Myocardial performance index in active and inactive paediatric systemic lupus erythematosus

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Abstract

Objective

To evaluate cardiac structure and function in paediatric SLE patients without clinical evidence of cardiovascular disease in active and inactive diseases.

Methods

Patients aged ≤20 years who fulfilled the diagnostic criteria of active SLE underwent transthoracic echocardiography to evaluate cardiac structure and function, and were then followed up echocardiographically every 3-4 months until SLE disease was inactive. Patients with heart failure, myocarditis, pericarditis, endocarditis, coronary artery disease, or abnormal structural heart disease were excluded.

Results

Twenty-six active SLE patients, mean age 13.2±3.3 years, of whom 20 were female (77%), were enrolled. Most patients had cardiac abnormalities especially LV global dysfunction assessed by left ventricular myocardial performance index (LV MPI). LV MPI by conventional method, by tissue Doppler imaging (TDI) at medial and lateral mitral valve annulus were significantly decreased when compared to LV MPI in patients with inactive disease (0.44±0.14 vs. 0.30±0.05, 0.52±0.09 vs. 0.36±0.04, and 0.51±0.09 vs. 0.35±0.05, p<0.001). Using receiver operating characteristic, LV MPI cut-off at 0.37, 0.40, and 0.40 by conventional, medial TDI, lateral TDI had sensitivity and specificity of 90% and 84%, 90% and 96%, 90% and100%, respectively.

Conclusion

Left ventricular global dysfunction was found to be common in paediatric patients with active SLE. LV MPI by TDI might be useful to diagnose active SLE in paediatric patients.

Key words

systemic lupus erythematosus, cardiovascular disease, echocardiography

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Introduction

Systemic lupus erythematosus (SLE) is an idiopathic connective tissue disease, characterised by the production of autoantibodies that lead to immune complex deposition and inflammation, involving many organs, and eventually leading to permanent organ damage. Cardiac involvements have been reported in 50–60% of SLE patients (1) involving all cardiac structures. Many studies have shown myocardial dysfunction associated with SLE which might be caused by lupus myocarditis, coronary artery disease (CAD), valvular disease, and drug-related cardiotoxicity (*e.g.* cyclophosphamide and chloroquine) (2-4). After the introduction of corticosteroid therapy, the prevalence of autopsy-identified SLE-related myocarditis decreased from 50–75% to 25–30% (5, 6). However, clinically evident lupus myocarditis was identified in less than 10% of patients (7). Thus, the prevalence of myocarditis might be underestimated due to late detection until the occurence of clinical congestive heart failure. This may be an important contributor to cardiovascular morbidity and mortality. New imaging modalities superior to standard echocardiography provide earlier insight into cardiovascular involvement in SLE through the detection of subclinical myocardial dysfunction. Many studies in adult SLE have demonstrated that myocardial dysfunction was significantly associated with enhanced disease activity (8-10), whereas some studies have shown no correlation between subclinical myocardial dysfunction and disease activity of SLE (11, 12). However, there were limited studies regarding the correlation between myocardial dysfunction and disease activity in paediatric SLE. Thus, the aim of the study was to evaluate myocardial function in SLE paediatric patients without clinically evident cardiovascular disease, and the reversibility of myocardial function after inactive disease.

Patients and methods

All active SLE children, age ≤20 years with fulfilled diagnostic criteria of SLE in a 1000-bed University Hosptial between November 2014 and March 2016, were enrolled in this study. The diagnosis of SLE was based on the 2012 Systemic Lupus International Collaborating Clinics (SLICC) criteria (13). According to the Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) (14), active SLE was defined by moderate to very high disease activity (SLEDAI ≥6) or, a flare of SLE (increase in SLEDAI >3) and inactive SLE was defined by no activity or mild disease activity (SLEDAI 0-5) (12, 15). All patients were in stable condition and under optimised therapy. Patients with a history or symptoms of heart failure, myocarditis, pericarditis, endocarditis, coronary artery disease, or abnormal structural heart disease were excluded.

Study design and protocol

This study was a prospective cohort study. All active SLE patients underwent echocardiography including 2 dimenstional (2D), motion mode (M-mode), colour flow, pulse wave (PW), continous wave (CW) Doppler, and tissue Doppler imaging (TDI); along with collecting of blood samples to determine disease activity. Then, individally, echocardiography was repeated at 3–4 months and 6–8 months until inactive disease in all patients. Disease activity were assess according to SLEDAI (14), composed of 24 items, including physical examination and blood samples for complete blood count, blood urea nitrogen, creatinine, liver function test, erythrocyte sediment rate, complement (C3, C4), anti-double-stranded DNA (anti-dsDNA) antibody, commonly contributing to disease activity present within 10 days of the evaluation after performed echocardiography. Baseline characteritics were obtained such as age, sex, age at first diagnosis, duration of disease, body weight, height, blood pressure, heart rate and co-morbidity. Medical treatment were obtained, including use of prednisolone, azathioprine, cyclophosphamide, cyclosporine A, and hydroxychloroquine. The study protocol was approved by the Institute Research Board Committee of Faculty of Medicine Ramathibodi Hospital, Mahidol University. The study protocol conformed to the ethical guide lines of the Declaration of Helsinki (1975).

Written informed consent was obtained from all parents of patients.

Echocardiography

A complete transthoracic echocardiography consisting of 2D, M-mode, colour PW, CW Doppler, and TDI was performed in all patients using Philips IE33 by one operator (WP/NS) following recommendation of The American Society of Echocardiography (16). Patients were not in acute illness on the day that echocardiography performed.

M-mode and 2-D

Interventricular septum thickness during diastole and systole (IVSd, IVSs), left ventricular internal diameter during diastole and systole (LVIDd, LVIDs), left ventricular posterior wall thickness during diastole and systole (LVPWd, LVPWs) were mearsured in parasternal-short axis view at the level of papillary muscles. Left atrial (LA) dimension major and minor axis were measured in apical four chamber view and LA dimension in parasternal-long axis view.

2-D & PW Doppler

Mitral valve inflow Doppler was measured for peak early velocity (E-wave) & peak velocity at the time of atrial contraction (A-wave), E-wave deceleration time, and mitral valve close to open time (MVCO) in apical four-chamber view. Left ventricular outflow Doppler was measured for velocity time intergral (VTI), left ventricular ejection time (LVET) in apical five-chamber views. Left ventricular outflow tract diameter (LVOTD) was measured in parasternal long axis view. Pulmonary vein velocity both systolic and diastolic phase were measured in apical four chamber view.

2-D and colour flow Doppler

Pericardial effusion and structural heart disease were scanned all echocardiography view.

2-D, colour flow and CW Doppler

Tricuspid valve regurgitation pressure gradient and pulmonary valve regurgitation pressure gradient were measured in parasternal short axis and long axis view.

2-D and tissue Doppler imaging (TDI)

E', A', S', isovolumetric contraction time (IVCT), isovolumetric relaxation time (IVRT), and ejection time ET were measured in apical four chamber view both medial and lateral mitral annulus. From all measurements, all parameters were calculated as the following:

Body surface area (BSA) (m^2) was calculated by Mosteller formula (17).

Left ventricular dimensions

- The percentage of ratio of measured LVIDd to predicted LVIDd (% LVIDd) is equal to the percentage of the ratio of LVIDd to predicted LVIDd (18).
  Predicted $LVIDd^2$=[45.3 x BSA (m^2) x 0.3] - [0.03 x age (years)] - 7.2
- LVIDd Z-score (19).

Left ventricular mass (LVM) (20)

- LVM (g) = 0.8 x (1.04 x [(LVIDd+ LVPWd+IVSd)^3–$LVIDd^3$] + 0.6)
- LVM index = LVM/$height^{2.7}$ (21)
- Relative wall thickness (RWT) = (IVSd+LVPWd)/LVIDd (22)
- Left ventricular (LV) geometry categorised into normal, eccentric hypertrophy, concentric hypertrophy, and concentric remodelling as described (23)

Left ventricular function

- Systolic function (24)
  - Left ventricular ejection fraction (LVEF) (%) = [$LVIDd^3$ – $LVIDs^3$)]/ $LVIDd^3$ x 100
  - Left ventricular fractional shortening (LVFS) (%) = (LVIDd – LVIDs) / LVIDd x 100
- Diastolic function
  - E/A, E/E', deceleration time (mitral valve inflow PW Doppler)
  - LA volume =D1 x D2 x D3 x 0.523] (25) (D1 & D2, measured in 2D, apical four chamber; D3, measured in 2-D parasternal long axis)
  - LA volume index = LA volume/ BSA
- Global function
  - Conventional method: (using PW Doppler at the tip of mitral valve inflow) (26) LV MPI = (MVCO – LVET)/LVET
  - Tissue Doppler imaging (TDI) method (27): LV MPI = (IVCT+ IVRT)/LVET (IVCT, isovolumetric contraction time; IVRT, isovolumetric relaxation time; MVCO, mitral valve close to open time; LVET, left ventricular ejection time; LV MPI, left ventricular myocardial performance index)

Cardiac output (CO) and cardiac index (CI)

CO = 0.786 X $(LVOTD)^2$ X VTI X HR (28)

CI = CO/BSA

(HR, heart rate; LVOTD, left ventricular outflow tract diameter; VTI, velocity time integral)

Definition of cardiac parameters abnormalities were described (Table I).

Statistics

Data were expressed in mean ± SD or median and range for continuous variables, number, relative frequencies for categorical variables. Data were compared using student's *t*-test and Mann-Whitney test. A *p*-value of <0.05 was required for statistical significance. Receiver operating characteristic (ROC) was used for the diagnostic performance of a test.

Results

A total of 26 paediatric patients, who fulfilled the diagnosis criteria of active SLE, had a mean age of 13.2±3.3 years, and 20 patients were females (77%). Twenty-one patients (80%) with lupus nephritis and 6 patients (23%) with systemic hypertension (Table II) were enrolled. All patients were treated for their active SLE and were followed up until their disease activities were inactive. Twenty patients were inactive during the follow-up of approximately one year. Six patients still had active SLE by SLEDAI score. All of them had lupus nephritis requiring longer to become inactive. None of them died. We did not include those patients in the inactive group since they still had active disease. The data from two the groups (active and inactive SLE) were analysed and compared. These two groups came from the same populations, before and after treatment for SLE, therefore, sex and age were not significantly different in these two groups. Body mass index (BMI) was not significantly different when compared between active and inactive SLE patients. The daily dose of prednisolone was significantly lower in

Table I. The definition of the abnormalities of cardiac parameters.

Parameters	Definitions
Systolic dysfunction [a]	LVEF <55% LVFS <25% Prolongation of IVCT
Diastolic dysfunction [b]	Abnormal mitral valve inflow and MV inflow E/E' Prolongation of IVRT Abnormal pulmonary vein inflow Enlargement of LA volume
Global dysfunction [c]	LV myocardial performance index (LV MPI) > 0.4
Dimension [d]	LVIDd% > 117 %
LVM [e]	LVM index > 38.5 g/m$^{2.7}$ RWT > 0.45
LV geometry [f]	Eccentric, concentric, concentric remodelling hypertrophy

IVCT, isovolumetric contraction time; IVRT, isovolumetric relaxation time; LA, left atrium; LV, left ventricle; LVEF, left ventricular ejection fraction; LVFS, left ventricular fractional shortening; LVIDd%, left ventricular internal diameter in diastole; LVM left ventricular mass; MPI, myocardial performance index; RWT, relative wall thickness.

[a] LANG RM, BADANO LP, MOR-AVI V *et al*.: Recommendations for cardiac chamber quantification by echocardiography in adults: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. *J Am Soc Echocardiogr* 2015;28:1-39.

[b] O'LEARY PW, DURONGPISITKUL K, CORDES TM *et al*.: Diastolic ventricular function in children: a Doppler echocardiographic study establishing normal values and predictors of increased ventricular end-diastolic pressure. *Mayo Clin Proc* 1998;73:616-28.

[c] TEI C, LING LH, HODGE DO *et al*: New index of combined systolic and diastolic myocardial performance: a simple and reproducible measure of cardiac function - a study in normals and dilated cardiomyopathy. *J Cardiol* 1995;26:357-66.

[d] BAIG MK, GOLDMAN JH, CAFORIO AL, COONAR AS, KEELING PJ, MCKENNA WJ: Familial dilated cardiomyopathy: cardiac abnormalities are common in asymptomatic relatives and may represent early disease. *J Am Coll Cardiol* 1998;31:195-201.

[e] NATIONAL HIGH BLOOD PRESSURE EDUCATION PROGRAM WORKING GROUP ON HIGH BLOOD PRESSURE IN CHILDREN AND ADOLESCENTS: The fourth report on the diagnosis, evaluation and treatment of high blood pressure in children and adolescents. *Pediatrics* 2004;114: 555-76.

[f] GANAU A, DEVEREUX RB, ROMAN MJ *et al*.: Patterns of left ventricular hypertrophy and geometric remodelling in essential hypertension. *J Am Coll Cardiol* 1992;19:1550-8.

Table II. Baseline characteristics.

Characteristics	Active SLE (n=26)	Inactive SLE (n=20)	*p*-value
Age (year)*	13.15 ± 3.30	13.31 ± 3.37	0.87
Sex: female (%)	20 (76.9)	15 (75)	0.88
BMI* (kg/m^2)	21.64 ± 5.04	24.23 ± 4.37	0.07
History of nephritis, n (%)	21 (80)	15 (75)	0.63
Hypertension , n (%)	6 (23.1)	1 (5)	0.09
Diabetic, n (%)	1 (3.8)	1 (5)	-
Daily dose of prednisolone** (mg/kg/day)	0.91 (0.45-1.13)	0.24 (0.20-0.33)	<0.001
Accumulative dose of IVCY** (mg/m^2/day)	568 (0-3789)	3934 (1269-5415)	0.03
Daily dose of HCQ** (mg/kg/day)	3.19 (0-4.69)	3.34 (1.28-3.91)	0.95
Mycophenolate n, (dose, range:mg/day)**	2 (1000-1500)	5 (1000-2000)	-
Azathioprine n, (dose, range:mg)**	4 (50-100)	5 (50-125)	-

*Expressed as mean ± SD. **Expressed as median (IQR).
BMI: body mass index; HCQ: hydroxychloroquine; IVCY: intravenous cyclophosphamide; SLE: systemic lupus erythematosus.

the inactive SLE group and cummulative dose of intravenous cyclophosphamide was significantly higher in the inactive SLE group (Table II).

Most patients with active SLE had at least one cardiac abnormality including left ventricular global dysfunction (73.1%) which was the most common finding. After disease was inactive, most cardiac abnormalities were not significantly decreased. Interestingly, LV global dysfunction was significantly reduced (Table III).

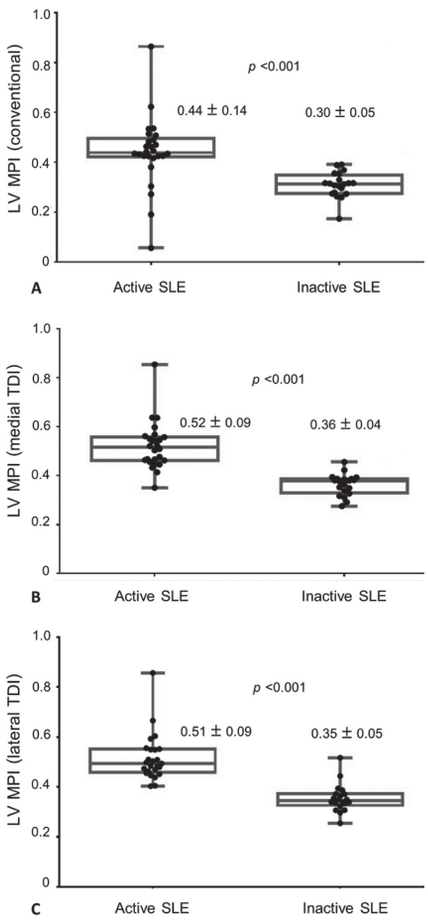

Fig. 1. Evaluation of left ventricular global function by myocardial performance index in systemic lupus erythematosus with active and inactive disease. Mean ± SD of left ventricular myocardial performance index by conventional pulse wave Doppler at tip of the mitral valve and left ventricular outflow tract (**A**), by tissue Doppler imaging at medial mitral valve annulus (**B**), by tissue Doppler imaging at lateral mitral valve annulus (**C**). Data were plotted with reference to mean ± SD and individual dot plot.
LV MPI: left ventricular myocardial performance index; SLE: systemic lupus erythematosus.

When compared between active and inactive SLE, MVCO was not significantly different (377.8±44.7 *vs*. 374±28 ms, p=0.72) whereas IVRT and IVCT were significantly longer (70.0±11.3 *vs*. 53.8±9.9 ms, p<0.001; 66.3±14.7 *vs*. 53.3±9.4 ms, p=0.001), and LVET was significantly shorter (265.1±35.5 *vs*. 295.5±22.9 ms, p=0.0007), resulting in significant reduction in LV MPI measured either by conventional meth-

od, LV MPI TDI (medial MV annulus), and LV MPI TDI (lateral MV annulus) after inactive disease (Fig. 1).

However, other diastolic function parameters were not significantly different after inactive disease (Table IV). Regarding LV systolic function, there was no statistically significant difference between active and inactive SLE (LVEF 65.0±7.0 *vs*. 66.8±5.0, *p*=0.33; LVFS36.6±4.7 *vs*. 38.1±5.3, *p*=0.32), respectively. Other cardiac parameters including LVIDd% (83.1±18.1 *vs*. 78.4±13.1, p=0.33), LVM index (41.6±10.2 *vs*. 40.2±7.0, *p*=0.59), and RWT (0.40±0.06 *vs*. 0.39±0.06, *p*=0.58) were not significantly different between active and inactive SLE (Table IV). Importantly, pericardial effusion, which was detected only in active disease, was not found in any patient with inactive SLE (30% *vs*. 0%).

Using ROC curve analysis, the cut-off values of LV MPI by conventional method (>0.37), LV MPI by medial TDI (>0.40), and LV MPI by lateral TDI (>0.40) were validated to determine active disease with sensitivity and specificity of 90% and 84%, 90% and 96%, 90% and 100%, respectively). (Fig. 2)

Table III. Cardiac abnormalities in paediatric systemic lupus erythromatosus.

Parameters	Cardiac abnormalities	Active SLE (n=26)	Inactive SLE (n=20)	*p*-value
LV function	LV systolic dysfunction	1 (4%)	0 (0%)	0.28
	LV diastolic dysfunction	7 (26.9%)	6 (30%)	0.81
	LV global dysfunction	19 (73.1%)	8 (40%)	0.02
LV dimension	LV dilatation	2 (7.7%)	0 (0%)	0.20
LV hypertrophy	Increased LVM	10 (38.5%)	9 (45%)	0.65
	Increased RWT	8 (30.8%)	3 (15%)	0.21
LV geometry	Abnormal LV geometry	14 (53.9%)	10 (50%)	0.57

Data expressed as number, n (%).
LV: left ventricular (ventricle); LVM: left ventricular mass; RWT: relative wall thickness; SLE: systemic lupus erythematosus.

Discussion

Studies reported new imaging modalities, including mean myocardial peak systolic velocity by tissue Doppler imaging or strain imaging that advanced echocardiography method, provided earlier insight into cardiovascular involvements in SLE which significantly associated with enhanced disease activity (9, 10). Some studies in adult SLE (11, 12) demonstrated no correlation between subclinical myocardial dysfunction and disease activity, however, those studies used only standard echocardiography modalities and might underestimate the assessment. Conventional echocardiography may not be sensitive enough to reveal the cardiac abnormalities. Our cohort study demonstrated that cardiac abnormalities, especially LV global dysfunction can be commonly found in children with active SLE even in the absence of specific clinical symptoms and signs of cardiac disease. Other cardiac abnormalities could be found. LV global dysfunction was significantly improved after inactive disease. However, the percentage of the abnormal LV dimension, LV mass and LV geometry were not significantly decreased after the disease was inactive. This might be due to the short period of follow-up. Long-term follow-up of these cardiac abnormalities may change this improvement. MPI has proved to be a reliable method for the evaluation of LV systolic and diastolic performance, with clear advantages over previously established indexes and prognostic value in various heart diseases (26, 29). MPI was affected by age during the first 3 years of life, showing a progressive reduction until the age of 3, but then it showed no further changes, the normal value being about 0.33±0.04 (26). Calculation of the MPI is not based on a geometric model or on volume measurements; it is first and foremost a ratio of time intervals, independent of ventricular geometry, blood pressure, heart rate and age, and it appears to be of great prognostic value in many different clinical settings. The MPI was also found to be more sensitive in the evaluation of diastolic relaxation than parameters such as the deceleration time of the E wave (DT) and the E/A ratio, which showed a weaker correlation with peak -dP/dt and tau (29). The value of the MPI in determining subclinical cardiotoxicity was investigated in patients undergoing chemotherapy with anthracyclines but normal fractional shortening (30). Myocardial dysfunction in SLE may be consequence of a variety of causes, including lupus myocarditis, coronary artery disease (CAD), valvular disease, and drug related cardiotoxicity (*e.g.* cyclophosphamide and chloroquine). Paediatric SLE is different from adult

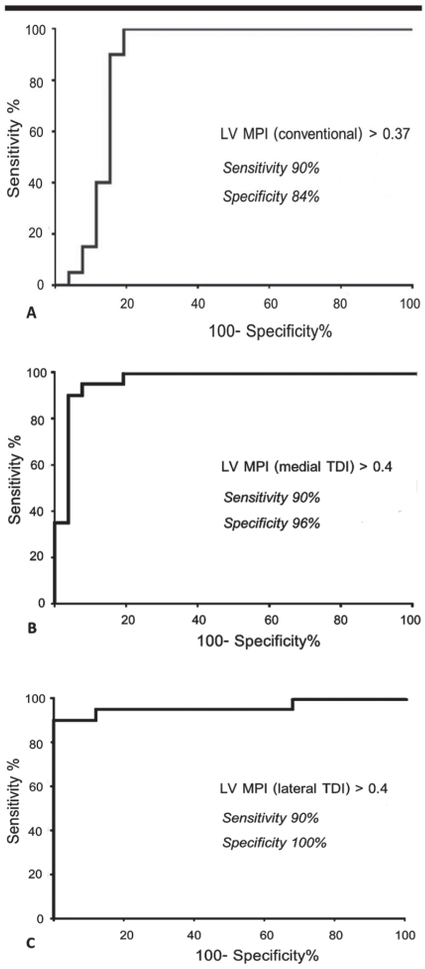

Fig. 2. Receiver operating characteristic curve for cut-off value of left ventricular myocardial performance index by conventional pulse wave Doppler at tip of the mitral valve and left ventricular outflow tract (**A**), by tissue Doppler imaging at medial mitral valve annulus (**B**), by tissue Doppler imaging at lateral mitral valve annulus (**C**).
LV MPI: left ventricular myocardial performance index.

Table IV. Parameters of left ventricular systolic and diastolic function in paediatric patients with active and inactive systemic lupus erythematosus.

Parameters	Active SLE	Inactive SLE	*p*-value
LV mass index ($g/m^{2.7}$)	41.6 ± 10.2	40.2 ± 7.0	0.59
RWT (cm)	0.40 ± 0.06	0.39 ± 0.06	0.58
LVIDd %	83.1 ± 18.1	78.4 ± 13.1	0.33
LVEF (%, Simpson)	65.0 ± 7.0	66.8 ± 5.0	0.33
FS (%)	36.6 ± 4.7	38.1 ± 5.3	0.32
Medial E' velocity (cm/s)	9.6 ± 1.9	10.5 ± 1.4	0.11
Medial A'velocity (cm/s)	7.3 ± 1.8	7.0 ± 1.2	0.57
Medial S' velocity (cm/s)	7.7 ± 1.1	7.2 ± 0.7	0.09
Lateral E' velocity (cm/s)	12.6 ± 3.5	13.8 ± 2.9	0.22
Lateral A' velocity (cm/s)	6.9 ± 2.0	7.0 ± 1.5	0.73
Lateral S' velocity (cm/s)	8.9 ± 2.1	8.8 ± 1.7	0.87
PV S velocity (cm/s)	51.4 ± 9.1	47.7 ± 6.8	0.14
PV D velocity (cm/s)	65.6 ± 12.4	56.1 ± 7.7	0.005
PV S/D	0.80 ± 0.20	0.86 ± 0.17	0.31
MV E/A	1.57 ± 0.36	1.73 ± 0.43	0.19
MV E/E' (medial)	9.5 ± 2.2	8.5 ± 1.5	0.10
MV E/E' (lateral)	7.6 ± 2.6	6.7 ± 1.6	0.17
LA volume index	12.2 ± 3.3	10.9 ± 1.7	0.09

D: diastole; LA: left atrium; MV: mitral valve; PV: pulmonary vein; S: systole; SLE: systemic lupus erythromatosus.

SLE, particularly coronary artery disease due to premature atherosclerosis, hypertension, renal failure, valvular disease, and toxicity from chloroquine were commonly found as the major causes in adult SLE (2-4) but not common in paediatric SLE. Martínez-Barrio *et al*. reported that juvenile-onset SLE had more frequent renal and cutaneous manifestations at the onset of disease and higher incidence of renal disease, malar rash, Raynaud's phenomenon, cutaneous vasculitis, and neuropsychiatric manifestations during follow-up than adult- or late-onset SLE (31). The higher incidence of renal complications might possibly lead to fluid retention and increased workload to the heart. Our study demonstrated that most active SLE patients with abnormal LV MPI indicating LV global dysfunction found that their global dysfunction significantly improved as to be in normal range after their inflammatory process was controlled by corticosteroids and immunosuppressive drugs until their diseases activities were inactive. For these two reasons, it was postulated that subclinical lupus myocarditis occuring during active SLE should be the explanation for detection of subclinical myocardial dysfunction by LV MPI. When these patients were treated, their LV global function improved. The mechanism of LV global dysfunction in SLE might be immune complex-mediated inflamatory processes, leading to subclinical myocarditis, subclinical vasculitis, and preclinical CAD in SLE patients (2, 3, 32). We propose that all of these cardiac abnormalities might be improved to normal if we have a longer follow-up period, so we recommend treating active SLE properly and performing the echocardiography over a the longer period after disease subsided. One of the criteria for the diagnosis of active SLE is serositis, including pleuritis or pericarditis. Evidence of pericarditis could be detected by echocardiographic pericardial effusion. Our study found only 30% in active SLE and 0% in inactive SLE which means that this finding was specific but not sensitive in the diagnosis of active SLE. LV MPI as the diagnostic tool for SLE with cut-off values of 0.37 (convention LV MPI) and 0.40 (TDI MPI) were found to have high specific and sensitivity. Tissue Doppler imaging (TDI) has been reported to be more precise than the conventional Doppler method in the evaluation of MPI and single time intervals, because their measurements were accomplished in concomitance with the left ventricular wall motion rather than the flow movement, and it was better correlated with conventional Doppler MPI in normal and diseased heart (27, 33). LV MPI by TDI has higher sensitivity (90%) and specificity (96% by medial TDI and 100% by lateral TDI). From these data, we propose using LV MPI by TDI as a diagnostic criteria for active SLE. We recommend performing echocardiography, including assessment of LV MPI by TDI in paediatric patients suspected of active SLE.

Conclusions

Left ventricular global dysfunction has been commonly found in paediatric patients with active SLE, indicating subclinical myocarditis. The left ventricular myocardial performance index by tissue Doppler imaging might be a useful tool for the diagnosis of active SLE in paediatric patients.

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References

1. YU XH, LI YN: Echocardiographic abnormalities in a cohort of Chinese patients with systemic lupus erythematosus--a retrospective analysis of eighty-five cases. *J Clin Ultrasound* 2011; 39: 519-26.
2. ABUSAMIEH M, ASH J: Atherosclerosis and systemic lupus erythematosus. *Cardiol Rev* 2004; 12: 267-75.
3. ASANUMA Y, OESER A, SHINTANI AK *et al*.: Premature coronary-artery atherosclerosis in systemic lupus erythematosus. *N Engl J Med* 2003; 349: 2407-15.
4. DORIA A, SHOENFELD Y, WU R *et al*.: Risk factors for subclinical atherosclerosis in a prospective cohort of patients with systemic lupus erythematosus. *Ann Rheum Dis* 2003; 62: 1071-7.
5. BULKLEY BH, ROBERTS WC: The heart in systemic lupus erythematosus and the changes induced in it by corticosteroid therapy. A study of 36 necropsy patients. *Am J Med* 1975; 58: 243-64.
6. GRIFFITH GC, VURAL IL: Acute and subacute disseminated lupus erythematosus; a correlation of clinical and postmortem findings in eighteen cases. *Circulation* 1951; 3: 492-500.
7. CODISH S, LIEL-COHEN N, ROVNER M, SUKENIK S, ABU-SHAKRA M: Dobutamine stress echocardiography in women with

systemic lupus erythematosus: increased occurrence of left ventricular outflow gradient. *Lupus* 2004; 13: 101-4.
8. BUSS SJ, WOLF D, KOROSOGLOU G *et al*.: Myocardial left ventricular dysfunction in patients with systemic lupus erythematosus: new insights from tissue Doppler and strain imaging. *J Rheumatol* 2010; 37: 79-86.
9. MURAI K, OKU H, TAKEUCHI K, KANAYAMA Y, INOUE T, TAKEDA T: Alterations in myocardial systolic and diastolic function in patients with active systemic lupus erythematosus. *Am Heart J* 1987; 113: 966-71.
10. YIP GW, SHANG Q, TAM LS *et al*.: Disease chronicity and activity predict subclinical left ventricular systolic dysfunction in patients with systemic lupus erythematosus. *Heart* 2009; 95: 980-7.
11. PARAN D, CASPI D, LEVARTOVSKY D *et al*.: Cardiac dysfunction in patients with systemic lupus erythematosus and antiphospholipid syndrome. *Ann Rheum Dis* 2007; 66: 506-10.
12. WISLOWSKA M, DEREN D, KOCHMANSKI M, SYPULA S, ROZBICKA J: Systolic and diastolic heart function in SLE patients. *Rheumatol Int* 2009; 29: 1469-76.
13. PETRI M, ORBAI AM, ALARCÓN GS *et al*.: Derivation and validation of the Systemic Lupus International Collaborating Clinics classification criteria for systemic lupus erythematosus. *Arthritis Rheum* 2012; 64: 2677-86.
14. LAM GK, PETRI M: Assessment of systemic lupus erythematosus. *Clin Exp Rheumatol* 2005; 23 (Suppl. 39): S120-32.
15. HUANG BT, YAO HM, HUANG H: Left ventricular remodeling and dysfunction in systemic lupus erythematosus: a three-dimensional speckle tracking study. *Echocardiography* 2014; 31: 1085-94.
16. GOTTDIENER JS, BEDNARZ J, DEVEREUX R *et al*.: American Society of Echocardiography recommendations for use of echocardiography in clinical trials. *J Am Soc Echocardiogr* 2004; 17: 1086-119.
17. MOSTELLER RD: Simplified calculation of body-surface area. *N Engl J Med* 1987; 317: 1098.
18. HENRY WL, GARDIN JM, WARE JH: Echocardiographic measurements in normal subjects from infancy to old age. *Circulation* 1980; 62: 1054-61.
19. PETTERSEN MD, DU W, SKEENS ME, HUMES RA: Regression equations for calculation of z scores of cardiac structures in a large cohort of healthy infants, children, and adolescents: an echocardiographic study. *J Am Soc Echocardiogr* 2008; 21: 922-34.
20. DEVEREUX RB, ALONSO DR, LUTAS EM *et al*: Echocardiographic assessment of left ventricular hypertrophy: comparison to necropsy findings. *Am J Cardiol* 1986; 57: 450-8.
21. DE SIMONE G, DANIELS SR, DEVEREUX RB *et al*.: Left ventricular mass and body size in normotensive children and adults: assessment of allometric relations and impact of overweight. *J Am Coll Cardiol* 1992; 20: 1251-60.
22. GANAU A, DEVEREUX RB, ROMAN MJ *et al*.: Patterns of left ventricular hypertrophy and geometric remodeling in essential hypertension. *J Am Coll Cardiol* 1992; 19: 1550-8.
23. DANIELS SR, LOGGIE JM, KHOURY P, KIMBALL TR: Left ventricular geometry and severe left ventricular hypertrophy in children and adolescents with essential hypertension. *Circulation* 1998; 97: 1907-11.
24. BHATT DR, ISABEL-JONES JB, VILLORIA GJ *et al*.: Accuracy of echocardiography in assessing left ventricular dimensions and volume. *Circulation* 1978; 57: 699-707.
25. JIAMSRIPONG P, HONDA T, REUSS CS *et al*.: Three methods for evaluation of left atrial volume. *Eur J Echocardiogr* 2008; 9: 351-5.
26. TEI C, LING LH, HODGE DO *et al*.: New index of combined systolic and diastolic myocardial performance: a simple and reproducible measure of cardiac function--a study in normals and dilated cardiomyopathy. *J Cardiol* 1995; 26: 357-66.
27. TEKTEN T, ONBASILI AO, CEYHAN C, UNAL S, DISCIGIL B: Novel approach to measure myocardial performance index: pulsed-wave tissue Doppler echocardiography. *Echocardiography* 2003; 20: 503-10.
28. HUNTSMAN LL, STEWART DK, BARNES SR, FRANKLIN SB, COLOCOUSIS JS, HESSEL EA: Noninvasive Doppler determination of cardiac output in man. Clinical validation. *Circulation* 1983; 67: 593-602.
29. TEI C, NISHIMURA RA, SEWARD JB, TAJIK AJ: Noninvasive Doppler-derived myocardial performance index: correlation with simultaneous measurements of cardiac catheterization measurements. *J Am Soc Echocardiogr* 1997; 10: 169-78.
30. ISHII M, TSUTSUMI T, HIMENO W *et al*.: Sequential evaluation of left ventricular myocardial performance in children after anthracycline therapy. *Am J Cardiol* 2000; 86: 1279-81.
31. MARTÍNEZ-BARRIO J, OVALLES-BONILLA JG, LÓPEZ-LONGO FJ *et al*.: Juvenile, adult and late-onset systemic lupus erythematosus: a long term follow-up study from a geographic and ethnically homogeneous population. *Clin Exp Rheumatol* 2015; 33: 788-94.
32. MANGER K, KUSUS M, FORSTER C *et al*.: Factors associated with coronary artery calcification in young female patients with SLE. *Ann Rheum Dis* 2003; 62: 846-50.
33. CACCIAPUOTI F, GALZERANO D, CAPOGROSSO P *et al*.: Impairment of left ventricular function in systemic lupus erythematosus evaluated by measuring myocardial performance index with tissue Doppler echocardiography. *Echocardiography* 2005; 22: 315-9.