



Self-Reported Physical Activity Is Associated with Lupus Nephritis in Systemic Lupus Erythematosus: Data from KOREan Lupus Network (KORNET) Registry

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Purpose: The aim of this study was to identify the associations among physical activity, disease activity, and organ damage in patients with systemic lupus erythematosus (SLE).

Materials and Methods: A total of 415 patients with SLE were consecutively enrolled from the KOREan lupus Network (KORNET) registry. This registry assessed clinical features, disease activity [Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2K)], and organ damage [Systemic Lupus International Collaborating Clinics/American College of Rheumatology (SLICC/ACR) Damage Index (SDI)] upon enrollment in the study. Self-reported physical activity was measured by the International Physical Activity Questionnaire. Statistical analyses were conducted using the Mann-Whitney U test and multivariate logistic regression analysis.

Results: A significant difference in vigorous activity was noted between patients with lupus nephritis (LN) (n=93) and those without LN (n=322) ($p=0.012$), but not in moderate and walking activities. In contrast, no differences in physical activity, walking, moderate, and vigorous intensity, according to SLEDAI-2K and SDI were found. In addition to younger age ($p=0.032$), high physical component summary of SF-36 ($p=0.004$) and SLEDAI-2K ($p=0.038$), and less vigorous physical activity were associated with LN ($p=0.024$). However, cardiovascular disease was not associated with physical activity in SLE patients.

Conclusion: This study showed that patients with LN had less vigorous physical activity than patients without LN. The results suggest that lupus nephritis might be associated with physical activity.

Key Words: Systemic lupus erythematosus, lupus nephritis, physical activity, SLEDAI-2K, SLICC/ACR Damage Index

INTRODUCTION

Systemic lupus erythematosus (SLE) is a multisystem autoim-

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mune disease with diverse clinical manifestations involving variable tissues and organs, such as the skin, hematologic system, cardiovascular system, lungs, musculoskeletal system, and kidneys.¹ Recent studies have provided evidence that physical activity should be considered as a crucial factor in understanding disease progression, manifested as disability, fatigue, and quality of life in patients with SLE.²⁻⁵ Considering the effect of physical activity on disease activity or damage, physical activity was found to be related with an increased risk of organ damage, but not disease activity.^{6,7} In contrast, low aerobic activity was not found to be correlated with overall disease activity and organ damage.⁸ Multiple studies have shown a prevalence of less physical activity in 23–59% of patients with SLE.^{2,9-11} Given the evidence linking physical activity and unfavorable SLE-related clinical progression, defining the effect of physical activity

on disease status in SLE patients should be of great importance.

Various methods have been developed to measure physical activity. Early studies in patients with SLE used self-reported estimates. The International Physical Activity Questionnaire (IPAQ)^{2,12} or accelerometer measures^{12,13} were used according to the purposes of each study. Comparing the two methods to assess their association in SLE patients, Ahn, et al.¹² concluded that the IPAQ was useful to provide descriptive data and was modestly correlated with accelerometer measurements. This study also suggested that an accelerometer may be helpful in detecting changes in physical activity in therapeutic intervention trials. However, these two estimates have limitations: subjective responses, abdominal adiposity, underestimated reporting in activities, such as swimming and bicycling, and cost-effectiveness in large population studies.

There is insufficient data about the relationship between physical activity and disease activity/organ damage in SLE patients, although debate over this issue remains.⁶⁻⁸ In our cross-sectional study, we used self-reported IPAQ estimates to investigate the association between physical activity and SLE-specific disease activity/organ damage measurements in patients with SLE.

MATERIALS AND METHODS

Subjects

Patients enrolled in the KOREan lupus Network (KORNET) registry were consecutively recruited from rheumatology outpatient clinics at four university-based medical centers between January 2014 and December 2015. A total of 505 patients with SLE who met the 1982 revised and 1997 updated American College of Rheumatology classification criteria for SLE^{14,15} were initially identified from this registry. However, only 415 SLE patients were enrolled in this study: 90 patients were excluded for failure to complete the questionnaire on self-reported measured physical activity. All patients provided written informed consent for enrollment in the registry. The Institutional Review Board of all four medical centers approved the registry protocol (IRB No. CR-14-123-L).

Clinical data collection

The KORNET registry collected clinical information through medical record review and interviews with each patient. Upon enrollment in the KORNET registry, each patient's demographic data and health behaviors, such as smoking and alcohol consumption, were recorded. Body mass index, marital status, and education duration were identified. Questionnaires related to health status were also assessed using Beck's Depression Inventory¹⁶ and the 36-item Short Form Health Survey (SF-36).¹⁷ Serologic markers included in this study were erythrocyte sedimentation rate (mm/hr), C-reactive protein (mg/dL), complement 3 (mg/dL), complement 4 (mg/dL), and CH50 (U/

mL). Positivity for anti-double stranded DNA (anti-dsDNA) antibody was also identified. In addition, anti-rheumatic medications being taken at the time of enrollment, such as hydroxychloroquine, corticosteroids, methotrexate, azathioprine, mycophenolate mofetil, and tacrolimus, were recorded. Enrolled patients with hypertension, ischemic heart disease, myocardial infarction, congestive heart failure, and/or a cardiac arrhythmia were defined as having cardiovascular disease (CVD). The definitions for each CVD were as follows: Hypertension was diagnosed if diastolic blood pressure was over 90 mm Hg or systolic blood pressure was 140 mm Hg or more when not taking or if taking anti-hypertensive medicine. Ischemic heart disease included stable or unstable angina pectoris based on clinical features or laboratory findings. Myocardial infarction was defined as a non-ST segment elevation or ST segment elevation myocardial ischemia diagnosed by abnormal changes in electrocardiogram, chest pain, and elevated cardiac enzymes. Congestive heart failure was diagnosed by echocardiography and clinical findings related with impaired heart function. Cardiac arrhythmia included premature heartbeat, tachyarrhythmia, or bradycardia identified by electrocardiogram.

SLE-related disease activity using the SLE Disease Activity Index 2000 (SLEDAI-2K)¹⁸ and organ damage using the Systemic Lupus International Collaborating Clinics/American College of Rheumatology (SLICC/ACR) Damage Index (SDI)¹⁹ were evaluated by a rheumatologist (SK Kim). According to disease activity and organ damage scores, this study was classified into two groups: inactive (SLEDAI<2) versus active (SLEDAI≥2) and non-damaged (SDI<1) versus damaged (SDI≥1). The Charlson comorbidity index (CCI) score is defined as the sum of the comorbidity scores.²⁰ CCIa is age-adjusted value of CCI.

Assessment of physical activity

The IPAQ, developed by the World Health Organization in 1998 (<https://sites.google.com/site/theipaq/scoring-protocol>), was utilized as a self-reported questionnaire for physical activity surveillance.²¹ For recording physical activity for seven days, patients used the 7-item short-form IPAQ instead of the 27-item long form. A Korean version of the short-form IPAQ has been confirmed through validation against both the long-form IPAQ and accelerometer measurements.²²

Metabolic equivalent of task (MET) values and formula for computation of MET-minutes/week were measured from the IPAQ assessment. The short-form IPAQ was categorized as follows: walking MET-minutes/week (3.3×walking-intensity activity minutes×walking-intensity days), moderate MET-minutes/week (4.0×moderate-intensity activity minutes×moderate-intensity days), and vigorous MET-minutes/week (8.0×vigorous-intensity activity minutes×vigorous-intensity days).²³ Total physical activity MET-minutes/week was the sum of walking, moderate, and vigorous MET-minutes/week scores. In addition, we assigned three categorical scores: category 1 low, category 2 moderate, and category 3 high, according to levels of

physical activity.

Statistical analysis

Statistical analysis for continuous variables was assessed by two normality tests: the Kolmogorov-Smirnov and Shapiro-Wilk tests. The data were not normally distributed and were described as median±interquartile range (IQR) for continuous variables. For categorical variables, data are expressed as a number (%). The statistical differences between two groups [lupus nephritis (LN) (+) vs. LN (-), CVD (+) vs. CVD (-), SLEDAI-2K<2 vs. SLEDAI-2K≥2, and SDI=0 vs. SDI≥1] were calculated using the chi-square test or Fisher's exact test for categorical variables and the Mann-Whitney U test for continuous variables. Binary logistic regression analysis was used to determine risk factors related to LN and CVD. All statistical analyses were conducted using IBM SPSS Statistics 19.0 (IBM Corp., Armonk, NY, USA). Statistical significance was considered at a *p* value less than 0.05.

RESULTS

Table 1 shows the baseline demographic data, clinical features, and laboratory findings in the 415 SLE patients. Median age at enrollment was 39.8 years (IQR 32.0–47.0) and 93.0% were female (*n*=386). Notably, 93 patients with LN (22.4%) were identified, all of whom were pathologically diagnosed in the course of the disease. Median SLEDAI-2K of all patients was 2.0 (IQR 1.0–4.0). The percentage of patients with SLEDAI-2K ≥2 and with at least one organ damaged (≥1 of SDI) was 73.7% (*n*=306) and 18.6% (*n*=77), respectively. In total, 16% of patients (*n*=67) had at least one manifestation of CVD.

Comparison of characteristics between patients with and without LN is illustrated in Table 2. There were significant differences in age, marital status, anti-dsDNA positivity, physical component summary of SF-36, frequency of CVD, and use of corticosteroid, methotrexate, mycophenolate mofetil, and tacrolimus between the two groups. However, the frequency for some disease activity and damage-related variables including SLEDAI-2K ≥2 and SDI ≥1 were similar between the two groups.

The differences in physical activity based on IPAQ scores according to SLEDAI-2K (<2 vs. ≥2), SDI (<1 vs. ≥1), and LN (presence vs. absence) were assessed (Fig. 1). There were no significant differences in walking, moderate, and vigorous physical activity between active (SLEDAI-2K≥2) and inactive (SLEDAI-2K<2) (*p*>0.05) patients. Similarly, there were no differences in each physical activity score between organ-damaged (SDI≥1) and non-organ-damaged (SDI<1) (*p*>0.05) patients. Walking and moderate activity showed similar levels despite the presence or absence of LN. However, patients with LN showed less vigorous activity, compared to those without LN (*p*=0.012). In addition, there were no differences in num-

bers of patients in low, moderate, and high categories between patients with and without LN (*p*>0.05). Patients with CVD also showed similar levels of each physical activity score, compared to those without CVD (*p*>0.05 of all, data not shown).

Table 1. Baseline Characteristics of Enrolled Subjects (*n*=415)

Variables	Results
Age (yr)	39.8 (32.0–47.0)
Gender (female)	386 (93.0)
Disease duration (month)	2.0 (0.2–7.2)
Education duration (yr)	14.0 (12.0–16.0)
Body mass index (kg/m ²)	21.4 (19.4–23.5)
Marital status	
Single/married/divorced/bereaved	123 (29.6)/264 (63.6)/19 (4.6)/9 (2.2)
Alcohol consumption	113 (27.2)
Smoking status	
Never/current/ex-smoker	368 (88.7)/29 (7.0)/18 (4.3)
Erythrocyte sediment rate (mm/hr)	18.0 (10.0–31.0)
C-reactive protein (mg/dL)	0.08 (0.05–0.30)
Anti-dsDNA positivity	298 (71.8)
Complement 3 (mg/dL)	79.7 (67.0–95.2)
Complement 4 (mg/dL)	15.4 (10.9–20.6)
CH50 (U/mL)	47.7 (37.9–56.7)
Becker depression inventory	7.0 (3.0–13.0)
Short form-36 health survey	
Physical component score	48.9 (42.9–53.8)
Mental component score	49.3 (40.6–56.1)
SLEDAI-2K	2.0 (1.0–4.0)
SLEDAI-2K≥2	306 (73.7)
LN	93 (22.4)
WHO class I/II/III/IV/V	4 (4.3)/14 (15.1)/19 (20.4)/40 (43.0)/16 (17.2)
SLEDAI-2K of LN	14.0 (11.0–18.0)
SDI≥1	77 (18.6)
CVD	67 (16.1)
Musculoskeletal symptom	9 (2.2)
Depression	4 (1.0)
CCLa	1.0 (1.0–2.0)
IPAQ categorical score	
Low/moderate/high	234 (56.4)/70 (16.9)/111 (26.7)
Medications	
Hydroxychloroquine	380 (91.6)
Corticosteroid	336 (81.0)
Methotrexate	22 (5.3)
Azathioprine	72 (17.3)
Mycophenolate mofetil	58 (14.0)
Tacrolimus	38 (9.2)

SLEDAI-2K, Systemic Lupus Erythematosus Disease Activity Index 2000; LN, lupus nephritis; SDI, Systemic Lupus International Collaborating Clinics/American College of Rheumatology (SLICC/ACR) Damage Index; CVD, cardiovascular disease; IPAQ, International Physical Activity Questionnaire; CCLa, age-adjusted Charlson comorbidity index.

Data are described as medians with interquartile range or number (%).

Table 2. Comparison of Characteristics according to LN

Variables	LN		p value
	Absence (n=322)	Presence (n=93)	
Age (yr)	40.5 (33.0–48.3)	35.0 (28.0–44.0)	0.003
Gender (female)	301 (93.5)	85 (91.4)	0.488
Disease duration (month)	2.0 (0.2–8.1)	1.9 (0.2–6.1)	0.209
Education duration (yr)	14.0 (12.0–16.0)	14.0 (12.0–16.0)	0.149
Body mass index (kg/m ²)	21.4 (19.3–23.4)	21.1 (18.9–24.2)	0.458
Marital status			0.019
Single/married/divorced/bereaved	84 (26.1)/216 (67.1)/16 (5.0)/6 (1.9)	39 (41.9)/48 (51.6)/3 (3.2)/3 (3.2)	
Alcohol consumption	90 (28.0)	23 (24.7)	0.539
Smoking status			0.455
Never/current/ex-smoker	284(88.2)/25(7.8)/13(4.0)	84(90.3)/4(4.3)/5(5.4)	
Erythrocyte sediment rate (mm/hr)	19.0 (11.0–31.0)	16.0 (9.0–28.8)	0.161
C-reactive protein (mg/dL)	0.09 (0.06–0.30)	0.07 (0.05–0.30)	0.646
Anti-dsDNA positivity	156 (48.4)	64 (68.8)	0.001
Complement 3 (mg/dL)	81.3 (67.2–95.4)	77.4 (63.9–95.1)	0.254
Complement 4 (mg/dL)	15.6 (11.3–20.7)	15.0 (9.9–20.6)	0.390
CH50 (U/mL)	47.3 (38.5–56.4)	50.1 (36.4–58.7)	0.353
Becker depression inventory	8.0 (4.0–14.0)	5.0 (3.0–11.0)	0.060
Short form-36 health survey			
Physical component score	8.3 (42.1–53.4)	51.1 (44.7–55.1)	0.010
Mental component score	48.8 (42.1–53.5)	50.7 (44.1–56.8)	0.090
SLEDAI-2K	2.0 (1.0–4.0)	4.0 (0.0–6.0)	0.145
SLEDAI-2K≥2	237 (73.6)	69 (74.2)	0.909
SDI≥1	56 (17.4)	21 (22.6)	0.257
CVD	42 (13.0)	25 (26.9)	0.001
Musculoskeletal symptom	7 (2.2)	2 (2.2)	0.674
Depression	3 (0.9)	1 (1.1)	0.639
CCla	1.0 (1.0–2.0)	1.0 (1.0–2.0)	0.194
IPAQ categorical score			0.295
Low/moderate/high	177 (55.0)/53 (16.5)/92 (28.6)	57 (61.3)/17 (18.3)/19 (26.7)	
Medications			
Hydroxychloroquine	295 (91.6)	85 (91.4)	0.947
Corticosteroid	253 (78.6)	83 (89.2)	0.021
Methotrexate	21 (6.5)	1 (1.1)	0.025
Azathioprine	58 (18.0)	14 (15.1)	0.507
Mycophenolate mofetil	21 (6.5)	37 (39.8)	< 0.001
Tacrolimus	11 (3.4)	27 (29.0)	< 0.001

LN, lupus nephritis; SLEDAI-2K, Systemic Lupus Erythematosus Disease Activity Index 2000; SDI, Systemic Lupus International Collaborating Clinics/American College of Rheumatology (SLICC/ACR) Damage Index; CVD, cardiovascular disease; IPAQ, International Physical Activity Questionnaire; CCl_a, age-adjusted Charlson comorbidity index.

Data are described as medians with interquartile range or number (%).

Logistic regression analysis was performed to determine the risk factors associated with LN (Table 3). Younger age, shorter disease duration, higher physical component score (PCS) of SF-36, higher SLEDAI-2K, and less vigorous physical activity were significantly associated with the presence of LN in univariate logistic regression analysis. However, multivariate logistic regression analysis showed that younger age, higher PCS of SF-36, higher SLEDAI-2K, and less vigorous physical activity were associated with LN. Age, gender, and BMI were

noted to be related to CVD in multivariate logistic regression analysis (data not shown). Remarkably, physical activity measured by the IPAQ estimate was not related to CVD.

DISCUSSION

Studies have established that physical activity could be limited by a high level of disease activity, poor functional disability,

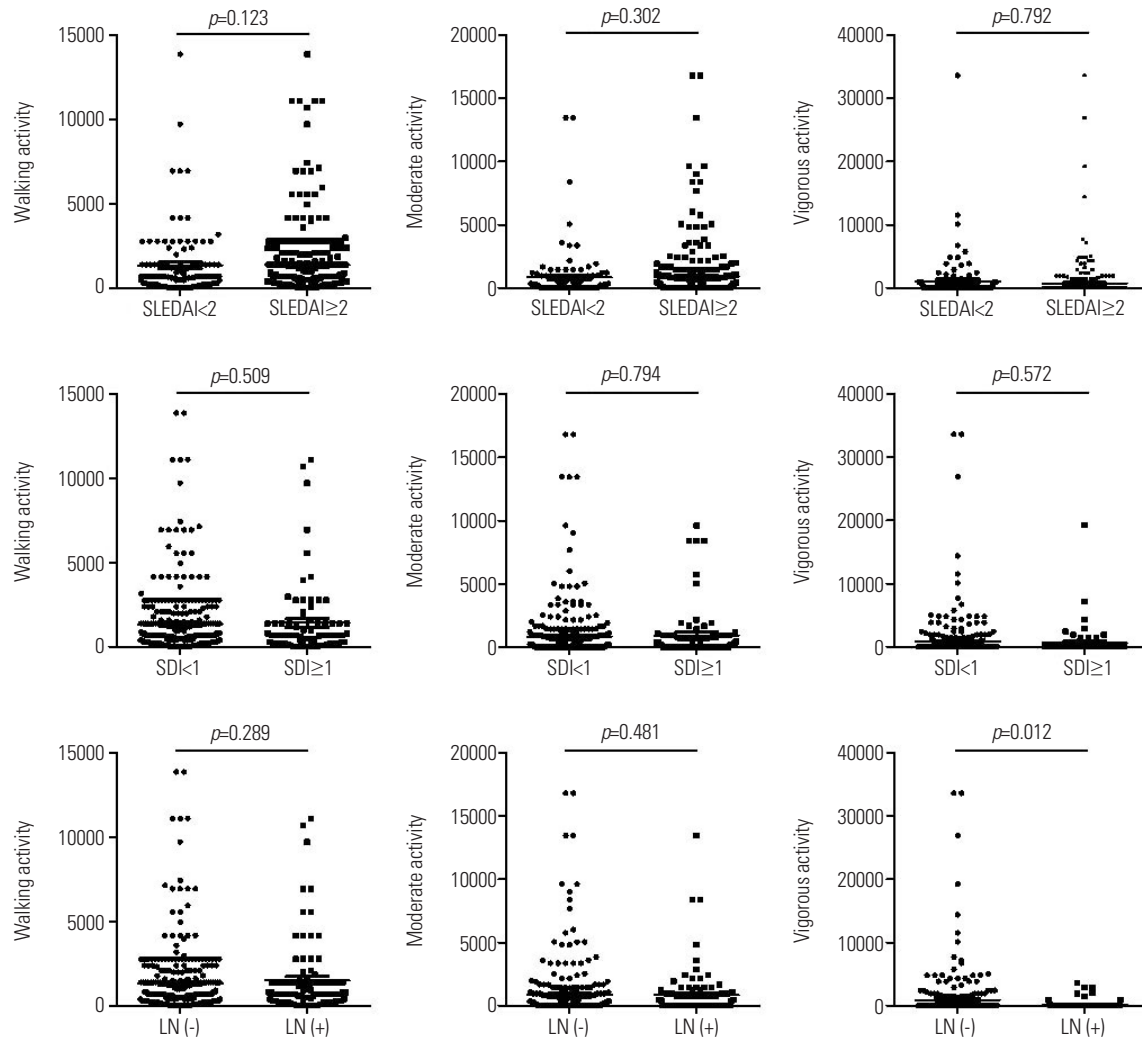


Fig. 1. Comparison of individual physical activity levels according to disease activity, organ damage, and LN. Each unit was described as MET minutes/week. *p* values were calculated by Mann-Whiney U test. SLEDAI-2K, Systemic Lupus Erythematosus Disease Activity Index 2000; SDI, Systemic Lupus International Collaborating Clinics/American College of Rheumatology (SLICC/ACR) Damage Index; LN, lupus nephritis; MET, metabolic equivalent of task.

and organ damage in patients with SLE.^{2,5-7} Nevertheless, there has been insufficient data about the relationship between physical activity and clinical features in SLE patients. The main objective of this study was to clarify an association between physical activity assessed by the IPAQ scores and disease activity/organ damage in SLE patients. We observed that physical activity was not associated with SLE-specific measures like SLEDAI and SDI. However, patients with LN were shown to perform less vigorous physical activity, compared to those without LN.

There is evidence of a close relationship between physical inactivity and high disease activity or specific organ involvement in patients with SLE. Several clinical studies have revealed that exercise or regular physical activity, without the interference of disease activity, improves quality of life, fatigue, and other SLE-related symptoms.^{5,24} Eriksson, et al.⁷ demonstrated less low to moderate intensity physical activity in SLE patients with SDI ≥ 2 , compared to matched controls. In con-

trast, they did not find a significant difference in physical activity between patients with high disease activity (SLEDAI > 5) or low disease activity (SLEDAI ≤ 5) and controls. Two different 12-week randomized trials in small populations with SLE demonstrated no significant changes in disease activity after an exercise training program.^{25,26} Although there was a marked difference in cutoffs for SLEDAI and SDI scores compared to a former study,⁷ this study failed to confirm the difference of physical activity based on IPAQ scores. The beneficial role of exercise and physical activity in SLE-related disease activity or organ damage should be confirmed in a larger study population.

Physical activity is an independent risk factor for CVD in the general population. Regular physical activity has beneficial health effects and also contributes to decreased mortality risk and development of morbidity.²⁷ The data from the Framingham Heart Study indicate that moderate to high physical activity leads to increased total and CVD-free life expectancy, compared to low physical activity.²⁸ Premature CVD is attributed

Table 3. Regression Analysis for Risk Factors Associated with Lupus Nephritis

Variables	Univariate analysis		Multivariate analysis*	
	Coefficient (B) (95% CI for B)	p value	Exp(B) [95% CI for Exp(B)]	p value
Age	-0.139 (-0.009–-0.002)	0.005	0.975 (0.953–0.998)	0.032
Gender (ref.=male)	0.034 (-0.102–0.214)	0.489	0.759 (0.300–1.924)	0.562
Disease duration	-0.118 (-0.004–0.000)	0.016	0.982 (0.962–1.003)	0.085
Education duration	0.055 (-0.006–0.020)	0.263		
Body mass index	-0.028 (-0.016–0.009)	0.564		
Erythrocyte sediment rate	-0.052 (-0.004–0.001)	0.305		
C-reactive protein	-0.017 (-0.080–0.057)	0.743		
Complement 3	-0.054 (-0.003–0.001)	0.269		
Complement 4	-0.040 (-0.007–0.003)	0.420		
CH50	0.051 (-0.002–0.005)	0.361		
Becker depression inventory	-0.054 (-0.008–0.002)	0.274		
Short form-36 health survey				
Physical component score	0.134 (0.002–0.013)	0.006	1.055 (1.018–1.094)	0.004
Mental component score	0.078 (-0.001–0.007)	0.111		
SLEDAI-2K	0.110 (0.002–0.026)	0.026	1.080 (1.004–1.161)	0.038
SDI	0.051 (-0.029–0.095)	0.296	1.217 (0.843–1.757)	0.294
Musculoskeletal symptom	1.0111 (0.206–4.952)	0.989	1.566 (0.304–8.077)	0.592
Depression	0.865 (0.089–8.417)	0.901	0.646 (0.060–6.917)	0.646
CCla	1.191 (0.851–1.668)	0.308	1.313 (0.903–1.909)	0.154
Physical activity by IPAQ				
Walking	0.038 (0.000–0.000)	0.444		
Moderate	-0.111 (0.000–0.000)	0.912		
Vigorous	-0.121 (-0.222–-0.025)	0.014	1.000 (0.999–1.000)	0.024
Total	-0.044 (0.000–0.000)	0.374		

SLEDAI-2K, Systemic Lupus Erythematosus Disease Activity Index 2000; SDI, Systemic Lupus International Collaborating Clinics/American College of Rheumatology (SLICC/ACR) Damage Index; IPAQ, International Physical Activity Questionnaire; CCl_a, age-adjusted Charlson comorbidity index; CI, confidence interval.

*Multivariate regression analysis was performed using covariates, including age, gender, disease duration, physical component score of SF-36, SLEDAI-2K, SDI, musculoskeletal symptom, depression, and CCl_a.

as the most common cause of mortality in SLE patients affected by the disease for over 5 years.²⁹ Earlier studies on physical activity have primarily focused on the risk of CVD in SLE patients.^{6,30} A multicenter inception cohort study found low physical activity level (score<28) to be a potent risk factor for coronary artery disease in 278 SLE patients who were followed for 3 years (71.6% increased risk from enrollment).⁶ Volkman, et al.³⁰ demonstrated that physical activity, assessed from self-reports by calculating METS per week, was negatively correlated with carotid intima-media thickness and number of carotid plaques, thus implicating the harmful effect of low physical activity on subclinical atherosclerosis in SLE. Subsequently, they recommended increased exercise to reduce the risk of atherosclerosis in SLE patients. These findings might be compatible with a sedentary lifestyle as a traditional risk factor for CVD in general.³¹ SLE-induced cognitive impairment has been known to be caused by multiple complex factors, such as inflammation and lower energy expenditure. Physical inactivity coupled with obesity was associated with an increased risk of cognitive dysfunction in female patients with SLE.² We found no association between physical activity and the risk of CVD dis-

ease in this study. Based on these results, future studies identifying the role of physical activity and other lifestyles in the risk of CVD are warranted.

LN is the most debilitating manifestation of SLE and is associated with increased morbidity and mortality.¹ The pathogenesis of LN is well understood: formation of glomerular immune complexes, B cell activation with autoantibodies, and inflammatory mediators.³² Although the precise mechanism for the favorable effect of physical activity has not been clearly determined, there is evidence that physical inactivity could induce an increased inflammatory response. Prolonged murine restraint stress induced changes in inflammatory cytokine profiles, increasing IL-6 and reducing IL-10, indicating an enhanced inflammatory cascade.³³ In contrast, daily moderate exercise attenuated systemic inflammation in response to lipopolysaccharide injection in mice.³⁴ Recently, Aqel, et al.³⁵ demonstrated that daily moderate exercise improves the inflammatory response of LN in NZM2410/J mice through blocking the expression of inflammatory mediators IL-6, tumor necrosis factor- α , CXCL1, and anti-dsDNA antibodies. Their findings also implicated the possibility of adjunct therapeutic

Table 4. Summary for the Effect of Physical Activity on Disease Activity and Organ Damage

Study	Study design and population	Measures of physical activity and outcome
Urowitz, et al. ⁶	Incept cohort study: 278 SLE	Low physical activity as risk factor for coronary artery disease
Eriksson, et al. ⁷	Case control study: 272 SLE and 272 controls	Less physical activity and excise capacity in patients with SDI ≥ 2
Boström, et al. ⁸	Cross-sectional study: 34 SLE	Aerobic capacity not associated with SLEDAI and SDI
Volkman, et al. ³⁰	Cross-sectional study: 242 SLE	Low physical activity associated with subclinical atherosclerosis
Abrahão, et al. ²⁵	RCT for 12 weeks: 62 SLE	No difference of SLEDAI by training program
Miossi, et al. ²⁶	RCT for 12 weeks: 24 SLE and 8 controls	No change of SLEDAI scores after exercise intervention
Present study	Cross-sectional study: 415 SLE	Less vigorous physical activity associated with lupus nephritis

SLE, systemic lupus erythematosus; SLEDAI, Systemic Lupus Erythematosus Disease Activity Index; SDI, Systemic Lupus International Collaborating Clinics/American College of Rheumatology (SLICC/ACR) Damage Index; RCT, randomized controlled study.

strategy for LN. Compatible with these observation, we found that patients with LN performed less vigorous physical activity.

There are several limitations that should be considered to understand this result. First, this study used only self-reported IPAQ estimates to assess levels of physical activity. Because our study contained a large number of patients, we could not perform objective measurements with an accelerometer. The IPAQ estimate has some advantages in studies that enroll many patients and also for acquisition of discriminable data related with the types of each physical activity, whereas estimation using an accelerometer is not cost-effective. Overall, moderate correlation between self-reported and objectively measured physical activity was confirmed through a cross-sectional study that included 129 patients with SLE.¹² Second, healthy and disease control groups were not included in this analysis. Approximately 56% of patients were classified into the low category in the assessment of physical activity in our registry, which is consistent with earlier evidence showing less physical activity in patients with SLE.^{9,10} Control groups with inactive, healthy subjects are needed to compare the levels of physical activity in patients with SLE. Third, our results were acquired through cross-sectional analysis. Therefore, we could not identify whether enforcement of physical activity hinders disease activity and lessens organ damage measured through SLEDAI and SDI. Some debate over the effect of therapeutic intervention through a regular exercise program or physical activity on SLE-related symptoms and disease activity remains.^{5,24-26} The possibility for exercise and physical activity as therapeutic modalities should be assessed in a prospective study. Considering 90 patients were excluded with missing data for physical activity, the study population may lack representativeness. Patients with a high disease activity or severe disease impairment may be less willing to participate in the questionnaire for physical activity. Excluding such patients who do not complete the questionnaire introduces a high likelihood of selective bias. In addition, physical activity according to disease activity or severity may be underestimated as a result of this study.

There is still debate over the effect of physical activity in the clinical status of patients with SLE (Table 4). Using the self-reported questionnaire IPAQ, this study was performed to identify the associations between physical activity and disease ac-

tivity and organ damage in a population of patients with SLE. We found that patients with LN showed no difference in walking and moderate physical activity, compared to patients without LN. Patients with LN also tended to be reluctant to conduct vigorous physical activity. Efforts to strengthen the intensity of physical activity should be encouraged to avoid incremental exposure to SLE-related morbidity and mortality.

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