

Bioimpedance analysis in determining body composition in women with systemic lupus erythematosus: a pilot study

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Objective: to determine body composition (BC) in women with systemic lupus erythematosus (SLE), by using bioimpedance analysis.

Patients and methods. The investigation enrolled 12 women with a reliable diagnosis of SLE, who were followed up at the Clinic of the V.A. Nasonova Research Institute of Rheumatology. Their median age was 46.5 [38.5; 54.7] years. All the patients underwent estimation of waist circumference (WC) and body mass index (BMI). BC was analyzed using an InBody 770 multi-frequency bioimpedance analyzer (Biospace Co. Ltd, South Korea) at the Clinical Nutrition Clinic, Federal Research Institute of Nutrition and Biotechnology.

Results and discussion. BMI corresponding to overweight or obesity was observed in 67% of patients; abdominal obesity (AO) was seen in 83%. BC study showed that in most patients, adipose tissue mass was greater than the normal values (75%), lean body mass, skeletal muscle mass, and the amount of body water were within normal limits (83%), and the basal metabolic rate was reduced (67%). There were positive correlations between the percentage of adipose tissue and BMI ($r=0.9$; $p<0.01$), WC ($r=0.7$; $p<0.01$), C-reactive protein (CRP) levels ($r=0.6$; $p<0.05$), and complement C3 concentrations ($r=0.9$; $p<0.01$). Similar results were obtained when assessing the relationship between visceral fat area and BMI ($r=0.9$; $p<0.01$), WC ($r=0.78$; $p<0.01$), CRP ($r=0.6$; $p<0.05$), complement component C3 ($r=0.8$; $p<0.01$). There was an inverse correlation between visceral fat area and the Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2K) ($r=-0.6$; $p<0.05$).

Conclusion. Most women with SLE have AO, increased adipose tissue mass, normal lean body mass, and decreased basal metabolism. There is a direct correlation of visceral fat content and inflammatory markers (CRP, complement component C3) and an inverse correlation of those with the SLEDAI-2K.

Keywords: systemic lupus erythematosus; bioimpedance analysis; body composition; obesity; basal metabolism.

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The introduction of new drugs and the optimization of glucocorticoid (GC) therapy for systemic lupus erythematosus (SLE) have led to an increase in the life expectancy of patients, but practically did not influence one of the main causes of death – cardiovascular complications (CVC). In this regard, risk factors for CVC, for example, obesity, are attracting increasing attention. It has been shown that not general, but visceral obesity, being the main component of the metabolic syndrome, increases the risk of type 2 diabetes, sub-clinical atherosclerosis and its progression, cardiovascular and cerebrovascular events, death from any causes in the population [1].

For the diagnosis of obesity, the body mass index (BMI) and waist circumference (WC) are traditionally used as a screening method. The advantage of these indices is the ease of use and the possibility of use in large-scale population studies. The disadvantages include weak correlation of BMI with the distribution of adipose tissue in the total body and the content of visceral fat, lack of information about other components of body composition (BC) at an individual level, including patients with various rheumatic diseases.

The aim of the study was to examine BC in women with SLE using bioelectrical impedance analysis.

Patients and methods.

In total, the study included 12 women, mean age 46.5 [38.5; 54.7] years old (median [25th, 75th percentile]) with the

diagnosis of SLE. All patients met the classification criteria of the American College of Rheumatology (ACR) 1997 [2] and the criteria of the Systemic Lupus International Collaborating Clinics (SLICC) / ACR 2012 [3], all patients were observed in V.A. Nasonova Research Institute of Rheumatology and signed an informed consent to participate in the study. The local ethics committee approved the study. Exclusion criteria: age younger than 18 or older than 65 years, the presence of severe concomitant pathology (infection, malignant neoplasms) or pregnancy, participation in other clinical trials. Conventional clinical, laboratory and instrumental examinations were carried out with standard methods. Systemic Lupus Erythematosus Disease Activity Index 2K (SLEDAI-2K) was used to assess SLE activity [4]. The Systemic Lupus International Collaborating Clinics Damage Index was used to evaluate irreversible changes [5].

Anthropometric parameters (height (cm), weight (kg), WC (cm), hip circumference (HC) (cm) were obtained in all patients and the WC/HC ratio and BMI (kg/m^2) were calculated. BMI categories interpretation was carried out according to World Health Organization (WHO) classification: BMI $<18.5 \text{ kg}/\text{m}^2$ – underweight, BMI = $18.5 - 24.9 \text{ kg}/\text{m}^2$ – normal weight, BMI = $25 - 29.9 \text{ kg}/\text{m}^2$ – overweight, BMI $\geq 30 \text{ kg}/\text{m}^2$ – obesity [6]. Abdominal obesity (AO) in women was diagnosed when WC ≥ 80 cm [7].

Analysis of BC was performed using an InBody770 multi-frequency bioimpedance analyzer (Biospace Co. Ltd., South Korea / BioSpace Co. Ltd., South Korea) at the Federal State Budgetary Scientific Institution «Federal Research Centre of Nutrition, Biotechnology and Food Safety» (Federal Research Centre of Nutrition and Biotechnology).

Statistical data processing was performed using the parametric and nonparametric methods of Statistica 8.0 program (StatSoft. Inc., USA). The variables are presented as a median (Me), upper and lower quartiles [25th; 75th percentile]. The relationship of the characteristics was evaluated with the Spearman rank correlation criterion (r). The statistical significance level was at $p < 0.05$ [8].

Results

The duration of SLE ranged from 2 months to 20 years, the disease activity was predominantly low (median SLEDAI-2K 4 [1; 8] points). The main clinical manifestations included skin lesions (33%), hematological disorders (33%), arthritis (33%) and nephritis (25%). Eleven patients (92%) had immunological abnormalities at the time of the examination. One of the patients never took GC, while other women were treated with GC for 8.0 [0.9; 11.0] years. Clinical characteristics of patients are presented in Table 1.

The median BMI of SLE patients was 26.4 [23.3; 27.4] kg/m², WC – 93.5 [85.0; 95.5] cm, WC/HC ratio – 0.93 [0.90; 0.97]. Most women (67%) were overweight or obese based on BMI values, 83% patients had AO. Underweight was diagnosed only in 1 woman (8%). Anthropometric parameters are shown in Table 2.

The median fat mass was 25.3 [21.2; 29.7] kg, total body fat percentage 34.2 [31.6; 47.7] %, fat mass index (FMI) was 8.8 [7.5; 11.4] kg/m², visceral fat area – 125.8 [96.4; 152.6] cm². For other BC indicators, the following data were obtained: median lean mass – 40.0 [36.9; 46.3] kg, skeletal muscle mass – 23.0 [22.0; 26.9] kg, fat-free mass index (FFMI) – 16.2 [15.4; 17.0] kg/m², total body water is 31.2 [29.9; 36.1] L. Automatically calculated basal metabolism was 1285 [1248; 1434] kcal. The results were matched with the expected ones (for same gender, age and height) in Table 3.

There were positive correlations between total body fat percentage and BMI ($r=0.9$, $p<0.01$), WC ($r=0.7$, $p<0.01$), C-reactive protein (CRP) levels ($r=0.6$, $p<0.05$), and C3 complement concentrations ($r=0.9$, $p<0.01$). Similar results were obtained for visceral fat area

(cm²) and BMI ($r=0.9$, $p<0.01$), WC ($r=0.8$, $p<0.01$), CRP ($r=0.6$, $p<0.05$) and C3 levels ($r=0.8$, $p<0.01$). A negative correlation between the visceral fat area and the SLEDAI-2K activity index ($r=-0.6$, $p<0.05$) was established. No associations were found with age, disease duration, clinical manifestations and laboratory parameters (anti-ds-DNA, C4 complement, antiSm, aPL, proteinuria, etc.), damage index SLICC/DI, HAQ, current GC dose and duration, the fact of taking other drugs. Moreover, these parameters did not correlate with skeletal muscle mass, lean mass, basal metabolism and total body water.

Discussion

Bioelectrical impedance analysis of BC is based on differences in the electrical conductivity of different body tissues. The

Table 1. Clinical characteristics of women with SLE included in the study (n=12)

Characteristics	Values
Age, years, Me [25th; 75th percentile]	46.5 [38.5; 54.7]
Disease duration, years, Me [25th; 75 th percentile]	8.5 [0.8; 14.0]
SLE manifestations, n (%):	
skin involvement	4 (33)
oral ulcers	2 (17)
arthritis	4 (33)
serositis	2 (17)
nephritis	3 (25)
neuropsychiatric disorders	0
hematological disorders	4 (33)
Immunological disorders, n (%):	11 (92)
ANA (+)	11 (92)
anti-ds-DNA	8 (67)
anti-Sm	1 (8)
antiphospholipid antibodies (aPL)	5 (42)
hypocomplementemia	3 (25)
SLE activity, n (%):	
Remission (SLEDAI-2K=0)	3 (25)
Low (SLEDAI-2K=1-5)	3 (25)
Moderate (SLEDAI-2K=6-10)	4 (33)
High (SLEDAI-2K=11-19)	2 (17)
SLEDAI-2K, score, Me [25th; 75th percentile]	4 [1; 8]
Damage index SLICC, score, Me [25th; 75 th percentile]	1 [1; 2]
Treatment:	
current GC users, n (%)	11 (92)
current daily dose of GC, mg	10.0 [7.5; 14.4]
GC duration, years	8.0 [0.9; 11.0]
hydroxychloroquine, n (%)	9 (75)
immunosuppressants, n (%)	4 (33)
rituximab, n (%)	3 (25)
Antiphospholipid syndrome, n (%)	4 (33)
Sjogren's syndrome, n (%)	2 (17)

Table 2. Anthropometric characteristics in women with SLE (n=12)

Characteristics	Values
Weight, kg, Me [25th; 75 th percentile]	74.1 [58.6;78.2]
BMI categories:	
underweight, n (%)	1 (8)
normal, n (%)	3 (25)
overweight + obesity, n (%)	8 (67)
AO	
Yes (WC ≥ 80cm), n (%)	10 (83)
No (WC < 80cm), n (%)	2 (17)
WC/HC	
0.75-0.85, n (%)	1 (8)
> 0.85, n (%)	11 (92)

accuracy and high reproducibility of measurement results, portability of the equipment, relatively low cost, comfort of the measurement procedure for the patient and convenience of automatic data processing have made bioimpedanceometry one of the most popular methods for determining BC, first in sports medicine, and then in dietetics, endocrinology and cardiology scientific research. Its advantage is based on the possibility of simultaneous assessment of such clinically significant parameters as active cell mass and basal metabolism, as well as the study of not only integral, but also local parameters of BC up to the resolution characteristic of computed tomography (CT). Compared to CT and X-ray absorptiometry, which are still considered the "gold standard" in this field of research, bioimpedanceometry is not accompanied by radiation exposure and can be performed repeatedly under dynamic observation [9].

Our pilot study of BC in 12 SLE women using bioelectrical impedance analysis showed that adipose tissue mass exceeded normal values, lean body mass and skeletal muscle mass, as well as the total body water were normal, and the basal metabolism was reduced in most patients.

The fat mass in the body can vary significantly among different individuals and vary throughout life. The total body fat percentage in adults for different populations usually ranges from 10% to 20–30% of body weight. Subcutaneous fat is distributed relatively evenly along the body, and visceral (internal) fat is concentrated mainly in the abdominal cavity. Often the concept of abdominal adipose tissue is also used, which means a combination of visceral and subcutaneous fat deposits localized in the abdomen. It has been established that the risk of developing CVC and other diseases associated with overweight has a higher correlation with the content of visceral fat, not subcutaneous fat [1].

It is believed that the main reasons for a high risk of obesity in patients with SLE are the restriction of physical activity due to the severity and some clinical features of the disease, such as musculoskeletal or nervous system involvement, as well as forced long-term use of GC. In a retrospective observation including more than 45 million people of different age categories (from 0 to 90+) examined in US clinics from 1999 to 2016 for various reasons, obesity in patients with SLE (n = 95400) was 3,8 times more common than in the control group (19% versus 5%) [10].

Using X-ray absorptiometry, Lilleby V. et al. showed that patients with SLE debut in childhood have a greater fat mass and

a smaller lean mass than healthy people from the control group. An independent predictor of fat mass increase was the administration of GC [11].

On the other hand, according to Mok C.C. et al. data, SLE duration and chronic smoking are responsible for the accumulation of adipose tissue in men, and a high dose of GC was associated mainly with less lean mass [12]. In our study, despite the fact that fat mass in 75% of patients was higher than normal, no similar correlations were found.

In a study by Santos M.J. et al., where the bioelectrical impedance analysis was used, sarcopenia (FFMI < 2 SD below the mean for the reference Caucasian population) and sarcopenic obesity (a combination of sarcopenia with

total body fat percentage > 40.0%) were observed in SLE more often than in healthy people (in 10.9% versus 6.5%, $p = 0.01$ and in 6.5% versus 0%, $p = 0.009$) [13]. In general, the frequency of obesity, including abdominal obesity, did not differ from the control group, although in patients with SLE with a normal BMI, the fat mass was higher. A positive correlation of fat mass with CRP level, and a negative correlation with smoking and SLEDAI-2K were revealed, which partly coincides with our data on a negative relationship between SLEDAI-2K and visceral fat area and a positive correlation between CRP concentration and both visceral fat and total body fat percentage.

So far there have been only two studies of the visceral fat assessment using x-ray absorptiometry in patients with SLE, which demonstrated its higher content in comparison with the control group. So, L.P.C.Seguro et al. compared BC of young SLE women (31 years old) and healthy donors matched for age, body mass and BMI. Patients did not differ in the total fat mass, but had more visceral fat (mass, volume and area, $p=0.001$). Visceral fat positively correlated with weight, total fat mass, age, lipid and CRP levels, total dose of GC, but not with indicators of SLE [14]. The predominance of visceral fat ($p=0.0015$), the reduction of lean mass ($p=0.0009$) (especially in premenopausal women) and FFMI ($p=0.0007$) was also found in a Chinese cohort of women with SLE (mean age 46 years) compared with the controls. Increased visceral fat mass was associated with age, hypertension, higher BMI, uric acid, creatinine, proatherogenic lipids concentrations, SLE duration, the damage index SLICC and C3/C4 hypocomplementemia [15]. We also found the dependence of total body fat percentage and the visceral fat area on anthropometric indices (BMI, WC), but the correlation with C3 levels was found to be positive. Epidemiological studies have shown that C3 complement system component is elevated in people with obesity, insulin resistance and metabolic syndrome [16]. Also, C3 concentration correlated with insulin sensitivity in rheumatoid arthritis (RA) and psoriatic arthritis (PsA) [17,18].

Inflammation and adipose tissue exert mutual influence on each other. On the one hand, adipose tissue is able to secrete proinflammatory cytokines, causing systemic subclinical "smoldering" inflammation [19,20]. Consequently, the excess of adipose tissue, metabolically active organ, can lead to the development of inflammatory non-communicable diseases. In order to confirm/reject this concept, clinical studies were conducted to

Table 3. BC in women with SLE using bioelectrical impedance analysis (n=12)

Characteristics	N (%)
Fat mass:	
normal, n (%)	2 (17)
increased, n (%)	9 (75)
decreased, n (%)	1 (8)
Skeletal muscle mass:	
normal, n (%)	10 (83)
increased, n (%)	0
decreased, n (%)	2 (17)
Lean mass:	
normal, n (%)	10 (83)
increased, n (%)	0
decreased, n (%)	2 (17)
Total body water:	
normal, n (%)	10 (83)
increased, n (%)	0
decreased, n (%)	2 (17)
Basal metabolism:	
normal, n (%)	3 (25)
increased, n (%)	1 (8)
decreased, n (%)	8 (67)

evaluate the effect of adipose tissue on the development of RA. For example, in a Danish cohort (n = 55037), during the follow-up period of 20 years, RA was diagnosed in 666 patients. In women (68%), the overall RA risk was 10% higher for each 5% increment of total body fat (HR 1.10; 95%CI 1.02–1.18), 5% higher for each 5-cm increment of WC (HR 1.05; 95%CI 1.01–1.10), and nearly 50% higher in those whose BMI was in the obese range compared with normal range BMI (HR 1.46; 95%CI 1.12–1.90). No association of increased risk of RA with adipose tissue was found among male patients [21]. On the other hand, patients with chronic inflammatory arthritis (RA, PsA), according to the results of some studies, have a loss of muscle and lean mass associated with the severity of inflammation and a decrease in physical activity due to functional disorders, often

with an simultaneous increase in adipose tissue mass (so-called sarcopenic obesity) [13,22,23]. According to several studies, a decrease in lean mass is also found in SLE [11,12,24]. Negative correlations of this indicator with age, maximum and total dose of GC, but not with the course of the disease itself were revealed. A possible explanation is the increase in protein catabolism under the influence of high doses of GC. Patients with normal lean mass prevailed in our group, with only 2 patients showing its deficiency and low skeletal muscle mass, while adipose tissue mass was normal in one these women and low in the other, and BMI in both cases was <20 kg/m². Possibly, in RA and SLE there are differences in the mechanism of losing weight: in RA, muscle mass seems to decrease first, followed by a decrease in fat, while in SLE the process in muscle and adipose tissues runs simultaneously.

A distinctive feature of our study was the evaluation of BC using bioelectrical impedance analysis rather than densitometry, as in most foreign studies, which allowed us to separately assess the skeletal muscle mass, visceral fat area, total body water and calculate the basal metabolism level. None of our patients, even despite lupus nephritis in several cases, had an excess of total body water, therefore, hypervolemia and edema could not significantly affect the results of evaluating the fat mass.

We found a decrease in basal metabolism in the majority (67%) of our patients. This indicator is automatically calculated by the analyzer (including on the basis of the BC parameters obtained during the examination) and is indicative. Previously, a comprehensive study of various serum metabolites in patients with SLE revealed signs of suppression of all energy-generating pathways, including glycolysis, Krebs cycle, lipids β -oxidation [25]. However, there are no data about basal metabolism in patients with SLE, obtained by using either indirect methods or indirect calorimetry.

The small number of observations and the absence of a control group do not allow us to draw unambiguous conclusions based on our results and require further more extensive studies.

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