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ORIGINAL ARTICLE

Cardiac manifestations of Han Chinese patients with systemic lupus erythematosus: a retrospective study

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Abstract

Objective To investigate cardiac manifestations and the risk factors in Han Chinese patients with systemic lupus erythematosus (SLE).

Methods Seven hundred fifty SLE patients who were hospitalized at our department were recruited in the present study. The patients were divided into two groups—those with or without cardiac manifestations. Cardiac manifestations in those SLE patients, such as pericarditis, myocarditis, heart valve disease, arrhythmia, were analyzed. The risk and protective factors of cardiac diseases in patients with SLE, as well as the predictors of mortality, were assessed, respectively.

Results In all 750 SLE patients, there were 339 (45.20%) patients suffered from one or more cardiac manifestations, involving pericarditis in 9.5%, myocarditis in 5.7%, heart valve disease in 15.6%, arrhythmia in 16.67%, and cardiovascular diseases (CVD) in 14%. 15.7% of SLE patients were accompanied with pulmonary arterial hypertension (PAH), of which 13.7% were mild, 1.2% were moderate, and 0.8% were severe. No significant differences were found between the two groups in age, disease duration, gender, antibody, and Systemic Lupus Erythematosus Disease Activity Index (SLEDAI). The incidence of pericarditis, heart valve disease, arrhythmia, and PAH was positively correlated with age. The incidence of arrhythmia, CVD, and PAH was correlated with SLEDAI. PAH and myocarditis were the risk factors of mortality in SLE patients with disease duration ≤ 10 years ($P = 0.034$ and 0.001, respectively).

Conclusion Cardiac involvement is common in Han Chinese SLE patients and associated with age and disease activity. PAH and myocarditis are the risk factors of mortality in SLE.

Keywords Cardiac manifestations · Pulmonary arterial hypertension (PAH) · Risk factor · Systemic lupus erythematosus (SLE)

Introduction

SLE is an autoimmune disease characterized by multiorgan manifestations, such as skin rash, arthralgias, ulcer, baldness, and autoimmune disorders. It has been well-known that cardiac involvement is often as the poor prognosis in SLE [1, 2]. It also relates to disease severity and adverse drug reactions [3].The cardiac manifestations can arise from endocardium, myocardium, pericardium, valves, conduction system, and vessels [4, 5].

Cardiovascular diseases are frequent in SLE patients. There were regional and racial differences in cardiac manifestations and related risk factors in patients with SLE [6]. The pathological and clinical characteristics of SLE have not been completely elucidated until now. Many studies about cardiac manifestations in SLE patients were focused on only few cases rather than population. Thus, cardiac manifestations and their risk predictors in Han Chinese SLE patients were explored in our study.

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Study population

Seven hundred fifty SLE patients were recruited from the department of rheumatology of the Fourth Clinical Medical College and the First Affiliated Hospital of Guangzhou University of Chinese Medicine consecutively between May 2005 and May 2017. The race of all the patients was Han. The diagnosis of SLE was defined according to the American College of Rheumatology (ACR) Classification Criteria [7]. This study complied with the Declaration of Helsinki and was approved by the Ethics Commission of Guangzhou University of Chinese Medicine.

Clinical data of all subjects, including gender, age, disease duration, autoantibodies (anti-ACA antibody, anti-SSA antibody, anti-SSB antibody, anti-dsDNA antibody, anti-Sm antibody and ANA), were collected. Transthoracic Doppler-echocardiography and troponin were used to diagnose pericardial effusion, PAH, CAD, myocarditis, and heart valve disease. The electrocardiogram was used to assess arrhythmia, CAD, and myocarditis. According to pulmonary artery systolic pressure, PAH was classified as mild (35–59 mmHg), moderate (59–89 mmHg), and severe (> 89 mmHg) [8].

The mean age of all patients was (36.59 ± 14.52) years old, and 88.8% of the patients ($n = 666$) was female. The mean disease duration was (4.72 ± 5.94) years. The positive rate of anti-ACA, anti-SSA, anti-SSB, anti-dsDNA, anti-Sm antibodies, and ANA was 5.3%, 51.7%, 15.6%, 52.5%, 30.5%, and 80.4%, respectively. Disease activity was evaluated by the Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) [9]. The patients were divided into two groups—those with or without cardiac manifestations.

Statistical analysis

Statistical analysis was performed using SPSS (version 162, SPSS Inc., Chicago, IL, USA). For continuous variables, data were presented as the mean ± standard error of the mean ($\bar{x} \pm s$). Chi-square test and the independent samples *t* test were used to evaluate the statistical difference between the two groups. The risk and protective factors of cardiac manifestations in SLE were examined by binary logistic regression analysis. Data with 10% significance were used to build the multivariate linear regression model, in which a stepwise methodology was applied to yield the best model. A two-sided p value < 0.05 was considered to be statistically significant.

Results

Cardiac manifestations in SLE patients

Table 1 shows cardiac manifestations in SLE patients. In all 750 SLE patients, there were 339 (45.20%) patients suffered from one or more cardiac manifestations, involving pericarditis in 9.5% ($n = 71$), myocarditis in 5.7% ($n = 43$), heart valve disease in 15.6% ($n = 117$), arrhythmia in 16.67% ($n = 125$), and cardiovascular diseases (CVD) in 14% ($n = 105$). 15.7% of SLE patients were accompanied with pulmonary arterial hypertension (PAH), of which 13.7% were mild, 1.2% were moderate, and 0.8% were severe.

Parameter differences between with and without cardiac manifestations group

Then, the parameters were compared between with and without cardiac manifestations group (Table 2). No significant differences were found in age, disease duration, gender, autoantibodies, and SLEDAI between the two groups.

The risk and protective factors of cardiac manifestations in SLE patients

Furthermore, we analyzed the risk and protective factors of cardiac manifestations in SLE (Table 3). The risk factors included age, disease duration, gender, antibody (ACA, SSA, SSB, ds-DNA, Sm, ANA), and SLEDAI ($P < 0.05$). Age was the predictive factor of pericarditis and arrhythmia ($P = 0.011$, 0.027; OR 0.975, 0.984; 95% CI, 0.956–0.994, 0.969–0.998, respectively); however, it was the risk factor of the heart valve disease ($P = 0.023$; OR1.023; 95% CI, 1.009–1.038). Different degrees of SLEDAI were the risk factors (moderate, $P = 0.001$; OR 2.356; 95% CI, 1.407–3.945 and severe, $P = 0.016$; OR 2.021; 95% CI, 1.137–3.591). However, mild degree of SLEDAI was the protective factor of myocarditis ($P = 0.005$; OR 0.326; 95% CI, 0.150–0.709), moderate degree of SLEDAI was the risk factor of arrhythmias ($P = 0.029$; OR 1.774; 95% CI, 1.062–2.063). Age was

Table 1 Cardiac manifestations in the SLE patients

Pericarditis, *n* (%)	Myocardial diseases, *n* (%)	Heart valve disease, *n* (%)	Arrhythmia, *n* (%)	CVD, *n* (%)	Pulmonary arterial hypertension		
					Mild, *n* (%)	Moderate, n (%)	Severe, *n* (%)
71 (9.5%)	43 (5.7%)	117 (15.6%)	125 (16.67%)	105 (14%)	103 (13.7%)	9 (1.2%)	6 (0.8%)

Table 2 Comparison of parameters between SLE patients with and without cardiac manifestations

Parameters		With cardiac manifestations group ($n = 339$)	Without cardiac manifestations group ($n = 411$)	$t/\chi^2/Z$	p value
Age, (years) $\bar{x} \pm s$		37.32 ± 15.29	35.99 ± 13.85	1.241	0.215
Disease duration, (years) $\bar{x} \pm s$		4.73 ± 5.89	4.72 ± 5.98	0.026	0.979
Females, n		308	358	2.628	0.105
ACA (+), n		16	24	0.105	0.497
SSA (+), n		181	207	0.682	0.409
SSB (+), n		60	57	2.070	0.150
ds-DNA (+), n		181	213	0.183	0.669
Sm (+), n		107	122	0.309	0.578
ANA (+), n		277	326	0.675	0.411
SLEDAI	No active	60	125	− 1.655	0.098
	Mild active	109	87		
	Moderate active	60	62		
	Severe active	110	137		

the risk factor of PAH ($P = 0.013$), while SLEDA (remission) was the protective factor of PAH ($P = 0.030$).

The predictors of mortality in SLE patients with disease duration ≤ 10 years

In order to explore the relationship between cardiac involvement and SLE-related death, we analyzed the predictors of mortality in 654 SLE patients with disease duration ≤ 10 years (Table 4). PAH and myocarditis were the risk factors of mortality in SLE patients with disease duration ≤ 10 years (P = 0.034 and 0.001, respectively; OR 6.275; 95% CI 2.033–19.372); but pericarditis, arrhythmia, heart valve disease, and CVD were not the risk factors of mortality in SLE patients with disease duration ≤ 10 years.

Discussion

Cardiac involvement is a common and severe symptom in SLE patients. It has been reported that the cumulative incidence rate of cardiovascular disease in SLE increased widely [4]. Cardiac manifestations in Chinese SLE patients have unique characteristics.

A retrospective study on PAH in 93 SLE patients found that pulmonary artery pressure (PAP) elevated in 13% of SLE patients (including White, Black, North Africa, and Other races) by noninvasive assessment [10]. And among the cases, morbidity, anti-Sm, and anti-cardiolipin antibodies were statistically different. The PAH-related morbidity in SLE patients was similar to the result of our study (15.7%); however, there were no differences in autoantibodies between the two studies.

The mechanism of arrhythmias in SLE patients has not been completely understood. The reports about the specific antibodies in arrhythmias, such as anti-Ro/SSA and anti-RNP, were controversial [11–13]. In our study, SLEDAI was the predictor of arrhythmias. SLEDAI may be correlated with pericarditis, myocarditis, atherosclerotic myocarditis, and small vessel vasculitis with collagen and fibrotic deposits, which leads to abnormality of conduction system [14, 15].

Previous studies have shown the prevalence of heart valve disease in SLE has ranged from 12 to 73% [16–21]. Vivero

Table 3 Binary analysis for predictors of the cardiac manifestations

Parameters	Predictors	B	P value	OR	95% CI for OR
Pericarditis	Age	− 0.025	0.011	0.975	0.956, 0.994
Myocardial diseases	None	NA	NA	NA	NA
Heart valve disease	Age	0.023	0.001	1.023	1.009, 1.038
Arrhythmia	Age	− 0.017	0.027	0.984	0.969, 0.998
	SLEDAI (moderate)	0.857	0.001	2.356	1.407, 3.945
	SLEDAI (severe)	0.703	0.016	2.021	1.137, 3.591
CVD	SLEDAI (mild)	− 1.122	0.005	0.326	0.150, 0.709
	SLEDAI (moderate)	0.573	0.029	1.774	1.062, 2.063
Pulmonary hypertension	Age	0.013	0.046	NA	NA
	SLEDA (remission)	− 0.593	0.030	NA	NA

Table 4 Binary analysis for predictors of mortality in SLE patients (disease duration ≤ 10 years)

Predictors	B	*P* value	OR	95% CI for OR
Pericarditis	0.276	0.690	1.318	0.340, 5.102
Myocardial diseases	1882	0.001	6.566	2.154, 20.012
Heart valve disease	0.852	0.153	2.344	0.729, 7.534
Arrhythmia	0.386	0.484	1.471	0.499, 4.334
CVD	0.590	0.272	1.803	0.630, 5.158
Pulmonary hypertension	NA	0.000	NA	NA

et al. found that valve lesions could be seen in 25% of Caucasian SLE patients, and age was the predictor of valvular thickening and dysfunction [22], while the prevalence of this report was higher than that of our study (15.6%). Similarly, age was also as the predictor in Vivero et al.'s report [22]. Valvulitis and cicatrisation could promote the development of thickening and deformation of vessels, resulting in valvular dysfunction in elderly SLE patients [23].

Pericarditis is one of the most common cardiac manifestations in SLE. Approximately 25% of SLE patients developed symptomatic pericarditis [24, 25]. Autopsy studies revealed even a higher incidence rate of subclinical pericarditis in SLE [25].The morbidity of SLE patients in other races was higher than Chinese SLE patients. Inflammatory exudate with neutrophil predominance and autoantibodies were found in pericardial effusion of SLE patients. Histopathology of pericarditis often found immune complex deposition, monocytes, and fibrinous substance [26, 27]. In our study, age was confirmed to be the predictor of pericarditis in SLE patients.

A recent study have shown morbidity of CVD was the highest among the blacks (10.57%) and lowest among the Asians (6.63%) [28]. The percentage of morbidity in Asian SLE patients was 3%, with a tenfold risk compared to the general population and a 50-fold risk at reproductive age [29, 30]. But CVD-related morbidity of in Chinese SLE patients was lower in our study. The risk factors included oxidized low-density lipoprotein, autoantibodies against endothelial cells and phospholipids, type I interferons (IFN-I), and extracellular neutrophils [31]. SLEDAI was the predictor of CVD in our study, which may be affected by immunological regulation.

The autopsy studies showed that subclinical myocarditis may commonly occur in 57% of SLE patients. It can be the initial cardiac manifestation during the progression of SLE in, particularly, among the untreated patients [32]. A French study showed that myocarditis was the first symptom in 58.6% of SLE patients [33], while 5.7% of Chinese SLE patients suffered from myocarditis in our study. Steroids and cyclophosphamide provide therapy for lupus myocarditis [34, 35]. Some reports showed that plasmapheresis [36] or high dose of intravenous immunoglobulin treatment [37] could improve myocarditis in SLE patients.

The wide use of glucocorticoid and immunosuppressive agents has improved symptoms and survival of SLE patients. However, glucocorticoids can increase the risk of lupus cardiovascular disease and cardiac death. Until now, the status of cardiovascular diseases in Han Chinese SLE patients has not been clarified. In this study, we selected SLE patients with disease duration ≤ 10 years and found that the risk factors for cardiac death of Han Chinese SLE patients were PAH and myocarditis. PAH significantly decreased survival time and quality of life in patients with connective tissue diseases [38]. A meta-analysis of six studies including 323 SLE patients accompanying PAH, which were carried out in the UK, the USA, China, and Japan, demonstrated that 1-, 3-, and 5-year survival rate was 88%, 81%, and 68%, respectively [39]. Apte et al. analyzed myocarditis in multiethnic cohorts of the USA and found that 53 of 496 SLE patients had myocarditis, and myocarditis was associated with short life span, particularly in patients with disease duration ≥ 5 years [40].

Our study had some limitations. It was a retrospective study and needed to be further verified. The assessment methods of heart diseases were not strictly unified, so only indirect detection was used to evaluate cardiac diseases in SLE patients. The effects of treatment on heart diseases in SLE were not assessed, which need to explore in the further study.

In conclusion, we confirmed cardiac manifestations are common in Han Chinese SLE patients. Age and disease activity increase the risk of cardiac manifestations. PAH and myocarditis are the risk predictors of mortality in SLE patients.

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Compliance with ethical standards All procedures performed in this study were in accordance with the ethical standards of the institutional and/ or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. For this type of study, formal consent is not required.

Competing interests The authors declare that they have no competing interests.?}$^"journal_txt">

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