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Circulatory System Organs Comorbid Lesions in Patients with Systemic Lupus Erythematosus: Nature and Frequency; Characteristics Depending on Gender, Age and Disease Duration

Introduction. Systemic lupus erythematosus (SLE) is an autoimmune disease of unknown etiology, which is characterized by the hyperproduction of organ-nonspecific antibodies to the different components of the cell nucleus with the development of immunoinflammatory damage of the tissues and internal organs [13].

For a long time, SLE was considered a rare disease, but the results of the recent studies disprove this [6]. There is a global trend of increasing both the prevalence and morbidity of SLE. Over the past decades, the number of new cases has almost tripled. This is probably due primarily to the quicker recognition of mild forms of the disease [8]. According to experts, the prevalence of SLE is 30–50 per 100,000, with approximately 500,000 patients in Europe and 250,000 in the United States of America (USA) [13]. The women to men SLE frequency ratio is on average 10–15:1 [12]. SLE can develop at any age [10] and has a tendency to debut later in men (at the age of 50–70 years) than in women (at the age of 30–50 years) [12].

SLE has numerous clinical manifestations and an unpredictable course, often lasting for several months or years, with alternating remissions and exacerbations [5]. Several organs can be affected simultaneously with different degrees of severity, which leads to the occurrence of comorbid lesions associated with the treatment and actually the disease [1], including cardiovascular diseases [2], metabolic syndrome, osteoporosis, infections and malignant neoplasms, diseases of the musculoskeletal, nervous systems, kidneys, eyes, gastrointestinal tract, and chronic lung diseases [3, 4, 9, 11]. The presence of comorbid lesions in case of SLE can significantly increase the mortality from all causes [7, 16]. Damage of the circulatory system organs is one of the main causes of death in SLE patients [14].

Improving the life quality of the patients largely depends on timely, completeness of the diagnosis and treatment of SLE, taking into account the characteristics of the circulatory system organs comorbid lesions, in particular, depending on the gender, age and disease duration, which obliges us to perform this study.

The aim of the study. To find out the nature and frequency of the circulatory system organs comorbid lesions in patients with systemic lupus erythematosus, to characterize them depending on the gender, age and the disease duration.

Materials and methods. To perform the study after signing the voluntary consent to participate, in accordance with the requirements of 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 (the diagnosis was made taking into account the diagnostic criteria of the American College of Rheumatology (1997) and the diagnosis was set based on 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 Providing the Medical Care on the Specialty "Rheumatology"», recommendations of the European Antirheumatic League (2010), the American College of Rheumatology (2010, 2012)), and by the presence of the circulatory system organs lesions (Order of the Ministry of Health of Ukraine N 436 dated 03.07.2006 «On the Approval of Protocols for Providing the Medical Care on the Specialty "Cardiology"» with changes according to the Order of the Ministry of Health of Ukraine N 455 dated July 2, 2014) included 112 patients, among which the majority was females (89.29%), patients of working age (57.14% – young and 39.29% – middle age), unemployed (58.04%), III disability group patients (45.54

%), city residents (62.50 %). According to the results of the disease duration assessment, a significant part of patients with SLE with circulatory system organs comorbid lesions have been ill for 1–5 years (36.61 %) and more than 10 years (38.39 %). All of them were patients of the rheumatology department of the Communal Non-Profit Enterprise of the Lviv Regional Council «Lviv Regional Clinical Hospital» from 2016 to 2021.

At the *first stage* of the study, the nature and frequency of the circulatory system organs comorbid lesions in all SLE patients were clarified. Complex clinical, laboratory and instrumental diagnostics of the circulatory system organs lesions were carried out in accordance with the Order of the Ministry of Health of Ukraine N 436 dated 03.07.2006 «On the Approval of Protocols for Providing the Medical Care on the Specialty "Cardiology", studying the information from the passport, patients' complaints, medical and life history, obtained during the comprehensive objective examination and the results of additional laboratory and instrumental examinations. We used: electrocardiography (Eli 230 electrocardiograph, Mortara Instrument company, USA); echocardiography (according to the standard method using the device Samsung H-60 (Korea) with a cardiac sensor in one-dimensional, two-dimensional modes and the Doppler echocardiography mode (using pulsed wave spectral Doppler, as well as color Doppler determination of blood flow); ultrasound examination of the vessels of the lower extremities and aortic arch branches using Samsung H-60 diagnostic device (Korea) with LF 5-13 linear sensor; bicycle ergometry according to the well-known technique on the bicycle ergometer Seca (Germany) in a sitting position with electrocardiogram registration by the 6-channel device 6-NEK-4-01 (Germany); Holter 24-hour monitoring of blood pressure and electrocardiogram using the Beecardia device, SDM23 (Ukraine) according to the standard protocol; assessment of the capillaries state and capillary blood flow by capillaroscopy of the nail bed using the "Capillaroscope M-70" device (capillaroscopy of the 4th finger of the left hand was performed); as well as an ophthalmoscopic examination using the slit lamp SL-2B (Ukraine) with the previous use of 1.0% atropine sulfate 5.0 ml.

In addition to complex routine laboratory examinations, a number of additional studies were conducted. "Lupus (lupus erythematosus – LE) cells" were studied by direct microscopic examination (Primo Star Zeiss, Germany). The titer of antiphospholipid antibodies, determination of circulating immune complexes was carried out by enzyme immunoassay (Euroimmun Analyzer I; Demeditec Diagnostics GmbH, Germany), C3 and C4 complement components (immunochemical analyzer COBAS E 411, RocheDiagnostics, Switzerland) – by using commercial test kits according to the attached instructions [15].

The titer of antibodies to double-stranded deoxyribonucleic acid (anti-dsDNA) was determined by the method of flow cytometry on the BioPlex 2200 device using the BioRad (USA) test system.

The titer of antinuclear antibodies (ANA) was determined by the method of indirect immunofluorescence (fluorescence

microscope Eurostar III Plus using the Euroimmun test system (Germany)).

At the *second stage* of the study, the peculiarities of the circulatory system organs comorbid lesions frequency were determined, depending on the gender (*first step*), age (*second step*), and duration (*third step*) of the disease.

SLE patients with comorbid lesions of the circulatory system were stratified by gender (100 females (89.29 %) and 12 males (10.71 %)), age, according to the classification of the World Health Organization, 2015 (young (18–44 years) – 64 patients (57.14 %), middle-aged (45–59 years) – 44 patients (39.29 %), elderly (60–75 years) – 4 patients (3.57 %)), as well as by the duration of SLE (less than 1 year – group A (5 patients (4.46 %), 1–5 years – group B (41 patients (36.61 %)), 6–10 years – group C (23 patients (20.54 %)) and those who have been ill for more than 10 years – group D (43 patients (38.39 %)).

The actual material was statistically processed on a personal computer in Excel, 2010 and Statistica 6.0 programs using descriptive statistics, χ^2 -criterion, z-criterion for comparing two proportions. The difference was considered statistically significant if $p < 0.05$.

Results and discussion. The results of the *first stage* of the study are shown in the table 1.

Table 1
The nature and frequency of the circulatory system organs comorbid lesions in the patients with systemic lupus erythematosus

№	Circulatory system organs comorbid lesions	SLE patients, n = 112	
		n	%
1	A. G. M. Raynaud's syndrome	61	54.46
2	Mitral valve insufficiency	48	42.86
3	Atherosclerosis	46	41.07
4	Myocarditis	40	35.71
5	Retinal angiopathy	39	34.82
6	Symptomatic arterial hypertension	38	33.93
7	Livedo reticularis	32	28.57
8	Varicose veins of the lower extremities	14	12.50
9	Hypertensive disease	11	9.82
10	Diffuse cardiosclerosis	10	8.93
11	Tricuspid valve insufficiency	8	7.14
12	Vein thrombosis	7	6.25
13	Postthrombophlebitis syndrome	6	5.36
14	Aortic valve insufficiency	6	5.36
15	Capillaritis	4	3.57
16	Pulmonary hypertension	3	2.68
17	CAD: stable angina pectoris	2	1.79
18	Cardiomyopathy	1	0.89
19	CAD: post-infarction cardiosclerosis	1	0.89

Note. CAD - coronary artery disease.

Most often, among the circulatory system organs comorbid lesions, about half of SLE patients were diagnosed with A. G. M. Raynaud's syndrome (61 patients (54.46 %), mitral valve insufficiency (48 patients (42.86 %)), atherosclerotic vascular lesions (46 patients (41.07 %)). Other lesions were recorded with a lower frequency: myocarditis – in 40 patients (35.71 %), retinal angiopathy – in 39 patients (34.82 %), symptomatic arterial hypertension – in 38 patients with SLE (33.93 %), livedo reticularis – in 32 patients (28.57 %), varicose veins of the lower extremities – in 14 patients (12.50 %), hypertensive disease – in 11 patients (9.82 %),

diffuse cardiosclerosis – in 10 patients (8.93 %), tricuspid valve insufficiency – in 8 patients (7.14 %), thrombosis of peripheral veins – in 7 patients (6.25 %), post-thrombophlebitis syndrome – in 6 patients (5.36 %), aortic valve insufficiency – also in 6 patients (5.36 %), capillaritis – in 4 patients (3.57 %), pulmonary hypertension – in 3 patients (2.68 %), stable angina pectoris, a form of CAD – in two patients (1.79 %), cardiomyopathy – in 1 patient (0.89 %), post-infarction cardiosclerosis, a form of CAD – in 1 patient with SLE (0.89 %).

Table 2

Statistical reliability of the difference between the frequency of certain circulatory system organs comorbid lesions in patients with systemic lupus erythematosus

Circulatory system organs comorbid lesions	A. G. M. Raynaud's syndrome	Mitral valve insufficiency	Atherosclerosis	Myocarditis	Retinal angiopathy	Symptomatic arterial hypertension	Livedo reticularis	Varicose veins of the lower extremities	Hypertensive disease	Diffuse cardiosclerosis	Tricuspid valve insufficiency	Vein thrombosis	Postthrombophlebitis syndrome	Aortic valve insufficiency	Capillaritis	Pulmonary hypertension	CAD: stable angina pectoris	Cardiomyopathy	CAD: post-infarction cardiosclerosis
A. G. M. Raynaud's syndrome	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■
Mitral valve insufficiency	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■
Atherosclerosis	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■
Myocarditis	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■
Retinal angiopathy	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■
Symptomatic arterial hypertension	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■
Livedo reticularis	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■
Varicose veins of the lower extremities	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■
Hypertensive disease	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■
Diffuse cardiosclerosis	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■
Tricuspid valve insufficiency	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■
Vein thrombosis	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■
Postthrombophlebitis syndrome	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■
Aortic valve insufficiency	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■
Capillaritis	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■
Pulmonary hypertension	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■
CAD: stable angina pectoris	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■
Cardiomyopathy	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■
CAD: post-infarction cardiosclerosis	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■

Notes:

■ – statistically significant difference between the frequency of the certain circulatory system organs comorbid lesions ($p < 0.05$);

■ – statistically insignificant difference between the frequency of the certain circulatory system organs comorbid lesions ($p > 0.05$).

So, the obtained results shown in the table 2, demonstrate that A. G. M. Raynaud's syndrome was diagnosed significantly more often than atherosclerosis, myocarditis, retinal angiopathy, symptomatic arterial hypertension, livedo reticularis, varicose veins of the lower extremities, hypertensive disease, diffuse cardiosclerosis, tricuspid valve insufficiency, venous thrombosis, post-thrombophlebitis syndrome, aortic valve insufficiency, capillaritis, pulmonary hypertension, CAD: stable angina pectoris, cardiomyopathy, CAD: postinfarction cardiosclerosis.

Mitral valve insufficiency and atherosclerosis were found significantly more often than livedo reticularis, varicose veins of the lower extremities, hypertensive disease, diffuse cardiosclerosis, tricuspid valve insufficiency, vein thrombosis, post-thrombophlebitis syndrome, aortic valve insufficiency, capillaritis, pulmonary hypertension, CAD: stable angina, cardiomyopathy, CAD: post-infarction cardiosclerosis.

Myocarditis, retinal angiopathy, symptomatic arterial hypertension, livedo reticularis were observed significantly more often than varicose veins of the lower extremities, hypertensive disease, diffuse cardiosclerosis, tricuspid valve insufficiency, venous thrombosis, postthrombophlebitis syndrome, aortic valve insufficiency, capillaritis, pulmonary hypertension, CAD: stable angina pectoris, cardiomyopathy, CAD: post-infarction cardiosclerosis.

Varicose veins of the lower extremities were recorded significantly more often than capillaritis, pulmonary hypertension, CAD: stable angina pectoris, cardiomyopathy, CAD: post-infarction cardiosclerosis.

Hypertensive disease and diffuse cardiosclerosis were diagnosed significantly more often than pulmonary hypertension, CAD: stable angina pectoris, cardiomyopathy, CAD: post-infarction cardiosclerosis, and aortic valve insufficiency – more than CAD: stable angina pectoris, cardiomyopathy, CAD: post-infarction cardiosclerosis.

Vein thrombosis, post-thrombophlebitis syndrome, aortic valve insufficiency were observed significantly more often than cardiomyopathy and CAD: post-infarction cardiosclerosis.

Capillaritis was found significantly less frequently than A. G. M. Raynaud's syndrome, mitral valve insufficiency, atherosclerosis, myocarditis, retinal angiopathy, symptomatic arterial hypertension, livedo reticularis, and varicose veins of the lower extremities.

Pulmonary hypertension was diagnosed significantly less often than A. G. M. Raynaud's syndrome, mitral valve insufficiency, atherosclerosis, myocarditis, retinal angiopathy, symptomatic arterial hypertension, livedo reticularis, varicose veins of the lower extremities, hypertensive disease and diffuse cardiosclerosis.

CAD: stable angina occurred significantly less often than A. G. M. Raynaud's syndrome, mitral valve insufficiency, atherosclerosis, myocarditis, retinal angiopathy, symptomatic arterial hypertension, livedo reticularis, varicose veins of the lower extremities, hypertensive disease, diffuse cardiosclerosis, tricuspid valve insufficiency.

Cardiomyopathy and CAD: post-infarction cardiosclerosis were found significantly less often than A. G. M. Raynaud's

syndrome, mitral valve insufficiency, atherosclerosis, myocarditis, retinal angiopathy, symptomatic arterial hypertension, livedo reticularis, varicose veins of the lower extremities, hypertensive disease, diffuse cardiosclerosis, tricuspid valve insufficiency, vein thrombosis, post-thrombophlebitis syndrome, aortic valve insufficiency.

According to our results, approximately half of SLE patients with circulatory system comorbid lesions have A. G. M. Raynaud's syndrome, mitral valve insufficiency, atherosclerosis, and about a third of patients have myocarditis, retinal angiopathy, symptomatic arterial hypertension, and livedo reticularis. Varicose veins of the lower extremities, hypertensive disease, diffuse cardiosclerosis, tricuspid valve insufficiency, venous thrombosis, post-thrombophlebitis syndrome, aortic valve insufficiency, capillaritis, pulmonary hypertension, CAD: stable angina pectoris, cardiomyopathy and CAD: post-infarction cardiosclerosis were seen with the decreasing frequency. A statistically significant difference was found between the frequency of the certain circulatory system organs comorbid lesions.

Our results confirm the previously reported number of comorbid diseases in patients with SLE [16] and are consistent with the studies of other authors who describe these lesions [2].

The results of the *second stage* of the study, namely its *first step*, was consisted of clarifying the features of the nature and frequency of circulatory system organs comorbid lesions in SLE patients, depending on the gender of a patient, and are shown in table 3.

Table 3

The nature and frequency of the circulatory system organs comorbid lesions, depending on the gender of patients with systemic lupus erythematosus

№	Circulatory system organs comorbid lesions	SLE patients	
		Females, n = 100	Males, n = 12
		n (%)	N (%)
1	2	3	4
1	A. G. M. Raynaud's syndrome	58 (58.00)	3 * (25.00)
2	Mitral valve insufficiency	41 (41.00)	7 (58.33)
3	Atherosclerosis	38 (38.00)	8 (66.67)
4	Myocarditis	32 (32.00)	8 * (66.67)
5	Retinal angiopathy	38 (38.00)	1 * (8.33)
6	Symptomatic arterial hypertension	37 (37.00)	1 * (8.33)
7	Livedo reticularis	32 (32.00)	0 * (0.00)
8	Varicose veins of the lower extremities	10 (10.00)	4 * (33.33)
9	Hypertensive disease	8 (8.00)	3 (25.00)
10	Diffuse cardiosclerosis	9 (9.00)	1 (8.33)
11	Tricuspid valve insufficiency	8 (8.00)	0 (0.00)

Table 3 (continued)

1	2	3	4
12	Vein thrombosis	6 (6.00)	1 (8.33)
13	Postthrombophlebitis syndrome	5 (5.00)	1 (8.33)
14	Aortic valve insufficiency	6 (6.00)	0 (0.00)
15	Capillaritis	4 (4.00)	0 (0.00)
16	Pulmonary hypertension	3 (3.00)	0 (0.00)
17	CAD: stable angina pectoris	1 (1.00)	1 (8.33)
18	Cardiomyopathy	0 (0.00)	1 (8.33)
19	CAD: post-infarction cardiosclerosis	0 (0.00)	1 (8.33)

Note. * – statistically significant difference with the frequency of lesions in females ($p < 0.05$).

As we can see from table 3, among 112 SLE patients, A. G. M. Reynaud’s syndrome was reliably diagnosed more often in females than in males (58 females (58.00 %) and 3 males (25.00 %), $p < 0.05$), mitral valve insufficiency – in 41 females (41.00 %) and in 7 males (58.33 %), between which there is no statistically reliable difference ($p > 0.05$). Atherosclerosis was diagnosed in 38 females (38.00 %) and 8 males (66.67 %), there was no statistically significant difference between the groups.

Myocarditis was found significantly more often in males than in females (8 cases (66.67 %) vs. 32 (32.00 %), $p < 0.05$).

Retinal angiopathy was seen significantly more often in females (females – 38 cases (38.00 %), males – 1 case (8.33 %), $p < 0.05$), as well as symptomatic arterial hypertension (37 females (37.00 %), 1 male (8.33 %), $p < 0.05$) and livedo reticularis (32 females (32.00 %), not found among males (0.00 %), $p < 0.05$). Varicose veins of the lower extremities, on the contrary, were significantly more common among males (10 females (10.00 %), 4 males (33.33 %), $p < 0.05$), as well as hypertensive disease – in 8 females (8.00 %) and in 3 males (25.00 %), between which no statistically reliable difference was found ($p > 0.05$).

Diffuse cardiosclerosis occurred with almost the same frequency in females and males (nine (9.00 %) and one (8.33 %) cases, respectively), tricuspid valve insufficiency – in eight females (8.00 %) and was not detected in males, vein thrombosis – in six females (6.00 %) and one man (8.33 %), post-thrombophlebitis syndrome – in five females (5.00 %) and one man (8.33 %). In all four cases, no statistically reliable difference was found ($p > 0.05$).

Aortic valve insufficiency, capillaritis, and pulmonary hypertension were diagnosed only in females with SLE (six (6.00 %), four (4.00 %), and three (3.00 %) cases, respectively), with no statistically significant difference between the groups, $p > 0.05$.

CAD: stable angina was diagnosed in one woman (1.00 %) and one man (8.33 %), no statistically significant difference was found, $p > 0.05$.

Cardiomyopathy and CAD: post-infarction cardiosclerosis were detected only in males with SLE (one case each (8.33 %)), there were no statistically significant difference between the groups, $p > 0.05$.

Therefore, A. G. M. Reynaud’s syndrome, retinal angiopathy, livedo reticularis, and symptomatic arterial hypertension are more characteristic for females with SLE, and myocarditis, varicose veins of the lower extremities are more characteristic for males, which coincides with the results of other authors [2].

The results of the *second step* of this study stage, devoted to finding out the nature and frequency of the circulatory system comorbid lesions in SLE patients, depending on the patient’s age, are shown in table 4.

Table 4

The nature and frequency of the circulatory system organs comorbid lesions depending on the age of patients with systemic lupus erythematosus

№	Circulatory system organs comorbid lesions	SLE patients		
		young age, n = 64	middle age, n = 44	old age, n = 4
		n (%)	n (%)	n (%)
1	2	3	4	5
1	A. G. M. Reynaud’s syndrome	38 (59.38)	22 (50.00)	1 * (25.00)
2	Mitral valve insufficiency	33 (51.56)	14 * (31.82)	1 (25.00)
3	Atherosclerosis	19 (29.69)	23 * (52.27)	4 * (100.00)
4	Myocarditis	24 (37.50)	14 (31.82)	2 (50.00)
5	Retinal angiopathy	20 (31.25)	17 (38.64)	2 (50.00)
6	Symptomatic arterial hypertension	22 (34.38)	15 (34.09)	1 (25.00)
7	Livedo reticularis	14 (21.88)	17 * (38.64)	1 (25.00)
8	Varicose veins of the lower extremities	6 (9.38)	8 (18.18)	0 (0.00)
9	Hypertensive disease	1 (1.56)	9 * (20.45)	1 * (25.00)
10	Diffuse cardiosclerosis	3 (4.92)	3 (6.82)	4 ** (100.00)
11	Tricuspid valve insufficiency	5 (7.81)	3 (6.82)	0 (0.00)
12	Vein thrombosis	1 (1.56)	5 * (11.36)	1 * (25.00)
13	Postthrombophlebitis syndrome	2 (3.13)	4 (9.09)	0 (0.00)
14	Aortic valve insufficiency	1 (1.56)	4 (9.09)	1 * (25.00)
15	Capillaritis	3 (4.92)	1 (2.27)	0 (0.00)
16	Pulmonary hypertension	3 (4.92)	0 (0.00)	0 (0.00)

Table 4 (continued)

1	2	3	4	5
17	CAD: stable angina pectoris	0 (0.00)	0 (0.00)	2 *# (50.00)
18	Cardiomyopathy	1 (1.56)	0 (0.00)	0 (0.00)
19	CAD: post-infarction cardiosclerosis	0 (0.00)	0 (0.00)	1 *# (25.00)

Notes: * – statistically significant difference with the frequency of lesions in young patients ($p < 0.05$);

– statistically significant difference with the frequency of lesions in middle-aged patients ($p < 0.05$).

As it can be seen from table 4, A. G. M. Raynaud's syndrome was more often diagnosed in young patients (38 cases, 59.38 %), fewer cases were detected in middle-aged patients (22 cases, 50.00 %), and the least often – in elderly patients (1 case, 25.00 %), there was a statistically significant difference only with the number of young patients with such vascular lesions. Mitral valve insufficiency was observed in half of young patients (33 cases, 51.56 %), in a third of middle-aged patients (14 cases, 31.82 %), and the least – in elderly patients (1 case, 25.00 %), there was a statistically significant difference only with the number of young patients. Atherosclerotic vascular damage was diagnosed in all the examined elderly patients (4 cases, 100.00 %), in half of middle-aged patients (23 cases, 52.27 %), and in a third of young patients (19 cases, 29.69 %), but this difference was not statistically reliable. Myocarditis was detected with approximately the same frequency in patients of each age group (24 young patients (37.50 %), 14 middle-aged patients (31.82 %) and 2 elderly patients (50.00 %)).

Retinal angiopathy was diagnosed in half of elderly patients (2 cases, 50.00 %), in one third of young (20 cases, 31.25 %) and middle-aged patients (17 cases, 38.64%), but there was no statistically reliable difference between the groups found. Symptomatic arterial hypertension was diagnosed in every third patient of each age group (22 young patients (34.38 %), 15 middle-aged patients (34.09 %) and 1 elderly patient (25.00 %)). Livedo reticularis was observed in one quarter of young (14 cases, 21.88 %), elderly (one case, 25.00 %) patients, and in a third of middle-aged patients (17 cases, 38.64 %), no statistically significant difference between the groups was found. Varicose veins of the lower extremities were diagnosed in six young patients (9.38 %), eight middle-aged patients (18.18 %), and not found in elderly patients. One quarter of middle-aged (nine cases, 20.45 %) and elderly (one case, 25.00 %) patients were diagnosed with hypertensive disease, only one case (1.56 %) of this disease was diagnosed among young patients, a statistically significant difference was found only with the number of young patients. Diffuse cardiosclerosis was significantly more often observed in all four elderly patients (100.00 %) than in young and middle-aged patients (three cases each (4.92 % and 6.82 %, respectively)).

In isolated cases, tricuspid valve insufficiency (five young patients (7.81 %), three middle-aged patients (6.82 %)), post-thrombophlebitis syndrome (two young patients (3.13 %), four middle-aged patients (9.09 %)), capillaritis (three young patients (4.92 %), one middle-aged patient (2.27 %)) were diagnosed. These lesions were not detected among elderly SLE patients, and there was no statistically significant difference. Thrombosis of peripheral veins was recorded more often among elderly (one case, 25.00 %) than among young (1.56 %) or middle-aged patients (11.36 %). Aortic valve insufficiency was more often diagnosed in elderly patients (one case (25.00 %), among young patients – one case (1.56 %), middle-aged – four cases (9.09 %), the statistically significant difference was found with the group of young patients. Pulmonary hypertension and cardiomyopathy were detected only in the group of young patients (4.92 and 1.56 %, respectively). CAD: stable angina pectoris and CAD: postinfarction cardiosclerosis were reliably more characteristic for the elderly patients – two (50.00 %) and one (25.00 %) cases, respectively, no lesions were found among the patients of other age groups.

Analysis of the information indicates that A. G. M. Raynaud's syndrome is characteristic for the young patients with SLE, and such circulatory system organs comorbid lesions as atherosclerosis, hypertensive disease, diffuse cardiosclerosis, vein thrombosis, aortic valve insufficiency, stable angina pectoris and postinfarction cardiosclerosis are most characteristic for elderly patients with SLE, which echoes the results of other authors [2].

Table 5 shows the results of the *third step* of the second stage of the study.

Table 5

The nature and frequency of the circulatory system organs comorbid lesions depending on the duration of systemic lupus erythematosus

№	Circulatory system organs comorbid lesions	SLE duration			
		Group A (less than 1 year), n = 5	Group B (1–5 years), n = 41	Group C (6–10 years), n = 23	Group D (more than 10 years), n = 43
		n (%)	n (%)	n (%)	n (%)
1	2	3	4	5	6
1	A. G. M. Raynaud's syndrome	2 (40.00)	21 (51.22)	14 (60.87)	24 (55.81)
2	Mitral valve insufficiency	2 (40.00)	17 (41.46)	18 # (78.26)	11 * (25.58)
3	Atherosclerosis	0 (0.00)	12 (29.27)	15 *# (65.22)	19 * (44.19)
4	Myocarditis	2 (40.00)	15 (36.59)	8 (34.78)	15 (34.88)
5	Retinal angiopathy	0 (0.00)	11 (26.83)	7 (30.43)	21 *# (48.84)
6	Symptomatic arterial hypertension	1 (20.00)	6 (14.63)	11 # (47.83)	20 # (46.51)

Table 5 (continued)

1	2	3	4	5	6
7	Livedo reticularis	0 (0.00)	10 (24.39)	3 (13.04)	19 *# * (44.19)
8	Varicose veins of the lower extremities	0 (0.00)	2 (4.88)	6 # (26.09)	6 (13.95)
9	Hypertensive disease	0 (0.00)	3 (7.32)	4 (17.39)	4 (9.30)
10	Diffuse cardiosclerosis	0 (0.00)	2 (4.88)	3 (13.04)	5 (11.63)
11	Tricuspid valve insufficiency	0 (0.00)	1 (2.44)	2 (8.70)	5 (11.63)
12	Vein thrombosis	0 (0.00)	1 (2.44)	0 (0.00)	6 # * (13.95)
13	Postthrombophlebitis syndrome	0 (0.00)	1 (2.44)	2 (8.70)	3 (6.98)
14	Aortic valve insufficiency	0 (0.00)	1 (2.44)	3 (13.04)	2 (4.65)
15	Capillaritis	1 (20.00)	3 (7.32)	0 * (0.00)	0 *# (0.00)
16	Pulmonary hypertension	0 (0.00)	0 (0.00)	0 (0.00)	3 (6.98)
17	CAD: stable angina pectoris	0 (0.00)	0 (0.00)	0 (0.00)	2 # (4.65)
18	Cardiomyopathy	0 (0.00)	0 (0.00)	1 (4.35)	0 (0.00)
19	CAD: post-infarction cardiosclerosis	0 (0.00)	0 (0.00)	0 (0.00)	1 (2.33)

Notes:

* – statistically significant difference with the frequency of lesions in patients whose SLE lasts for less than 1 year ($p < 0.05$);

– statistically significant difference with the frequency of lesions in patients whose SLE lasts for 1–5 years ($p < 0.05$);

* – statistically significant difference with the frequency of lesions in patients whose SLE lasts for 6–10 years ($p < 0.05$).

As can be seen from table 5, A. G. M. Raynaud’s syndrome was diagnosed the least often in patients of group A (2 cases, 40.00 %) compared to patients of group B (21 cases, 51.22 %), C (14 cases, 60.87 %) and D (24 cases, 55.81 %), where A. G. M. Raynaud’s syndrome was common with almost the same frequency. Mitral valve insufficiency was significantly more often observed in patients of group C (18 cases, 78.26 %), with the same frequency in patients of groups A and B (2 (40.00 %) and 17 (41.46 %) cases, respectively), the least – in patients of group D (11 cases (25.58 %)). In 15 SLE patients from group C, atherosclerosis was detected (65.22 %), which is significantly more often than in patients from groups A and B (not detected (0.00%) and 12 (29.27 %) cases, respectively). This lesion was also found in 19 SLE patients of group D (44.19 %). 2 cases of myocarditis were diagnosed in SLE patients from group A (40.00 %), 15 cases (36.59 %) – in patients from group B, 8 cases (34.78 %) – in patients of group C and 15 cases (34.88 %) – in patients of group D.

Retinal angiopathy reliably the most often occurred in SLE patients from group D (21 cases, 48.84 %). In group B, this lesion was detected in 11 patients (26.83 %), in group C – in 7 (30.43 %), but it was not detected in SLE patients of group A. Livedo reticularis the most often was detected in SLE patients of group D (19 cases, 44.19 %), in 10 SLE patients of group B (24.39 %) and in 3 SLE patients of group C (13.04 %), but this lesion was not diagnosed in SLE patients of group A. Symptomatic arterial hypertension reliably more often occurred in SLE patients of group C (11 cases, 47.83 %) and group D (20 cases, 46.51 %) than in group A (1 case, 20.00 %) or B (6 cases, 14.63 %) patients. Varicose veins of the lower extremities were detected in two patients of group B (4.88 %), in six patients of group C (26.09 %), in six patients of group D (13.95 %), and were not detected in SLE patients of group A. Hypertensive disease was diagnosed with the following frequency: in patients of group A – none, in patients of group B – three cases (7.32 %), in patients of group C – four cases (17.39 %), in patients of group D – four cases (9.30 %). Diffuse cardiosclerosis was diagnosed in two SLE patients of group B (4.88 %), in three patients of group C (13.04 %), in five patients of group D (11.63 %), but in none from group A.

Isolated cases of tricuspid valve insufficiency were found in three groups: one case – in group B (2.44 %), two cases – in group C (8.70 %), five cases – in group D (11.63 %), but not detected in group A. Thrombosis of peripheral veins occurred mainly in SLE patients of group D (six cases (13.95 %)), in group B with a frequency of 2.44 % (one case), and was not detected in groups A and C. In a few cases, patients with SLE were diagnosed with post-thrombophlebitis syndrome and aortic valve insufficiency: in group B – one case each (2.44 %), in group C – two and three cases (8.70 and 13.04 %), respectively, in group D – three and two cases (6.98 and 4.65 %), respectively, these lesions were not detected in patients of group A.

Capillaritis was the most often diagnosed in patients with SLE of group A (one case, 20.00 %) and group B (three cases, 7.32 %) compared to patients of groups C and D (0.00 %).

Pulmonary hypertension, stable angina pectoris and post-infarction cardiosclerosis were found in patients of group D (three (6.98 %), two (4.65 %), one (2.33 %) cases, respectively), and cardiomyopathy – in a patient of group C (one case (4.35 %)), these diseases were not found in other groups.

So, having studied the circulatory system organs comorbid lesions in SLE patients, we found out that some of them depend on the duration of the disease. Namely, capillaritis most often occurs in patients with the shortest duration of SLE, and mitral valve insufficiency, atherosclerosis, retinal angiopathy, livedo reticularis, vein thrombosis, symptomatic arterial hypertension and stable angina – in patients whose SLE lasts the longest (6–10 years and more than 10 years).

Conclusions. Almost half of patients with systemic lupus erythematosus and circulatory system organs comorbid lesions have A. G. M. Raynaud’s syndrome, mitral valve

insufficiency and atherosclerosis, about a third of patients have myocarditis, retinal angiopathy, symptomatic arterial hypertension and livedo reticularis. The varicose veins of the lower extremities, hypertensive disease, diffuse cardiosclerosis, tricuspid valve insufficiency, vein thrombosis, post-thrombophlebitis syndrome, aortic valve insufficiency, capillaritis, pulmonary hypertension, CAD: stable angina pectoris, cardiomyopathy and CAD: post-infarction cardiosclerosis were found with the decreasing frequency. A statistically significant difference between the frequency of the certain circulatory system organs comorbid lesions was found.

A. G. M. Raynaud's syndrome (58.00 %), retinal angiopathy (38.00 %), livedo reticularis (32.00 %) and symptomatic arterial hypertension (37.00 %) are more characteristic for females with SLE, and myocarditis

(66.67 %), varicose veins of the lower extremities (33.33 %) are more characteristic for males.

A. G. M. Raynaud's (59.38 %) syndrome is characteristic for the young patients with SLE, atherosclerosis (100.00 %), hypertensive disease (25.00 %), diffuse cardiosclerosis (100.00 %), vein thrombosis (25.00 %), aortic valve insufficiency (25.00 %), stable angina pectoris (50.00 %) and postinfarction cardiosclerosis (25.00 %) are most characteristic for elderly patients with SLE.

Capillaritis (20.00 %) most often occurs in patients with the shortest duration of SLE, and mitral valve insufficiency (78.26 %), atherosclerosis (65.22 %), retinal angiopathy (48.84 %), livedo reticularis (44.19 %), vein thrombosis (13.95 %), symptomatic arterial hypertension (47.83 %) and stable angina (4.65 %) – in patients whose SLE lasts the longest (6–10 years and more than 10 years).

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Conflict of interest

The authors of this article argue that there is no conflict of interest.

Circulatory System Organs Comorbid Lesions in Patients with Systemic Lupus Erythematosus: Nature and Frequency; Characteristics Depending on Gender, Age and Disease Duration

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Introduction. Systemic lupus erythematosus (SLE) is a disease with numerous clinical manifestations and an unpredictable course. It often lasts for several months or years, with alternating remissions and exacerbations.

Multiple organs can be affected simultaneously with varying degrees of severity, resulting in treatment- and disease-related comorbidities, including circulatory system diseases, which are one of the leading causes of death of SLE patients.

The aim of the study. To find out the nature and frequency of the circulatory system organs comorbid lesions in patients with systemic lupus erythematosus, to characterize them depending on the gender, age and the disease duration.

Materials and methods. Prior to performing the study all patients signed the voluntary consent to participate in accordance with the requirements of Helsinki Declaration of Human Rights, the Council of Europe Convention on Human Rights and Biomedicine. The cohort under investigation included 112 patients with diagnosed SLE of different severity with preliminary stratification as follows: females 89.29 %, patients of working age (57.14 % – young and 39.29 % – middle aged), unemployed (58.04 %), III disability group patients (45.54 %), city residents (62.50 %). According to the results of the disease duration assessment, a significant number of patients with SLE and circulatory system organs comorbid lesions have been ill for 1–5 years (36.61 %) and more than 10 years (38.39 %). All of them were patients of the rheumatology department of the Communal Non-Profit Enterprise of the Lviv Regional Council "Lviv Regional Clinical Hospital" from 2016 to 2021. The research was carried out in several stages, during which the nature and frequency of the circulatory system comorbid lesions with respect to gender, age and disease duration were estimated.

Results. While completing the study, almost half of patients with SLE were diagnosed with Raynaud's syndrome, mitral valve insufficiency and atherosclerosis, about 1/3 – with myocarditis, retinal angiopathy, symptomatic arterial hypertension and livedo reticularis. The varicose veins of the lower extremities, hypertensive disease, diffuse cardiosclerosis, tricuspid valve insufficiency, vein thrombosis, post-thrombophlebitis syndrome, aortic valve insufficiency, capillaritis, pulmonary hypertension, coronary artery disease (CAD) including stable angina pectoris, cardiomyopathy and post-infarction cardiosclerosis were found with the decreasing frequency.

Raynaud's syndrome was significantly more often diagnosed in females and young people; retinal angiopathy, livedo reticularis and symptomatic arterial hypertension – in females and those patients whose SLE lasted for more than 10 years; myocarditis, varicose veins of the lower extremities – in males; capillaritis – in patients with the shortest duration of SLE; atherosclerosis and mitral valve insufficiency – in elderly patients and patients with SLE lasting for 6–10 years; vein thrombosis and stable angina – in elderly patients and those with SLE lasting for more than 10 years; hypertensive disease, diffuse cardiosclerosis, aortic valve insufficiency, post-infarction cardiosclerosis were the most characteristic for the elderly patients with SLE.

Conclusions. In patients with systemic lupus erythematosus, a number of circulatory system organs comorbid lesions were found. Having studied their nature and frequency, characterizing them depending on gender, age and the disease duration, we found out the certain features that should be taken into consideration during the screening examination of circulatory system disorders in patients with systemic lupus erythematosus and providing them the integrated care to improve their life quality. With this in mind, systemic lupus erythematosus requires further detailed study.

Keywords: systemic lupus erythematosus, circulatory system comorbid lesions, diagnosis.

Коморбідні ураження органів системи кровообігу у хворих на системний червоний вовчак: характер і частота; характеристика залежно від статі, віку й тривалості хвороби

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Вступ. Системний червоний вовчак (СЧВ) – хвороба з численними клінічними проявами й непередбачуваним перебігом. Часто перебігає упродовж декількох місяців або років, із чергуванням ремісій і загострень. Можуть бути уражені одночасно декілька органів із різним ступенем тяжкості, що призводить до виникнення коморбідних уражень, пов'язаних із лікуванням та хворобою, включаючи хвороби органів системи кровообігу, які є однією з основних причин смерті хворих на СЧВ.

Мета. З'ясувати характер і частоту коморбідних уражень органів системи кровообігу у хворих на системний червоний вовчак, охарактеризувати залежно від статі, віку, тривалості хвороби.

Матеріали й методи. Для виконання дослідження після підписання добровільної згоди на участь, відповідно до вимог Гельсінкської декларації прав людини, Конвенції Ради Європи про права людини і біомедицину, в рандомізований спосіб із попередньою стратифікацією за наявністю СЧВ включено 112 хворих, серед яких більшість жінок (89,29 %), хворих працездатного віку (57,14 % молодого і 39,29 % середнього віку), що не

працювали (58,04 %), мали III групу інвалідності (45,54 %), були жителями міста (62,50 %). За результатами оцінювання тривалості хвороби, значна частина хворих на СЧВ з коморбідними ураженнями органів системи кровообігу хворіли 1–5 років (36,61 %) і понад 10 років (38,39 %). Усі вони були пацієнтами ревматологічного відділу Комунального некомерційного підприємства Львівської обласної ради «Львівська обласна клінічна лікарня» з 2016 по 2021 рік.

Дослідження проводили в декілька етапів, на яких визначали характер і частоту коморбідних уражень органів системи кровообігу в усіх хворих на СЧВ із наступною характеристикою залежно від статі, віку, тривалості хвороби.

Результати. Під час проведеного дослідження майже у половини хворих на СЧВ діагностовано синдром А. Г. М. Рейно, недостатність мітрального клапана та атеросклероз, близько у третини – міокардит, ангіопатію сітківки, симптоматичну артеріальну гіпертензію та ретикулярне ліведо, а також зі спадною частотою були виявлені варикозна хвороба вен нижніх кінцівок, гіпертонічна хвороба, дифузний кардіосклероз, недостатність трикуспідального клапана, тромбоз вен, посттромбофлебітний синдром, недостатність клапана аорти, капілярит, легенева гіпертензія, ІХС: стабільна стенокардія, кардіоміопатія, ІХС: постінфарктний кардіосклероз.

Синдром А. Г. М. Рейно достовірно частіше фіксували у жінок і осіб молодого віку, ангіопатію сітківки, ретикулярне ліведо і симптоматичну артеріальну гіпертензію – у жінок і тих хворих, СЧВ яких триває понад 10 років, міокардит, варикозну хворобу вен нижніх кінцівок – у чоловіків, капілярит – у хворих із найменшою тривалістю СЧВ, атеросклероз і недостатність мітрального клапана – у хворих похилого віку та хворих, СЧВ у яких триває 6–10 років, тромбоз вен і стабільну стенокардію – у хворих похилого віку й тих, які хворіють на СЧВ понад 10 років; гіпертонічна хвороба, дифузний кардіосклероз, недостатність клапана аорти, постінфарктний кардіосклероз – найбільш характерні для хворих на СЧВ похилого віку.

Висновки. У хворих на системний червоний вовчак виявлено низку коморбідних уражень органів системи кровообігу. Вивчивши й проаналізувавши їхній характер і частоту, залежно від статі, віку, тривалості хвороби, ми з'ясували певні особливості, які потрібно брати до уваги під час скринінгового обстеження уражень органів системи кровообігу хворих на системний червоний вовчак і надання інтегрованої допомоги для поліпшення якості життя. Із огляду на це системний червоний вовчак потребує подальшого детального дослідження.

Ключові слова: системний червоний вовчак, коморбідні ураження органів системи кровообігу, діагностика.

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