ORIGINAL INVESTIGATIONS

Survival and lethal outcomes in Orenburg population of patients with systemic lupus erythematosus

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Currently, the prognosis for systemic lupus erythematosus (SLE) has improved significantly, but the relative risk of death in these patients is still higher than in the general population. Thrombotic complications are one of the leading causes of death in SLE.

Objective: *to analyze the survival rate and structure of lethal outcomes in Orenburg population of patients with SLE, including deaths due to thrombotic complications.*

Material and methods. *A two-stage study of SLE progression and patient survival was conducted from 2007 to 2022. Clinical signs of the disease were analyzed in all patients at baseline (n=68) and in survivors (n=50) after 15 years. The median age at the time of enrolment in the study was 35 [29; 45] years, the disease duration – 7.5 [3; 13.5] years. During the second stage, the characteristics of the course of the disease in the survived patients and the causes of death in those who died over 15-year period were determined.*

Results and discussion. *The 10-, 15- and 20-year survival rates in Orenburg population of patients with SLE reached 98.5, 95.5 and 86.3%, respectively. During this period, 18 (26.5%) deaths were registered, the median age of the deceased was 48.5 [39; 57] years, and the duration of the disease was 22 [16; 30] years. The most common causes of death were thrombotic complications (n=14, 78%) due to antiphospholipid syndrome, lupus nephritis, and arterial hypertension. Less frequently, infectious complications were the cause of death (n=4, 22%). Patients with thrombotic complications had a 20-year survival rate of 80.2% that was significantly lower than in the SLE group without thrombosis.*

Conclusion. *The results obtained allow to consider the presence of thrombotic complications in patients with SLE in Orenburg population as an unfavorable prognostic factor.*

Keywords: *systemic lupus erythematosus; thrombotic complications; risk factors; survival; mortality.*
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Systemic lupus erythematosus (SLE) is a systemic autoimmune rheumatic disease of unknown etiology, characterized by the formation of a wide range of non-specific autoantibodies to various components of the nuclei and immune complexes causing immune inflammatory damage to internal organs, and associated with a high mortality rate [1, 2]. Today, thanks to the improvement of early diagnosis, rational use of immunosuppressive drugs and availability of modern treatments, the prognosis for SLE has significantly improved, but the relative risk of death in these patients is still higher than in the general population [3, 4]. In addition, the structure of the causes of death from this pathology is also changing.

According to the literature data, in the middle of the past century almost half of patients with SLE died within the first 5 years. In the early stages of the disease, the death was mainly associated with kidney damage due to high disease activity, and in a later period – with cardiovascular complications and functional insufficiency of internal organs [5–8]. Infectious complications as a cause of death were common at all stages of the disease [3, 9–11]. In the multicenter analysis of morbidity and mortality of 1000 patients with SLE, conducted by the European Working Group from 1990 to 2000, there was a significant increase in life expectancy: the 5-year survival rate reached 95%, and the 10-year survival old reached 92%. The most common causes of death during the initial 5-year observations were high SLE activity and infections (28% each). Over the past 5 years of observation, the most frequent cause of death was thrombosis (26.1%) [12].

Since the early 2000s, the survival rate of patients with SLE has significantly increased, and the structure of causes of death has changed [4, 13]. So, according to a meta-analysis of a large number studies published from 2008 to 2016, the 5-, 10-and 15-year survival rates were 95%; 89% and 82%, respectively [13]. In the structure of causes of mortality, the proportion of active SLE decreased, and the proportion of infections and cardiovascular complications increased [4]. In Turkey, South Korea, China, Egypt, Taiwan the 5-, 10- and 15-year survival rates of patients with SLE varied from 82.9% to 97.8%, 90% to 95.5%, and 51.4% to 88.2%, respectively [14–19]. Meanwhile the leading causes of death in these populations of patients with SLE were infections [15, 17, 18, 20, 21], cardiovascular pathology [15, 16, 20, 21], cerebrovascular diseases and malignant neoplasms [15, 17, 20]. According to the meta-analysis of 15 studies which was conducted by Y.H. Lee et al. [22] and included 26,101 patients with SLE from Northern America, Europe and Asia, 4640 patients (17.7%) died. The authors found an increase in the mortality of patients with SLE from infections 5 times, from kidney damage 4.7 times and from cardiovascular disease 2.3 times, while mortality from malignant neoplasms was comparable to that in the general population.

In domestic works devoted to the study of the survival rates of patients with SLE, an increase in life expectancy since the middle

of the past century was also noted. So, according to I.E. Tareeva et al. [5], in the 1980s the 5-year survival rate of patients with SLE with lupus nephritis (LN) was 50%, and the 10- and 15-year survival rates were 49% and 37%, respectively. Thus, kidney damage was the main cause of death of patients. According to the observations of a group of researchers, in the Republic of Tatarstan from 2004 to 2018 the 5-, 10-, and 15-year survival rates in 256 patients with SLE reached 93.7%, 90.8% and 86.4%, respectively [23]. The authors did not analyze the structure of the causes of death; however, they revealed factors significantly affecting the probability of death: arterial hypertension (AH), active LN, antiphospholipid syndrome (APS) and thrombotic events [23].

Thus, thrombotic complications occupy the leading positions in the structure of mortality in SLE. In patients with SLE, thromboses develop 10–14 times more often than in the general population, their incidence ranges from 4.2 to 16 per 1000 patient-years [24–26]. E. Lundstrцm et al. [27] revealed thrombosis in 210 (31,7%) of 665 patients with SLE, including arterial thrombosis – in 103 (15,6%), and venous thrombosis - in 107 (16.1%). R. Kaiser et al. [28] reported thrombosis in 629 (31%) of 2030 patients with SLE. So, deep vein thrombosis (DVT) was diagnosed in 172 (8.5%), pulmonary embolism (PE) – in 56 (2.8%), acute cerebrovascular accident (ACVA) – in 106 (5.2%) and myocardial infarction (MI) in 52 (2.6%) patients. Obviously, the risk of thrombotic complications in patients with SLE is increased due to the presence of multiple factors contributing to their occurrence.

The main risk factor for thrombosis in patients with SLE is antiphospholipid antibody positivity (aPL) [28]: an increase in lupus anticoagulant, anti-cardiolipin antibody (aCL), anti-cardiolipin β_2 glycoprotein 1 complex antibody ($a\beta_2GP_1$) determines the high risk of thrombosis in patients with SLE (for aCL odds ratio (OR) is 4.03; 95% confidence interval (CI) is 2.06-7.86, for $a\beta_2GP_1$ OR – 5.10; 95% CI – 2.58-10.1) [25]. Other risk factors for thrombosis related to SLE are disease duration, activity of the pathological process, presence of LN, an increase in level of von Willebrand factor in the serum. There are very important population risk factors of thrombotic complications, such as age, body mass index (BMI), smoking, glucocorticoid (GC) therapy, presence of AH, diabetes mellitus (DM), cancer [29–31].

Thus, currently it is still important to study the causes of death in patients with SLE, especially cardiovascular events and fatal thrombosis. Our objective was to study survival rates and structure of deaths in the Orenburg population of patients with SLE, including deaths due to thrombotic complications.

Material and methods. The two-stage study of the course of SLE and patient survival rates was conducted from 2007 to 2022. The diagnosis of SLE was verified according to the generally accepted criteria (1997, 2012) [32, 33]. In all patients initially, and in survivors after 15 years, SLE activity was assessed by SLEDAI-2K (Systemic Lupus Erythematosus Disease Activity Index in modification 2K) [34], SDI damage index (Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index) [35], features of the multiple organ damage, presence of APS according to the generally accepted international criteria [36–38]. The second stage included determination of the nature of the course of the disease in survivors, and causes of death of patients included in the first stage of the study who died during the 15-year follow-up period.

The study was approved by local ethics committee of Orenburg State Medical University of the Ministry of Health of Russia (protocol № 285 of 23.11. 2020). All patients signed informed consent to participate in the study.

The statistical analysis of the results was carried out using the Statistica 12.0 software package. Normal distribution was assessed using Shapiro-Wilk test. To determine the significance of differences in quantitative characteristics between unrelated samples in the case of normal distribution t-test was used, for qualitative characteristics – Pearson's χ^2 test, in abnormal distribution – Mann–Whitney test. For comparison of dependent samples Wilcoxon test was used; for assessment of the dynamics of binary variables - McNemar test. The central trend was described using the median (Me), variability of characteristics was determined using the interquartile interval [25th; 75th percentiles]. The survival rate was analyzed using Kaplan-Meier curves, to assess the effect of thrombosis on survival – the Cox test. Differences were considered statistically significant at $p<0.05$.

Results. The study included 68 patients with SLE, who were predominantly women (98.5%). The median age was 35 [29; 45] years, disease duration – 7.5 [3; 13.5] years, SLEDAI-2K – 8.5 [4.5; 14], SDI – 1 [1; 2]. The initial characteristics of patients with SLE are presented in Table 1. At the time of inclusion in the study, various systemic manifestations of the disease were found. We noted various skin changes, more often in the form of erythema of the face, neck, chest (n=34; 51%), livedo reticularis (n=20; 29%), lupus cheilitis (n=11, 16%). Thirty-nine (57,3%) patients were affected by joint damage. Constitutional disorders commonly found in SLE (weight loss, hair loss, fever) were detected in 52 (76,4%) patients. Heart damage in the form of Liebman-Sachs endocarditis was observed in 5 (7.3%) patients, myocarditis – in 3 (4.3%) patients. Almost a third of patients (n=19, 28%) had peripheral polyneuropathy, 3 (4,3%) – ACVA in all cases combined with APS. Lesions of serous membranes, mainly adhesive pleurisy, were noted in 11 (16.1%) cases. In 28 (41.1%) patients kidney damage was diagnosed in the form of active LN, in 18 (26.4%) – APS.

Depending on the presence of thrombotic complications in their medical histories and laboratory and instrumental methods of analysis, all patients were divided into two groups (see Table 1). Group 1 included 8 (12%) patients with thrombosis. Among the patients of this group, 3 patients (4.4%) had ACVA, another 3 (4.4%) – DVT in the medical history; 1 patient (1.4%) had PE and 1 more (1.4%) – obstetric pathology (miscarriage, frozen pregnancy). The remaining 60 (88%) patients without thrombosis were included in Group 2. Patients of both groups turned out to be comparable in age and disease duration. In Group 1 in comparison with Group 2 there were statistically significantly higher SLEDAI-2K and SDI, the medians of which were 9.5 [6; 14] and 8 [4; 14.5] ($p<0.05$); and 2 [1; 3] and 1 [0.5; 2] ($p<0,05$), respectively. In Group 1 skin damage was detected significantly more often than in Group 2: it was represented by necrotizing ulcerative vasculitis (NUV, in 25% and 1.7% of cases respectively; $p<0.05$) and livedo reticularis (in 75% and 23.3%; $p<0.05$), as well as joint damage (in 87.5% and 53%; $p<0.05$). When determining the concentration of aPL in Group 1 in comparison with Group 2, a significant increase in IgG aβ2GP1 was detected (median 35.5 [23.5; 134.3] and 6.2 [3.8; 13.7] U/ml; $p < 0.05$), and total aCl (20.4 [13.7; 75.4] and 5.8 [2.9; 11.1] U/ml respectively; $p<0.05$; see Table 1).

After 15 years, 50 (73.5%) of 68 patients were alive. During the observation period 15 (30%) of them had a non-fatal thrombotic event, though 8 (53.3%) of these patients initially did not have

Table 1. Characteristics of patients with SLE (n=68)

Indicator	All patients (n=68)	Group 1 (n=8)	Group 2 (n=60)
Age, years, Me [25th; 75th percentiles]	35 [29; 45]	36,5 [29,5; 44]	35 [29; 45,5]
Disease duration, years, Me [25th; 75th percentiles]	7,5 [3; 13,5]	9 [4; 15,5]	7[3; 13]
SLEDAI-2K, Me [25th; 75th percentiles]	8,5 [4,5; 14]	9,5 [6; 14]*	8 [4; 14,5]
SDI, Me [25th; 75th percentiles]	1 [1; 2]	2 [1; 3]*	1 [0,5; 2]
Skin damage, n (%):			
erythema	34 (51)	3 (37,5)*	31 (51,6)
NUV	3 (4,3)	2 (25)*	1 (1,7)
livedo reticularis	20 (29)	6 (75)*	14 (23,3)
lupus cheilitis	11 (16)	3 (37,5)	8 (13,3)
Joint damage, n (%):			
arthralgia	27 (39,7)	4 (50)*	23 (38)
polyarthritis	12 (17,6)	3 (37,5)*	9 (15)
Constitutional disorders, n (%):			
weight loss	13 (19,1)	1 (12,5)	12 (20)
hair loss	29 (42,6)	3 (37,5)	26 (43,3)
Disturbance of thermoregulation (fever), n (%):	10 (14,7)	1 (12,5)	9 (15)
Lesion of serous membranes, n (%):			
adhesive pleurisy	11 (16,1)	1 (12,5)*	10 (16,6)
exudative pleurisy	1 (1,5)	0 (0)	1 (1,6)
Neurological disorders, n (%):			
CNS damage	9 (13,2)	2 (25)	7 (11,6)
ACVA	3 (4,3)	3 (37,5)	0 (0)
polyneuropathy	19 (28)	2 (25)	17 (28,3)
Heart damage, n (%):			
Libman-Sacks endocarditis	5 (7,3)	2 (25)	3 (5)
myocarditis	3 (4,3)	1 (12,5)	2 (3,3)
Kidney damage (LN), n (%)	28 (41,1)	4 (50)*	24 (40)
APS, n (%)	18 (26,4)	6 (75)*	12 (20)
$a\beta_2GP_1$, U/ml, Me [25th; 75th percentiles]	6,8 [4,4; 23,8]	35,5 [23,5; 134,3]*	6,2 [3,8; 13,7]
aCL, Me [25th; 75th percentiles]:			
total aCL, U/ml	6,5 [3,4; 14,9]	20,4 [13,7; 75,4]*	5,8 [2,9; 11,1]
IgG, g/l (7–16 g/l)	12,3 [10,3; 15,8]	13,3 [11,7; 15]	12,3 [10,1; 16,5]
IgA, g/l (0,7–4 g/l)	2,5 [1,8; 3,3]	3 [2; 3,4]	2,4 [1,8; 3,3]
IgM, g/l (0,4–2,3 g/l)	1,4 [1; 2,2]	2 [1,4; 3,5]	1,4 [0,9; 2]

Note. CNS – central nervous system; NUV – necrotizing ulcerative vasculitis. *p 0.05 – for comparison of Group 1 and Group 2 of patients with SLE.

Table 2. Clinical characteristics of patients with SLE after 15 years of observation (n=50), Me [25th; 75th percentile]

Indicator	All patients	Group 1 (with thromboses, n=15)	Group 2 (without thromboses, n=35)
Age, years	50 [44; 60]	54 [44; 61]	50 [41; 60]
Disease duration, years	21,5 [17; 26]	23 [21; 30]	20 [17; 24]
SLEDAI-2K	4 [2; 5]	4 [2; 10]	3 [2; 5]
SDI	2 [2; 4]	3 [2; 4]	2 [1; 4]

thrombosis. Thus, over 15 years, the proportion of patients with thrombotic complications significantly increased – from 12% to 30% ($p<0.05$).

Clinical characteristics of the survivors with SLE after 15 years based on the presence of a thrombotic event are given in Table 2. After 15 years patients of both groups (with and without

Table 3. Risk factors for thrombotic complications in patients with SLE in the first and second stages of the study

Indicator	All patients (n=68)	Initially, Group 1 (n=8)	Initially, Group 2 (n=60)	All patients (n=50)	After 15 years: Group 1 (n=15)	After 15 years: Group 2 (n=35)
Smoking, n (%)	6 (8,8)	1 (12,5)*	5 (8,3)	5 (10)	1 (6,6)	4 (11,4)
BMI, w/m², Me [25th; 75th percentiles]	30 [23,7; 34] #	25,5 [22; 29,5] *,#	31 [24.2; 34]#	37 [33; 42]	35 [31; 38]	38 [34; 43]
Dose of GC, mg/d recalculated for prednisolone, Me [25th; 75th percentiles]	5 [2,5; 12,5]#	5 [2,5; 10]#	5 [2,5; 7,5]#	10 [5; 35]	10 [5; 30]	10 [5; 20]
AH, n (%)	25 (36,7)	3 (37,5)	22 (36,6)	36 (72)	13 (86,6)**	23 (65,7)
APS, n (%)	18 (26,4)	6 (75)*	12 (20)	23 (46)	12 (80)**	11 (31,4)
LN, n (%)	28 (41,1)	4 (50)*	24 (40)	37 (74)	12 (80)**	25 (71,4)
DM, n (%)	2 (2,9)	0 (0)	2 (3,3)	4 (8)	2 (13,3)	2 (5,71)
Malignant neoplasms, n (%)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	1 (2,8)
Infectious complications, n (%)	0 (0)	0 (0)	0 (0)	5 (10)	0 (0)	5 (14,2)

*p 0.05 – for comparison of Group 1 and Group 2 of patients with SLE initially; **p 0.05 – for comparison of Group 1 and Group 2 of patients with SLE in dynamics; #p 0.05 – for comparison of the corresponding groups in dynamics.

thrombosis) were comparable by age, disease duration and SLEDAI-2K index (see Table 2). SDI in the group with thrombotic complications was slightly higher than in the group without them (the median was 3 [2; 4] and 2 [1; 4], respectively). However, these differences did not reach the statistical significance (p>0.05). Clinical characteristics of SLE manifestations after 15 years were not significantly different from those at baseline.

The assessment of population risk factors for thrombosis in patients with SLE (n=68) at the first stage of the study showed that 36.7% of them had AH, 8.8% were smokers, 2.9% had DM (Table 3). The median BMI was 30 [23.7; 34] kg/m², doses of GC recalculated for prednisolone – 5 [2.5; 12.5] mg/day. After 15 years (n=50) the incidence of AH, smoking, and DM increased respectively to 72%; 10% and 8%, but the only significant increase was noted in BMI – up to 37 [33; 42] kg/m² (p<0.05) and GC doses – up to 10 [5; 35] mg/day (p<0.05). As for the risk factors of SLE-related thrombosis, 26.4% of patients initially had APS, 41.1% – LN. During the observation, the frequency of these risk factors increased to 46% and 74%, respectively; however, these dynamics were statistically insignificant (p>0.05).

In Groups 1 and 2 initially and at the end of the observation (see Table 3) risk factors associated with SLE were also found. Active LN and APS in the group with thrombosis were significantly more frequent than in the group without thrombosis: initially in 50% and 40% of cases (p<0.05), 75% and 20% (p<0.05), respectively; and after 15 years in 80% and 71.4% (p<0,05), 80% and 31.4% (p<0.05), respectively. Analysis of the population risk factors for thrombosis in patients with SLE at the first stage of the study showed that there was no significant difference between the groups, except for smoking, which in Group 1 was more common than in Group 2: in 12.5% and 8.3% of cases, respectively (p<0.05; see Table 3). After 15 years in Group 1 AH was detected significantly more often than in Group 2: in 86.6% and 65.7% of patients (p<0.05), respectively. DM in Group 1 was slightly more frequent than in Group 2: in 13.3% and 5.7% of cases respectively, however, the differences were statistically insignificant (p>0.05). Group 2 reported 1 (2.8%) malignant neoplasm and 5 (14.2%) cases of infectious complications. In Group 1 these pathologies were not found (see Table 3).

After 15 years of observation, 18 (26.5%) out of 68 patients (initially included in the study) died the median age of the deceased patients was 48.5 [39; 57] years, disease duration – 22 [16; 30] years. In most patients (n=14, 78%) the cause of death was thrombotic complications (Table 4). In 7 patients (39%) the cause of death was PE: 2 (11%) of them had APS, and 5 (28%) – LN. In 5 (28%) patients the cause of death was ACVA: 2 (11%) of them developed APS, and 3 (17%) had the risk factors – AH and LN (n=2), oncological pathology (n=1). In 2 (11%) patients the death was due to acute MI; one of them had APS and LN. Population risk factors included thrombosis, risk factors related to SLE were LN and APS. Infections caused deaths in 4 (22%) participants of the study.

In the first 5 years of the observation there wasn`t a single fatal case in the study population. Thrombotic complications turned out to be the leading causes of death in patients with a disease duration of more than 15 years (see Table 4), and cardiovascular and infectious complications – in patients with a longer disease duration (over 20 years).

According to the analysis of Kaplan-Meier curves, the 10-, 15-, 20-year survival rates of patients with SLE in Orenburg population was 98.5%; 95.5% and 86.3%, respectively (Fig. 1).

Then we have analyzed the effect of thrombotic complications on the outcome of the disease. The 15-year survival rate for patients with SLE and thrombotic complications reached 96.2% and was

Table 4. Causes of death from 2007 to 2022 (n=18)

Cause of death	Death, n (%)	Age, years, Me [25th;75th percentiles]	Disease duration, years, Me [25th;75th percentiles]
PE, *including:*	7 (39)		
with APS	2 (11)	53 [48; 58]	19 [15; 22]
without APS	5 (28)	41 [35; 53]	20 [18; 29]
ACVA, *including:*	5 (28)		
with APS	2 (11)	39 [39; 39]	19 [16; 22]
without APS	3 (17)	49 [47; 61]	19 [16; 34]
Acute MI, *including:*	2 (11)	52 [46; 58]	26 [24; 28]
with APS	1 (5,5)		
without APS	1 (5,5)		
Infections (osteomyelitis, tuberculosis, COVID-19)	4 (22)	51 [41; 54]	30 [21; 34]

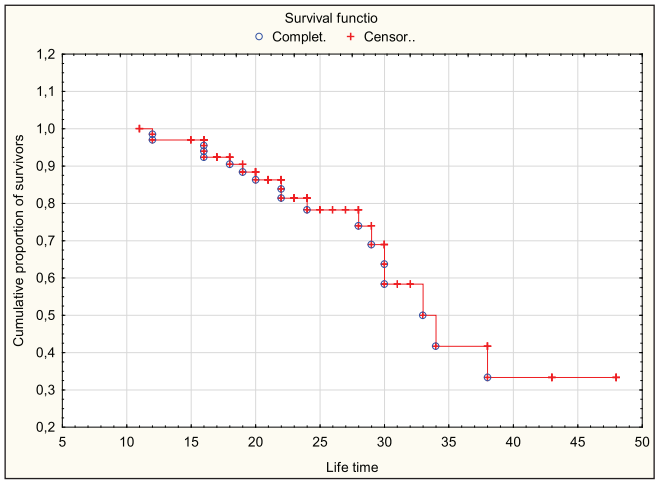

Fig. 1. *Overall survival of patients with SLE. Lifetime – years from the time of diagnosis are indicated*

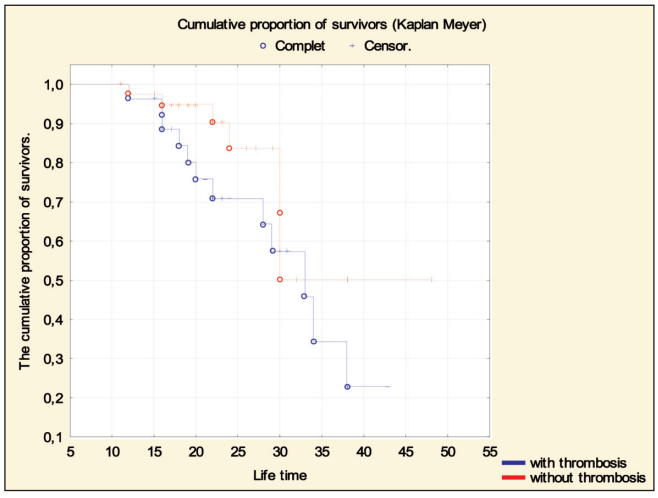

Fig. 2. *Survival rate of SLE patients with and without thrombosis*

slightly lower than for patients without thrombosis – 97.5%. The 20-year survival rate in the group with thrombotic complications was statistically significantly lower than in the non-thrombosis group – 80.2% and 94.3%, respectively (p=0.03; Fig. 2).

Discussion. In our study we analyzed the survival rate in the Orenburg population of patients with SLE, including those with thrombotic complications, and determined the structure of death.

Among the examined patients most were women (n=68) (98.5%) with high frequency of damage to the skin and mucous membranes, musculoskeletal system, heart, kidneys, that is consistent with other populations [15, 17, 23]. Moreover, 8 (12%) of 68 patients initially had non-fatal thrombotic events, and 60 (88%) did not have thrombosis in their medical histories. As the duration of SLE increased, the number of thrombotic events also significantly increased, and their frequency in the surviving group of (n=50) reached 30% (p<0.05).

Risk factors for SLE-related thrombosis initially and in dynamics were mainly active LN and APS. With an increase in the duration of the disease, GC treatment and the number of comorbid conditions, AH became the dominating population risk factor. Thus, our findings about the prevalence of non-fatal thrombotic events in patients with SLE are mainly consistent with the general population [12, 27, 28].

In our study the overall survival rates were mostly similar to those from the retrospective studies in the Moscow region [3], the Republic of Tatarstan [23], as well as in South Korea [18], China [16, 17], Egypt [19], Turkey [15] and Taiwan [20]. So, the 10-, 15-, 20-year survival rates of patients with SLE in the Orenburg population were 98.5%; 95.5% and 86.3%, respectively. In this study, there was a trend to some increase in survival of patients with SLE. Perhaps this is due to the early verification of the diagnosis, adequately prescribed therapy and control of patients.

During the observation there were 18 (26.5%) deaths, the median of age of the deceased patients was 48.5 years, disease duration - 22 years. Leading causes of death were thrombotic complications (n = 14, 78%), including PE, ACVA, MI against the background of APS, LN and AH. Less often, the death was due to infections (n=4, 22%).

Thus, the main risk factors for fatal thrombotic complications in the Orenburg population of patients with SLE were: APS,

AH, LN. It is very important that all deaths in our study occurred when the disease duration was more than 10 years. According to the literature data, it is mainly associated with vascular disorders caused, among other things, by atherothrombotic changes: usually the disease duration exceeded 15 years. Generally, the structure of death is consistent with the data from other cohorts [3, 15, 17, 20, 23], however, there are differences in the leading causes of death.

Conclusion. Increased life expectancy of patients with SLE is the achievement of modern rheumatology practice. Survival rates in the Orenburg population of patients with SLE are comparable to those in Russia, and are 98.5%; 95.5% and 86.3% at 10, 15 and 20 years, respectively. The main causes of death are thrombotic events, most commonly associated with the activity of the autoimmune disease. In the presence of thrombotic complications, the 20-year survival rate is 80.2%, which is significantly lower than in the SLE group without thrombosis. The results of our study allow us to confirm the opinion of the majority of researchers that the presence of thrombotic complications in patients with SLE is an unfavorable prognostic factor.

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