Revista Colombiana de
REUMATOLOGÍA

www.elsevier.es/rcreuma

Original Investigation

Echocardiographic findings in patients with systemic lupus erythematosus: Retrospective analysis in a tertiary referral centre

Oswaldo E. Aguilar-Molina[a], *Diana Quintero-González*[b], *Juan Corredor-Castro*[c], *María Antonia Escobar-Mera*[d,*], *Silvia Gironza Betancourt*[e], *David Del Castillo-Gil*[f,g], *Luis Fernando Medina-Quintero*[f,g], *Raúl Vallejo-Serna*[e,g]

[a] *Cardiology Section, Department of Internal Medicine, Universidad de Antioquia, Medellín, Colombia*
[b] *Rheumatology Section, Department of Internal Medicine, Universidad de Antioquia, Medellín, Colombia*
[c] *Cardiology Section, Department of Internal Medicine, Universidad del Valle, Cali, Colombia*
[d] *Residency in Internal Medicine, Department of Internal Medicine, Universidad Libre Seccional, Cali, Colombia*
[e] *Internal Medicine, Hospital Universitario del Valle, Cali, Colombia*
[f] *Rheumatology Section, Department of Internal Medicine, Universidad del Valle, Cali, Colombia*
[g] *Department of Internal Medicine, Universidad del Valle, Cali, Colombia*

ARTICLE INFO

Article history:
Received 10 April 2022
Accepted 3 August 2022
Available online 3 September 2024

Keywords:
Lupus
Echocardiography
Cardiac anomaly

ABSTRACT

Introduction: Transthoracic echocardiography is a useful noninvasive tool in the assessment of cardiac involvement in patients with systemic lupus erythematosus.
Objective: We aimed to investigate the main echocardiographic alterations in patients with a diagnosis of systemic lupus erythematosus and to describe the relationship between various disease factors and echocardiographic findings.
Materials and methods: We performed a retrospective review of patients with a diagnosis of SLE between 2016 and 2020 at a referral centre. All 98 patients were included, 87% were female, the mean age for the whole population was 35 years (IQR 27.0- 49.7), 40% had a recent diagnosis, 55% with previous or new diagnosis of arterial hypertension, 37% were using steroids at admission.
Results: Among the echocardiographic findings, 64.3% had valvular disease, 63% had pericardial involvement, 25.5% systolic function compromise, 27.5% some degree of diastolic dysfunction, 13% ventricular hypertrophy, 46% left atrial enlargement, 87% right ventricular systolic dysfunction, 24.5% some probability of pulmonary hypertension, 3% non-infectious vegetations. The presence of lupus activity was associated with a higher percentage of abnormal echocardiographic findings. There was no significant relationship between disease duration and cardiac abnormalities, anti-DNA and positive antiphospholipid antibodies were more frequently observed in the cardiac involvement group.

DOI of original article: https://doi.org/10.1016/j.rcreue.2022.08.002.
* *Corresponding author.*
E-mail address: antoniaescobarmera@gmail.com (M.A. Escobar-Mera).

Conclusion: We consider that echocardiography should be part of the routine evaluation in patients with lupus. Right ventricular systolic dysfunction, pericardial involvement and non-significant valvular disease were the most frequently reported abnormalities.

Hallazgos ecocardiográficos en pacientes con lupus eritematoso sistémico: análisis retrospectivo en un centro de referencia terciaria

Palabras clave:
Lupus
Ecocardiografía
Anomalía cardiaca

RESUMEN

Introducción: El ecocardiograma transtorácico es una herramienta no invasiva útil en la valoración del compromiso cardíaco en los pacientes con lupus eritematoso sistémico (LES).
Objetivo: Nos propusimos investigar las principales alteraciones ecocardiográficas en pacientes con este diagnóstico y describir la relación entre varios factores de la enfermedad y los hallazgos ecocardiográficos.
Materiales y métodos: Realizamos una revisión retrospectiva de pacientes con diagnóstico de LES entre los años 2016 y 2020 en un centro de referencia. Se incluyeron 98 pacientes, de los cuales el 87% fueron mujeres, la media de edad para toda la población fue de 35años (RIQ 27,0-49,7), el 40% tenía diagnóstico reciente, el 55% diagnóstico previo o nuevo de hipertensión arterial, en tanto que el 37% usaba esteroides al ingreso.
Resultados: Entre los hallazgos ecocardiográficos se encontró un 64,3% con enfermedad valvular, el 63% presentaba afección pericárdica, el 25,5% tenía compromiso de la función sistólica, el 27,5% mostraba algún grado de disfunción diastólica, el 13% experimentaba hipertrofia ventricular, el 46% acusaba crecimiento de la aurícula izquierda, el 87% sufría una disfunción sistólica del ventrículo derecho, el 24,5% tenía alguna probabilidad de hipertensión pulmonar, y el 3% presentaba vegetaciones no infecciosas. La presencia de actividad lúpica se asoció con mayor porcentaje de hallazgos ecocardiográficos anormales. No hubo una relación significativa entre la duración de la enfermedad y las anomalías cardíacas, se observó con mayor frecuencia anti-DNA y anticuerpos antifosfolípidos positivos en el grupo de afectación cardíaca.
Conclusión: Consideramos que la ecocardiografía debe hacer parte de la evaluación rutinaria en los pacientes con lupus. La disfunción sistólica del ventrículo derecho, el compromiso pericárdico y la enfermedad valvular no significativa fueron las anormalidades reportadas con mayor frecuencia.

Introduction

Systemic lupus erythematosus (SLE) is a heterogeneous autoimmune disease characterized by an intermittent course of relapses and remissions.[1] It mainly affects women of childbearing age and usually presents a more aggressive phenotype in the male population and in ethnic groups such as African Americans, Hispanics and Asians. It is a consequence of the interaction of genes and environmental factors that lead to the loss of immune tolerance of antibodies to self-antigens, mainly nucleic acids. Damage to multiple tissues such as skin, muscle, joints, kidney, heart, central nervous system and lung is due to the deposition of immune complexes or antibodies that lead to an increase in morbidity and mortality.[2]

The affection of the heart was described for the first time by Libman and Sacks in 1920, after finding valve and mural lesions in autopsies.[3] According to historical descriptions, cardiac manifestations occur in more than half of patients with SLE.[4] In contrast to the global epidemiology, in Latin America the prevalence of primary involvement of the heart is lower (14%). Given that it can affect any anatomical region, the clinical spectrum is broad, being valvular disease and pericarditis the most frequent findings.[5] Among the cardiac manifestations, patients with SLE also have a higher risk of cardiovascular events (coronary heart disease, stroke, heart failure and atrial fibrillation), which are the main cause of death with a rate of 4.1 events per 1,000/patients/year,[6] the disease being an independent factor with a relative risk of 1.98.[7] Endothelial dysfunction is explained by accumulated damage, chronic inflammation, development of traditional risk factors (hypertension, diabetes) and the adverse effects of immunosuppressants such as glucocorticoids.[8] The risk factors related to accelerated atherosclerosis in this population are age, cigarette smoking, high levels of C-reactive protein, and antiphospholipid antibodies.[9]

The serious implications of cardiac involvement on the prognosis of patients with SLE require a diligent approach in the presence of suggestive findings, even, some authors recommend screening of asymptomatic patients, especially if they have positive antiphospholipid antibodies, since early detection and initiation of specific interventions can have a positive impact on outcomes. In this sense, echocardiography continues to be the most widely used imaging modality. Its primary role in SLE includes the evaluation of valvular lesions, insufficiency/stenosis, systolic/diastolic function, contractility abnormalities, and pericardial disease.[10]

Mitral regurgitation, tricuspid regurgitation, thickening of the mitral valve, pericardial effusion and pulmonary hypertension are among the main echocardiographic findings. Some publications suggest a correlation between the SLEDAI (Systemic Lupus erythematosus Disease Activity Index) scale and pericardial effusion ($p = 0.001$) and between the SLICC (Systemic Lupus International Collaborating Clinics) damage index and left ventricular (LV) diastolic dysfunction.[11] Taking into account the knowledge gap regarding imaging findings of cardiac disease in the Colombian population, the following descriptive study about echocardiographic alterations in patients with SLE is proposed.

Materials and methods

We conducted a retrospective cross-sectional study, with the objective of describing echocardiographic changes using transthoracic echocardiography, in patients over 15 years of age with a confirmed diagnosis of SLE according to the classification criteria of the American College of Rheumatology.[12] These patients were evaluated in the hospital setting (emergency, hospitalization and intensive care) in a tertiary referral center in the city of Cali, during the period from January 1, 2016 to May 31, 2020. The medical records were reviewed in detail and patients with SLE who had overlap with other autoimmune diseases, such as rheumatoid arthritis, scleroderma, or mixed connective tissue disease were excluded. Those with diagnoses of congenital heart disease, previously known valvular disease or ischemic heart disease, pregnant women and incomplete medical records were also excluded.

Patient demographics, including age, sex, and smoking habit, were collected. The duration of the disease and the age at the time of diagnosis were recorded. The disease activity was assessed using the SLE Disease Activity Index-2K (SLEDAI-2K).[13,14] Severe lupus was defined as a severe manifestation of SLE of at least one organ, or treatment with cyclophosphamide or rituximab (for any manifestation except arthritis) at any time during the course of the disease. Mild disease was defined as mild manifestations, absence of involvement of any major organ, and maximal treatment with the following: oral glucocorticoids (GC) $\leq$10 mg/day (prednisone equivalent) or intramuscular GC or hydroxychloroquine (HCQ), at any time during the course of the disease. Patients who could not be included within these two definitions were classified as having moderate disease. These definitions were taken according to the glossary of the British Isles Lupus Assessment Group (BILAG).[15] Echocardiographic reports were evaluated retrospectively.

Two-dimensional echocardiography was used to evaluate the cardiac characteristics of all patients, the probability of pulmonary arterial hypertension (PHT) was considered when the pulmonary systolic arterial pressure was $\geq$35 mmHg, and the result of the right atrial pressure was added to the tricuspid regurgitation velocity (TRV), or the TRV was associated with other findings suggestive of PHT.[16] The ejection fraction (<53%) was considered abnormal.[17] Data on LV diastolic[18] and systolic function, ejection fraction, disorders or abnormalities of local or global myocardial contractility, pericardial effusion, heart valve status, and size of the chambers were collected. The reference values were established according to the cardiac chamber quantification guidelines of the American Society of Echocardiography (ASE).[17]

The valvular disease was assessed according to the criteria of the European guidelines available at the time of the data analysis.[19] Pericardial involvement was defined as the case of those patients with distinctive signs and symptoms that can be grouped into specific "syndromes". The classic pericardial syndromes include pericarditis, pericardial effusion, cardiac tamponade, and constrictive pericarditis.[20] Meanwhile, myocarditis was defined as 2 or more of the following: elevated level of serum troponin according to the normal values of the local laboratory; new or worsening changes on echocardiography, including new wall motion abnormalities and altered left ventricular ejection fraction (LVEF).[21] Approval from the institutional ethics committee for the study was obtained.

The variables were collected in a pre-designed database in Microsoft Excel, with data subjected to double checking to minimize errors in their introduction. Statistical analyses were performed using the statistical software Stata 14. A description of the clinical and demographic characteristics obtained in the medical history was carried out. The qualitative variables are presented with percentages and the quantitative variables with the mean and the standard deviation or with the median and the interquartile range (IQR) according to the distribution observed.

The quantitative variables were evaluated with the Shapiro-Wilk test to determine if they followed a normal distribution. In the first instance, a descriptive statistical analysis was performed; an *a priori* level of statistical significance of $\alpha = 0.05$ was established if any comparison between the study variables is required.

Results

330 patients with a diagnosis of SLE, of which 235 had a transthoracic echocardiogram, were admitted during the study period. Once the inclusion and exclusion criteria were applied, data from 98 patients were recorded for analysis (see Fig. 1). Of the 98 patients, 87% were women, with a median age of 35 years for the entire population (IQR: 27.0–49.7); 91% (89) had active disease; 73.5% (72) experienced severe compromise; 40% had recently received a diagnosis of SLE (less than 3 months), 35.7% between 3 months and 5 years; 37% received steroids and 43% another immunomodulator (See Table 1). As for the characteristics of the disease, during the index assessment, the median of total leukocytes was 6,015 mm^3 (IQR:

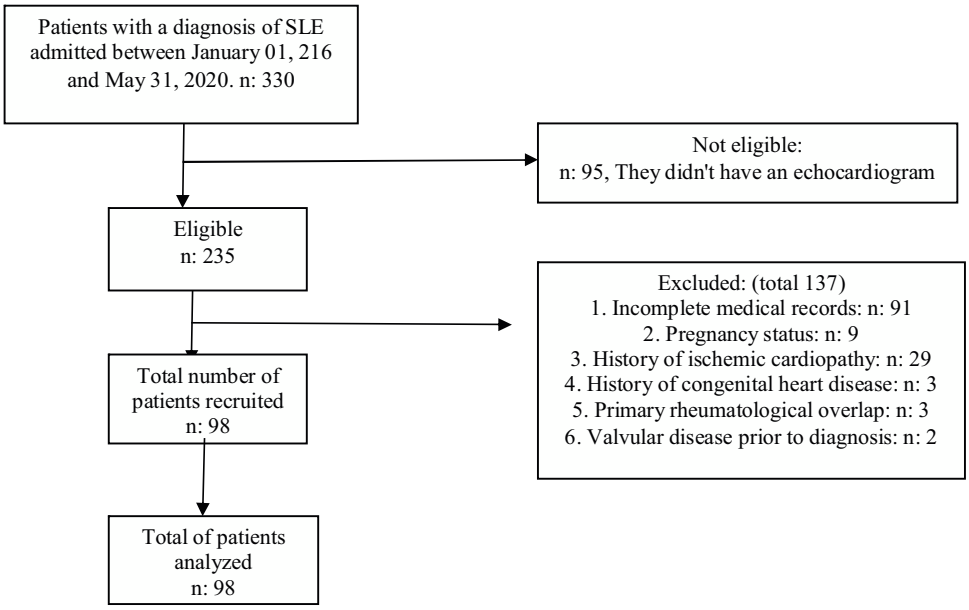

Fig. 1 – Patients algorithm. Source: own elaboration.

Table 1 – Demographic manifestations.

	Not serious	Serious	Total
Total of patients	26 (26.5%)	72 (73.5%)	98 (100%)
Women	21 (80.8%)	64 (88.9%)	85 (86.7%)
Men	5 (19.2%)	8 (11.1%)	13 (13.3%)
Age	47.0 (35.5–59.0)	32.0 (25.0–44.0)	35 (27.0–49.7)
Active disease	17 (65.3%)	72 (100%)	89 (90.8%)
Duration of the SLE, *n* (%)			
Less than 3 months	6 (23.1)	33 (45.8)	39 (39.8)
3 months to 1 year	2 (7.7)	14 (19.4)	16 (16.3)
1 year to 5 years	5 (19.2)	14 (19.4)	19 (19.4)
5 years to 10 years	5 (19.2)	6 (8.3)	11 (11.2)
More than 10 years	8 (30.8)	4 (5.6)	12 (12.2)
Ethnicity, *n* (%)			
Afro-descendant	6 (23.1)	18 (25)	24 (24.5)
Caucasian	2 (7.7)	1 (1.4)	3 (3.1)
Indigenous	1 (3.8)	1 (1.4)	2 (2)
Mestizo	10 (38.5)	17 (23.6)	27 (27.6)
Other	1 (3.8)	4 (5.6)	5 (5.1)
No data	6 (23.1)	31 (43.1)	37 (37.8)
Use of steroids, *n* (%)	7 (26.9)	29 (40.3)	36 (36.7)
Immunomodulators, *n* (%)	13 (50)	29 (40.3)	42 (42.9)
Origin, *n* (%)			
Rural	5 (19.2)	31 (43.1)	36 (36.7)
Urban	21 (80.8)	40 (55.6)	61 (62.2)

Source: own elaboration.

4,475–9,555), hemoglobin: 9.6 mg/dl (SD 2.9), and the mean platelet level was 24,7663.3 (3,000–679,000).

In relation to the immunological assessment, C3 hypocomplementemia was globally documented in 68.45% of cases, a finding more frequent in severe cases (in 82% of these). The level of C4 was found low in 53.1% of the total (65% in the group of severe disease). 45% had positive anti-DNA, while 14% and 16% had a diagnosis of secondary Sjögren's and antiphospholipid syndrome, respectively (see Table 2). Among the main echocardiographic findings, the size of the LV in diastole was 45 mm (IQR: 42.0–49.7), 13% had ventricular hypertrophy, 46% left atrial enlargement, 25.5% compromise of the systolic function, and 16,3% contractility disorders, of which 50% were generalized hypokinesia.

Some degree of diastolic dysfunction was reported in 27.5%, while systolic dysfunction of the right ventricle (RV) was found in 87% when it was evaluated only by TAPSE. 64.3% (63) had valvular involvement, and of this group, 70% corresponded to mild mitral regurgitation, 25% to some degree of tricuspid regurgitation and only 9% to more than mild aortic or

Table 2 – Characteristics of the disease.

	Non-severe	Severe	Total	*p*
Hemogram				–
Total leukocytes	5,720 (4,790–7,292)	6,825 (4,378–10,648)	6,015 (4,475–9,555)	
Hemoglobin	10.3 (3.8)	9.4 (2.6)	9.6 (2.9)	
Platelets	258,807.7 (71,000–606,000)	243,638.9 (37,000–631,000)	247,663.3 (3,000–679,000)	
Low complement C3, *n* (%)	8 (30.8)	59 (81.9)	67 (68.4)	**0.0001**
Low complement C4, *n* (%)	5 (19.2)	47 (65.3)	52 (53,1)	**0.0001**
Positive anti-DNA, *n* (%)	7 (26.9)	37 (51.4)	44 (44.9)	–
Sjogren's syndrome, *n* (%)	4 (15.4)	10 (13.9)	14 (14.3)	–
Antiphospholipid syndrome, *n* (%)	2 (7.7)	14 (19.4)	16 (16.3)	–

Source: own elaboration.

In bold: Statistically significant.

mitral involvement. 24.5% showed some probability of pulmonary hypertension, 4% with criteria for severe PHT; and 3% presented non-infectious vegetations. 63% had pericardial involvement, of which 84% corresponded to mild pericardial effusion. Of the total number of pericardial effusions, 77% occurred in severe SLE and 23% in non-severe disease.

The criterion for pericarditis was met in only 2% of cases, and the established criteria for myocarditis were met in 4% (See Table 3). Of the patients who had compromised LV systolic function (25.5%), 80% had severe SLE. Active disease (91%) was more likely to present cardiac involvement, a finding independent of the duration of the SLE. Regarding the time with the disease and the cardiac involvement, the same result was obtained if the analysis was done according to the established severity criteria, so that greater cardiac involvement was found in those patients who were classified as severe SLE.

Discussion

The heart is frequently involved in SLE, therefore, cardiac manifestations develop in most patients at some point during the course of the disease.[22] Historically, cardiac involvement in SLE depends, in particular, on pericardial disease, usually due to asymptomatic effusion; on valvular disease, most frequently mitral insufficiency without hemodynamic significance; on myocardial dysfunction and on coronary artery disease.[23] The frequency of appearance of echocardiographic anomalies in this study tends to be similar to other previous observations,[22,23] being mitral and tricuspid valve involvement the most frequent, with a higher predominance of mild mitral and tricuspid insufficiency, with a low proportion of moderate or severe valvular disease.

LV systolic dysfunction was found in 25.5% of cases, possibly related to a higher rate of patients with severe active SLE and the in-hospital nature of the publication, 20% higher compared to previous reports.[11,24] One of our main findings was a high percentage of RV systolic dysfunction assessed by TAPSE (less than 17 mm), both in severe and non-severe SLE (87.5% and 84.6%, respectively). RV systolic dysfunction has shown adequate correlation with hemodynamic variables of RV function and has been associated with a shorter 6 min walk test, lower mixed venous oxygen saturation and higher level of plasma N-terminal brain natriuretic peptide.[25] Low TAPSE has already been reported in patients with SLE compared to healthy controls,[26] which has put into evidence that patients with SLE have a higher prevalence of subclinical RV systolic dysfunction. It is known that pericardial involvement is the most frequent cause of symptomatic heart disease and, in turn, the most common echocardiographic finding in SLE. In our study, 63.3% had pericardial involvement, mainly due to pericardial effusion, which was less than in other publications from our region (83%)[5] and much higher than what was previously reported in other geographical areas (11–54% of cases).[27] However, in these publications pericarditis is reported as the main involvement. Both pericardial effusion and pericarditis, like other types of serositis, occur more frequently when SLE is severely active or when it is active in other organs. Our low rate of pericarditis (higher proportion of mild pericardial effusion) may be associated with underdiagnosis in the clinical history records.

We reported that 24% of the population is Afro-descendant. Previously, it has been demonstrated that non-white patients have worse SLE-specific outcomes in the long term that white patients[28]; likewise, it has been reported that Afro-descendants are younger at the time of admission for cardiovascular disease than white individuals, which suggests important disparities that could explain the echocardiographic changes reported, although it seems like an observation to consider in future publications since it was not included in the objectives and methodology of this publication.

There was no significant relationship between the duration of the disease and cardiac abnormalities, age was not significantly associated with echocardiographic alterations, and positive anti-DNA and antiphospholipid antibodies were more frequently observed in the group with cardiac involvement. The presence of lupus activity was associated with a higher percentage of abnormal echocardiographic findings. The reports for the association between disease activity and cardiac involvement are contradictory. For Zaid and Abudelnbi,[29] only PHT and myocarditis were correlated with the lupus disease activity, which did not happen with valvular, pericardial or coronary artery diseases.

The main limitations of this publication lie in its retrospective nature, the lack of a control group and the underreporting derived from the clinical history reports. It should also be mentioned that data on traditional risk factors and their association with cardiac alterations were not analyzed, mainly

Table 3 – Echocardiographic findings.

	Non serious (*n* = 26)	Serious (*n* = 72)	Total (*n* = 98)
Size of the left ventricle diastolic diameter, median (IQR)	44.0 (40.2–47.5)	45.0 (42.0–50.0)	45.0 (42.0–49.7)
Left ventricular hypertrophy, *n* (%)	5 (19.2)	8 (11.1)	13 (13.3)
Left atrial dilation, *n* (%)	13 (50.0)	32 (44.4)	45 (45.9)
Reduced LVEF less than 53%, *n* (%)	5 (19.2)	20 (27.7)	24.5 (25.5)
Reduced myocardial contractility, *n* (%)	4 (15.3)	12 (16.6)	16 (16.3)
Global hypokinesia	1 (3.84)	7 (9.7)	8 (50)
Others	3 (11.5)	5 (6.9)	8 (50)
Diastolic dysfunction, n (%)	7 (26.9)	20 (27.7)	27 (27.5)
Systolic dysfunction RV TAPSE <17 mm, *n* (%)	22 (84.6)	63 (87.5)	85 (86.7)
Valvular abnormality, *n* (%)	16 (61.5)	47 (65.2)	63 (64.3)
Mitral regurgitation	12 (46.1)	37 (51.3)	49 (50)
Aortic regurgitation	1 (3.8)	5 (6.9)	6 (9)
Tricuspid regurgitation	4 (15.3)	12 (16.6)	16 (25)
Pulmonary hypertension, *n* (%)	7 (26.9)	17 (23.6)	24 (24.5)
Vegetations, *n* (%)	0	3 (4.2)	3 (3.1)
Pericardial involvement, *n* (%)	14 (53.8)	48 (66.8)	62 (63.2)
Mild effusion	13 (50)	39 (54.2)	52 (84)
Moderate effusion	1 (3.8)	4 (5.6)	5 (5.1)
Severe effusion	0 (0)	3 (4.2)	3 (3.1)
Pericarditis	0 (0)	2 (2.8)	2 (2.0)
Myocarditis	0 (0)	4 (100)	4 (4.0)

Source: own elaboration.

because patients with coronary heart disease were excluded from the analysis.

Conclusion

Echocardiography is an excellent non-invasive tool for cardiac evaluation. Our data highlight the need for increased evaluation and early intervention to reduce subsequent cardiac morbidity and mortality among the patients with lupus. We consider that echocardiography should be part of the routine evaluation of patients with SLE. Mild valvular disease, pericardial involvement, and RV systolic dysfunction were the most frequently reported abnormalities. Screening echocardiography should be recommended, especially at initial in-hospital presentation, during exacerbation of SLE, or in the presence of cardiac symptoms.

Funding

Own of the authors.

Conflict of interest

The authors do not declare any conflict of interest.

Acknowledgements

Thanks to the Research Center of the Hospital Universitario del Valle.

REFERENCES

1. Fanouriakis A, Tziolos N, Bertsias G, Boumpas DT. Update in the diagnosis and management of systemic lupus erythematosus. Ann Rheum Dis. 2021;80:14–25, http://dx.doi.org/10.1136/annrheumdis-2020-218272.
2. Tsokos GC. Autoimmunity and organ damage in systemic lupus erythematosus. Nat Immunol. 2020;21:605–14, http://dx.doi.org/10.1038/s41590-020-0677-6.
3. Libman E, Sacks B. Hitherto undescribed form of valvular and mural endocarditis. Arch Intern Med. 1924;33:701–37, http://dx.doi.org/10.1001/archinte.1924.00110300044002.
4. Zagelbaum Ward NK, Linares-Koloffon C, Posligua A, Gandrabur L, Kim WY, Sperber K, et al. Cardiac manifestations of systemic lupus erythematous: an overview of the incidence, risk factors, diagnostic criteria, pathophysiology and treatment options. Cardiol Rev. 2022;30:38–43, http://dx.doi.org/10.1097/CRD.0000000000000358.
5. García MA, Alarcón GS, Boggio G, Hachue L, Marcos AI, Marcos JC, et al. Primary cardiac disease in systemic lupus erythematosus patients: protective and risk factors-data from a multi-ethnic Latin American Cohort. Rheumatology (Oxford). 2014;53:1431–8, http://dx.doi.org/10.1093/rheumatology/keu011.
6. Bernatsky S, Boivin JF, Joseph L, Manzi S, Ginzler E, Gladman DD, et al. Mortality in systemic lupus erythematosus. Arthritis Rheum. 2006;54:2550–7, http://dx.doi.org/10.1002/art.21955.
7. Restivo V, Candiloro S, Daidone M, Norrito R, Cataldi M, Minutolo G, et al. Systematic review and meta-analysis of cardiovascular risk in rheumatological disease: symptomatic and non-symptomatic events in rheumatoid arthritis and systemic lupus erythematosus. Autoimmun Rev. 2022;21:102925, http://dx.doi.org/10.1016/j.autrev.2021.102925.
8. Sairam S, Sureen A, Gutierrez J, Dang TQ, Mishra K. Cardiovascular outcomes in systemic lupus erythematosus. Curr Cardiol Rep. 2022;24:75–83, http://dx.doi.org/10.1007/s11886-021-01626-9.

9. Toloza SMA, Uribe AG, McGwin G, Alarcón GS, Fessler BJ, Bastian H, et al. Systemic lupus erythematosus in a multiethnic US cohort (LUMINA): XXIII. Baseline predictors of vascular events. Arthritis Rheum. 2004;50:3947–57, http://dx.doi.org/10.1002/art.20622.
10. Khayata M, Wang TKM, Chan N, Alkharabsheh S, Verma BR, Oliveira G, et al. Multimodality cardiac imaging in patients with systemic lupus erythematosus. Curr Probl Cardiol. 2021:101048, http://dx.doi.org/10.1016/j.cpcardiol.2021.101048.
11. Mohammed MA, Rady SAK, El-Mokadem MO, Fadda SMH. Echocardiographic findings in systemic lupus erythematosus and its relation to disease activity and damage index. Egypt Rheumatol. 2018;40:173–8, http://dx.doi.org/10.1016/j.ejr.2017.10.009.
12. Aringer M, Costenbader K, Daikh D, Brinks R, Mosca M, Ramsey-Goldman R, et al. 2019 European League Against Rheumatism/American College of Rheumatology Classification criteria for systemic lupus erythematosus. Arthritis Rheumatol (Hoboken). 2019;71:1400–12, http://dx.doi.org/10.1002/art.40930.
13. Gladman DD, Ibañez D, Urowitz MB. Systemic lupus erythematosus disease activity index 2000. J Rheumatol. 2002;29:288–91.
14. Yee CS, Farewell VT, Isenberg DA, Griffiths B, Teh LS, Bruce IN, et al. The use of Systemic Lupus Erythematosus Disease Activity Index-2000 to define active disease and minimal clinically meaningful change based on data from a large cohort of systemic lupus erythematosus patients. Rheumatology (Oxford). 2011;50:982–8, http://dx.doi.org/10.1093/rheumatology/keq376.
15. Murphy CL, Yee CS, Gordon C, Isenberg D. From BILAG to BILAG-based combined lupus assessment 30 years on. Rheumatology. 2016;55:1357–63, http://dx.doi.org/10.1093/rheumatology/kev387.
16. Augustine DX, Coates-Bradshaw LD, Willis J, Harkness A, Ring L, Grapsa J, et al. Echocardiographic assessment of pulmonary hypertension: a guideline protocol from the British Society of Echocardiography. Echo Res Pract. 2018;5:G11–24, http://dx.doi.org/10.1530/ERP-17-0071.
17. Lang RM, Badano LP, Mor-Avi V, Afilalo J, Armstrong A, Ernande L, et al. Recomendaciones para la cuantificación de las cavidades cardíacas por ecocardiografía en adultos: actualización de la Sociedad Americana de Ecocardiografía y de la Asociación Europea de Imagen Cardiovascular, http://sisiac.org/files/GUIA_011.pdf.
18. Nagueh SF, Smiseth OA, Appleton CP, Byrd BF, Dokainish H, Edvardsen T, et al. Recommendations for the evaluation of left ventricular diastolic function by echocardiography: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. J Am Soc. 2016;29:277–314, http://dx.doi.org/10.1016/j.echo.2016.01.011.
19. Baumgartner H, Falk V, Bax JJ, De Bonis M, Hamm C, Holm PJ, et al., ESC Scientific Document Group. 2017 ESC/EACTS Guidelines for the management of valvular heart disease. Eur Heart J. 2017;38:2739–91, http://dx.doi.org/10.1093/eurheartj/ehx391.
20. Adler Y, Charron P, Imazio M, Badano L, Barón-Esquivias G, Bogaert J, et al., ESC Scientific Document Group. 2015 ESC Guidelines for the Diagnosis and Management of Pericardial Diseases: The Task Force for the Diagnosis and Management of Pericardial Diseases of the European Society of Cardiology (ESC)Endorsed by: The European Association for Cardio-Thoracic Surgery (EACTS). Eur Heart J. 2015;36:2921–64, http://dx.doi.org/10.1093/eurheartj/ehv318.
21. Caforio ALP, Pankuweit S, Arbustini E, Basso C, Gimeno-Blanes J, Felix SB, et al., European Society of Cardiology Working Group on Myocardial and Pericardial Diseases. Current state of knowledge on aetiology, diagnosis, management, and therapy of myocarditis: a position statement of the European Society of Cardiology Working Group on Myocardial and Pericardial Diseases. Eur Heart J. 2013;34:2636–48, http://dx.doi.org/10.1093/eurheartj/eht210.
22. Jain D, Halushka MK. Cardiac pathology of systemic lupus erythematosus. J Clin Pathol. 2009;62:584–92, http://dx.doi.org/10.1136/jcp.2009.064311.
23. Brigden W, Bywaters EG, Lessof MH, Ross IP. The heart in systemic lupus erythematosus. Br Heart J. 1960;22:1–16, http://dx.doi.org/10.1136/hrt.22.1.1.
24. Cervera R, Font J, Paré C, Azqueta M, Pérez-Villa F, López-Soto A, et al. Cardiac disease in systemic lupus erythematosus: prospective study of 70 patients. Ann Rheum Dis. 1992;51:156–9.
25. Wang H, Wang Q, Tian Z, Guo X, Lai J, Li M, et al. Right ventricular function is associated with quality of life in patients with systemic lupus erythematosus associated pulmonary arterial hypertension. Heart Lung Circ. 2019;28:1655–63, http://dx.doi.org/10.1016/j.hlc.2018.09.002.
26. Elnady BM, Abdelghafar ASM, Khalik ESA, Algethami MM, Basiony AS, Al-Otaibi MDA, et al. The implication of tissue Doppler echocardiography and cardiopulmonary exercise in early detection of cardiac dysfunction in systemic lupus erythematosus patients. Eur J Rheumatol. 2016;3:109–17, http://dx.doi.org/10.5152/eurjrheum.2016.16002.
27. Smiti M, Salem TB, Larbi T, Sfaxi AB, Ghorbel IB, Lamloum M, et al. [Pericarditis in systemic lupus erythematosus: prevalence and clinical and immunologic characteristics]. Presse Med. 2009;38:362–5, http://dx.doi.org/10.1016/j.lpm.2008.08.010.
28. Barbhaiya M, Feldman CH, Guan H, Gómez-Puerta JA, Fischer MA, Solomon DH, et al. Race/ethnicity and cardiovascular events among patients with systemic lupus erythematosus. Arthritis Rheumatol (Hoboken). 2017;69:1823–31, http://dx.doi.org/10.1002/art.40174.
29. Cardiovascular disease is common among patients with systemic lupus erythematosus. MOJ Orthop Rheumatol. 2016;5(3), http://dx.doi.org/10.15406/mojor.2016.05.00177.