The quality of life of patients with lupus erythematosus influences cardiovascular capacity in 6-minute walk test

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ABSTRACT

Objective: To assess the association between quality of life and distance walked in the 6-minute walk test (6MWT) in Brazilian premenopausal patients with systemic lupus erythematosus (SLE) and compare their results with those of healthy controls. **Methods:** Twenty-five premenopausal (18–45 years) patients diagnosed with low-activity SLE (mean SLEDAI: 1.52 ± 1.61) and 25 controls were matched for age, physical characteristics, and physical activity level (International Physical Activity Questionnaire/s-IPAQ). Both groups should not be involved in regular physical activity for at least six months before the study. The 6MWT distance (American Thoracic Society protocol), posttest heart rate (HRpost), posttest oxygen saturation (SpO_2post) and the Borg scale of subjective perception of effort (SPE/CR10) were evaluated. The quality of life was assessed by use of the Short Form Health Survey 36 (SF-36). **Results:** Patients with SLE had a significantly poorer quality of life, a shorter 6MWT distance (598 ± 45 m versus 642 ± 14 m, $P < 0.001$), and greater values of SPE/CR10 (6.28 ± 2.0 versus 5.12 ± 1.60, $P \leq 0.05$) and HRpost (134 ± 15 bpm versus 123 ± 23 bpm, $P \leq 0.05$) when compared with controls. The linear regression model suggested that quality of life was a significant predictor of 70% of the 6MWT distance. **Conclusion:** When compared with controls, patients with SLE walked a shorter distance in the 6MWT, which was associated with poorer quality of life.

Keywords: systemic lupus erythematosus, physical fitness, quality of life, 6-minute walk test.

INTRODUCTION

Patients with systemic lupus erythematosus (SLE) are at increased risk for acute myocardial infarction, up to seven times that of the healthy population.[1,2] In addition to a greater cardiovascular risk, women with SLE have lower cardiorespiratory capacity as compared with that of healthy women.[3]

Another aspect that might aggravate their cardiovascular risk is the high percentage of physically inactive patients,[4] directly affecting their quality of life.[5] Previous studies have reported an association between lower oxygen consumption (direct measure of peak oxygen) and worse quality of life in patients with SLE.[5] However, the conventional test is time-consuming, requires specialized equipment, which has a high cost and is not practical for hospitals, clinics and physical activity centers.

A practical strategy to aid in the assessment of the clinical status for the patient's cardiovascular prognosis is the 6-minute walk test (6MWT). The 6MWT requires a walkway with at

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least 30 meters and an oximeter.[6] However, so far, no study has assessed the 6MWT in patients with SLE and compared its results with those of healthy women. In addition, it is not clear whether there is an association between the distance walked in the 6MWT and the quality of life of patients with SLE. The results of that investigation might aid health professionals to control the quality of life and to assess clinical aspects and the cardiovascular capacity of patients with SLE, in addition to providing comparative parameters with the healthy population.

The present study aimed at: 1) assessing the association between the distance walked in the 6MWT and the quality of life of premenopausal patients with low activity SLE; 2) comparing the results with those of healthy women matched for gender, age, physical activity level and physical characteristics. The hypothesis of the present study was that patients with SLE would walk a shorter distance in the 6MWT, which would be associated with an impaired quality of life.

MATERIAL AND METHODS

Study participants and design

This study was conducted from January, 20th 2009 to January, 31st 2011, and was approved by the Committee of Ethics and Research of the Medical School of the Universidade de Brasília (FM-UnB) (protocol CEP-FM 074//2005), in accordance with the Helsinki declaration.[7] It is part of the LUPUSFIT study, a research project aimed at assessing the various aspects related to physical fitness and health of Brazilian females with SLE – linked to the laboratory of physical fitness and rheumatology (LAR) of Hospital Universitário de Brasília (HUB). All participants provided written informed consent to undergo all tests. Twenty-five premenopausal patients with SLE met the American College of Rheumatology (ACR) criteria[8,9] and were on regular follow-up at the service of rheumatology of the HUB. Twenty-five healthy women (controls) were matched for gender, age, physical activity level and physical characteristics.

This study included female patients with SLE according to the ACR criteria,[8,9] who were on regular follow-up at the service of rheumatology of the HUB and had low disease activity (SLEDAI ≤ 5). All study participants should be between 18 and 45 years of age, and not exercising for at least 6 months before the beginning of this study (on average, less than once a week). To identify the type of exercises, their regularity, frequency, intensity and duration, a questionnaire[10] with the following three questions was used: 1) What type of physical exercise do you practice regularly during the week?; 2) What is the week frequency of that exercise?; and 3) What is the mean duration, in minutes, of a single session of physical exercise?

Patients with SLE and the following characteristics were excluded from the study: SLEDAI > 5; serum creatinine ≥ 4,770 mg/dL or 265 mmol/L, hematocrit ≤ 30%, nephritis and/or leukopenia; beta-blocker use, previous history of myocardial infarction, cardiomyopathy and/or systemic arterial hypertension; diabetes mellitus; neurological disorders; hypothyroidism; fibromyalgia; locomotor disorders (fractures and prostheses) and/or osteoporosis; rheumatoid arthritis (RA); Sjögren's syndrome; cancer; age < 18 years; age > 45 years; geographical difficulties (living far from the city of Brasília); body mass index (BMI) < 18 kg/m^2; body surface > 30 kg/m^2 (obesity); tobacco use; pregnancy; and regular exercise practice (on average, at least twice a week).

METHODS

The study participants visited the laboratory of human performance of the Centro Universitário Euroamericano (UNIEURO) twice, at a minimum interval of 48 hours and maximum interval of 72 hours, always at the same time (between 2PM and 4PM). In the 24 hours preceding their visits to that laboratory, the participants had to avoid any intense activity and the consumption of caffeine and alcoholic beverages. Their last meal should precede the test by at least 2 hours and the participants should not be menstruating on the day of the test. On their first visit, the quality of life questionnaire was applied, anthropometric measures were taken, and the 6MWT performed. On their second visit, the 6MWT was repeated.

Physical activity level

Aiming at assessing the patient's daily physical activity level, the Physical Activity Questionnaire-Short Form (IPAQ-S),[11,12] validated to the Brazilian population,[12] was used. That questionnaire was applied individually by the major investigator and comprised questions about the frequency (days per week) and duration (minutes per day) of activities involving moderate and vigorous physical exertion in four domains: work commuting; household chores; leisure; and the number of hours that patients with SLE and controls remained seated during the week and during the weekend. According to their physical activity levels, patients were classified as follows: active; irregularly active; and sedentary.

Quality of life

Quality of life was assessed by use of the Short Form Health Survey 36 (SF-36),[13] containing 36 items grouped into eight

domains: physical functioning; role limitation due to physical health; bodily pain; general health perception; vitality; social functioning; role limitation due to emotional problems; and mental health. Each domain's score ranges from 0 to 100, the highest score indicating better health conditions related to quality of life.

Anthropometric measures

One single observer assessed the following measures: height; body mass, BMI (kg/m^2); and body composition [fat percentage; three skinfold measurements: triceps, suprailiac and thigh; Lange Skinfold Calipers (Cambridge Scientific Industries, Cambridge, MD)].[14]

The 6-minute walk test

The 6MWT was performed according to the American Thoracic Society protocol.[6] Functional capacity was determined by the distance walked in a covered 30-meter walkway. After the 6MWT, the following were used: an oximeter (NONIN, model 9500, USA), to assess posttest heart rate (HRpost) and posttest oxygen saturation (SpO_2post); and the Borg scale of subjective perception of effort (SPE), ranging from 0 to 10 (SPE/CR-10; 0 = rest, 10 = maximum effort possible).[15]

Statistical analysis

A minimum sample of 25 volunteers for each group, with test power of 90%, was estimated to indicate a difference between the groups, the size of the effect being 0.97. The sample size was calculated based on a pilot study.[3,16] Normality of the data was assessed by using the Kolmogorov-Smirnov test. The variables with a normal distribution were shown as mean ± standard deviation; those without a normal distribution were shown as median with an interquartile interval.

To compare the means of the measures of the distance walked during the 6MWT, HRpost, SpO_2post and SPE/CR10 between both groups, the Student *t* test was used for independent samples in the variables with a Gaussian distribution, in which the difference between the means with a 95% confidence interval (95% CI) was obtained. When no normality was observed in the groups, the nonparametric Mann-Whitney test was used.

The Pearson's chi-square test was used to assess the association between the group and the physical activity level. In accordance with Tench et al.,[5] the forward linear regression model was used to assess the relationship between the dependent variable 'distance walked' in the 6MWT and the independent variable 'quality of life' (SF-36), and between the independent variable 6MWT in patients with SLE. The SAS for Windows 9.2 (SAS Institute Inc., Cary, NC, USA) was used in the analyses. A 5% significance level was adopted.

RESULTS

Study participants

From January 20th 2009 to January 31st 2011, 25 patients with low activity SLE [mean SLEDAI: 1.52 ± 1.61; variation: 0–5; 9 patients (36%) had a score of 0] were assessed. Mean disease duration was 5.3 ± 4.6 years (range: 1–20 years). The patients were on regular treatment as follows: prednisone = 21/25 (84%), mean dose = 6.07 ± 2.18 mg/day, range = 5–20 mg/day; azathioprine = 8/25 (32%), mean dose = 87.50 ± 46.88 mg/day, range = 50–200 mg/day; chloroquine diphosphate = 17/25 (68%), mean dose = 205.88 ± 66.44 mg/day; and hydroxychloroquine = 2/25 (8%), mean dose = 400 ± 0.0 mg/day. Twenty-five healthy women matched for age and physical characteristics were selected (Table 1).

International Physical Activity Questionnaire

Compared with controls, the patients with SLE did not statistically differ regarding their physical activity level (P = 0.127), which was as follows: 17/25 (68%) were considered active; 3/25 (12%) were considered irregularly active; and 5/25 (20%) were considered sedentary. The physical activity level of the control group was as follows: 23/25 (92%) patients were considered active; 1/25 (4%) were considered irregularly active; and 1/25 (4%) were considered sedentary. The patients with SLE did not statistically differ regarding the time they remained seated during the week (SLE = 251.00 ± 148.16 hours *versus* controls = 287.00 ± 215.76 hours; P = 0.80), and during the weekend (SLE = 266.00 ± 146.46 hours *versus* controls: 253.80 ± 200.08 hours; P = 0.40).

Quality of life

Table 2 shows data regarding the patients' quality of life. The SF-36 showed that patients with SLE had a worse quality of life in the following domains: general health perception; physical functioning; role limitation due to emotional problems; social functioning; role limitation due to physical health; and mental health (all, P < 0.05). Neither vitality nor bodily pain differed (both, P > 0.05).

The 6-minute walk test

Table 3 shows data regarding the 6MWT. Compared with controls, the patients with SLE walked a shorter distance (P < 0.001) and had higher SPE/CR10 (P < 0.05) and HRpost

Table 1
Physical characteristics of patients with systemic lupus erythematosus and healthy women (control group)*

Variable	SLE (n = 25)	Control (n = 25)	Difference between means (95% CI)#	P
Age, years, median (IQR)+	29.9 (6.8)	29.2 (8.0)	—	0.7671
Body mass, kg	57.7 ± 6.7	58.3 ± 8.2	0.69 (–3.5; 4.9)	0.7462
Height, cm	158.0 ± 0.1	158.0 ± 0.1	–0.01 (–0.5; 0.0)	0.6573
Lean body mass, kg	38.0 ± 4.8	38.5 ± 3.8	0.49 (–2.0; 2.9)	0.6966
BMI, kg/height^2	23.0 ± 2.9	23.5 ± 3.3	0.47 (–1.3; 2.2)	0.5998

SLE: systemic lupus erythematosus; 95%CI: 95% confidence interval; IQR: interquartile range; BMI: body mass index.
*Values expressed as mean ± standard deviation, unless otherwise specified.
#Calculated only when the Student *t* test was used.
+These variables do not have normal distribution, being, thus, expressed as median.

Table 2
Results regarding quality of life (SF-36) of patients with systemic lupus erythematosus and in healthy women (control group)*

Variable	SLE (n = 25)	Control (n = 25)	Difference between means (95%CI)#	P
Quality of life, SF-36				
Physical functioning, median (IQR)+	61.6 (24.4)	81.2 (14.5)	—	0.0029
Role limitations due to physical health, median (IQR)+	53.0 (41.0)	78.0 (25.3)	—	0.0375
Bodily pain, median (IQR)+	64.4 (25.7)	72.9 (22.0)	—	0.2752
General health perceptions	51.1 ± 17.8	67.5 ±16.3	16.3 (6.6; 26.1)	0.0014
Vitality, median (IQR)+	54.8 (11.5)	55.2 (10.3)	—	0.9686
Social functioning, median (IQR)+	68.4 (24.0)	83.8 (18.3)	—	0.0266
Role limitations due to emotional problems	41.2 (39.9)	73.1 (36.0)	—	0.0073
Mental health, median (IQR)+	50.0 ± 13.2	58.5 ± 10.5	8.5 (1.74; 15.4)	0.0150

SLE: systemic lupus erythematosus; 95%CI: 95% confidence interval; IQR: interquartile range; SF-36: Short Form Health Survey 36.
* Values expressed as mean ± standard deviation, unless otherwise specified.
#Calculated only when the Student t test was used.
+These variables do not have normal distribution, being, thus, expressed as median.

Table 3
Results of the 6-minute walk test of patients with systemic lupus erythematosus and healthy women (control group)*

Variable	SLE (n = 25)	Control (n = 25)	Difference between means (95% CI)#	P
6MWT	598.1 ± 45.5	642.4 ± 39.1	44.3 (20.2; 68.5)	0.0006
SPE/CR10, median (IQR)+	6.2 ± 2.0	5.1 ± 1.6		0.0358
SpO_{2PRE}, (%), median (IQR)+	98.1 (0.6)	97.6 (1.3)		0.3588
SPO_{2POST}, (%), median (IQR)+	98.1 ± 1.3	98.0 ± 1.0		0.5864
HR_{PRE}, BPM	80.5 ± 10.3	81.7 ± 14.9	1.2 (–6.1; 8.5)	0.7432
HR_{POST}, BPM	134.3 ± 15.5	123.0 ± 23.6	–11.2 (–22.6; 0.0)	0.0544

SLE: systemic lupus erythematosus; 95%CI: 95% confidence interval; IQR: interquartile range; 6MWT: 6-minute walk test; SPE/CR10: subjective perception of effort in each series, scale from 0 to 10; SpO_{2PRE}: peripheral oxygen saturation at rest prior to the 6MWT; SpO_{2POST}: peripheral oxygen saturation after the 6MWT; HRPRE: heart rate at rest prior to the 6MWT; FCPOST: heart rate after the 6MWT; BPM: beats per minute.
* Values expressed as mean ± standard deviation, unless otherwise specified.
#Calculated only when the Student *t* test was used.
+These variables do not have normal distribution, being, thus, expressed as median.

(P = 0.05) than controls. Patients with SLE did not differ regarding SpO_2post (P = 0.35).

Linear regression model

The final linear regression model for 6MWT, which included the SF-36 variables (mental health, physical functioning, social functioning and role limitation due to emotional problems), accounted for 70% of the distance walked in the 6MWT (P ≤ 0.01) (Table 4).

DISCUSSION

The present study aimed at: 1) assessing the association between distances walked in the 6MWT and the quality of life of premenopausal patients with low activity SLE; 2) comparing those results with those of healthy women matched for gender, age, physical activity level and physical characteristics. In addition, HRpost, SpO_2post, and SPE/CR10 were assessed. The results of the tests confirm our hypothesis that the patients with SLE walked a shorter distance in the 6MWT as compared with controls. The linear regression model showed that the quality of life was a significant predictor of 70% of the distance walked in the 6MWT.

We know no previous evidence of the association between the distance walked in the 6MWT and the quality of life of patients with SLE. This study provides evidence that the quality of life of patients with SLE, per se, is associated with a reduction in the cardiovascular capacity assessed by use of the 6MWT. In addition, in a practical and simple way, the 6MWT confirmed the results of the study by Tench et al.,[5] in which high-cost equipment has been used to assess cardiovascular capacity, and which has shown an association of the cardiovascular capacity, assessed by use of the treadmill test and bicycle ergometer, with quality of life.[5]

Table 4
Linear regression model of the 6-minute walk test

Dependent variable	Independent variable	PE	Standard error	R^2	P
6MWT	Functional capacity (SF-36)	2.26	0.33	0.20	< 0.0001
	Social aspects (SF-36)	−1.14	0.31	0.44	0.0014
	Emotional aspects (SF-36)	−0.68	0.18	0.60	0.0010
	Mental health (SF-36)	−1.16	0.44	0.70	0.0155

R^2: coefficient of determination; PE = parameter estimate; 6MWT: 6-minute walk test; SF-36: *Short Form Health Survey* 36.

However, Bostrom et al.[17] have reported that 26% of the patients undergoing treadmill tests do not achieve the minimum velocity of 5 km/h,[5] possibly due to biomechanical issues.[17] Similarly, when the tests are performed on a bicycle ergometer, the major limitation is that 50% of the patients have peripheral fatigue prior to central fatigue.[18] In addition, the conventional test is time-consuming, requires specialized equipment, which has a high cost and is not practical for hospitals, clinics and physical activity centers. Thus, the 6MWT might be a more practical tool to aid with the cardiovascular clinical prognosis of patients with SLE.

The only study performed so far with the 6MWT was that by Hougthon et al.,[18] showing that young patients with SLE walked a shorter distance than that predicted for the same age group. However, this is the first study using the 6MWT to compare the cardiovascular capacity of adult patients with SLE and controls. The results of the present study confirm the findings of several studies in which patients with SLE have lower cardiovascular capacity and higher values of SPE and HR than those of controls.[3] However, the previous studies have been performed with treadmills or bicycle ergometers.[3]

The shorter distance walked and the worse quality of life of patients with SLE might relate to the time for disease diagnosis,[19] depression, and cognitive dysfunction.[20] Tench et al.[5] have reported that the lower cardiovascular capacity might be associated with the fatigue of patients with SLE. That symptom is also associated with a reduced functional performance[21] and might relate to the cycle that reduces physical fitness (muscle strength/cardiovascular capacity), thus reducing the ability to perform daily activities[3] and impairing the quality of life of those patients. Another explanation might be the type I and II muscle fiber atrophy,[22,23] and the mitochondrial damage due to long-term corticosteroid therapy.[24]

Some limitations of this study should be considered. 1) The generalization of our results should be limited due to the homogeneity of the sample studied. The patients studied originated from one single hospital, and their physical characteristics, age, and physical activity level were similar to those of the control group. In addition, the sample size was relatively small. However, the homogeneity of both groups strengthens the internal validity of this study, minimizing potential confounding factors attributed to that aspect, such as perimenopause, fibromyalgia, tobacco use, obesity, and beta-blocker and statin use. In the present study, those factors were similar in patients with SLE and controls. In addition, only patients with low activity SLE participated in this study. All those aspects were methodologically controlled to minimize interference in the distance walked in the 6MWT.

2) The cross-sectional nature of this study establishes no cause-effect relationship. However, the objective of this study was to raise hypotheses for future studies aimed at assessing the clinical effects of exercise on the health and quality of life of patients with SLE. In addition, the 6MWT was used, a test that, considering the reality of the Brazilian Unified Health System (SUS), might have greater practical applicability for cardiovascular prognosis, differently from conventional tests.

Concluding, the present study evidenced that factors related to quality of life are predictors of cardiovascular capacity. We investigated that association by using the 6MWT in patients with SLE. In addition, reduced cardiovascular capacity and SLE are associated with increased morbidity and mortality. Thus, assessing cardiovascular capacity by use of the 6MWT and encouraging the practice of exercises might improve the quality of life of patients with SLE. Those possible benefits, however, should be assessed in further studies.

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