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PAPER

# Features associated with cardiac abnormalities in systemic lupus erythematosus

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**Objectives.** To determine the prevalence of echocardiographic abnormalities and identify associated clinical and laboratory features in a large systemic lupus erythematosus (SLE) cohort.
**Methods.** Patients fulfilling ACR criteria for SLE underwent a transthoracic echocardiogram (TTE) between January 2005 and June 2006. Variables used as potential correlates included age, sex, ethnicity, lupus duration, lupus disease activity (SLEDAI), cumulative damage (SLICC/ACR damage index (DI)), arterial hypertension, diabetes, current smoking, medication use and laboratory data. Multivariate logistic regression was used to examine the association between TTE abnormalities and potential determinants.
**Results.** For the 217 subjects with a TTE performed during the study, the main abnormalities were of the mitral valve (37.3%) and included thickening (25.4%) and insufficiency (25.8%). Other findings included pulmonary artery pressure (PAP) $\geq$ 30 mm Hg (10.1%), pericardial effusion (4.6%), hypokinesis (2.8%), and aortic insufficiency (3.7%). In multivariate analysis, mitral insufficiency was associated with the use of corticosteroids (OR 2.90; 95%CI 1.42–5.94) and hypokinesis with angiotensin-converting enzyme inhibitors (12.89; 1.06–157.18). Elevated PAP was associated with age (1.04; 1.01–1.07) and with DI (1.20; 1.01–1.42).
**Conclusion.** Valvular abnormalities are frequent in patients with SLE, with mitral valve lesions occurring in over one third. TTE screening may be indicated in patients with SLE, especially for those with identified risk factors such as corticosteroid use. *Lupus* (2011) **20,** 1518–1525.

**Key words:** cardiovascular disease; systemic lupus erythematosus; ultrasonography

## Introduction

The cardiovascular system is frequently affected in patients with systemic lupus erythematosus (SLE). Involvement of the pericardium, endocardium, myocardium, coronary and pulmonary vessels has been found in several clinical and autopsy studies in these patients.[1]

Current guidelines for the management of SLE[2,3] suggest early identification and treatment of cardiovascular risk factors. However, the non-specific and multifactorial nature of symptoms such as dyspnea and fatigue in SLE patients, along with the low value of the clinical cardiac examination, could lead to delays in the recognition of cardiac involvement. Early identification of high-risk SLE patients is a challenge, and although risk factors for accelerated atherosclerosis are increasingly being identified, studies aiming to identify risk factors for other cardiac complications such as valvular dysfunction, pulmonary artery hypertension (PAH), pericardial disease or heart failure have provided conflicting results.

Previous authors have reported an association between antiphospholipid antibodies (aPL) and cardiac abnormalities such as valvular disease and PAH,[4–7] whereas others did not find any correlation.[8,9] One report also suggested an association between serum levels of both anti-Ro/SS-A and anti-La/SS-B antibodies and valvular lesions in patients with SLE,[10] but this finding has not been replicated. Most studies that have attempted to describe cardiac abnormalities and their correlation

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with clinical and laboratory factors in patients with SLE were limited by a relatively small number of participants.[11,12] The largest study published so far included 200 patients, but it was designed to examine the association of cardiovascular manifestations with aPL[4] and did not aim to estimate the effect of other clinical and laboratory determinants. Hence, the predictors of structural cardiac lesions in adult SLE patients are far from clear. Our study, the largest to date of echocardiography in patients with SLE, aims to describe the various echocardiographic abnormalities, and to examine the potential clinical and laboratory characteristics associated with them.

## Materials and methods

### *Study population*

The McGill University Health Center lupus cohort enrolls consecutive adults with American College of Rheumatology (ACR) revised criteria for SLE[13] at the time when they present for their first clinic visit. Clinical and laboratory data on these patients are collected prospectively on an annual basis.

### *Study variables*

Clinical and laboratory variables studied as potential correlates of echocardiographic abnormalities were age, sex, ethnic origin, lupus duration, SLE Disease Activity Index 2000 (SLEDAI-2K),[14] Systemic Lupus International Collaborating Clinics(SLICC)/ACR Damage Index (DI; total score and individual cardiovascular, pulmonary, renal and diabetes elements),[15] arterial hypertension (defined as systolic blood pressure $\geq$ 140 mm Hg or diastolic blood pressure $\geq$ 90 mm Hg measured for at least three visits,[16] or the current use of a medication to control hypertension), current smoking status, and use of medications (warfarin, heparin, acetylsalicylic acid (ASA), non-steroidal anti-inflammatories, antimalarials, beta-blockers, calcium channel blockers, angiotensin-converting enzyme (ACE) inhibitors, angiotensin receptor blockers (ARBs), nitrates, lipid-lowering agents, and immunosuppressive drugs including azathioprine, mycophenolate mofetil, methotrexate and cyclophosphamide), and steroid use (yes/no since last cohort visit, and mean steroid dose in the preceding year). At the time of the study visit, following an overnight fast, blood was drawn for analyses which included the following: high-sensitivity C-reactive protein (hs-CRP), total cholesterol, low-density lipoprotein, high-density lipoprotein, triglycerides, apolipoprotein B, antinuclear antibodies detected by indirect immunofluorescence, anti-DNA and ENA profile (anti-Ro/SSA, anti-La/SSB, anti-Sm, anti-RNP) measured using a standardized enzyme-linked immunosorbent assay (ELISA), anticardiolipin antibodies measured by ELISA, and lupus anticoagulant (LA; positive screening and confirmation to document the phospholipid dependence of the inhibitor). We defined positive aPL status as 1) either a positive anticardiolipin or a positive LA test at the time of the study; 2) either a positive anticardiolipin or a positive LA test at least once in the preceding 5 years; 3) either a positive anticardiolipin or a positive LA test on two or more occasions at least 12 weeks apart in the preceding 5 years.

### *Echocardiography*

Complete two-dimensional transthoracic echocardiographic (TTE) examination was performed at rest within 1 month of the clinical assessment by an experienced technician, and interpreted by a single echocardiographer (TH) who is trained to American Society of Echocardiography (ASE) level 3.[17] Both were blinded to the clinical and laboratory characteristics of the patients. All studies were performed on an HP-5500 and 2.5 mHz probe and completed according to ASE guidelines.[17] The following criteria were used for quantification of the echocardiographic abnormalities. Mitral valve thickness was measured by M-mode in the long axis parasternal view; a thickness $\geq$ 3 mm qualified as abnormal.[8] Valvular regurgitations were evaluated in all echocardiographic views by 2-d color imaging and Doppler flow interrogation, and the severity of any valvular regurgitation (mitral, aortic, tricuspid and pulmonary) was graded as mild, moderate or severe. We assessed pericardial morphology and function by sub-costal view and 4-chamber mitral and tricuspid inflows respiratory variations (to rule out constrictive pericarditis). Pericardial effusion was noted when there was echolucent space between the pericardial layers. Left ventricular hypokinesis was observed when systolic thickening was $<$50%. Systolic pulmonary artery pressure (PAP) was estimated by the Bernoulli equation ((4 $\times$ peak velocity of the tricuspid insufficiency[18]) plus estimated right atria pressure). The mean right atria pressure was estimated by evaluating the respiratory variation of the inferior vena cava.[17] Mean PAP was estimated to be equal to 0.6 PAP systolic + 2.

### *Statistical analyses*

Descriptive statistics are presented using means, medians, standard deviations (SD), interquartile ranges and proportions, as appropriate. We first estimated the effects of various demographic, clinical and laboratory factors on the presence of echocardiographic abnormalities using univariate logistic regression analysis. We also performed multivariate models which included sex, age, ethnic origin, SLE disease duration, SLEDAI-2K, SLICC/ACR DI, arterial hypertension, current smoking, hs-CRP, lipids, ENA, anti-DNA, aPL and drug exposure. We investigated confounding by comparing odds ratios (OR) for each main variable of interest as possible confounders exited or entered the model. Analyses were performed using SAS software, version 9.2 (SAS Institute, Cary, NC, USA).

The study was approved by the Institutional Ethics Board of the Montreal General Hospital and written consent was obtained according to the Declaration of Helsinki.

## Results

### *Baseline characteristics of the patients*

From January 2005 to June 2006, 260 patients with SLE were invited to participate in this study and 217 (83.5%) gave informed written consent to participate. Baseline characteristics of the patients are shown in Tables 1 and 2. The majority (91.7%) were women, 70.0% were Caucasian, 14.8% were African-American, 10.7% were Asian and 4.5% were of other ethnic origins. The mean age at assessment was 45.5 years (SD 14.5) and the mean lupus disease duration was 13.5 years (10.8). Mean SLEDAI-2K was 4.1 (4.5) and the median DI was 1.0 (interquartile range 0, 3). Comorbidities were as follows: 66 patients (30.4%) with arterial hypertension, 15 (6.9%) with proteinuria $\geq$ 3.5 g/day, 14 (6.5%) with renal insufficiency, seven (3.2%) with pulmonary fibrosis, five (2.3%) with coronary artery disease (CAD) including three patients with past history of myocardial infarction, and four (1.8%) with diabetes. Thirty-nine (18.0%) patients were current smokers. At the time of the assessment, 24 patients (11.1%) were using anticoagulants and 58 (26.7%) were using ASA. Antimalarials were used by 171 (78.8%) patients, corticosteroids by 47 (21.7%) and immunosuppressive agents by 61 (28.1%). ACE inhibitors were used by 41 subjects (18.9%), ARBs by 35 (16.1%), diuretics by 30 (13.8%), calcium channel blockers by 27 (12.4%), and beta-blockers by 10 (4.6%). Lipid-lowering agents were used by 19 (8.8%). Only one patient (0.5%) was taking nitrates. At the time of the assessment, 166 patients (76.5%) had positive anti-nuclear antibodies. The prevalence of positive aPL was 32.7% (70/214), among which 50 patients (71.4%) had positive anticardiolipin antibodies (positive IgM: 34 subjects; positive IgG: 28; positive for both: 12), and 39 (18.2%) had positive LA.

**Table 1** Clinical and laboratory data of the study participants

| *Variables* | *Study participants (n = 217)* |
|---|---|
| Age at assessment (years(SD)) | 45.5 (14.5) |
| Gender woman (%) | 91.7 |
| Caucasian (%) | 70.0 |
| Disease duration (years(SD)) | 13.5 (10.8) |
| SLEDAI-2K (mean(SD)) | 4.1 (4.5) |
| SLICC/ACR DI (mean(interquartile range)) | 1.0 (0.3) |
| *Antibodies (%)* | |
| ANA | 76.5 |
| Anti-Ro/SSA | 38.3 |
| Anti-La/SSB | 13.4 |
| Anti-Sm | 18.1 |
| Anti-RNP | 37.8 |
| Anti-DNA | 19.4 |
| Antiphospholipids | 32.7 |
| *Medications (%)* | |
| Anticoagulation | 11.1 |
| Acetylsalicylic Acid | 26.7 |
| Antimalarials | 78.8 |
| Immunosuppressive agents | 28.1 |
| Prednisone use | 21.7 |
| Prednisone dose (mg(SD)) | 6.8 (5.1) |
| Lipid-lowering agents | 19 (8.8) |
| ACE inhibitors or ARB | 35.0 |
| Calcium channel blockers | 12.4 |
| Beta-blockers | 4.6 |

SLE, systemic lupus erythematosus; SLEDAI-2K, SLE Disease Activity Index (year 2000 version, SLEDAI-2K); SLICC/ACR DI, Systemic Lupus International Collaborating Clinics (SLICC)/ACR Damage Index; Mean prednisone dose (SD) has been calculated among patients using prednisone; ACE, Angiotensin-converting enzyme; ARB, angiotensin receptor blockers.

### *Cardiac abnormalities*

Valvular abnormalities, defined as insufficiency, thickening or stenosis of the mitral, aortic, tricuspid or pulmonary valves, were detected in 87 patients (40.1%). The mitral valve was the most commonly affected, being involved in 81 patients (37.3% of the entire cohort). Abnormalities of this valve included insufficiency (56 patients, 25.8%) and thickening

(55 patients, 25.4%). Mitral regurgitation severity was distributed as the follows: mild, 38 patients (67.8%); moderate, 17 patients (30.4%); and severe, one patient (1.8%). In patients with mitral thickening, the mean thickness was 3.4 mm (SD 0.4). Mitral thickening was localized in the ventricular face of the valve and involved the whole anterior leaflet. Aortic insufficiency was detected in eight patients (3.7%) and aortic stenosis in one (0.5%). One patient (0.5%) had pulmonary valve insufficiency. No patient had significant tricuspid regurgitation. Among the 87 patients with valvular abnormalities, 31 subjects (35.6%) had two or more valvular lesions. The most frequent combination was mitral thickening plus mitral insufficiency, which occurred in 28 patients. No verrucous vegetations were observed in any patient.

Cardiac auscultation was performed by the rheumatologist at each annual assessment and cardiac murmurs were detected in only 11 patients (5.1%). Therefore, only 16.7% (11 out of 66) of cases of valvular insufficiency or stenosis would have been diagnosed clinically.

**Table 2** Cardiovascular risk factors among the study participants

| *Variables* | *Study participants (n = 217)* |
|---|---|
| Current smokers (*n*(%)) | 39 (18.0) |
| Hypertension (*n*(%)) | 66 (30.4) |
| Diabetes (*n*(%)) | 4 (1.8) |
| Hs-CRP (mean(SD)) | 4.04 (7.10) |
| Total cholesterol (mean(SD)) | 4.75 (1.07) |
| LDL cholesterol (mean(SD)) | 2.52 (0.81) |
| HDL cholesterol (mean(SD)) | 1.71 (0.48) |
| Total triglycerides (mean(SD)) | 1.20 (0.61) |
| Apolipoprotein B (mean(SD)) | 0.77 (0.23) |

Hs-CRP, high-sensitivity CRP; LDL, low-density lipoprotein; HDL, high-density lipoprotein.

Other findings included a systolic PAP $\geq$ 30 mm Hg in 22 patients (10.1%). Six patients (2.8%) had a PAP $\geq$ 40 mm Hg and two patients (0.9%) $\geq$ 50 mm Hg. Pericardial effusions were detected in 10 patients (4.6%) and the left ventricle's ejection fraction (LVEF) was $\leq$ 50% in six patients (2.8%), with the lowest LVEF value being 42.5%.

### *Clinical and laboratory associations*

Concerning valvular abnormalities, the use of corticosteroids in the last year was associated with an increased risk of mitral insufficiency (OR 2.58; 95% CI 1.29, 5.16) in multivariate analysis. However, we were unable to demonstrate a clear dose effect. In univariate models, the use of anticoagulants was associated with a decreased risk of aortic insufficiency (difference in proportion: 4.2%; 95% CI 1.3, 7.0) and with a tendency to have fewer overall valvular abnormalities (Table 3; difference in proportion: 11.23%; 95% CI -8.8, 31.3). However, in multivariate analysis, anticoagulation did not show a significant effect on these outcomes.

Factors associated with elevated PAP were studied. In multivariate analysis, age was associated with an elevated systolic PAP ($\geq$ 30 mm Hg; OR 1.04; 95% CI 1.01, 1.07), with a mean age of 44.7 years (95% CI 42.7, 46.7) in the group with normal PAP compared with 52.8 years (95% CI 46.1, 59.6) in the group with abnormal PAP. PAP $\geq$ 30 mm Hg was also associated with cumulative damage (OR 1.20; 95% CI 1.01, 1.42), with a mean DI in the groups with and without elevated PAP of 2.64 (2.28) and 1.66 (2.15), respectively. In the univariate analysis, there was a tendency towards higher PAP in the anticoagulated group (difference in proportion: 12.0%; 95% CI -4.8, 28.7).

Concerning other associations, left ventricular hypokinesis showed an association with the use of

**Table 3** Echocardiographic abnormalities according to anticoagulation therapy

| *Variables* | *All study participants (n = 217)* | *No anticoagulation (n = 192)* | *Anticoagulation (n = 24)* |
|---|---|---|---|
| Valvular abnormalities (*n*(%)) | 87 (40.1) | 80 (41.7) | 7 (30.4) |
| Mitral thickening | 55 (25.4) | 52 (27.1) | 3 (13.0) |
| Mitral insufficiency | 56 (25.8) | 50 (26.0) | 6 (26.1) |
| Aortic insufficiency | 8 (3.7) | 8 (4.2) | 0 (0.0) |
| Pericardial effusion (*n*(%)) | 10 (4.6) | 9 (4.7) | 1 (4.2) |
| Elevated PAP (*n*(%)) | 22 (10.1) | 17 (8.9) | 5 (20.8) |
| Left ventricular hypokinesis (*n*(%)) | 6 (2.8) | 5 (2.6) | 1 (4.2) |

Valvular abnormalities, thickening, insufficiency or stenosis of the mitral, aortic, tricuspid or pulmonary valves; Mitral thickening, thickness $\geq$ 3 mm; PAP, pulmonary artery pressure; Elevated PAP, systolic PAP $\geq$ 30 mm Hg; Left ventricular hypokinesis, systolic thickening of less than 50%.

ACE inhibitors in multivariate models (OR 12.89; 95% CI 1.06, 157.18) and with a past history of CAD in the univariate model (OR 89.5; 95% CI 10.72, 747,18); the latter association was not observed in the multivariate analysis. In the univariate analysis, pericardial effusions appeared more frequently in women (10 patients, 5%) compared with men (0%) (difference in proportion: 5.03%; 95% CI 1.99, 8.06). We did not demonstrate a relationship between any echocardiographic abnormalities and ethnic origin, lupus duration, disease activity or the traditional cardiovascular risk factors studied. Also, no auto-antibody appeared as a strong predictor of cardiac lesions. In particular, aPL, taken as a whole or studied individually (anticardiolipin or LA), were not associated with any abnormalities (Table 4). Besides the abovementioned associations involving corticosteroids, no other association between echocardiographic lesions and medication exposure was observed.

## Discussion

The aim of our study was to describe the presence of structural cardiac abnormalities in a large cohort of patients with SLE, and to identify possible associations with clinical or laboratory data. Our study, the largest to date of echocardiography in patients with SLE, confirmed that valvular disease is one of the most prevalent and important forms of cardiac involvement in these patients. Valvular lesions were detected in 40.1% of all patients, a prevalence similar to that found in other studies.[10] We noted a large spectrum of valvular diseases, ranging from thickened leaflets to moderate-to-severe dysfunction. The mitral valve was the most commonly affected, with more than a third of patients showing anomalies and more than one quarter showing regurgitation. By comparison, the prevalence of mitral regurgitation after adjustment for the age and sex distribution of the US 2000 population was only 1.7% (95% CI 1.5, 1.9) in the Framingham heart study.[19]

Corticosteroids are known to have an overall deleterious effect on the heart, causing systemic hypertension and left ventricular hypertrophy. On the other hand, corticosteroids in patients with SLE could help to decrease potential inflammatory cardiac lesions. In our study, use of prednisone in the preceding year was associated with an almost threefold increased risk of mitral insufficiency. This association was independent of underlying lupus disease activity as measured by the SLEDAI-2K. Although no dose effect was seen, this would have been difficult to observe considering the small number of patients on prednisone ($n = 47$) and the narrow range of doses used in our cohort (mean (SD): 6.8 (5.1)).

An interesting finding in this study was the high frequency of mitral thickening (25.4%). The clinical significance of valvular thickening remains uncertain, but it may represent an early stage of progressive mitral valve involvement. Indeed, among the 55 subjects with mitral thickening, 28 (50.9%) also had mitral insufficiency.

Although not significant in multivariate analysis, we noted a tendency for a lower rate of valvular abnormalities with the use of anticoagulation. Antithrombotic therapy could in theory have a protective effect on the development of cardiac lesions, but this relationship needs to be confirmed.

In patients with SLE, aPL are associated with arterial and venous thrombosis and with recurrent fetal loss, but the extent to which they influence valvular defects and myocardial disease is controversial and uncertain. Indeed, some reports describe the association of aPL with cardiac lesions, such as valvular thickening[20] and Libman–Sacks endocarditis.[21] However, other authors did not find any correlation.[8,9] In our study, no patient had an echocardiographic pattern suggestive of

**Table 4** Cardiac abnormalities detected by echocardiography according to autoantibodies

| *Variables* | *All study participants* (n = *217*) | *Anti-Ro* (n = *83*) | *Anti-Sm* (n = *39*) | *Anti-DNA* (n = *42*) | *Anti-RNP* (n = *82*) | *APL +* (n = *70*) | *LA +* (n = *39*) |
|---|---|---|---|---|---|---|---|
| Valvular abnormalities (*n*(%)) | 87 (40.1) | 39 (47.6) | 18 (46.2) | 41 (49.9) | 36 (43.9) | 34 (48.6) | 19 (48.7) |
| Mitral thickening | 55 (25.4) | 27 (32.9) | 14 (35.9) | 12 (29.3) | 25 (30.5) | 22 (31.4) | 11 (28.2) |
| Mitral insufficiency | 56 (25.8) | 25 (30.5) | 11 (28.2) | 11 (26.8) | 23 (28.0) | 17 (24.3) | 11 (28.2) |
| Aortic insufficiency | 8 (3.7) | 4 (4.9) | 2 (5.1) | 2 (4.8) | 3 (3.7) | 4 (5.7) | 2 (5.1) |
| Pericardial effusion (*n*(%)) | 10 (4.6) | 3 (3.6) | 3 (7.7) | 2 (4.8) | 4 (4.9) | 2 (2.9) | 1 (2.6) |
| Elevated PAP (*n*(%)) | 22 (10.1) | 11 (13.3) | 4 (10.3) | 4 (9.5) | 10 (12.2) | 10 (14.3) | 6 (15.4) |
| Hypokinesis (*n*(%)) | 6 (2.8) | 2 (2.4) | 0 (0.0) | 2 (4.8) | 3 (3.7) | 1 (1.4) | 0 (0.0) |

Libman–Sacks endocarditis, and we did not find a definite association between aPL and any valvular lesions. It should, however, be noted that testing for anti-beta 2 glycoprotein 1 was not performed. On the other hand, it is the practice at our center to give prophylaxis with ASA to all aPL-positive patients. Although there is currently no evidence to suggest that this practice decreases the risk of aPL-related cardiac involvement, the absence of such lesions in our patients could contribute to the generation of such a hypothesis, which could potentially be tested in the future.

It is also noteworthy to mention that very few patients had a clinically audible murmur, confirming the inadequacy of the physical examination and the usefulness of echocardiography to detect morphologic abnormalities of the heart. However, it is possible that these are often not clinically significant lesions. All patients with mild or moderate mitral regurgitation were New York Heart Association class I (no symptoms and no limitation in ordinary physical activity) and did not receive specific treatment at the time the echocardiography was performed. One patient with severe mitral insufficiency required mitral valve replacement.

PAP $\geq$ 30 mm Hg was seen in over 10% of our patients, while severe PAH was rare. One of the possible mechanisms invoked for the increased rates of elevated PAP seen in patients with SLE is the potential hypercoagulability related to aPL.[7] However, we did not detect this relationship in our study, suggesting that other mechanisms, including vasoconstriction and endothelial dysfunction, may also play important pathophysiological roles. In multivariate analysis, we found that elevated PAP was associated with age and cumulative damage, but no association was seen with disease activity or anti-RNP antibodies. Not including one subject who had previously diagnosed PAH, the echocardiographic examinations performed in this study allowed the detection of new cases of PAP elevation which were not previously scored as damage on the DI. The association between damage in various domains of the DI and elevated PAP, although mild (OR 1.20; 95% CI 1.01, 1.42) is thus not biased. The association between PAH and damage score was demonstrated in a recent publication, in which the mean DI score in patients with and without PAH were, respectively, 4.0 (2.4) and 0.4 (1.0).[22] The fact that we see more patients with elevated PAP in the anticoagulated group in the univariate analysis could certainly reflect an indication bias, whereby patients with past pulmonary thromboembolic events, who are already on anticoagulation, might overall have higher pulmonary pressures.

Except for the association between DI and elevated PAP, disease activity and damage did not show any association with echocardiographic abnormalities in our cohort. Our results are in agreement with a recent report in which the prevalence of preclinical cardiovascular abnormalities was not statistically different in patients with a DI of 0 compared with patients with a DI ranging from 1–4.[23] Hence, patients with SLE often have an elevated cardiovascular risk profile in spite of low clinical damage.

Given the strong association between SLE and premature CAD, we studied different variables related to CAD and its traditional risk factors as potential correlates of echocardiographic abnormalities. Neither a past history of CAD nor the traditional predictors studied were shown to be associated with valvular dysfunction, pericardial disease or PAH. Treatment for hypertension, diabetes and dyslipidemia has improved over the years, and this could have contributed to lessen their impact on echocardiographic manifestations. Although, due to small numbers, our data cannot totally discount the role of these risk factors, our finding supports the concept that echocardiographic abnormalities in SLE, such as premature atherosclerosis,[24] cannot be attributed solely to classic predictors and likely derives from a complex interaction between traditional and non-traditional risk factors. However, CAD being a common cause of left ventricular hypokinesis, we found an expected association between these two variables in the univariate analysis. The small number of patients with CAD in our cohort ($n = 5$) precludes conclusive association in multivariate models. An association between ACE inhibitors and hypokinesis was also expected, since this medication is regularly used in the treatment of heart failure. Indeed, the use of ACE inhibitors was associated with hypokinesis in our study, albeit with a large confidence interval (OR 12.89; 95% CI 1.06, 157.18). Because of the relatively low prevalence of patients on other medications with the potential to affect ventricular function in our cohort, we did not find an association between hypokinesis and medications such as beta-blockers.

Potential limitations of the present study include its cross-sectional design as well as the use of TTE, which is less sensitive than transesophageal echocardiography in detecting valvular lesions. However, most clinically significant cardiac lesions should have been detected by TTE. Also, our study has a small number of patients with severe valvular

disease, limiting our conclusions regarding potential clinical or laboratory associations in this subpopulation. It is possible that very sick patients with severe valvular disease early on in the course of SLE have a high mortality, and would not necessarily be present in our sample. This likely makes our estimates of the burden of pathology conservative. As a final limitation, we are unable to comment definitively on sex differences, due to the relatively small number of men ($n = 18$) in our cohort.

In conclusion, we have shown in a large cohort that cardiac abnormalities detectable with TTE are frequent in SLE. We found clinical and laboratory associations with certain cardiac abnormalities that would benefit from confirmation by future studies. Corticosteroid use showed the strongest association with valvular abnormalities, leading to an almost threefold increase in the risk of having mitral insufficiency. In a long-term follow-up study,[6] the number of patients with any valvular abnormality increased from 40% to 70% over an 8-year follow-up. Although the significance of the mitral thickening seen in 25.4% of our patients is uncertain, it may represent an early stage of progressive valve involvement. Consideration should be given to the early detection of echocardiographic abnormalities and to the close follow-up of these abnormalities, especially in those patients with identified risk factors, such as the use of steroids. We currently have a longitudinal study in progress with the goal of assessing risk for progression of established lesions over time.

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## Conflict of interest

The authors declare no conflicts of interest.

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