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Tolerance to Minimal Physical Activity in Adolescents with Systemic Lupus Erythematosus

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Abstract- In modern medicine, the issue of rheumatic diseases remains one of the most significant and socio-economically impactful problems due to the high rates of disability and loss of working capacity among these patients. The main cause of decreased quality of life and mortality in patients with systemic lupus erythematosus (SLE) is cardiovascular pathology, leading to the development of heart failure. An early symptom of myocardial dysfunction is the patient's loss of ability to perform routine physical activities in daily life. The aim of the study was to assess tolerance to minimal physical exertion in adolescents with systemic lupus erythematosus. A total of 46 adolescents with SLE were examined. They underwent the Six-Minute Walk Test (6MWT) with measurement of several parameters at rest and during the first minute of recovery following exertion.

Keywords: *systemic lupus erythematosus, six-minute walk test, adolescents.*

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Tolerance to Minimal Physical Activity in Adolescents with Systemic Lupus Erythematosus

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Abstract- In modern medicine, the issue of rheumatic diseases remains one of the most significant and socio-economically impactful problems due to the high rates of disability and loss of working capacity among these patients. The main cause of decreased quality of life and mortality in patients with systemic lupus erythematosus (SLE) is cardiovascular pathology, leading to the development of heart failure. An early symptom of myocardial dysfunction is the patient's loss of ability to perform routine physical activities in daily life. The aim of the study was to assess tolerance to minimal physical exertion in adolescents with systemic lupus erythematosus. A total of 46 adolescents with SLE were examined. They underwent the Six-Minute Walk Test (6MWT) with measurement of several parameters at rest and during the first minute of recovery following exertion.

Results: Patients with SLE covered a shorter distance during the 6-minute period. Both before and after the Six-Minute Walk Test, elevated heart rate (HR) and respiratory rate (RR) values were recorded. This may indicate strain on the adaptive capacities of the cardiovascular and respiratory systems against the background of sympathetic activation of the autonomic nervous system, which likely leads to impaired autonomic regulation of these systems and disruption of myocardial perfusion.

Keywords: systemic lupus erythematosus, six-minute walk test, adolescents.

I. Introduction

The issue of rheumatic diseases in modern medicine is being studied as one of the most significant medical and socio-economic challenges [1, 2, 3]. One of the most prevalent diseases within this group is systemic lupus erythematosus (SLE). Typically manifesting in childhood or early adulthood, the disease persists throughout life and exhibits continuous progression. Among the primary causes of reduced quality of life and mortality in these patients are cardiovascular system (CVS) pathologies, leading to the development of heart failure (HF) [4, 5, 6]. According to the functional classification of HF by the New York Heart Association (NYHA), the key diagnostic indicators of subclinical HF are the patient's subjective symptoms, such as dyspnea during physical exertion and an inability to perform daily physical activities [7, 8].

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In adolescent patients and young adults, such complaints are generally uncommon and are most often identified retrospectively during active questioning by the physician [8]. Therefore, for the diagnosis of early cardiovascular system (CVS) impairments in patients with various somatic diseases during this age period, the assessment of tolerance to minimal physical exertion through the use of different exercise tests becomes particularly important [9, 10, 11].

Recently, the six-minute walk test (6MWT) conducted in a corridor setting has gained widespread use for addressing these diagnostic challenges. This test is simple to perform, does not require expensive equipment, and can be conducted in any environment that is safe for both the patient and the investigator [11, 12].

II. Objective of the Study

To assess the tolerance to minimal physical exertion in adolescents with systemic lupus erythematosus.

a) Data Collection

The study group comprised 46 pediatric patients diagnosed with systemic lupus erythematosus (5 males and 41 females). The mean age of the patients was 13.89 ± 0.39 years.The control group consisted of 36 practically healthy adolescents (5 males and 31 females) with a mean age of 14.53 ± 0.38 years ($p_t < 0.1$).

The children in the main group underwent a comprehensive health assessment at the Cardiorheumatology Department, while the control group was examined at the Pediatric Department of the State Institution "Institute for the Protection of Children's and Adolescents' Health of the National Academy of Medical Sciences of Ukraine" during the period from 2017 to 2022. The healthy children had no history of inflammatory diseases, joint lesions, or congenital malformations.

The study was conducted in accordance with the principles of the Declaration of Helsinki on human rights (1948), as well as ethical and moral-legal requirements of the Statute of the Ukrainian Association of Bioethics, the standards of Good Clinical Practice (GCP, 1992), the Council of Europe Convention on

Human Rights and Biomedicine (1997), and considering the requirements of the Law of Ukraine "On Medicinal Products" (1996, Articles 7, 8, 12), the principles of Good Laboratory Practice (GLP, 1998), and the ICH GCP guidelines (2008) [13, 14, 15].

The study protocol and the use of human biological materials were approved by the Ethics Committee of the State Institution "Institute for the Protection of Children's and Adolescents' Health of the National Academy of Medical Sciences of Ukraine" (Kharkiv, Ukraine), and written informed consent was obtained in accordance with the Declaration of Helsinki.

Clinical diagnoses were established in accordance with the International Classification of Diseases, 10th Revision (ICD-10). For the diagnosis of systemic lupus erythematosus (SLE), the guidelines of the Ministry of Health of Ukraine dated January 31, 2017, No. 00446 "Systemic Lupus Erythematosus" were followed, as well as the classification criteria of the European League Against Rheumatism (EULAR) and the American College of Rheumatology (ACR), published in 2019. According to these criteria, a diagnosis of SLE was made in the presence of positive antinuclear antibodies (ANA) along with clinical manifestations from the proposed domains totaling 10 or more points [16, 17].

To assess disease activity in patients with SLE, the Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2K) was calculated. This index includes 24 parameters (16 clinical and 8 laboratory), each assigned a score ranging from 1 to 8 points. The maximum possible total score is 105. Only those manifestations present within the 10 days prior to evaluation were considered, regardless of the severity of the symptoms or any improvement or deterioration observed at the time of examination.Based on the SLEDAI score, the following degrees of disease activity were defined: 0 points – no activity (grade 0); 1–5 points – low activity (grade 1); 6–10 points – moderate activity (grade 2); 11–19 points – high activity (grade 3); and more than 20 points – very high activity (grade 4) [16].

b) Research Methods

To assess tolerance to minimal physical exertion in adolescents with systemic lupus erythematosus (SLE), a six-minute walk test (6MWT) was performed. The test was conducted in the morning hours in the corridor of the cardiology and cardiorheumatology department, with a corridor length of 58.6 meters. Each patient completed the test once. Prior to the test, the children rested in a seated position for three minutes. No dietary restrictions or harmful habits (such as smoking, alcohol consumption, or drug use) were reported among the participants. The test was performed at an individually maximal self-paced speed, avoiding the onset of pain, dyspnea, muscle fatigue or heaviness in the legs, dizziness, or weakness, allowing the patient to cover the maximum distance possible within six minutes. The distance covered (6-minute walk distance, 6MWD) was measured in meters.

The clinical status of each patient was monitored before and after the test by recording heart rate (HR), respiratory rate (RR), oxygen saturation (SpO_2) using pulse oximetry, and arterial blood pressure (BP). Upon completion of the test, during the first minute of the recovery phase, in addition to the aforementioned parameters, the percentage increase in heart rate (%HR increase) and respiratory rate (%RR increase) in response to minimal physical exertion was calculated. Heart rate was measured in a seated position over 15 seconds using a pulse oximeter, followed by counting respiratory rate for 15 seconds using a stopwatch. Blood pressure was also measured in a seated position using a cuff placed on the left upper limb by the Korotkoff method with a Microlife AG1-20 device [11, 12].

c) Statistical Analysis

The statistical analysis of the obtained data was performed using the SPSS 17 software package (license 4a180844250981ae3dae-s / nSPSS17). The arithmetic mean and its standard error were calculated, and the upper and lower quartiles were determined for all parameters. The measured values were compared to the corresponding values obtained from adolescents in the control group. Differences between means were assessed using parametric methods (Student's *t*-test, Fisher's angular transformation test) in cases where the distribution of values was normal. When the data did not meet the criteria for normal distribution, non-parametric methods (Wilcoxon–Mann–Whitney test) were employed.

Correlation analysis was conducted using Pearson's pairwise correlation to evaluate relationships between disease duration, disease activity, percentage increase in heart rate (%HR increase), percentage increase in respiratory rate (%RR increase), and the distance covered during the six-minute walk test (6MWD). The strength of the correlation was interpreted according to Chaddock's scale: a value of 0.10–0.29 indicated a weak correlation, 0.30–0.49 a moderate correlation, 0.50–0.69 a substantial correlation, 0.70–0.89 a strong correlation, 0.90–0.99 a very strong correlation, and 1.00 indicated a functional (perfect) correlation. Differences were considered statistically significant at $p < 0.05$.

III. Results

In terms of physical development, patients with SLE demonstrated the following differences compared to their healthy peers: they were of shorter stature (1.55 ± 0.02 m vs. 1.67 ± 0.02 m, $p_t < 0.001$), whereas body weight did not significantly differ between the two groups (51.44 ± 2.24 kg vs. 54.38 ± 2.14 kg, $p_t < 0.1$).

However, the body mass index (BMI) of patients with SLE was significantly higher (21.01 ± 0.59 kg/m^2 vs. 19.21 ± 0.45 kg/m^2, $p_t < 0.01$).

The majority of the patients were female ($p_x < 0.001$). There were no significant differences between boys and girls with SLE in terms of age or physical development parameters ($p_t < 0.3$). Therefore, analysis of six-minute walk test (6MWT) outcomes by sex was deemed unnecessary.

The mean age of SLE onset across the group was 10.87 ± 0.54 years. The disease onset occurred before the age of 5 years in 2 patients (4.35 ± 3.01%), between the ages of 5 and 10 years in 14 patients (30.43 ± 6.78%), and after the age of 10 years in 30 patients (65.22 ± 7.02%; $p < 0.05$ compared to the groups with disease onset before the age of 5 years and between 5 and 10 years).

At the time of examination, the mean disease duration was 3.63 ± 0.41 years (40.41 ± 4.30 months). Disease duration between 1 and 3 years was observed in 26 patients (56.52 ± 7.37%), while 20 patients (43.48 ± 7.31%) had a disease duration of more than 3 years.

The six-minute walk test (6MWT) was performed in 30 patients, including 3 boys (10%) and 27 girls (90%). The remaining patients did not undergo the 6MWT due to various reasons: 3 patients had arthralgia associated with complications of aseptic necrosis of the femoral head, 9 patients were in a severe condition due to the underlying disease, and 4 patients refused to participate in the test.

Before the test, 4 patients with SLE (13%) reported complaints: three patients experienced joint pain and one patient reported fatigue; however, all of them agreed to complete the test. Upon pre-test assessment, baseline values of heart rate (HR), respiratory rate (RR), and diastolic blood pressure (DBP) were within normal limits but were significantly higher compared to healthy controls ($p_t < 0.01$, $p_t < 0.01$, $p_t < 0.05$, respectively) (Table 1).

Table 1: Six-minute walk test indicators in patients with systemic lupus erythematosus(M±m)

Indicators	Patients with SLE, n = 30		Control group, n = 36	
	Before 6MWT	After 6MWT	Before 6MWT	After 6MWT
Complaints, M ± m, %	13,33 ± 6,21	36,67 ± 8,80	0	0
HR, bit/min	83,87±2,65**	112,47±3,04***	74,17 ± 2,15	99,78 ± 2,23
RR, breath/min	20,80± 0,64**	26,90±1,09***	18,75 ±0,41	21,33±0,38
SpO_2, %	98,33 ± 0,16*	98,70± 0,11*	97,39±0,49	97,72±0,49
SBP, mmHg	112,20±2,79	118,23±2,59	110,06 ± 2,44	116,67 ± 2,89
DBP, mmHg	71,00±1,86*	72,40± 1,61***	66,94 ± 1,36	65,72 ± 1,42
% increaseinHR	-	35,62±3,03	-	36,97 ± 3,63
% increasein RR	-	30,32±4,97***	-	14,36±1,36
6MWD, m	-	483,68±9,73**	-	519,29 ± 8,56

*Note: p < 0.05, ** p < 0.01, *** p < 0.001 – significance of differences between patient group and control group*

After the Six-Minute Walk Test (6MWT), complaints were noted in 11 patients (36.67%). Among them, the predominant complaints were shortness of breath (in 6 patients), arthralgia in 4 children, and fatigue persisted in 1 girl. In response to minimal exertion, heart rate (HR), respiratory rate (RR), and diastolic blood pressure (DBP) increased and remained significantly higher compared to the control group (p < 0.001). The percentage increase in heart rate was comparable to the control group, whereas the percentage increase in respiratory rate was significantly higher than in healthy adolescents. The distance covered in 6 minutes by patients with systemic lupus erythematosus (SLE) was shorter (p < 0.01) (Table 1).

When analyzed by age groups, significant differences were observed in blood pressure values, which is physiological. No differences were found in the distance covered (Table 2).

Table 2: Six-minute walk test indicators in patients with Systemic Lupus Erythematosusconsidering patient age (M±m)

Indicators	Patients aged 10 – 13 years, n = 11		Patients aged 14 – 18 years, n = 19	
	Before 6MWT	After 6MWT	Before 6MWT	After 6MWT
HR, bit/min	87,28±4,97	117,73±5,47	81,89± 3,06	109,42±3:53
RR, breath/min	20,91±1,25	27,45± 1,95	20,74± 0,74	26,58±1,35
SpO_2, %	98,36± 0,36	98,91± 0,09	98,32± 0,15	98,58± 0,16
SBP, mmHg	103,27±5,03***	108,09±4,55***	117,37±2,76	124,11±2,31
DBP, mmHg	65,72±3:53**	67,82±2,49**	74,05± 1,83	75,05± 1,88
% increaseinHR	-	36,26 ±3,99	-	35,25±4,26
% increasein RR	-	31,47±5,08	-	29,66±7,38
6MWD, m	-	476,79±18,48	-	487,66±11,34

*Note: ** $p_t < 0,01$, *** $p_t < 0,001$– significance of differences between patient groups of diferent age*

Patients with a disease duration of less than 3 years had significantly higher heart rate (HR) values both before ($p < 0.01$) and after ($p < 0.01$) the test, but the percentage increase in HR in response to minimal physical exertion was similar. The distance covered was also not different between patients with varying disease durations (Table 3).

Table 3: Six-minute walk test indicators in patients with Systemic Lupus Erythematosusconsidering disease duration(M±m)

Indicators	Patients with disease duration up to 3 years, n = 12		Patients with disease duration of more than 3 years, n = 18	
	Before 6MWT	After 6MWT	Before 6MWT	After 6MWT
HR, bit/min	92,42 ± 4,09**	121,33 ± 4,18**	78,17 ± 2,83	106,56 ± 3,68
RR, breath/min	20,33 ± 0,95	26,42 ± 1,40	21,11 ± 0,87	27,22 ± 1,60
SpO_2, %	98,33 ± 0,22	98,58 ± 0,19	98,33 ± 0,24	98,78 ± 0,13
SBP, mmHg	114,33 ± 3,04	120,83 ± 3,27	110,78 ± 4,22	116,50 ± 3,76
DBP, mmHg	74,58 ± 2,14*	75,25 ± 1,67	68,61 ± 2,64	70,50 ± 2,38
% increaseinHR	-	32,82 ± 4,42	-	37,49 ± 4,13
% increasein RR	-	30,60 ± 5,24	-	30,13 ± 7,64
6MWD, m	-	470,83 ± 15,58	-	492,24 ± 12,40

*Note: * $p_t < 0,05$, ** $p_t < 0,01$– significance of differences between patient groups with diferent disease duration*

Regarding disease activity, the majority of patients (43.48%) had a high degree of activity, 21.74% had very high activity, and 19.57% had moderate activity. Only 3 patients (6.52%) were in the inactive phase of the disease (Table 4).

The analysis of Six-Minute Walk Test (6MWT) indicators considering disease activity showed that baseline values in patients with systemic lupus erythematosus (SLE) did not differ, except for the respiratory rate, which was significantly lower in children with the third degree of disease activity ($p < 0.05$). After the test, the respiratory rate significantly differed in patients with the fourth degree of activity, and these patients also had the highest percentage increase in respiratory rate (Table 4). The distance covered in 6 minutes by patients with varying degrees of activity was almost the same.

Table 4: Six-minute walk test indicators in patients with Systemic Lupus Erythematosusconsidering disease activity(M±m)

Indicators	Patients with grade 1-2 activity, n = 9		Patients with grade 3 activity, n = 13		Patientswithgrade4 activity, n = 8	
	Before 6MWT	After 6MWT	Before 6MWT	After 6MWT	Before 6MWT	After 6MWT
HR, bit/min	84,33±4,62	114,22±5,33	82,23±4,73	109,77±5,19	86,00±4,29	114,88±5,37
RR, breath/min	22,00±1,15	25,78± 1,18 £	19,23± 0,74 £ *	25,46±1,83	22,00±1,46	30,50±2,26 *¥
SpO_2, %	98,56± 0,24	98,67± 0,24	98,00± 0,30	98,69± 0,17	98,63± 0,18	98,75± 0,16
SBP, mmHg	115,56± 2,62	125,67 ±3,64	108,23±4,61	111,54±4,25 ££	114,88±6,81	120,75±4,17
DBP, mmHg	75,44±2,66	76,33± 1,86	67,77±3,19 £	69,31 ±2,91 £	71,25±3,24	73,00 ±2,75
% increaseinHR	-	36,88±5,59	-	35,62±5,47		34,19±4,26
% increasein RR	-	17,77±2,60	-	32,35±7,97		41,15±12,46*
6MWD, m	-	492,57± 19,86	-	474,55±13,23		488,51±21,02

*Note: £ $p < 0,05$, ££ $p < 0,01$ when comparing patients with activity grades 1–2 to patients with activity grade 3; * $p < 0,05$ when comparing patients with activity grades 1–2 to patients with activity grade 4; ¥ $p < 0,05$ when comparing patients with activity grade 3 to patients with activity grade 4;* $p < 0,05$ when comparing patients with activity grade 2 to patients with activity grade 3.*

Subsequently, using quartile distribution, two groups of children were identified based on the smallest and largest distances covered (less than 437.25 m and more than 524.70 m, respectively). The first group included 8 patients, 3 of whom were aged 10 to 13 years, with the rest being older. In terms of disease activity, 2 (25%) had first-degree activity, 2 (25%) had fourth-degree activity, and 4 (50%) had third-degree activity. Regarding disease duration, the patients were equally divided: 4 (50%) had a disease duration of less than 3 years, and 4 (50%) had more than 3 years. The second group consisted of 9 children, 4 (45%) of whom were aged 10 to 13 years, and 5 (55%) were older. In terms of disease activity, 1 (11%) had first-degree activity, 2 (22%) had second-degree activity, 2 (22%) had third-degree activity, and 4 (45%) had fourth-degree activity. Regarding disease duration, 3 (33%) patients had a disease duration of less than 3 years, while the remaining had more than 3 years.

Table 4: Six-minute walk test indicators in patients with Systemic Lupus Erythematosusin the lower quartile compared to patients in the upper quartile(M ± m)

Indicators	Patients in the lower quartile, n = 8		Patients in the upper quartile, n = 9	
	Before 6MWT	After 6MWT	Before 6MWT	After 6MWT
Complaints, M ± m, %	12,50 ± 12,50	37,50 ± 18,30	11,11 ± 11,11	22,22 ± 14,70
HR, bit/min	95,38±3,08 ***	116,50±4,37	78,89±3,31	111,22±5,17
RR, breath/min	21,50± 0,82	26,38±1,69	22,67±1,15	27,78±2,07
SpO_2, %	98,38± 0,26	98,63± 0,26	98,67± 0,17	98,56± 0,24
SBP, mmHg	106,88 ±5,55	110,63±5,76	105,44±4,84	118,78±5,43
DBP, mmHg	69,88 ±4,61	68,75±4,30	66,44 ±3,01	72,33±3,06
% increaseinHR	-	22,40±3,79**	-	41,16±3,84
% increasein RR	-	22,80±6,71	-	21,98±4,39
6MWD, m	-	413,19 ±7,71***	-	542,59±7,88

*Note: p < 0.05, ** p < 0.01, *** p < 0.001 – significance of differences between patient groups*

IV. Discussion

It has been established that in patients with rheumatic diseases, the leading cause of death is cardiovascular disease, including myocardial infarction, ischemic heart disease, strokes, and others [1, 18, 19]. These conditions primarily lead to the development of heart failure, which remains the leading cause of mortality. Cardiovascular mortality in patients with rheumatic diseases is 1.7 times higher than in the general population [20, 21].

It is known that the cardiovascular system in these patients is involved in the pathological process due to systemic autoimmune inflammation, which exerts a direct toxic effect on cardiomyocytes, the microcirculatory bed, vascular endothelium, and the extracellular matrix, accelerating myocardial remodeling and contributing to its ischemia [22, 23, 24, 25].

Heart failure at an early stage often has no clinical manifestations and frequently remains undetected. However, it is known to be characterized by a reduced tolerance to minimal, everyday physical exertion [7, 8]. Exercise tolerance is an integral indicator of the physiological capabilities of the body. It is significantly influenced by the state of the cardiovascular, respiratory, and musculoskeletal systems, as well as the overall health of the individual [11, 12].

For the early detection of the first signs of heart failure, the six-minute walk test is widely used. In adult patients, a correlation has been established between the distance covered and indicators of their quality of life, as well as with the functional class of heart failure. Additionally, in adults, the distance covered in 6 minutes serves as a strong predictor of mortality and disability in various cardiopulmonary diseases [26, 27]. In recent years, this test has increasingly been used in pediatrics with no changes in the protocol [11, 12].

In our study, patients with systemic lupus erythematosus covered a shorter distance compared to healthy children ($p < 0.01$). The analysis of this indicator was not dependent on patient age (Table 2), disease duration (Table 3), or the degree of activity of the pathological process (Table 4).

It is known that the results of physical stress tests often simultaneously reflect the functional capabilities of several systems, and sometimes the organism as a whole. This is because the function of any particular visceral system is under significant neurohormonal regulation. For example, the pulse response to physical exertion may reflect the functional status of the heart, vascular response, as well as the features of the autonomic regulation of the cardiovascular system [9, 11].

Patients with systemic lupus erythematosus had higher heart rate and respiratory rate both at rest and after exertion, as well as a greater percentage increase in RR (Table 1). Blood oxygen saturation, however, was not affected. These changes may indicate the impact of the disease on the overall state of the body due to long-

term subclinical inflammation. Against this background, the likely development of comorbid conditions such as hyperlipidemia and hypercoagulability may occur, which in turn contribute to the formation of atherosclerosis and atherothrombosis, ultimately leading to chronic heart failure [7].

It is known that in systemic lupus erythematosus, all organs and systems are involved in the pathological process. The longer the active inflammatory process persists, the more internal organs are affected. However, it is during the acute inflammatory phase that the highest likelihood of developing multiple organ failure exists [22, 25].

In the group of children under study, the highest HR levels, both before and after exertion, were observed in patients with a disease duration of less than three years ($p < 0.01$). This may suggest activation of neurohormonal regulatory systems, primarily the sympathoadrenal system, both in the context of the pronounced inflammatory process and due to the use of aggressive immunosuppressive therapy, which leads to increased strain on the cardiovascular system.

The respiratory rate at the first minute of recovery, as well as its percentage increase, were highest in patients with a very high degree of disease activity ($p < 0.05$), with preserved saturation according to pulse oximetry. The baseline heart rate values in patients who covered a shorter distance were significantly higher ($p < 0.001$), while the percentage increase in HR was greater in patients who covered a longer distance ($p < 0.01$).

Thus, when assessing tolerance to minimal physical exertion, patients with systemic lupus erythematosus covered a shorter distance in 6 minutes. Both before and after the six-minute walk test, higher heart rate and respiratory ratevalues were observed in these patients. This may indicate strain on the adaptive capacities of the cardiovascular and respiratory systems against the background of sympathetic activation of the autonomic nervous system, which likely leads to impaired autonomic regulation of these systems and disruption of myocardial perfusion.

V. Conclusions

1. Patients with systemic lupus erythematosus demonstrated decreased tolerance to minimal physical exertion, as evidenced by the shorter distance covered during the six-minute walk test ($p < 0.01$).
2. Adolescents with a disease duration of less than three years had the highest heart rate levels both before ($p < 0.01$) and after ($p < 0.01$) the test.
3. In cases of very high disease activity in SLE, the respiratory system's functionality is strained in response to exertion, as indicated by the higher respiratory rate ($p < 0.05$).
4. Reduced tolerance to minimal physical exertion, alongside elevated heart rate and respiratory rate levels in children with systemic lupus erythematosus, may reflect a deterioration in the functional state of the heart, vascular response, respiratory system strain, and the characteristics of autonomic regulation of these systems.

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