 4.64	< 0.001

Data are presented as the mean ± SD or median (Q1, Q3).

CMR cardiac magnetic resonance; *LVEDVI* left ventricular end-diastolic volume index; *LVEF* left ventricular ejection fraction; *LVESVI* left ventricular stroke volume index; *LVGCS* left ventricular global circumferential strain; *LVGLS* left ventricular global longitudinal strain; *LVGRS* left ventricular global radial strain; *LVMI* left ventricular mass index; *LVSVI* left ventricular stroke volume index; *MetS* metabolic syndrome

**P* less than 0.05 versus High Hb group

Subgroup analysis

Subgroup analyses were conducted based on sex, age, obesity, eGFR, smoking and anti-diabetes drug. As shown in Fig. 5, the associations between Hb levels and LV global strains in MetS patients were consistent across sex, age, eGFR, smoking and anti-diabetes drug strata (all p for interaction > 0.05). However, a significant interaction was found between obesity and Hb levels in these associations (LVGRS: p for interaction = 0.013; LVGCS: p for interaction = 0.020; LVGLS: p for interaction = 0.006). The associations were more pronounced in MetS patients with obesity (LVGRS: β = −0.005 [95% CI −0.087 to

Table 3 The association between Hb levels and LV global strains in Mets patients

Hb (g/L)	Cases	Model 1	Model 2	Model 3
		β (95% CI)	β (95% CI)	β (95% CI)
LVGRS				
Anemia [109.0 (median)]	46	−1.805 (−4.914 to 1.305)	−1.724 (−4.724 to 1.276)	−1.285 (−3.941 to 1.370)
Low-normal Hb [131.0 (median)]	44	−1.587 (−4.713 to 1.539)	−2.069 (−5.112 to 0.974)	−2.151 (−4.840 to 0.537)
Moderate-normal Hb [143.0 (median)]	65	Reference	Reference	Reference
High-normal Hb [152.0 (median)]	51	−1.583 (−4.596 to 1.429)	−2.296 (−5.258 to 0.665)	−2.379 (−4.991 to 0.233)
High Hb [164.5 (median)]	48	−5.976 (−9.111 to −2.842) *	−5.854 (−8.940 to −2.767) *	−4.943 (−7.673 to −2.213) *
P for trend		0.112	0.107	0.090
LVGCS				
Anemia [109.0 (median)]	46	−0.553 (−2.047 to 0.941)	−0.483 (−1.919 to 0.953)	−0.238 (−1.471 to 0.994)
Low-normal Hb [131.0 (median)]	44	−0.546 (−2.048 to 0.956)	−0.800 (−2.257 to 0.656)	−0.855 (−2.103 to 0.392)
Moderate-normal Hb [143.0 (median)]	65	Reference	Reference	Reference
High-normal Hb [152.0 (median)]	51	−0.668 (−2.115 to 0.779)	−0.993 (−2.410 to 0.425)	−1.031 (−2.243 to 0.181)
High Hb [164.5 (median)]	48	−2.896 (−4.402 to −1.391) *	−2.817 (−4.294 to −1.339) *	−2.341 (−3.608 to −1.074) *
P for trend		0.044	0.039	0.022
LVGLS				
Anemia [109.0 (median)]	46	−0.227(−1.705 to 1.250)	−0.031 (−1.461 to 1.400)	0.036 (−1.182 to 1.253)
Low-normal Hb [131.0 (median)]	44	−0.367 (−1.852 to 1.119)	−0.607 (−2.058 to 0.844)	−0.523 (−1.755 to 0.710)
Moderate-normal Hb [143.0 (median)]	65	Reference	Reference	Reference
High-normal Hb [152.0 (median)]	51	−0.820 (−2.251 to 0.612)	−0.994 (−2.406 to 0.418)	−1.089 (−2.287 to 0.108)
High Hb [164.5 (median)]	48	−3.437 (−4.926 to −1.947) *	−3.284 (−4.755 to −1.812) *	−2.797 (−4.049 to −1.546) *
P for trend		0.003	0.002	<0.001

Model 1 was adjusted for sex, age; Model 2 was adjusted for BMI, triglyceride, estimating glomerular filtration rate, smoking, heart rate, anti-diabetes drug based on Model 1; Model 3 was adjusted for LVEDVI and LVMI based on Model 2. MetS patients were categorized into 5 groups based on Hb levels: anemia group (< 120 g/L in female; < 130 g/L in male), low-normal Hb group (120–129 g/L in female; 130–139 g/L in male), moderate-normal Hb group (130–139 g/L in female; 140–149 g/L in male), high-normal Hb group (140–149 g/L in female; 150–159 g/L in male), and high Hb group, (≥ 150 g/L in female; ≥ 160 g/L in male). The linear regression used absolute LVGLS and LVGCS values to analysis.

CI confidence interval; *Hb* hemoglobin; *HTN* hypertension; *LV* left ventricular; *LVEDVI* left ventricular end-diastolic volume index; *LVGCS* left ventricular global circumferential strain; *LVGLS* left ventricular global longitudinal strain; *LVGRS* left ventricular global radial strain; *LVMI* left ventricular LV mass index; *T2DM* diabetes mellitus; MetS, metabolic syndrome.

**P* less than 0.05

0.097] for non-obese patients versus −0.087 [95% CI −0.145 to −0.030] for obese patients; LVGCS: −0.006 [95% CI −0.045 to 0.034] for non-obese patients versus −0.048 [95% CI −0.075 to −0.021]for obese patients; LVGLS: $\beta = \beta$ = −0.011 [95% CI −0.053 to 0.032] for non-obese patients versus −0.063 [95% CI −0.089 to −0.036] for obese patients).

Intra-observer and inter-observer variability

Regarding the delineation of LV global strains in all three directions, intra-observer and inter-observer consistency were excellent (all ICCs > 0.8). The intra-observer and inter-observer correlation coefficients are summarized in Additional File 1, Table S3.

Discussion

This study investigated the associations between Hb levels and LV global strains in MetS patients. The key findings are as follows: (a) compared with the control group, MetS patients exhibited larger LV volume index, higher mass index, lower LVEF, and impaired LV global strains; (b) inverted L-shaped associations between Hb levels and LV global strains were observed in MetS patients, with an inflection point at 143 g/L: when Hb levels exceed 143 (g/L), LV global strains was significantly reduced, whereas levels below it, LV global strains showed no significant changes; (c) subgroup analyses indicated that the associations between the Hb levels and LV global strains were more pronounced in MetS patients with obesity.

Impact of MetS on LV remodeling

Each component of MetS contributes to cardiovascular pathophysiology, triggering complex mechanisms that lead to adverse cardiac remodeling and subsequent cardiovascular disease [22, 23]. Our study revealed

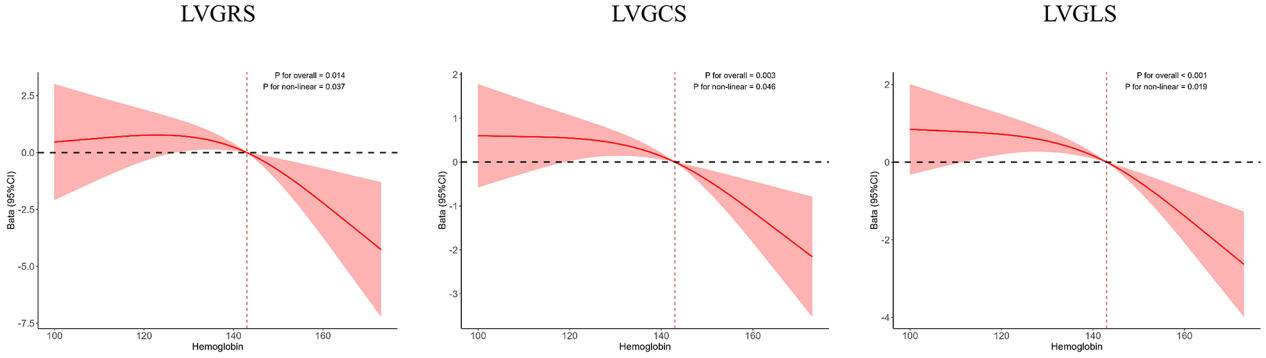

Fig. 3 Restricted cubic spline of associations between Hb levels and LV global strains in MetS patients. Restricted cubic spline plots show the nonlinear associations between Hb levels and LVGRS, LVGCS, LVGLS, respectively. Restricted cubic spline plots were adjusted for sex, age, BMI, triglyceride, estimating glomerular filtration rate, smoking, heart rate, anti-diabetes drug, LVEDVI and LVMI. The restricted cubic spline plots used absolute LVGLS and LVGCS values to analysis. β are indicated by solid lines and 95% CIs by shaded areas. BMI, body mass index; CI, confidence interval; Hb, hemoglobin; LV, left ventricular; LVEDVI, left ventricular end-diastolic volume index; LVGCS, left ventricular global circumferential strain; LVGLS, left ventricular global longitudinal strain; LVGRS, left ventricular global radial strain; LVMI, left ventricular LV mass index; MetS, metabolic syndrome

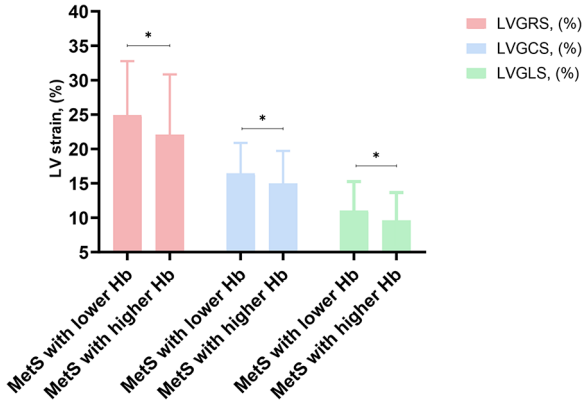

Fig. 4 Comparison of LV global strains between higher and lower Hb groups in MetS patients. According to the inflection point of the Hb level (143 g/L), MetS patients were divided into higher Hb group and lower Hb group. LVGCS and LVGLS were used as absolute values to analysis. Hb, hemoglobin; LV, left ventricular; LVEF, left ventricular ejection fraction; LVGCS, left ventricular global circumferential strain; LVGLS, left ventricular global longitudinal strain; LVGRS, left ventricular global radial strain; MetS, metabolic syndrome. * P less than 0.05

that increased LV cavity size, impaired LV function and higher LV mass in MetS patients than control participants, which was similar to a previous study [10]. LV advance remodeling in MetS may result from sympathetic nervous system overactivation, oxidative stress, endothelial dysfunction, chronic inflammation, disrupted cardiac metabolism, insulin resistance, cardiac lipotoxicity, microcirculatory disorders, and myocardial fibrosis [22]. LV global strains offer additional incremental value over LVEF in assessing LV dysfunction and risk stratification [16]. Strain analysis derived from CMR feature tracking technique provides superior signal-to-noise ratios compared with speckle-tracking echocardiography [24]. While prior studies on LV global strains in MetS used speckle-tracking echocardiography, our study addresses this gap by employing CMR feature tracking technique [9, 10].

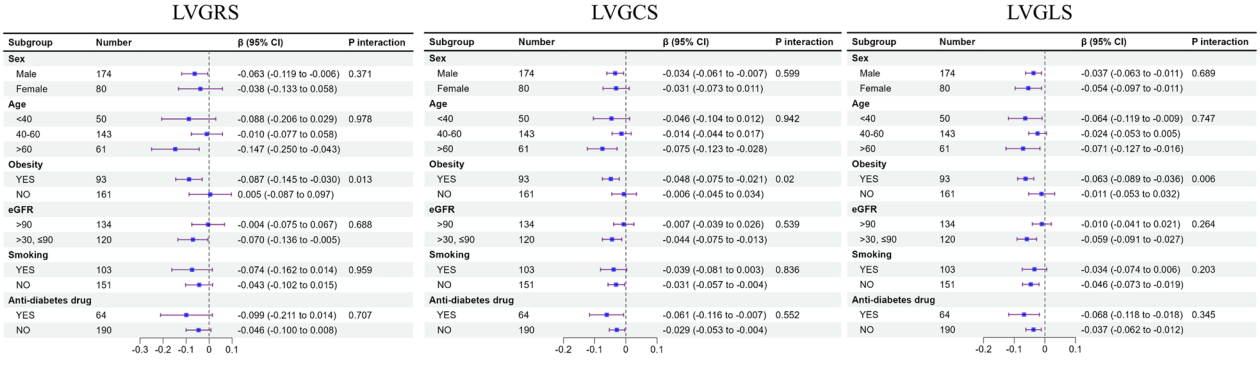

Fig. 5 Subgroup analysis on the associations between Hb levels and LV global strains in MetS patients. Subgroup analyses were conducted based on sex, age, obesity, eGFR, smoking, and anti-diabetes drug. The subgroup analysis used absolute LVGCS and LVGLS values to analysis. eGFR, estimated glomerular filtration rate; Hb, hemoglobin; LV, left ventricular; LVGCS, left ventricular global circumferential strain; LVGLS, left ventricular global longitudinal strain; LVGRS, left ventricular global radial strain; MetS, metabolic syndrome

Impact of Hb levels on LV global strains

Currently, the relationship between Hb levels and LV global strains is limited, and our study is the first to investigate this in the context of MetS. Tapio et al. [8] found that higher Hb levels are associated with poorer LVGLS in the general population. Our study confirmed the adverse impact of higher Hb levels on LV function in MetS. Additionally, our research demonstrated non-linear relationship between Hb levels and LV global strains in patients with MetS: With the increase in Hb, the variation of LV global strains was relatively flat until around 143 g/L of Hb and then started to decrease rapidly afterwards. Increased blood viscosity, endothelial dysfunction, and inflammatory status may serve as mediators of adverse effect of higher Hb. Increased blood viscosity can reduce the delivery of insulin and glucose to target organs, potentially accelerating insulin resistance and further damaging the myocardium [25, 26]. Increased blood viscosity may also worsen LV myocardial damage directly though impairing myocardial glucose metabolism [27]. Additionally, higher Hb levels linked to more severe endothelial dysfunction, probably as they bind more nitric oxide, reducing its availability and potentially promoting platelet aggregation, vasoconstriction, reduced blood flow, and increased insulin resistance [28–30]. Another explanation is that higher Hb levels were associated with elevated levels of soluble CD40 ligand, which may contribute to a pro-inflammatory, prothrombotic environment that exacerbates cardiovascular damage in MetS [31, 32]. On the other hand, Qian et al. [33] indicated that anemia has a worsen effect on LV global strains in T2DM patients; however, our study did not observe similar results. We speculate that this may be due to the limited number of MetS patients with anemia in our study. The impact of anemia on LV function in patients with MetS need further investigation.

More apparent LV dysfunction in obesity

Compared with non-obese MetS patients, obese MetS patients showed a more pronounced worsening of LV global strains with increasing Hb levels. Enlarged adipose tissues in obese patients would promote the recruitment of macrophages into pro-inflammatory states, leading to the excessive secretion of free fatty acids, reactive oxygen species, and pro-inflammatory cytokines [34].These secretions disrupt cellular organelle function, leading to chronic low-grade inflammation that impairs glucose homeostasis and causes insulin resistance [34]. Moreover, obesity can increase the risk of developing hypertension through various mechanisms, including hyperactivation of the sympathetic nervous system and the renin-angiotensin-aldosterone system, as well as metabolic disorders, kidney compression and arterial dysfunction [35, 36]. Obesity is also reported as a significant risk factor for obstructive sleep apnea syndrome, which was associated with LV hypertrophy, enlargement, and dysfunction [37, 38].

Limitations

Firstly, this single-center retrospective study that limited both its generalizability and causal inference. Therefore, further large-scale, multi-center prospective studies are needed to confirm our findings. Secondly, this study introduced potential bias by using BMI as a substitute for waist circumference. However, BMI is more accurate and convenient than waist circumference, and BMI > 25 is considered to meet the waist circumference threshold for the diagnosis of MetS [1, 18]. Additionally, the control group was relatively small. Although this may limit the robustness of our findings, it still provided important insights into the impaired cardiac function of MetS patients compared to age-, sex-, and Hb-matched controls. However, larger and more diverse control groups would enhance the validity of future research. Furthermore, we only assessed the impact of Hb levels on LV function in MetS patients. Future studies should evaluate left atrial and right ventricular function to comprehensively assess the effects of Hb levels on cardiac function.

Future directions

The causal relationship between higher Hb levels and impaired LV global strains needs to be further explored through prospective studies. Higher hemoglobin is independent risk factors for adverse metabolic and is associated with impaired LVGLS in the general population, suggesting that higher Hb may serve as a marker for the severity of metabolic disturbances in MetS—individuals with higher Hb levels may demonstrate poorer metabolic profiles, leading to greater deterioration of LV function [7, 8]. Additionally, our findings differed from those of Qian et al. [33], indicating that the impact of anemia on cardiac function in MetS requires further validation.

Conclusions

Our study revealed inverted L-shaped associations between Hb levels and LV global strains in patients with MetS. Higher Hb levels were associated with more severe LV dysfunction in MetS patients, particularly in those with obesity. Routine monitoring and early management of higher Hb levels may help prevent further deterioration of cardiac function and reduce the risk of cardiovascular events in MetS patients.

Abbreviations

MetS	Metabolic syndrome
Hb	Hemoglobin
LV	Left ventricular
LVGRS	Left ventricular global radial strain
LVGCS	Left ventricular global circumferential strain
LVGLS	Left ventricular global longitudinal strain

RCS	Restricted cubic spline
CMR	Cardiac magnetic resonance
LVEF	Left ventricular ejection fraction
T2DM	Type 2 diabetes mellitus
BMI	Body mass index
eGFR	Estimated glomerular filtration rate
LVEDVI	Left ventricular end-diastolic volume index
LVESVI	Left ventricular end-systolic volume index
LVSVI	Left ventricular stroke volume index
LVMI	Left ventricular mass index
ICCs	Intraclass correlation coefficients
CI	Confidence interval

Supplementary Information

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Additional File 1.

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Author contributions
L.X. and Y.S.Q., conception and design of study, analyzed images, collection and interpretation of data, drafted the manuscript, critical revision of the manuscript. Y.Z.G, conception and design of study, collection and interpretation of data, critically reviewed the manuscript. H.B.Y., S.K., W.J., L.X.M., Z.G. and L.W.R., collection and interpretation of data, critically reviewed the manuscript. X.R., conception and design of study, analyzed images, critical revision of the manuscript. L.Y., conception and design of study, critically reviewed the manuscript, supervised the overall study. All authors read and approved the final version of submitted manuscript.

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Data availability
The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
This study was approved by the Biomedical Research Ethics Committee of our hospital (No. 2019 – 756), and informed consent was waived due to its retrospective design.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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