Layer-specific strain and dyssynchrony index alteration in new-onset systemic lupus erythematosus patients without cardiac symptom

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Abstract

Background

Layer-specific speckle-tracking echocardiography (STE) is a noninvasive approach assessing subclinical left ventricular (LV) dysfunction. We aimed to investigate: (I) layer-specific strain and dyssynchrony index alteration; (II) disease parameters associated with layer-specific STE change; (III) effects of hydroxychloroquine (HCQ) therapy on layer-specific STE parameters in drug-naïve patients with new-onset systemic lupus erythematosus (SLE) without cardiac symptoms.

Methods

35 drug-naïve patients with new-onset SLE and 25 age-and-sex-matched healthy controls were enrolled. All individuals received both conventional echocardiographic and two-dimensional STE assessment. Layer-specific global longitudinal strain (GLS), global circumferential strain (GCS) and peak systolic dispersion (PSD) were acquired in layer-specific STE. The effect of HCQ monotherapy on GLS parameters and PSD was assessed in 7 SLE patients with stable disease.

Results

All patients had normal left ventricular ejection fraction (LVEF). Conventional echocardiographic parameters were comparable between patients and controls. Decreased layer-specific GLS and elevated PSD were observed in SLE patients. In contrast, there's no difference of layer-specific GCS at the basal level, papillary muscle level and apical level between patients and controls. More severely impaired GLS was observed in patients with higher disease activity, high-risk aPL profile or renal involvement. PSD increased in patients with higher disease activity or high-risk aPL profile. Correlational analysis showed that GLS at three layers and PSD correlated with high-sensitivity CRP (hsCRP) levels. PSD correlated with epicardial GLS, when treating hsCRP level, renal involvement, profile of aPL and disease activity as control variables. Multivariate regression showed hsCRP level and epicardial GLS are the predictors of layer-specific GLS impairment and elevated PSD, respectively. No change of GLS at three layers or PSD was observed in the first 6 months of HCQ treatment, compared with baseline. During the second 6 months of HCQ treatment, increase of endocardial GLS and whole layer GLS, and decrease of PSD were detected. There was no change of epicardial GLS during follow-up.

Conclusion

Drug-naïve patients with new-onset SLE, even having normal LVEF, are likely to have subclinical GLS impairment and LV dyssynchrony. SLE-related risk factors are associated with these dysfunctions. Continuous use of HCQ may provide beneficial effects to the silent cardiac impairment.

Background

With advances in immunosuppressive therapies, the short-term outcome of systemic lupus erythematosus (SLE) has significantly improved. However, cardiac involvement still makes up a main part of mortalities in SLE. SLE patients have up to 10-fold increased risk of cardiovascular morbidity and mortality (1). Cardiac impairment in SLE is constantly asymptomatic and not always in parallel with disease activity (2, 3). Transthoracic echocardiography is a routine method to screen cardiovascular system involvement in SLE. However, it often fails to detect subclinical ventricular dysfunction for multiple reasons. For example, abnormal left ventricular ejection fraction (LVEF) tends to reflect the global but not regional myocardial dysfunction. Furthermore, disadvantages including load and angle dependency and low reproducibility exist in measurement of LVEF (4).

Speckle-tracking echocardiography (STE) is a practical and noninvasive facility of cardiac function assessment arising increasing attention in the past two decades. STE provides important information on subclinical LV dysfunction (5). Layer-specific STE was recently introduced for its advantage to quantify longitudinal-and circumferential-layer strains of the endocardium, midmyocardium, and epicardium, which makes it more sensitive and accurate (6). Moreover, peak systolic dispersion (PSD) acquired in layer-specific STE, defined as the standard deviation of the time to peak strain of the 18 segments, reflects LV mechanical dyssynchrony (LVMD). LVMD is a marker of poor prognosis in patients with cardiovascular disease (CVD), especially in those with preserved ejection fraction (7)(8).

Hydroxychloroquine (HCQ), a cornerstone drug in SLE, has multiple potential CVD benefit to SLE patients through its pleiotropic effects (9). Nevertheless, scarce evidence of the effect of HCQ on subclinical left ventricular dysfunction in SLE patients has been reported. In the present study, to our knowledge, we evaluated subclinical cardiac dysfunction and mechanical dyssynchrony in drug-naïve patients with new-onset SLE and the effects of hydroxychloroquine monotherapy on certain STE parameters in patients with stable disease for the first time. Disease parameters associated with the layer-specific STE change were also explored.

Methods

Study subjects

In this study, drug-naïve patients with new-onset SLE were consecutively recruited in Second affiliated hospital of Fujian Medical University from January 2019 to January 2020. These patients fulfilled 2012 American College of Rheumatology (ACR)/Systemic Lupus International Collaborating Clinics (SLICC) criteria (8). SLE patients included had no cardiac symptoms. Disease activity was assessed by Systemic Lupus Erythematosus Disease Activity Index-2K (SLEDAI-2K). High-risk antiphospholipid antibody (aPL) profile was defined as the presence of lupus anticoagulant or of double or triple aPL positivity, or the presence of persistently high aPL titres. Age-and-sex-matched healthy controls with negative result of antinuclear antibodies and no history of systemic disease served as healthy controls. The exclusion

criteria included age <18 years, a history of treatment with cardio-toxic drugs, acute coronary symptoms or symptomatic heart failure, previous cardiac surgery, obesity, hypertension, smoking, diabetes, bundle-branch heart block, estimated glomerular filtration rate of <30 ml/minute/1.73 m² and tumor. This study was approved by the ethics committee of the Second Affiliated Hospital of Fujian Medical University.

Routine echocardiographic assessment

2D echocardiography examinations were performed. A GE VIVID E95 ultrasound system equipped with a 1.4~4.6 MHz transducer (M5Sc-D probe) was applied. LVEF was determined by the following parameter: left ventricular end-diastolic diameters (LVEDD), left ventricular end-systolic diameters (LVESD), interventricular septal (IVS), posterior wall thickness (PWT), end-diastolic volume and end-systolic volumes. Diastolic parameters included E, A, e' and E/e'. Here, the "E" represents transmitral peak velocity of early diastole, while the "e" and the "A" refer to the velocity of early diastole of the mitral annulus and transmitral peak velocity of late diastole, respectively.

2D Speckle-tracking echocardiographic assessment

2D STE was performed using a GE VIVID E95 ultrasound system. Images of the apical four-chamber, apical two-chamber, apical LV long-axis, and LV short-axis views at the basal, papillary and apical levels were collected within 3~5 cardiac cycles. Software package (EchoPAC, version 201 6.3, GE Vingmed Ultrasound) was used to analyze images. The software tracked endocardium outline and divided the whole ventricular wall into 3 layers (an endocardial, a mid-myocardial and an epicardial layer). Quantitative myocardial parameters for global longitudinal strain (GLS) and global circumference strain (GCS) of each layer, as well as PSD, were obtained.

Statistical analysis

Differences between patients and controls and correlations were analyzed using t-test and Pearson's correlation. analysis, respectively, if data is normally distributed. If not, nonparametric Mann-Whitney rank sum test and Spearman's correlation analysis were applied. Partial correlation analysis and multivariate linear regression were used to find out the disease parameters associated with abnormal measure value in STE. The effects of HCQ monotherapy on layer-specific STE parameters were investigated in 7 SLE patients via repeated measure ANOVA. Inter- and intra-observer reproducibility was assessed using intra-class correlation coefficients. Statistical significance was defined as $p < 0.05$. All statistical analyses were performed with GraphPad Prism software 5.0 and SPSS software 21.0.

Results

Study population

The characteristics of SLE patients and healthy controls were summarized in Table 1. In this study, a total of 35 SLE patients with new-onset disease and 25 healthy controls were enrolled. 51% had stable disease

to mild disease activity (n=18), 40% had moderate disease activity (n=14), and 9% had high disease activity (n=3). No cardiac symptoms were referred in SLE patients and controls. Accordingly, all individuals had normal serum markers of cardiac injury including N-terminal pro-B-type natriuretic peptide (NT-proBNP) and Troponin I, indicating absence of clinical evidence of cardiac impairment in SLE patients.

Table 1 Subjects’ characteristics of SLE patients and controls.

Variables	SLE(n=35)	Healthy controls(n=25)	<i>p</i>
Female/Male	29/6	20/5	0.05
Age(years)	33±6	32±6	0.863
Immune parameters			
Serum C3, gm/liter	0.62±0.18	1.13±0.08	0.001
Serum C4, gm/liter	0.12±0.05	0.24±0.03	0.001
ANA positive no. (%)	35(100)	0(0)	NA
Anti-dsDNA positive, no. (%)	25(71)	0(0)	NA
Antiphospholipid antibody positive, no. (%)	23(66)	0(0)	NA
High-risk profile aPL, no.(%)	15(42.9)	0(0)	NA
Disease Activity			
SLEDAI-2K≤4	7	NA	NA
5≤SLEDAI-2K≤9	11	NA	NA
10≤SLEDAI-2K≤14	14	NA	NA
SLEDAI-2K≥15	3	NA	NA
Traditional cardiac risk factors, no(%)			
Hypertension	0(0)	0(0)	NA
Diabetes	0(0)	0(0)	NA
Hyperlipidemia	3(9)	0(0)	NA
Smoking	0(0)	0(0)	NA
Obesity	0(0)	0(0)	NA
Gout	0(0)	0(0)	NA
Cardiac symptom, no. (%)	0(0)	0(0)	NA
Serum markers of cardiac injury			
NT-proBNP(pg/L)	116±31	114±19	0.988
Troponin I, ng/ml	0(0-0.01)	0(0-0.01)	0.05
Echocardiographic measurements			
Pulmonary hypertension, no. (%)	5(14)	0(0)	NA
LVEF (%)	58±3	59±3	0.132
Diastolic dysfunction, no. (%)	0(0)	0(0)	NA
hsCRP (mg/L)	26.11±12.92	6.97±2.12	0.001
ESR (mm/H)	34±11	14±5	0.001

ANA= antinuclear antibody; anti-dsDNA= anti-double-stranded DNA; SLEDAI-2K= Systemic Lupus Erythematosus Disease Activity Index-2K; aPL= antiphospholipid antibody; NT-proBNP= n-terminal pro-b-type natriuretic peptide; LVEF= left ventricular ejection fraction; hsCRP= high sensitivity C-reactive protein; ESR= erythrocyte sedimentation rate

Conventional echocardiographic parameters

Conventional echocardiographic results are summarized in Table 2. All participants included had normal LVEF. No significant differences of parameters assessing systolic and diastolic function including LVEDD, LVESD, IVS, PWT, E, A, e' and E/e' were found between SLE patients and healthy controls(p>0.05, all). In the follow-up period of seven patients accepting HCQ monotherapy, there were no significant changes of LV diameter and LVEF.

Table 2 Conventional and TDI echocardiographic parameters in SLE patients and controls

Variables	SLE(n=35)	Healthy controls(n=25)	<i>p</i>
LVEDD (mm)	45.8±2.5	45.6±3.3	>0.05
LVESD (mm)	31.6±1.9	31.4±2,8	>0.05
IVS (mm)	9.4±0.8	9.6±0.7	>0.05
PWT (mm)	8.9±0.7	9.1±0.9	>0.05
E(cm/s)	88.0±11.3	90.2±11.6	>0.05
A(cm/s)	59.5±11.3	62.4±9.1	>0.05
e'(cm/s)	12.3±1.7	12.2±1.8	>0.05
E/e'	7.2±0.7	7.4±0.7	>0.05

LVEDD= left ventricular end-diastolic diameter; LVESD= left ventricular end-systolic diameter; IVS= interventricular septum; PWT= posterior wall thickness; E= transmitral peak velocity of early diastole; A= transmitral peak velocity of late diastole; e' = velocity of early diastole of the mitral annulus

Layer-specific STE characteristics, left ventricular dyssynchrony index (PSD) and disease parameters in SLE patients

Representative images of layer-specific STE of one SLE patient and one health control individual are shown in Figure 1 and 2. The results of layer-specific STE parameters are displayed in Table 3. Although no clinical evidence of cardiac involvement was detected in SLE patients through routine assessment, impaired left ventricular GLS at three layers (whole layer GLS, endocardial GLS and epicardial GLS) were observed in drug-naïve patients with new-onset SLE, compared with controls (p=0.02, 0.01, 0.04, respectively). Elevation of PSD, which reflects left ventricular dyssynchrony, was found in SLE patients (p<0.01). In contrast, there's also no significant difference of the GCS of the three layers (midmyocardium

GCS, endocardium GCS and epicardium GCS) at the basal level, papillary level and apical level between SLE patients and controls ($p>0.05$, all).

In addition, more severe impairment of GLS was observed in SLE patients with moderate to severe active disease, high-risk aPL profile or lupus nephritis, compared with those with inactive to mild active disease, negative aPL to low-risk aPL profile or without evidence of renal involvement, respectively (Table 4). In contrast, PSD significantly increased in patients with higher disease activity or high-risk aPL, but not in those with lupus nephritis (Table 4).

Correlation analysis showed that endocardial GLS, whole layer GLS, epicardial GLS and PSD correlated with high-sensitivity CRP (hsCRP) levels. PSD also correlated with the three layer-specific GLS parameters above (Figure 3). Partial correlation analysis showed that PSD correlated with epicardial GLS, but not whole layer GLS or endocardial GLS, when treating hsCRP level, renal involvement, profile of aPL and disease activity as control variable (Table 5). Multivariate regression analysis showed that hsCRP level and epicardial GLS are the predictors of layer-specific GLS impairment and PSD change, respectively (Table 6).

Table 3 Lay-specific strain data and left ventricular dyssynchrony index parameters in SLE patients and controls

Variables	SLE	Healthy controls	<i>p</i>
Whole layer GLS	-17.6±3.0	-19.3±2.6	0.02
Endocardial GLS	-20.0±3.2	-22.1±3.0	0.01
Epicardial GLS	-15.6±2.7	-16.8±2.4	0.04
GCS at basal level			
Endocardium	-25.6±6.3	-24.4±6.0	0.458
Mid-myocardium	-18.0±4.4	-16.9±4.5	0.376
Epicardium	-12.8±4.0	-12.2±3.9	0.675
GCS at papillary muscle level			
Endocardium	-29.0±5.5	-27.1±7.0	0.239
Mid-myocardium	-20.3±3.9	-18.3±5.3	0.124
Epicardium	-14.2±4.5	-12.5±4.3	0.136
GCS at apical level			
Endocardium	-33.8±5.7	-32.7±8.4	0.605
Mid-myocardium	-23.4±4.9	-22.5±6.3	0.686
Epicardium	-16.0±5.6	-15.5±5.9	0.708
PSD	41.0±18.9	28.8±10.1	0.007

STE= speckle tracking echocardiography; GCS= global circumferential strain; GLS= global longitudinal strain; PSD= peak systolic dispersion.

Table 4 Layer-specific longitudinal parameters, PSD and certain disease-related contributors of cardiovascular risk in SLE patients

	Whole layer GLS	Endocardial GLS	Epicardial GLS	PSD
Disease activity				
Inactive to mild active disease	-19.3±2.3	-21.8±2.6	-17.1±2.2	34.1±16.1
Moderate to severe active disease	-15.8±2.5	-18.1±2.8	-13.9±2.3	48.2±19.3
<i>p</i>	<0.001	<0.001	<0.001	0.014
Renal involvement				
Without lupus nephritis	-19.5±2.1	-22.0±2.4	-17.4±2.0	35.1±17.4
With lupus nephritis	-16.6±2.9	-19.0±3.2	-14.6±2.6	44.0±19.3
<i>p</i>	<0.001	0.001	0.002	0.062
aPL profile				
Negative and low-risk aPL profile	-18.9±2.5	-21.3±2.7	-16.8±2.3	36.4±18.4
High-risk aPL profile	-15.9±2.8	-18.3±3.2	-14.0±2.5	47.1±18.4
<i>p</i>	0.002	0.002	0.004	0.037

GCS= global circumferential strain; GLS= global longitudinal strain; PSD = peak systolic dispersion; aPL= antiphospholipid antibody

Table 5 Partial correlation analysis between PSD and layer-specific GLS parameter

Control Variable	Variable	<i>r</i>	<i>p</i>
HsCRP level	Whole layer GLS	0.296	0.106
Renal involvement	Endocardial GLS	0.212	0.252
Profile of aPL	Epicardial GLS	0.360	0.047
Disease activity			

PSD= peak systolic dispersion; GLS= global longitudinal strain; hsCRP= high sensitivity C-reactive protein; aPL= antiphospholipid antibody

Table 6 Multivariate linear regression to analyze predictor of layer-specific GLS parameter and PSD

		Unstandardized coefficients		Standardized coefficients		<i>p</i>
Model		B	Std. error	Beta	t	
Whole layer GLS	Constant	-21.725	0.815		-26.656	<0.001
	HsCRP level	0.121	0.032	0.528	3.717	0.001
	Disease activity	1.728	1.211	0.296	1.426	0.164
	Renal involvement	-0.164	1.064	-0.027	-0.154	0.878
	Profile of aPL	0.545	0.952	0.092	0.572	0.572
Endocardial GLS	Constant	-24.454	0.909		-26.893	<0.001
	HsCRP level	0.139	0.036	0.556	3.849	0.001
	Disease activity	2.028	1.351	0.317	1.500	0.144
	Renal involvement	-0.433	1.187	-0.064	-0.365	0.718
	Profile of aPL	0.295	1.063	0.046	0.278	0.783
Epicardial GLS	Constant	-19.294	0.767		-25.161	<0.001
	HsCRP level	0.104	0.031	0.492	3.400	0.002
	Disease activity	1.385	1.140	0.258	1.215	0.234
	Renal involvement	0.055	1.001	0.010	0.055	0.957
	Profile of aPL	0.730	0.896	0.134	0.815	0.422
PSD	Constant	95.394	32.226		2.960	0.006
	HsCRP level	-0.123	0.315	-0.084	-0.390	0.699
	Disease activity	5.306	8.505	0.142	0.624	0.537
	Profile of aPL	-0.995	7.972	-0.026	-0.125	0.901
	Epicardial GLS	3.429	1.635	0.494	2.097	0.045

GLS= global longitudinal strain; PSD= peak systolic dispersion; hsCRP= high sensitivity C-reactive protein; aPL= antiphospholipid antibody

Effect of HCQ monotherapy on layer-specific GLS parameters and PSD in SLE patients with stable disease

The effect of HCQ monotherapy for 6 months and 12 months on GLS parameters and PSD was assessed in 7 SLE patients with stable disease. The results were summarized in Table 7. Figure 4 showed change of Bull's eye plot during HCQ monotherapy in one patient at different points in time. Cardiac enzyme, Troponin I, NT-proBNP and LVEF were within normal arrange during follow-up.

Endocardial GLS and whole layer GLS showed no change after HCQ treatment for 6 months, compared with baseline. During the second 6 months of HCQ treatment, significant increase of the two strain

parameters was detected. Similarly, significant decrease of PSD was observed in the second 6 months of HCQ treatment. No change of epicardial GLS was observed during follow-up.

Table 7 Effect on GLS parameters and PSD by HCQ monotherapy in SLE patients with stable disease

Variables	Baseline	6 months	12 months	<i>p</i>
Whole layer GLS	-19.0±1.8	-19.3±2.1	-21.1±2.6**	<0.05
Endocardial GLS	-21.5±2.0	-21.8±2.4	-23.8±2.8**	<0.05
Epicardial GLS	-16.8±1.8	-17.1±2.0	-18.7±2.5	>0.05
PSD	49.9±15.7	39.9±7.8	29.7±10.1*,**	<0.01

GLS= global longitudinal strain; PSD= peak systolic dispersion; HCQ= Hydroxychloroquine

*p<0.05 compared with baseline.

**p<0.05 compared with 6 months.

Discussion

In 2016, Ozawa K et al. firstly analyzed the relationship between layer-specific strain parameters and heart failure indicators in 20 systemic autoimmune disorder patients (including 7 SLE patients). They found that GCS values, but not GLS in whole, endocardial and epicardial layers correlated with serum B-type natriuretic peptide (BNP) levels (11). In addition, GCS in endocardial layer was significantly positively correlated with LVEF. To the best of our knowledge, in the present study, it is the first time to display the asymptomatic myocardial dysfunction in drug-naïve patients with new-onset SLE via speckle-tracking-based multilayer approach. The main findings are that decreased whole layer GLS, endocardial GLS and epicardial GLS were found in SLE patients, compared with age, sex-matched healthy individuals, suggesting that subclinical impairment of LV function can occur as early as the time SLE was new-onset and newly diagnosed.

Interestingly, these SLE patients had impaired myocardial GLS but not GCS. The relationship between LS and CS was still not very clear. Emerging evidence showed that different roles was played by CS and LS in left ventricular ejection (12). Circumferential shortening was proved to contributed more to LVEF (11, 13). In contrast, patients with impaired longitudinal shortening constantly have preserved LVEF. This result was also consistent with the study by Kraigher-Krainer et al who found that in heart failure with preserved ejection fraction (HFpEF), after adjustment for 10 baseline covariates, lower LS but not CS was associated with higher NT-proBNP, a prognostically relevant biomarker in HFpEF (14). In our study, decreased GLS was found in new-onset SLE patients with normal LVEF, suggesting GLS might be a marker for early detection of myocardial dysfunction in SLE patients.

PSD had been proved to be a relatively new and useful marker for early detection of LVMD (15, 16). Mounting evidence supports that LVMD has an independent and incremental negative impact on myocardial mechanics and remodeling. In the study by Leong et al, LV dyssynchrony is independently associated with changes in the LVEF over time in idiopathic dilated cardiomyopathy and occurrence of ventricular tachycardia after myocardial infarction (17). Fudim M et al. demonstrated that LV dyssynchrony were strongly associated with adverse outcomes among patients with coronary heart disease (18). In our study, elevation of PSD was detected in drug-naïve SLE patients for the first time, suggesting subclinical LVMD in SLE. Moreover, previous study showed that LVMD has been found to be particularly prevalent in patients with microvascular involvement (19), which is also a characteristic lesion mediated by immune complex deposition in SLE. Whether higher PSD predicts poorer prognosis of myocardial involvement in SLE needs to be clarified in further research.

Mouse model and clinical evidence had shown lupus-associated risk factors play key roles in pathogenesis of CVD in SLE patients (20, 21). Disease activity, inflammation, antiphospholipid antibody and lupus nephritis are among the most commonly studied SLE-associated cardiovascular risk factors (22, 23, 24). In our study, accordingly, more active disease, high-risk aPL profile, renal involvement and higher hsCRP level are linked with the tendency of more severe impaired GLS parameters and higher PSD (although not always had statistical significance). Active disease is associated with macrophage activation, enhancing the pro-inflammatory process of CVD occurrence in SLE (25). High-risk aPL profile not only mediates hypercoagulable state and endothelial dysfunction, but also exacerbate atherosclerosis inflammation in SLE with antiphospholipid syndrome (26). Gustafsson et al. reported that accelerated atherosclerosis in SLE is mainly confined to a subgroup with LN (27). The four factors above may work alone or coordinate to cause LS and PSD impairment. Interestingly, PSD correlated with the three layer-specific GLS parameters in the univariate analysis. Further partial correlation and multivariate regression analysis revealed that epicardial GLS is an independent predictor of PSD, suggesting that epicardial GLS maybe a contributor of LVMD.

HCQ, has been thought to exert a broad spectrum of beneficial effects on premature CVD in SLE via targeting various SLE-related and traditional CVD risk factors (9). In the present study, we provided evidence that HCQ monotherapy for 12 months could significantly improve impaired GLS parameters including whole layer GLS and endocardial GLS but not epicardial GLS, and LVMD. We speculate that endocardial region, where has higher microvessel density, is more accessible to evoke an immune complex-mediated process, so the endocardial lesion can be easier to achieve improvement under HCQ treatment. In addition, the beneficial effects seemed to be more substantial at the time point of the second 6 months of HCQ treatment than the first 6 months, suggesting that continuous use of HCQ for more than 6 months has protective effects on asymptomatic cardiac involvement in SLE.

Routine echocardiography was commonly used to assess the cardiac dysfunction in SLE patients. However, some serious limitations exist due to reasons referred above. In this study, all individuals including had normal LV systolic and diastolic function in routine echocardiography scan, suggesting

longitudinal parameters measured in STE is probably more sensitive tools for myocardial function impairment at the early stage.

Some limitations existed in this study. First, it is a study with a relatively short time follow-up. Thus, the predictive value of layer-specific STE parameters could not be well judged. Second, we did not enroll SLE patients having cardiac symptoms as first manifestation to assess the clinical significance more comprehensively. A large-scale study with long-term follow-up in SLE patients will be urged to evaluate the effects of these STE parameters.

Conclusions

In conclusion, this is the first study to demonstrate that drug-naive patients with new-onset SLE, even those with normal LVEF, are likely to have subclinical GLS impairment and LV dyssynchrony. Some SLE-related risk factors are associated with these dysfunctions. Continuous use of HCQ may provide beneficial effects to the silent cardiac impairment.

Abbreviations

SLE

systemic lupus erythematosus

LVEF

left ventricular ejection fraction

STE

Speckle-tracking echocardiography (STE)

PSD

peak systolic dispersion

LVMD

LV mechanical dyssynchrony

CVD

cardiovascular disease

HCQ

Hydroxychloroquine

ACR

American College of Rheumatology

SLICC

Systemic Lupus International Collaborating Clinics

SLEDAI-2K

Systemic Lupus Erythematosus Disease Activity Index-2K

aPL

antiphospholipid antibody

LVEDD

left ventricular end-diastolic diameters
LVESD
left ventricular end-systolic diameters
IVS
interventricular septal
PWT
posterior wall thickness
GLS
global longitudinal strain
GCS
global circumference strain
NT-proBNP
n-terminal pro-b-type natriuretic peptide
hsCRP
high sensitivity C-reactive protein
ESR
erythrocyte sedimentation rate
HFpEF
heart failure with preserved ejection fraction

Declarations

Ethics approval and consent to participate

The study was approved by the ethics committee of the Second Affiliated Hospital of Fujian Medical University. All patients and controls gave signed informed consent.

Consent for publication

All authors consented to the publication of this manuscript.

Availability of data and materials

The datasets used and/or analyzed during the present study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that there are no competing interests.

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Authors' contributions

T Luo and Z Wang contribute equally to this article. Conception and design: C Fang, T Luo; Administrative support: Z Wang, Z Chen; Collection and assembly of data: Z Wang, T Luo, C Fang; Data analysis and interpretation: C Fang, E Yu, T Luo; Manuscript writing: T Luo, C Fang; Final approval of manuscript: All authors.

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Figures

Apical 4-chamber view

Apical 2-chamber view

Apical 3-chamber view

Figure 1

Typical layer-specific global longitudinal strain (GLS) images of Left Ventricle (LV) from a patient with systemic lupus erythematosus(left) and one healthy individual(right). LV GLS was measured from 3 different views (apical 4 (upper level images)-, 2 (middle level images)-, and 3 (bottom level images)-chamber views). Measurement of whole layer GLS, endocardial GLS and epicardial GLS were performed.

GCS at apical level

GCS at papillary muscle level

GCS at basal level

Figure 2

Representative plot of layer-specific global circumferential strain (GCS) in the left ventricle (LV) of one SLE patient(left) and a healthy individual(right). LV GCS was measured from 3 different levels (apical level, papillary muscle level and basal level). Measurement of midmyocardium GCS, endocardium GCS and epicardium GCS were performed.

Figure 3

Univariate correlation between (1) global longitudinal strain (GLS) parameters and high sensitivity C reactive protein (hsCRP) levels; (2) peak systolic dispersion (PSD) and hsCRP levels; (3) PSD and GLS parameters.

Figure 4

Change of layer-specific STE Bull's eye plot during HCQ monotherapy in one patient with stable disease, which is measured at baseline, HCQ treatment for 6 months and HCQ treatment for 12 months, respectively.