УДК 615.5-002.525.2:616.1]-06-07



L. Kobak<sup>1</sup>, O. Khukhlina<sup>2</sup>, L. Babinets<sup>3</sup>, M. Panasiuk<sup>1</sup>, N. Drobinska<sup>1</sup>, O. Faiura<sup>1</sup>, Z. Bilous<sup>1</sup>

- <sup>1</sup> Danylo Halytsky Lviv National Medical University, Lviv, Ukraine
- <sup>2</sup> Bukovinian State Medical University, Chernivtsi, Ukraine
- <sup>3</sup> I. Ya. Gorbachevsky Ternopil National Medical University, Ternopil, Ukraine

### Clinical Markers of the Heart and Blood Vessels Syntropic Lesions in Patients with Systemic Lupus Erythematosus, Their Diagnostic Value (First Notice)

Introduction. Systemic lupus erythematosus (SLE) is an autoimmune rheumatic disease with numerous clinical manifestations and an unpredictable course, which affects any organs or systems, which quite often occurs over several months or years with stable or, on the contrary, variable clinical manifestations, a wave-like course, alternating remissions and exacerbations. It is a multifactorial disease caused by a complex interaction of genetic and environmental factors underlying various disorders of innate and acquired immunity, including hyperproduction of cytokines, pathological activation of B cells, disruption of intracellular signaling of T cells, defects in the clearance of cells subjected to apoptosis and necrosis [12].

Since the Middle Ages, the Latin name lupus (which means "wolf") has been used to describe various diseases that were manifested by ulcers on the lower limbs. The name "lupus erythematosus" was used by the French dermatologist Pierre-Louis Cazenava in 1851. An important event in the history of lupus occurred at the beginning of the 19th century, when an understanding of the difference between cutaneous and vulgar lupus in the modern sense gradually emerged. The work of scientists contributed to the discovery of the systemic nature of the disease. Later, it was determined that deoxyribonucleic acid (DNA) is the main target of antinuclear antibodies, and in modern studies interferons play a decisive role in the pathogenesis of SLE [2]. The prevalence of SLE is 9-241 cases per 100,000 people per year, the incidence is 0.3–23.2 cases per 100,000 people per year, according to studies conducted worldwide over the past 15 years [13].

Heart lesions in patients with SLE have been described since the beginning of the 20th century. Manifestations are numerous and may involve all components of the heart, including the pericardium, conduction system, myocardium, valves, and coronary arteries [4].

The prognosis of SLE has improved with better treatment and care, but cardiovascular disease is still an important clinical problem, as the risk of cardiovascular disease (CD) is significantly higher in this disease than in controls. Atherosclerosis is the main cause of CD in the general population, and in patients with SLE, as proven [1], the severity of atherosclerosis, especially the prevalence of atherosclerotic plaques, is greater. In addition to atherosclerosis, as the main cause of CD in patients with SLE, there are other mechanisms that are not mutually exclusive. The most important among them are antiphospholipid antibodies, which lead to the the syndrome of antiphospholipid antibodies with arterial and venous thrombosis. Antiphospholipid antibodies can cause direct proinflammatory and prothrombotic effects on endothelial and other cells, as well as interfere with blood coagulation, for example, by inhibiting the antithrombotic and protective effects of annexin A5. Antibodies against phosphorylcholine and other small epitopes associated with lipids, which are sometimes called natural antibodies, contribute to the development of cardiovascular atherosclerosis in patients with SLE. As a result of the combination of traditional risk factors, such as arterial hypertension (AH) and dyslipidemia, and non-traditional factors, especially antiphospholipid antibodies, inflammation, and a low titer of antibodies against phosphorylcholine, the risk of CD in patients with SLE increases, although there are some differences in the results [1, 3].

Clinical manifestations and symptoms of heart lesions, in particular with valve lesions [5, 6, 8], and vessels in patients with SLE are diverse. Not all of them appear at the same time, sometimes there may be a time interval of several months or even years between them. The rate of increase in severity SLE and the onset of new symptoms can vary greatly. In the majority of patients, early complaints are general constitutional symptoms (fatigue, unmotivated weakness), damage to mucous membranes, skin (including photosensitization) and musculoskeletal system. It should be noted that there is no specific combination of symptoms for SLE, SLE is primarily a combination of symptoms [5].

© Kobak L., Khuklina O., Babinets L. et al., 2024

Cardiovascular events can occur both in the early and late stages of the disease, and younger patients are at significantly greater risk than their peers [6]. Special attention should be paid to the so-called syntropic lesions of the CD in patients with SLE, i.e., those that share etiological and/or pathogenetic mechanisms with the main disease, which is confirmed by a reliable direct relationship between the frequency of CD and the degree of activity of SLE [9]. However, they are insufficiently described in modern literature, and the effectiveness of treatment of this category of patients is not optimal.

Increasing the effectiveness of their treatment requires the clinician in certain situations, in particular, to find new, effective, low-cost methods of their detection, to have information about the diagnostic value of clinical markers of syntropic lesions of the cardiovascular system (CVS).

The aim of the study. To find out the clinical markers of the heart and blood vessels syntropic lesions in patients with systemic lupus erythematosus, their diagnostic value.

Materials and methods. After signing the informed consent to participate, in accordance with the requirements of the Helsinki Declaration of Human Rights, the Council of Europe Convention on Human Rights and Biomedicine, in a randomized manner with preliminary stratification by the presence of SLE (diagnosis was set taking into account the diagnostic criteria of the American College of Rheumatology (1997) and establishing the diagnosis in the presence of 4 out of 11 criteria (Order of the Ministry of Health of Ukraine N 676 dated 12.10.2006 "On the approval of protocols for the provision of medical care in the specialty "Rheumatology", recommendations of the European Antirheumatic League (2010), the American College of Rheumatology (2010, 2012)) with the presence of syntropic (those that have the same etiological and/or pathogenetic mechanisms as the main disease) lesions of the CVS (Order of the Ministry of Health of Ukraine N 436 dated 03.07.2006 "On approval of protocols for providing medical care in the specialty "Cardiology" with changes introduced in accordance with the Order of the Ministry of Health of Ukraine N 455 dated 02.07.2014). The study included 118 patients of the rheumatology department of the Communal Non-Commercial Enterprise of the Lviv Regional Council "Lviv Regional Clinical Hospital" since 2016 till 2021 year (107 women (90.68 %)) and 11 men (9.32 %) aged 18 to 74 years (average age  $42.48 \pm 1.12$  years)), including A. G. M. Raynaud's syndrome found in 67 patients, mitral valve (MV) insufficiency - in 55 patients, MV consolidation – in 47 patients, symptomatic hypertension - in 43 patients, livedo reticularis - in 35 patients, retinal angiopathy - in 32 patients, myocarditis - in 29 patients, pericardial effusion - in 22 patients, pulmonary hypertension - in 16 patients, atherosclerosis - in 13 patients, venous thrombosis - in 7 patients, capillaritis - in 4 patients, endocarditis - in 2 patients [9, 10]. Clinical markers included information from passports, complaints, medical and life anamnesis, as well as the results of an objective examination. To determine the constellations of clinical markers, I. Newton's binomial coefficient was used using the Solver add-on for MS Excel.

During the study in patients with SLE and lesions of the heart (MV insufficiency, MV consolidation, myocarditis, pericardial effusion, endocarditis) (the first stage - the first notice) and blood vessels (A. G. M. Raynaud's syndrome, symptomatic hypertension, livedo reticularis, retinal angiopathy, pulmonary hypertension, atherosclerosis, venous thrombosis, capillaritis) (second stage - second notice) clinical markers were identified and those that occurred significantly more often (p < 0.050) in terms of the number of cases in patients with SLE with the studied syntropic lesion of the CVS were selected, compared to patients with SLE without it, and had a positive relationship with syntropic lesions (coefficient of association (CA) greater than 0). (the first step), the diagnostic value of some clinical markers (the second step) and their constellations (the third step) was determined in terms of sensitivity, specificity and accuracy, and one of them with the reliably greatest diagnostic value was selected based on the highest value of the sum of sensitivity and specificity (diagnostic accuracy reliably higher than 50.00 % by one-tailed test for proportion, p < 0.050). The difference was considered statistically significant if p < 0.050. To determine the closeness of the connection between the clinical marker and the syntropic lesion of CVS, CA was used. The relationship was considered confirmed if  $CA \ge 0.50$  [11].

Results of the first stage of research and their discussion. To carry out the first step of the first stage, the frequency of cases of clinical markers in patients with SLE with heart lesions was assessed (figure) and only those that met the criteria of our methodology were selected for the study.

Therefore, patients with SLE with MV insufficiency significantly (p < 0.05) more often than patients with SLE without it had morning stiffness, new rashes, shortness of breath, problems with memory, weakened cardiac tones during auscultation, systolic murmur on the apex of the heart, accent of the second tone on the pulmonary artery.

In patients with SLE with the MV consolidation significantly (p < 0.05) more often than in patients with SLE without it, new rashes, the presence of swelling on the lower extremities, shortness of breath, a feeling of interruptions in the work of the heart, pain in the area of the heart, weakened heart tones, systolic murmur on the apex of the heart were detected.

In patients with SLE and myocarditis, muscle pain, alopecia, presence of swelling on the lower extremities, shortness of breath, palpitations, and systolic murmur over the apex of the heart were recorded significantly (p < 0.05) more often than in patients with SLE without it.

Significantly more often (p < 0.05), SLE patients with pericardial effusion had lower limb swelling, shortness of breath, palpitations, and weakened heart sounds than SLE patients without it.

Significantly more often (p < 0.05), the presence of a second tone accent over the pulmonary artery was recorded in patients with SLE with endocarditis than in patients with SLE without it.

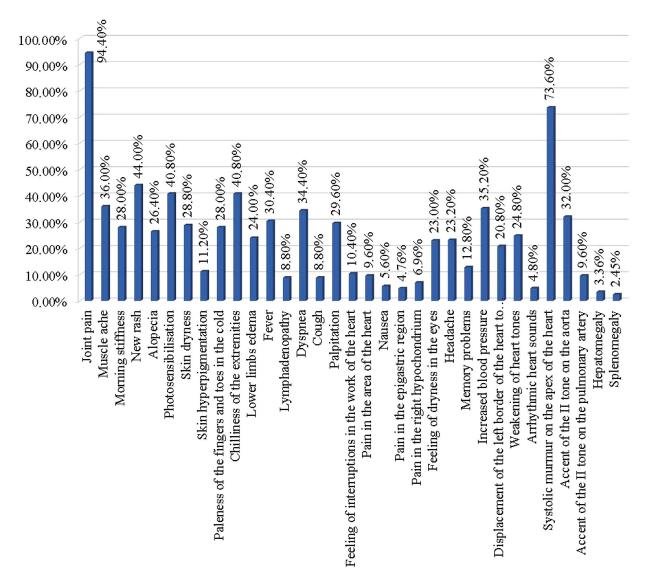


Fig. Frequency of cases of clinical markers in patients with systemic lupus erythematosus with the CVS syntropic lesions (p < 0.050).

The results of the second step of the first stage, in which the diagnostic value of clinical mono markers of syntropic heart lesions, that is, each clinical marker separately in patients with SLE, were determined is presented in the tabl. 1.

Table 1
Diagnostic value of significantly more frequently detected clinical markers in patients with systemic lupus erythematosus and syntropic heart lesions (%)

N	Clinical markers / markers constellations	Parameters of diagnostic value				
		Sensitivity, %	Specificity, %	Accuracy,		
1	2	3	4	5		
with MV insufficiency						
1	Morning stiffness	36.36	78.57	60.00		
2	New rash	54.55	64.29	60.00		
3	Dyspnea	47.27	75.71	63.20		
4	Memory problems	21.82	94.29	62.40		

Contin. of the tabl. 1

1	2	3	4	5	
5	The weakened heart tones during auscultation	34.55	82.86	61.60	
6	Systolic murmur on the apex	81.82	32.86	54.40	
7	Accent of the second tone on the pulmonary artery	16.36	95.71	60.80	
with MV consolidation					
1	New rash	19.15	94.87	66.40	
2	Legs edema	34.04	84.42	65.32	
3	Dyspnea	48.94	75.64	65.60	
4	Feeling of interruptions in the work of the heart	61.70	66.67	64.80	
5	Pain in the heart area	14.89	94.87	64.80	
6	Weakened cardiac tones	36.17	82.05	64.80	

End of the tabl. 1

1	2	3	4	5			
7	Systolic murmur on the apex	82.98	32.05	51.20			
with myocarditis							
1	Muscle ache	51.72	68.75	64.80			
2	Alopecia	51.72	81.25	74.40			
3	Legs edema	41.38	81.05	71.77			
4	Dyspnea	51.72	70.83	66.40			
5	Palpitations	62.07	80.21	76.00			
6	Systolic murmur on the apex	89.66	31.25	44.80			
with pericardial affusion							
1	Legs edema	40.91	79.41	72.58			
2	Dyspnea	45.45	79.61	73.60			
3	Palpitations	54.55	75.73	72.00			
4	Weakened cardiac tones	63.64	71.84	70.40			
with endocarditis							
1	Accent of the second tone on the pulmonary artery	100.00	91.87	92.00			

As we can see in the tabl. 1, in patients with SLE with MV insufficiency, the sensitivity of such a clinical marker as morning stiffness (direct relationship, p = 0.029) is 36.36 %, specificity - 78.57 %, accuracy - 60.00%; sensitivity to the presence of new rashes (direct connection, p = 0.016) is 54.55 %, specificity - 64.29 %, accuracy -60.00%; sensitivity of the presence of shortness of breath (direct relationship, p = 0.004) as a marker reaches 47.27 %, specificity - 75.71 %, accuracy - 63.20 %; the sensitivity of the memory impairment marker (direct relationship, p = 0.006) is 21.82 %, specificity - 94.29 %, accuracy - 62.40 %; sensitivity of the presence of weakened tones during auscultation of the heart (direct relationship, p = 0.014) reaches 34.55 %, specificity - 82.86 %, accuracy - 61.60 %; the sensitivity of the presence of a systolic murmur on the apex of the heart (direct relationship, p = 0.030) is 81.82 %, specificity - 32.86 %, accuracy - 54.40 %; sensitivity of the presence of an accent of the second tone on the pulmonary artery (direct relationship, p = 0.019) is 16.36 %, specificity - 95.71 %, accuracy - 60.80 %. Therefore, shortness of breath has the optimal diagnostic value for detecting MV insufficiency in patients with SLE among clinical markers (diagnostic accuracy reliably exceeds 50.00 %, p = 0.002).

It was determined that the sensitivity of such a marker as new rash (direct relationship, p=0.013) is 19.15 %, specificity - 94.87 %, accuracy - 66.40 %; the sensitivity of the legs edema (direct relationship, p=0.011) as a marker reaches 34.04 %, specificity - 84.42 %, accuracy - 65.32 %; sensitivity of shortness of breath (direct

relationship, p = 0.003) is 48.94 %, specificity - 75.64 %, accuracy - 65.60 %; the sensitivity of the presence of such a complaint as a feeling of heart failure (direct relationship, p = 0.001) is 61.70 %, specificity - 66.67 %, accuracy - 64.80 %; pain in the heart area (direct relationship, p = 0.048) as a marker reaches 14.89 %, specificity - 94.87 %, accuracy - 64.80 %; presence of weakened cardiac sounds (direct relationship, p = 0.013) reaches 36.17 %, specificity - 82.05 %, accuracy - 64.80 %; the presence of systolic murmur on the apex of the heart (direct relationship, p = 0.046) is 82.98 %, specificity - 32.05 %, accuracy - 51.20 %. The optimal diagnostic value for detecting the MV consolidation in patients with SLE is a complaint of a feeling of interruptions in the work of the heart (diagnostic accuracy reliably exceeds 50.00 %, p < 0.001).

The sensitivity of a complaint of muscle ache (direct relationship, p = 0.024) for the detection of myocarditis is 51.72 %, specificity - 68.75 %, accuracy - 64.80 %; sensitivity of the presence of alopecia (direct relationship, p = 0.001) reaches 51.72 %, specificity - 81.25 %, accuracy - 74.40 %; legs edema (direct relationship, p = 0.011) is 41.38 %, specificity - 81.05 %, accuracy - 71.77 %; sensitivity of the complaint to shortness of breath (direct connection, p = 0.016) for the detection of myocarditis is 51.72 %, specificity - 70.83 %, accuracy - 66.40 %; palpitations (direct relationship, p < 0.001) is 62.07%, specificity - 80.21 %, accuracy - 76.00 %; the sensitivity of the presence of systolic murmur over the apex of the heart (direct relationship, p = 0.014) reaches 89.66 %, specificity - 31.25 %, accuracy - 44.80 %. The optimal clinical marker for detecting myocarditis in patients with SLE are palpitations (diagnostic accuracy significantly exceeds 50.00 %, p < 0.001).

The legs edema (direct relationship, p=0.031) in relation to the detection of pericardial effusion reaches 40.91 %, specificity - 79.41%, accuracy - 72.58 %; the sensitivity of the presence of shortness of breath (direct relationship, p=0.013) as a marker of pericardial effusion is 45.45 %, specificity - 79.61 %, accuracy - 73.60 %; the sensitivity of the heart palpitation complaint (direct relationship, p=0.005) reaches 54.55 %, specificity - 75.73 %, accuracy - 72.00 %; sensitivity of the presence of weakened heart sounds (direct relationship, p=0.002) is 63.64 %, specificity - 71.84 %, accuracy - 70.40 %. The optimal clinical marker for detecting pericardial effusion in patients with SLE is the presence of weakened cardiac sounds (diagnostic accuracy significantly exceeds 50.00 %, p < 0.001).

The sensitivity of the presence of the accent of the second tone on the pulmonary artery (direct relationship, p=0.009) as a marker of endocarditis reaches 100.00%, specificity - 91.87 %, accuracy - 92.00 %. It is a diagnostically valuable marker for detecting endocarditis in patients with SLE (diagnostic accuracy significantly exceeds 50.00 %, p < 0.001).

The results of the third step of the first stage, which determined the diagnostic value of the optimal constellation of clinical markers of syntropic heart lesions in patients with SLE, are presented in tabl. 2.

Table 2

Diagnostic value of constellations of clinical markers
in patients with systemic lupus erythematosus
with syntropic heart lesions (%)

Parameters of diagnostic value Clinical markers / Ν Sensitivity, Specificity, Accuracy, markers constellations with MV insufficiency "Pain in the joints + new rash + accent of 27.27 98.57 67.20 the second tone on the with MV consolidation "Dyspnea + feeling of interruptions in the 38.30 89.74 70.40 work of the heart" with myocarditis "Palpitations + systolic 55.17 79.20 86.46 murmur on the apex" with pericardial effusion "Pain in the joints + 63.64 72.82 71.20 weakened heart tones" with endocarditis "Fever + systolic murmur on the apex of the heart + accent 100.00 100.00 100.00 of the second tone on the pulmonary artery"

Carrying out the research made it possible to determine: constellation of markers (CA = 0.93) in patients with SLE with MV insufficiency ("pain in the joints + new rash + accent of the second tone on the aorta" (sensitivity - 27.27%, specificity - 98.57 %, accuracy - 67, 2 %, p < 0.001)), which has a stronger relationship with MV insufficiency than a separate clinical marker (CA = 0.47);

constellation of markers (CA = 0.69) in patients with SLE with the MV consolidation ("shortness of breath + feeling of interruptions in the work of the heart" (sensitivity - 38.30 %, specificity - 89.74 %, accuracy - 70.40 %, p < 0.001)), which has a stronger relationship with syntropic lesions than a separate clinical marker (CA = 0.53);

constellation of markers (CA = 0.77) in patients with SLE with myocarditis ("palpitations + systolic murmur on the apex of the heart" (sensitivity - 55.17 %, specificity - 86.46 %, accuracy - 79.20 %, p < 0.001)), which has stronger connection with myocarditis than a separate clinical marker (CA = 0.74);

constellation of markers (CA = 0.65) in patients with SLE with pericardial effusion ("pain in the joints + weakened cardiac tones" (sensitivity - 63.64 %, specificity - 72.82 %, accuracy - 71.20 %, p = 0.001)), which has stronger relationship with pericardial effusion than a single clinical marker (CA = 0.63);

constellation of markers (contingency coefficient (CC) = 1.00) in patients with SLE and endocarditis ("fever + systolic murmur on the apex of the heart + accent of the second sound on the pulmonary artery" (sensiti-

vity - 100.00 %, specificity - 100.00 %, accuracy - 100.00 %, p < 0.001), which has stronger relationship with syntropic lesions than a separate clinical marker (CC = 0.39).

Having found out the clinical markers of syntropic heart lesions in SLE patients and their diagnostic value, it was concluded that the optimal diagnostic value for detecting MV insufficiency in SLE patients among the clinical monomarkers is dyspnea and the constellation "pain in the joints + new rash + accent of the second tone on aorta", MV consolidation - a complaint of a feeling of interruptions in the work of the heart and the constellation "shortness of breath + feeling of interruptions in the work of the heart", myocarditis - palpitations and the constellation "heartbeat + systolic murmur on the apex of the heart", pericardial effusion - the presence of weakened cardiac tones and the constellation "pain in the joints + weakened cardiac tones", endocarditis - accent of the second tone on the pulmonary artery and the constellation "fever + systolic murmur on the apex of the heart + accent of the second tone on the pulmonary artery". Comparing the obtained results with the studies of other authors [5, 6, 8] we found that shortness of breath and systolic murmur are frequent complaints in patients with SLE with valvular lesions. Similar results were described by Kevin G. Moder et al. [8], who observed precardial or substernal discomfort or pain that could be positional, fever, tachycardia, shortness of breath and weakening of heart sounds (especially in case of significant effusion) in patients with pericarditis, with myocarditis - tachycardia and, if the disease is severe, other signs of congestive heart failure. The mentioned researchers described clinical symptoms in SLE patients with the specified heart diseases, but did not study the diagnostic value of a single clinical marker or their constellations.

Conclusions. Clinical markers for detecting mitral valve insufficiency in patients with systemic lupus erythematosus are morning stiffness, new rash, dyspnea, memory problems, the presence of weakened sounds during auscultation of the heart, a systolic murmur on the apex of the heart, an emphasis of the second sound on the pulmonary artery; consolidation of the mitral valves - new rash, legs edema, dyspnea, feeling of interruptions in the work of the heart, pain in the area of the heart, presence of weakened heart tones, systolic murmur on the apex of the heart; myocarditis - pain in the muscles, alopecia, presence of legs edema.

The optimal value for the diagnosis of mitral valve insufficiency in patients with systemic lupus erythematosus is the constellation of clinical markers "pain in the joints + new rash + accent of the second tone on the aorta"; mitral valve consolidation - "dyspnea + a feeling of interruptions in the work of the heart"; myocarditis - "heart palpitations + systolic murmur on the apex of the heart"; pericardial effusion - "pain in the joints + weakening of heart tones"; endocarditis - "fever + systolic murmur over the top of the heart + emphasis of the second tone on the pulmonary artery".

#### References

- 1. Esdaile JM, Abrahamowicz M, Grodzicky T, Li Y, Panaritis C, Berger RD et al. Traditional Framingham risk factors fail to fully account for accelerated atherosclerosis in systemic lupus erythematosus. Arthritis Rheum. 2001;44:2331-2337.
- 2. Felten R, Lipsker D, Sibilia J, Chasset F, Arnaud L. The history of lupus through outtheages. J Am Acad Dermatol. 2022; 87(6): 1361-1369, 10.1016/j.jaad.2020.04.150.
- 3. Fernandez-Nebro A, Rua-Figueroa I, Lopez-Longo FJ, Galindo-Izquierdo MA, Calvo-Alén J, Olivé-Marqués A etal. Cardiovasculareventsinsystemiclupuserythematosus: a nationwidestudyin S painfromtheRelesserregistry. Medicine (Baltimore). 2015;94(29):e1183. doi: 10.1097/MD.0000000000001183.
- 4. Frostegard J. Systemic lupus erythematosus and cardiovascular disease. J InternMed. 2023;293:48-62.
- 5. Heinlen LD, McClain MT, Merrill J et al. Clinicalcriteriaforsystemiclupuserythematosusprecedediagnosis, andassociatedautoantibodiesarepresentbeforeclinicalsymptoms. ArthritisRheum. 2007;56:2344–2351. doi: 10.1002/art.22665.
- 6. Jha SB, Rivera AP, Flores Monar Getal. Systemic lupusery thematosus and cardiovascular disease. Cureus. 2022;14(2):e22027. doi:10.7759/cureus.22027.
- 7. JustizVaillant AA, Goyal A, Varacallo M. Systemic lupuserythematosus. 2023 Aug 4. In: StatPearls [Internet]. Treasure-Island (FL): StatPearlsPublishing; 2024 January PMID: 30571026.
- 8. Kevin G Moder, Todd D Miller, Henry D Tazelaar. Cardiac involvement in systemic lupus erythematosus. MayoClinProc. 1999;74(3):275-284.
- 9. Kobak L, Abrahamovych O, Abrahamovych U, G uta S, Tsyhanyk L. Thenatureandfrequencyofcomorbidheartlesionsin-patientswithsystemiclupuserythematosusdiagnosedbyechocardiography, detectionandcharacteristicsoftheirsyntropicvariants. LvivClinical Bulletin . 2023;2(42):36-43.
- 10. Kobak L, Abrahamovych O, Abrahamovych U, Ivanochko R, Chemes V. Circulatory system organs with morbid lesions in patients with systemic lupus erythematosus: nature and frequency; characteristics depending on gender, age and disease duration. Lviv Clinical Bulletin . 2022;3(39)-4(40):66-75.
- 11. Kobak L, Abrahamovych O, Abrahamovych U, Maksymuk A, Ivanochko R. Diagnostic value of laboratory markers of syntropic lesions of the circulatory system organs in patients with systemic lupus erythematosus. Georgian M edical N ews. 2023;7(340):6-11.
- 12. Kovalenko VM, GolovachIYu, Bortkevych OP. Achievementstreatmentofsystemiclupuserythematosus . Ukrainian Journal of Rheumatology . 2012;50(4):16-22.
- 13. Rees F, Doherty M, Grainge M, Davenport G, Lanyon P, Zhang W. The incidence and prevalence of systemic lupus erythematosus in the UK, 1999-2012. AnnRheumDis. 2016;75:136-141. doi: 10.1136/annrheumdis-2014-206334.

The article was submitted to the editorial board on March 5, 2024.

Conflict of interest

The authors declare no conflicts of interest.

## Clinical Markers of the Heart and Blood Vessels Syntropic Lesions in Patients with Systemic Lupus Erythematosus, Their Diagnostic Value (First Notice)

### L. Kobak, O. Khukhlina, L. Babinets, M. Panasiuk, N. Drobinska, O. Faiura, Z. Bilous

**Introduction.** Systemic lupus erythematosus (SLE) is an autoimmune rheumatic disease with numerous clinical manifestations that affects any organs or systems and requires a comprehensive study.

The aim of the study. To find out the clinical markers of the heart and blood vessels syntropic lesions in patients with systemic lupus erythematosus and evaluate their diagnostic value.

**Materials and methods.** The study included 118 patients with SLE with the presence of syntropic (having common etiological and/or pathogenetic mechanisms with the main disease) lesions of the heart and blood vessels (107 women (90.68 %) and 11 men (9.32 %) aged 18 to 74 years (average age  $42.48 \pm 1.12$  years)).

The study included the identification of clinical markers of syntropic lesions of the heart and blood vessels, determination of the diagnostic value of individual clinical markers and their constellations in terms of sensitivity, specificity and accuracy in patients with SLE, and the identification of one of them with the most reliable diagnostic value.

**Results.** Clinical markers for detecting mitral valve insufficiency in patients with SLE are morning stiffness, new rash, dyspnea, memory problems, presence of weakened cardiac sounds, systolic murmur on the apex of the heart, accent of the second sound on the pulmonary artery; mitral valve consolidation - new rash, the presence of legs edema, dyspnea, a feeling of interruptions in the work of the heart, pain in the heart area, the presence of weakened cardiac tones, systolic murmur on the top of the heart; myocarditis - muscle ache, alopecia, legs edema, shortness

of breath, palpitation, systolic murmur on the top of the heart; pericardial effusion - legs edema, dyspnea, palpitations, the presence of weakened cardiac tones; endocarditis - the presence of the accent of the second tone on the pulmonary artery.

The optimal value for the diagnosis of mitral valve insufficiency in patients with SLE is the constellation of clinical markers "pain in the joints + new rash + accent of the second tone on the aorta"; of mitral valve consolidation - "dyspnea + a feeling of interruptions in the work of the heart"; of myocarditis - "heart palpitations + systolic murmur on the apex of the heart"; of pericardial effusion - "pain in the joints + weakening of heart tones"; of endocarditis - "fever + systolic murmur over the top of the heart + emphasis of the second tone on the pulmonary artery".

Conclusions. In patients with SLE the optimal value among clinical monomarkers and their constellations for the diagnosis of mitral valve insufficiency is dyspnea and the constellation "pain in the joints + new rash + accent of the second tone on aorta"; for MV consolidation - a complaint of a feeling of interruptions in the work of the heart and the constellation "shortness of breath + feeling of interruptions in the work of the heart"; for myocarditis - palpitations and the constellation "heartbeat + systolic murmur on the apex of the heart", pericardial effusion - the presence of weakened cardiac tones and the constellation "pain in the joints + weakened cardiac tones"; for endocarditis - accent of the second tone on the pulmonary artery and the constellation "fever + systolic murmur on the apex of the heart + accent of the second tone on the pulmonary artery". Constellations of clinical markers, but not individual clinical markers, have optimal value for the diagnosis of the syntropic heart lesions in patients with SLE.

**Keywords:** systemic lupus erythematosus, syntropic lesions of the heart and blood vessels, clinical markers, diagnostic value.

# Клінічні маркери синтропічних уражень серця і судин у хворих на системний червоний вовчак, їхня діягностична цінність (повідомлення перше)

Л. О. Кобак, О. С. Хухліна, Л. С. Бабінець, М. Т. Панасюк, Н. В. Дробінська, О. П. Фаюра, З. О. Білоус

**Вступ.** Системний червоний вовчак (СЧВ) – хронічна автоімунна недуга, за якої уражаються майже всі внутрішні органи. Йдеться про синтропічні коморбідні ураження органів системи кровообігу (синтропічними ураженнями вважаємо ті, частота яких достовірно наростає з підвищенням ступеня активности СЧВ, позаяк мають спільні з основною недугою етіологічні й/або патогенетичні механізми), що не лише є одними з найпоширеніших, а й посідають перші позиції у структурі причин смертности. Підвищення ефективности їхньої курації вимагає від клініциста у певних ситуаціях пошуку нових, ефективних, малозатратних способів виявлення, володіння інформацією про діягностичну цінність клінічних маркерів синтропічних уражень серця.

**Мета.** З'ясувати клінічні маркери синтропічних уражень серця і судин у хворих на системний червоний вовчак, їхню діягностичну цінність.

**Матеріяли й методи.** У дослідження включено 118 хворих на СЧВ із наявністю синтропічних (тих, що мають спільні з основною недугою етіологічні й/або патогенетичні механізми) уражень серця і судин (107 жінок (90,68 %) та 11 чоловіків (9,32 %) віком від 18 до 74 років (середній вік  $42,48 \pm 1,12$  року)).

Виконання дослідження передбачало виявлення клінічних маркерів синтропічних уражень серця і судин, визначення діягностичної цінности окремих клінічних маркерів та їхніх констеляцій за чутливістю, специфічністю й точністю у хворих на СЧВ та виокремлення одного з них із достовірно найбільшою діягностичною значущістю.

Результати. Клінічними маркерами у хворих на системний червоний вовчак для виявлення недостатности мітрального клапана є ранкова скутість, нові висипання, задишка, погіршення пам'яти, наявність ослаблених тонів під час аускультації серця, систолічний шум над верхівкою серця, акцент другого тону над легеневою артерією, ущільнення мітрального клапана — нові висипання, наявність набряків на нижніх кінцівках, задишка, відчуття перебоїв у роботі серця, біль у ділянці серця, наявність ослаблених тонів серця, систолічний шум над верхівкою серця, міокардиту — біль у м'язах, алопеція, наявність набряків на нижніх кінцівках, задишка, серцебиття, систолічний шум над верхівкою серця, перикардіяльного випоту — набряки на нижніх кінцівках, задишка, серцебиття, наявність ослаблених тонів серця, ендокардиту — наявність акценту другого тону над легеневою артерією.

Оптимальну цінність для діягностики недостатности мітрального клапана у хворих на системний червоний вовчак має констеляція клінічних маркерів «біль у суглобах + нові висипання + акцент другого тону над аортою», ущільнення мітрального клапана — «задишка + відчуття перебоїв у роботі серця», міокардиту — «серцебиття + систолічний шум над верхівкою серця», перикардіяльного випоту — «біль у суглобах + ослаблення тонів серця», ендокардиту — «гарячка + систолічний шум над верхівкою серця + акцент другого тону над легеневою артерією».

Висновки. У хворих на СЧВ оптимальну цінність серед клінічних мономаркеріві їхніх констеляцій для діягностики недостатности МК мають задишка, «біль у суглобах + нові висипання + акцент другого тону над аортою», ущільнення МК – скарга на відчуття перебоїв у роботі серця, «задишка + відчуття перебоїв у роботі серця»; міокардиту — серцебиття, «серцебиття + систолічний шум над верхівкою серця», перикардіяльного випоту — наявність ослаблених тонів серця, «біль у суглобах + ослаблення тонів серця», ендокардиту — акцент другого тону над легеневою артерією, «гарячка + систолічний шум над верхівкою серця + акцент другого тону над легеневою артерією». Оптимальну цінність для діягностики досліджуваних синтропічних уражень серця у хворих на СЧВ мають констеляції клінічних маркерів, а не окремі клінічні маркери.

**Ключові слова:** системний червоний вовчак, синтропічні ураження серця і судин, клінічні маркери, діягностична цінність.

#### Information about the authors

- 1. Lyubov Kobak; Danylo Halytsky Lviv National Medical University, Department of Internal Medicine N 1 (69, Pekarska Str., Lviv, 79010; +380(32) 276 97 63); PhD, Assistant Professor; 7, Hrabianky Str., Lviv, 79053; +380(67) 585 20 10; k liubov@ukr.net; https://orcid.org/0000-0002-2700-4007
- 2. Oksana Khukhlina; Bukovinian State Medical University, Department of Internal Medicine, Clinical Pharmacology and Occupational Deseases (2, Fastivska Str., Chernivtsi, 58012; +038(03722) 6 92 21, +0380(3722) 6 18 06); MD, PhD, Professor, Head of the Department; oksanakhukhlina@bsmu.edu.ua; http://orcid.org/0000-0001-6259-2863
- 3. Liliia Babinets; I. Ya. Gorbachevsky Ternopil National Medical University, Department of Therapy and Family Medicine (14, Roman Kupchynskyi Str., Ternopil, 46004; +38(0352) 25 34 56); MD, PhD, Professor, Head of the Department; babinets@tdmu.edu.ua; https://orcid.org/0000-0002-0560-1943
- 4. Mariia Panasiuk; Danylo Halytsky Lviv National Medical University, Department of Internal Medicine N 1 (69, Pekarska Str., Lviv, 79010; +380(32) 276 97 63); PhD, Associate Professor; 35, Tiutiunnykiv Str., Lviv, 79011; marpanasjuk@gmail.com; https://orcid.org/0000-0003-4487-8467
- 5. Nataliya Drobinska; Danylo Halytsky Lviv National Medical University, Department of Internal Medicine N 1 (69, Pekarska Str., Lviv, 79010; +380(32) 276 97 63); PhD, Assistant Professor; doktornataliia@gmail.com; https://orcid.org/0000-0002-4714-3688
- Oksana Faiura; Danylo Halytsky Lviv National Medical University, Department of Internal Medicine N 1 (69, Pekarska Str., Lviv, 79010; +380(32) 276 97 63); PhD, Associate Professor; 7, Poludneva Str., Lviv, 79067; +380(96) 814 17 49, +380(32) 271 27 65); fayurchuk@ukr.net; https://orcid.org/0000-0003-1122-9030
- 7. Zoriana Bilous; Danylo Halytsky Lviv National Medical University, Department of Internal Medicine N 1 (69, Pekarska Str., Lviv, 79010; +380(32) 276 97 63); PhD, Associate Professor; 15, Osvytska Str., Lviv, 79066; +380(97) 333 51 47; zoryanabilous@gmail.com; https://orcid.org/0000-0002-8301-2474