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Low Physical Activity is Associated with Proinflammatory High Density Lipoprotein and Increased Subclinical Atherosclerosis in Women with Systemic Lupus Erythematosus

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Abstract

Objective—To investigate the association between physical activity, functional activity of HDL, and subclinical cardiovascular disease in patients with Systemic Lupus Erythematosus (SLE).

Methods—242 SLE patients (all women) participated in this cross-sectional study from February 2004 to February 2008. Carotid plaque and intima-media thickness (IMT), antioxidant function of HDL, and traditional cardiac risk factors were measured. Physical activity was assessed from self-reports by calculating the metabolic equivalent-minutes (METs) per week and by the physical function domain of the Medical Outcomes Study Short Form-36 (SF-36). Data were analyzed using bivariate and multivariate regression analyses.

Results—Number of METs per week spent performing strenuous exercise was negatively correlated with IMT ($r = -.30$, $P = 0.002$) and number of plaques ($r = -.30$, $P = 0.0001$). Physical function as assessed by the SF-36 was also negatively correlated with IMT ($r = .14$, $P = 0.03$) and number of plaques ($r = -.14$, $P = 0.04$). In multivariate analyses, number of strenuous exercise METs was significantly associated with IMT ($t = -2.2$, $P = 0.028$) and number of plaques ($t = -2.5$, $P = 0.014$) when controlling for markers of SLE disease activity and damage, but not after controlling for traditional cardiac risk factors. Low physical activity, defined as < 225 total METs per week, was associated with presence of piHDL ($P = 0.03$).

Conclusion—Low physical activity is associated with increased subclinical atherosclerosis and with piHDL in patients with SLE. Increased strenuous exercise may reduce the risk of atherosclerosis in SLE.

Accumulating evidence has demonstrated that exercise and physical activity decreases cardiovascular morbidity and mortality in the general population (1,2). Data from the

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Framingham Heart Study indicate that in the population aged 50 years or older, high physical activity is associated with an increased life expectancy of 3.7 years in men and 3.5 years in women (3). Moreover, low physical activity appears to be an independent predictor of coronary heart disease (4). Suggested mechanisms for the cardiac benefits of increased physical activity include enhanced glucose regulation and insulin sensitivity, fat redistribution/loss, improved endothelial function, decreased blood pressure and lipid levels, anti-thrombotic effects, and modification of novel cardiovascular risk factors (e.g. inflammatory cytokines) (5).

While the cardiovascular benefits of exercise are well recognized, few studies have examined the relationship between physical activity and subclinical markers of atherosclerosis, such as carotid intima-media thickness (IMT) and plaque. A systematic review of cross-sectional, interventional, retrospective or prospective clinical studies demonstrated that physical inactivity is associated with increased IMT (5). However, the same study reported inconsistent associations between structured lifestyle interventions and progression of IMT. Other studies have found no relationship between physical activity and IMT (6,7), while some have demonstrated an inverse association between physical activity in men, but not in women (8). A recent report from the Multi-Ethnic Study of Atherosclerosis found that walking pace was favorably associated with common carotid IMT; however, this association was no longer significant after controlling for traditional cardiac risk factors (9). Differences in physical activity assessment techniques may contribute to the disparities in these findings.

In addition, the majority of studies have evaluated these relationships within the general population. The use of heterogeneous study cohorts may also contribute to result discrepancies. To address this issue, the present study examined the relationships between physical activity and subclinical atherosclerosis in patients with systemic lupus erythematosus (SLE), a patient population with a predilection for premature cardiovascular disease (10). Patients with SLE have an increased risk of coronary artery disease (10) and stroke (11) compared with the general population. Myocardial infarction (MI), the leading cause of death in SLE patients, occurs on average at 49 years of age, 20 years earlier than the general population (12). SLE patients also have significantly increased subclinical atherosclerosis compared with healthy controls, measured as carotid artery plaque or coronary artery calcification (13,14). Furthermore, the rate of plaque progression over a short period (mean of 4.19 years) is significantly higher than in healthy controls (15).

Research suggests that the pathogenesis of SLE-related enhanced atherosclerosis is multi-factorial, involving abnormalities of lipids, inflammation, and autoimmune reactions (16). With regard to lipids, recent studies have demonstrated that dysfunction of high-density lipoproteins (HDL) contributes to atherosclerotic plaque formation in SLE patients (17). Specifically, dysfunctional, proinflammatory HDL (piHDL) is associated with increased IMT and plaque on carotid ultrasound (18). To our knowledge, no studies have assessed whether factors such as diet and lifestyle interventions may improve HDL function in SLE patients. However, a study of obese men exposed to a three-week intensive diet and exercise intervention found a substantial decrease in piHDL levels after the intervention (19).

The purpose of the present study was to investigate the relationship between physical activity and subclinical atherosclerosis in patients with SLE. A secondary goal was to examine the relationship between physical activity and piHDL in patients with SLE.

MATERIALS AND METHODS

Study population

Study subjects were drawn from our Biomarkers of Atherosclerosis in SLE Study. Details of this study protocol have been reported elsewhere (18); in brief, participants were recruited prospectively from the Rheumatology Practices of the University of California, Los Angeles (UCLA), Cedars Sinai Medical Center in Los Angeles, and Harbor UCLA Medical Center in Torrance, California, from February 2004 to February 2008. Eligible participants were women ≥18 years of age. Patients with SLE fulfilled at least four of the 1997 revised American College of Rheumatology (ACR) classification criteria for SLE (20). Exclusion criteria included previous or current statin use, renal failure and/or decreased renal function (Cr >2.0), all of which have been shown to alter HDL function (21,22). The study was approved by the Institutional Review Board at UCLA and Cedars-Sinai Medical Center. All participants provided written informed consent.

Procedure

Eligible women who gave consent provided a blood sample, underwent a carotid ultrasound, and completed a set of questionnaires. Blood samples were obtained on the same day of the carotid ultrasound in the majority of participants; in all they were obtained within 2 weeks of their carotid ultrasound. Plasma lipid concentrations, levels of high sensitivity C-reactive protein (hs-CRP), and erythrocyte sedimentation rate (ESR), were measured in the UCLA clinical laboratory using standard methods. On the day of the plasma sampling, participants met with a study physician who assessed their disease activity using Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) (23), and organ damage using the Systemic Lupus International Collaborating Clinics / ACR damage index (SLICC/ACR) (24). Current and cumulative lifetime prednisone doses were ascertained by chart review.

Subclinical disease measures

B (brightness)-mode grey scale, color and spectral Doppler techniques were used to investigate the carotid arteries according to a standardized protocol (25). The same radiologist (NR) interpreted all studies in a blinded fashion, and the same ultrasound unit (Iu22, Philips Medical Systems, Bothell, WA) was used for scanning all participants.

The following anatomical sites were examined for the presence of atherosclerotic plaque, defined as the presence of focal protrusion (intima-media thickening) into the arterial lumen with a thickness exceeding that of the surrounding wall by at least 50%: the bilateral common carotid arteries, the carotid bulbs, the bilateral internal carotid arteries, the bilateral external carotid arteries, and the bilateral vertebral arteries. The number, location and sonographic appearance of the plaques were recorded. Intima-media thickness (IMT) of the far wall of the distal common carotid artery was measured (a) 1 cm proximal to the flow divider, (b) at end diastole on cineloop real-time playback, and (c) using automated QLAB software (Philips Medical Systems, Bothell, WA). IMT was never measured at the level of a plaque and is presented as the average of three values of the left and right segments.

Measurement of HDL-C function

Dysfunctional HDL has historically been identified using a cell-based assay that requires endothelial cells, smooth muscle cells, and monocytes; however, this assay is not practical for large-scale studies (26). A cell-free assay has been developed that rapidly detects dysfunctional HDL and gives results that are highly comparable to the cell based-assay (21,27). The assay is based on the ability of normal HDL to prevent oxidation of LDL. The presence of oxidized LDL leads to the conversion of normally non-fluorescent dichlorofluorescein diacetate (DCFH-DA) into a fluorescent form (DCFH). DCFH is then

measured on a plate reader (Spectra Max, Gemini XS; Molecular Devices, Sunnyvale, CA) set at an excitation wavelength of 485 nm and an emission wavelength of 530 nm, and the change in fluorescence intensity resulting from oxidation of DCFH-DA by LDL in the presence or absence of test HDL can be quantitated. Dysfunctional HDL is unable to prevent the oxidation of LDL that occurs spontaneously in vitro, and actually increases oxidation, and thus can be considered pro-oxidant and pro-inflammatory. LDL-C was prepared from normal plasma as previously described (27). 20 μL of the normal LDL-C solution (final concentration of 50 μg/ml) and 90 μL of test HDL-C (at a final concentration of 10 μg/mL cholesterol) were incubated in quadruplicate in 96-well plates for one hour. 10 μL of DCFH-DA solution (0.2mg/mL) were added to each well and incubated for 2 hours. Fluorescence was then determined with a plate reader. Values of DCFH activated by LDL-C alone were normalized to 1.0. In addition to preventing the oxidation of LDL, the presence of dysfunctional HDL in the assay often amplified LDL oxidation and subsequent DCF formation. Thus, values equal to or greater than 1.0 after the addition of test HDL-C indicated dysfunctional, proinflammatory HDL; values less than 1.0 indicated normal, anti-inflammatory HDL.

Cardiovascular risk factors

Cardiovascular risk factors were assessed on the day of the plasma collection. Height and weight were measured with the subjects in light clothing without shoes. Body mass index (BMI) was calculated as weight in kilograms divided by the square of height in meters. Resting, seated blood pressure was measured with a sphygmomanometer from one arm. Information about current and past cigarette smoking, history of cardiovascular disease (e.g. stroke, myocardial infarction), diabetes, dyslipidemia, hypertension, renal failure, and family history of coronary artery disease were obtained from a self-administered health history questionnaire. Responses on the health history questionnaire were cross-checked by a study physician using chart review. Hypertension was defined on the basis of use of an antihypertensive medication (excluding use of calcium channel blockers for management of Raynaud's phenomenon) and/or systolic/diastolic blood pressure ≥140/90 mm Hg on two or more visits occurring at least six weeks apart. Persons were considered to have dyslipidemia if they had a history of elevated LDL (≥160 mg/dL), decreased HDL (<50 mg/dL), and/or elevated total cholesterol (≥200 mg/dL).

Physical activity

Physical activity was obtained from two self-administered questionnaires. The first questionnaire consisted of the Medical Outcomes Study Short Form-36 (SF-36) (28). This valid and reliable measure is a multi-dimensional assessment of physical function, mental health, perception of health, social health, pain, and role function. The physical function component of the SF-36 consists of 10 items assessing the participants' ability to carry out specific types of physical activity on a typical day (e.g. playing vigorous sports, cleaning, carrying groceries, climbing stairs, walking, bathing or dressing). A low score on the SF-36 indicates inferior physical function compared with a high score.

The second questionnaire consisted of an abridged version of the MESA Typical Week Physical Activity Survey (TWPAS) (9), adapted from the Cross-Cultural Activity Participation Study of women (29). The survey is designed to identify the frequency, intensity, and time spent in various physical activities during a typical week in the past month. The survey has 9 items in categories of exercise ranging from walking (not at work), to strenuous aerobic activity (jogging, aerobic dancing), to moderate exercise (biking, using an exercise machine), to mild leisure activities (bowling, golf). Where appropriate, questions differentiated between light-, moderate-, and heavy-intensity activities. Respondents were asked whether they participated in these categories of activity, and if yes, subsequently

answered questions regarding the average number of days per week and time per day engaged in these activities. Minutes of activity were summed for each discrete activity type and multiplied by the appropriate metabolic equivalent (MET) level (30). Total METs per week were calculated for each participant. After reviewing the patterns of response regarding physical activity, SLE patients were divided into tertiles based on total calculated METs per week. Low exercise was defined as <225 METs per week; Medium exercise was defined as 225-945 METs per week; and High exercise was defined as >945 METs per week.

Statistics

All statistical analyses were performed using the Statistical Package for Social Sciences (SPSS) 17.0 for Windows (SPSS, Inc., Chicago, Ill.). Data were checked for normality and equality of distribution, prior to any analysis being performed. Skewed continuous variables were logarithmically transformed to attain a normal distribution. Between-group comparisons were conducted using analysis of variance and student's t-test for continuous parametric variables and Mann-Whitney test for non-parametric variables. Pearson and Spearman rank correlations were calculated for parametric and non-parametric variables, respectively. All statistical tests were two-tailed and the accepted level of significance was set at an alpha level of 0.05. Multiple logistic regression analyses were used to identify risk factors associated with the presence of piHDL and plaque. Multiple linear regression analysis was used to identify risk factors associated with IMT.

RESULTS

Characteristics of the Study Group

Our previously reported cohort consisted of 276 SLE subjects (18). From those subjects, 242 SLE patients completed exercise and physical function questionnaires and were included in this analysis. There were no statistically significant differences in demographic or disease characteristics between this subset of patients and the entire cohort (Tables 1 and 2).

Physical Activity of the Study Group

To assess the internal reliability of the questionnaires used to assess physical activity, Cronbach's alpha was calculated for each measure. Cronbach's alpha for the physical activity component of the SF-36 and abridged TWPAS exercise survey were 0.917 and 0.759, respectively. Walking was the most common type of physical activity reported by SLE patients, followed by strenuous activity (Table 3). There were no correlations between physical activity on the SF-36 and total METs per week with the SLICC/ACR damage score, nor the SLEDAI disease activity score (all *P*-values >0.3).

Relationship between Physical Activity and Carotid IMT

The mean IMT in SLE patients was 0.55 ± 0.14 (mean ± S.D.). There was a negative correlation between mean IMT and physical activity level as assessed by the SF-36 ($r = -0.14$, $P = 0.03$). There were also negative correlations between mean IMT and strenuous activity METs per week ($r = -0.3$, $P = 0.002$), and moderate activity METs per week ($r = -0.3$, $P = 0.001$). In multivariate analyses, number of strenuous exercise METs was significantly associated with IMT ($t = -2.2$, $P = 0.028$) when controlling for markers of SLE disease activity and damage, but not after controlling for traditional cardiac risk factors.

Relationship between Physical Activity and Carotid Plaque

Among SLE patients, 16.9% had ≥1 area of plaque on carotid ultrasound. Of those patients with plaque, the mean number of plaques was 2.12 ± 1.56 (mean ± S.D.). In bivariate

analysis, there was a negative correlation between number of plaques and physical activity on the SF-36 ($r = -0.14$, $P = 0.04$). There were also negative correlations between number of plaques and strenuous activity METs per week ($r = -0.4$, $P < 0.0001$), mild activity METs per week ($r = -0.25$, $P = 0.03$), and moderate activity METs per week ($r = -0.23$, $P = 0.019$). SLE patients with plaque had significantly lower levels of strenuous activity METs per week compared with SLE patients without plaque, with a mean score of 273.7 ± 489.6 (mean ± S.D.) for plaque positive SLE patients vs. 105.9 ± 292.0 ($P = 0.035$) for plaque negative SLE patients. SLE patients with plaque also had significantly lower levels of mild activity METs per week compared with SLE patients without plaque, with a mean score of 71.6 ± 163.5 (mean ± S.D.) for plaque positive SLE patients vs. 112.9 ± 260.3 ($P = 0.007$) for plaque negative SLE patients. In multivariate analyses, number of strenuous exercise METs was significantly associated with number of plaques ($t = -2.5$, $P = 0.014$) when controlling for markers of SLE disease activity and damage, but not after controlling for traditional cardiac risk factors.

Relationship between Physical Activity and Proinflammatory HDL levels

Using a HDL function score of ≥1.0 to define proinflammatory HDL (piHDL), 48.8% of SLE patients had piHDL, which is similar to our previously reported data (18). SLE patients with piHDL had lower levels of physical activity on the SF-36 compared with SLE patients without piHDL, with a mean score of 22.0 ± 6.4 (mean ± S.D.) for piHDL positive SLE patients vs. 23.8 ± 5.5 ($P = 0.01$) for piHDL negative SLE patients. SLE patients with piHDL were also more likely to have low exercise levels (<225 METs per week) compared with SLE patients without piHDL (39.8% of piHDL positive patients were in the low exercise group compared to 27.4% of patients with normal HDL function, $P = 0.04$). In multivariate analysis, controlling for traditional cardiac risk factors, as well as markers of SLE disease activity and damage, patients in the low exercise group had significantly increased odds for having piHDL (odds ratio 2.0, 95% C.I. 1.05 – 3.9, $P = 0.03$) (Table 4). To avoid the possibility of overfitting (i.e. including too many variables in the model for the number of outcome events), regression analyses were performed including traditional cardiac risk factors alone, and markers of SLE disease activity and damage alone. Low exercise was significantly associated with the presence of piHDL in both the model containing cardiac risk factors alone (odds ratio 1.95; 95% C.I. 1.03 – 3.7, $P = 0.04$) and in the model containing SLE disease activity and damage markers alone (odds ratio 2.1; 95% C.I. 1.1 – 3.96, $P = 0.02$). There were no significant differences in plasma levels of total cholesterol, HDL, LDL, triglycerides, hsCRP, and ESR between SLE patients with low versus medium and high exercise levels (Table 5). There were furthermore no significant correlations between total METs per week and individual lipid levels (all P-values >0.3).

DISCUSSION

Discovering ways to reduce cardiovascular disease morbidity and mortality is a major focus of study in SLE research. The results reported herein underscore the potential importance of exercise and physical activity in modifying subclinical markers of atherosclerosis in patients with SLE. In bivariate analysis, decreased physical activity as assessed by the SF-36 was associated with increased carotid plaque and IMT. Moreover, decreased physical activity as assessed by self-reported total METs per week was associated with presence of piHDL in SLE patients.

After accounting for potentially confounding variables, decreased physical activity (<225 METs per week) remained significantly associated with piHDL in patients with SLE. We have previously reported that in patients with SLE, piHDL is significantly associated with carotid plaque and IMT in multivariate analyses (18). Taken together, these results suggest that exercise may moderate the relationship between SLE and cardiovascular disease

development, possibly by decreasing inflammatory mediators, such as piHDL. Indeed, several studies have demonstrated that regular exercise exerts anti-inflammatory effects (31,32), and a diet and exercise intervention has also been shown to improve anti-inflammatory HDL function (19). Because inflammation has been implicated at several points in the carotid atherosclerotic process (33), exercise may slow carotid atherogenesis. Although limited clinical data exists to support this hypothesis, experimental studies have found that exercise not only regresses atherosclerotic plaque, but also improves plaque stability (34).

In contrast to piHDL, the associations between physical activity as assessed by the SF-36 and IMT and plaque were no longer significant after controlling for potentially confounding variables. These results are consistent with recent findings from the MESA group (9). A plausible explanation for these results is that physical activity may have a greater impact on IMT progression versus absolute IMT levels. In support of this notion, Sato and colleagues (35) found that walking distance was inversely associated with IMT progression over six months in patients with coronary heart disease. Similarly, The Women's Healthy Lifestyle Project (WHLP) trial demonstrated that a diet and exercise intervention slowed IMT progression among peri- and post-menopausal women over four years (36). Given the cross-sectional nature of the current study, the effects of physical activity on IMT and plaque progression could not be determined.

The present study has important strengths and limitations. The major strengths include using of a specific patient cohort and controlling for confounding variables, such as markers of SLE disease activity and damage and traditional cardiac risk factors. Moreover, the physical activity measurements not only assessed the frequency and duration of exercise, but also considered the type and intensity of each activity, which together may more reliably capture actual metabolic output. However, the assessment of physical activity is based on participant recall. Self-report surveys are subject to both recall and social desirability bias (37). A second shortcoming is that causality cannot be determined. It is possible that advanced subclinical atherosclerosis decreases the ability to perform exercise.

Another strength of the present study is the use of an ethnically diverse patient cohort. While the present study was not powered to evaluate differences between specific racial groups, , we found no significant race/ethnicity differences in the associations between physical activity and subclinical atherosclerosis.. However, we did find that African American patients had significantly higher IMT (0.66 (0.13)) compared with non-African American patients (0.53 (0.13)), $t = 5.1$, $p < 0.0001$).

To address the possibility that clinical activity of SLE is also associated with decreased physical activity, we investigated the relationship between exercise and disease activity and damage assessment measures and found no significant correlations. This negative finding could signify either that the instrument is flawed or that there is not a clinically significant association between exercise and the activity of SLE. There are no validated measures of SLE severity, to our knowledge; thus, this particular association could not be evaluated.

An additional limitation of this study is selection bias. Because the study population consists predominantly of patients receiving outpatient care for their SLE, the findings may not be generalizable to inpatient populations. A final limitation is the use of surrogate markers of cardiovascular disease. Although IMT and plaque are accepted, validated surrogate markers of carotid atherosclerosis (38,39), piHDL is a novel biomarker linked to cardiovascular disease and is still under study. To adequately assess the impact of physical activity on cardiovascular disease and to implement effective strategies for reducing disease burden,

future prospective studies are needed to examine the impact of exercise on cardiac events in SLE patients.

These limitations notwithstanding, to our knowledge the present study is the first to evaluate the relationship between physical activity and subclinical atherosclerosis in patients with SLE. While multiple factors affect atherogenesis in patients with SLE, physical activity appears to play a role in reducing inflammation associated with cardiovascular disease. Through encouraging patients with SLE to engage in physical activity, physicians may improve health outcomes in this vulnerable patient population.

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Table 1

Demographic characteristics of SLE patients*

Demographic characteristic	Value
Age (years)	43.0 ± 13.0
Total cholesterol (mg/dL)	186.1 ± 41.6
HDL (mg/dL)†	56.9 ± 16.9
LDL (mg/dL)†	106.2 ± 33.4
Triglycerides (mg/dL)	112.5 ± 73.8
High-sensitivity CRP (mg/L)	2.8 ± 6.9
Body Mass Index (kg/m2)	26.4 ± 6.4
History of previous CAD % (n)‡	2.9% (7)
History of CVA % (n)§	7.4% (18)
History of Hypertension % (n)	33.9% (82)
History of Diabetes % (n)	5.0% (12)
History of Smoking (current) % (n)¶	8.3% (20)
Ethnicity % (n)	
Caucasian	50.0 % (121)
Asian or Pacific Islander	13.2 % (32)
African American	12.8 % (31)
Hispanic	17.8 % (43)
Mixed or Other	6.2 % (15)

*Except where indicated otherwise, values are mean, plus or minus the standard deviation.

†HDL = high density lipoprotein; LDL = low density lipoprotein.

‡Coronary artery disease (CAD) was defined as a history of MI and/or CAD documented on angiogram or stress test.

§Cerebrovascular events (CVA) included history of transient ischemic attacks (confirmed by physician) and/or strokes (confirmed by appropriate imaging).

¶Smoking was present if subjects had smoked any cigarettes within the last 3 months.

Table 2

Disease characteristics of SLE patients*

Disease characteristic	Value
History of glomerulonephritis (ever) % (n)	26.4 % (64)
Disease duration (years)	12.5 ± 8.6
SLEDAI disease activity score†	4.1 ± 4.0
SLICC/ACR damage score‡	1.3 ± 1.7
History of Lupus Anticoagulant positive % (n)	14.5 % (35)
History of anticardiolipin antibody positive (IgG, IgM, IgA) % (n)	32.6 % (79)
Current Medications: % (n)	
Mycophenolate Mofetil	21.5 % (52)
Hydroxychloroquine	63.3 % (154)
Cyclophosphamide	0.40 % (1)
Methotrexate	6.6 % (16)
Azathioprine	12.4 % (30)
Non-Steroidal Anti-Inflammatory	42.1 % (102)
Current Glucocorticoid Use	43.8 % (106)
Current Prednisone (mg)	4.2 ± 7.6
Cumulative Lifetime Prednisone dose (grams) % (n)	
<10 g	49.2 % (119)
10-20 g	20.2 % (49)
>20g	30.2% (73)

*Except where indicated otherwise, values are mean, plus or minus the standard deviation.

†Systemic Lupus Erythematosus Disease Activity Index.

‡Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index.

Table 3

Physical activity and exercise profiles of SLE patients*

Physical activity measure	Value
SF-36, Physical Activity	22.9 ± 6.0
Exercise- Total METs/week	822.5 ± 937.5
Low (<225 METs/week) % (n)	33.5 % (81)
Medium (225-945 METs/week) % (n)	32.6 % (79)
High (>945 METs/week) % (n)	33.9 % (82)
Walking METs/week	312.4 ± 365.3
Strenuous Activity METs/week	245.3 ± 465.9
Moderate Activity METs/week	188.1 ± 305.1
Mild Activity METs/week	78.4 ± 183.1

* Except where indicated otherwise, values are mean, plus or minus the standard deviation.

Table 4

Logistic regression of the relationship of piHDL to physical activity in SLE patients, controlling for cardiovascular disease risk factors and markers of SLE disease activity and damage

Explanatory variable	Odds Ratio	95% CI*	*P*-value
Exercise			
Low (<225 METs/week)	2.02	1.1 – 3.9	0.03
Medium & High (≥225 METs/week)	1.5	0.77 – 2.8	0.2
Age (years)	1.01	0.98 – 1.0	0.6
Disease Duration (years)	1.01	0.97 – 1.05	0.6
Hypertension (yes, no)	1.3	0.73 – 2.4	0.4
Dyslipidemia (yes, no)	1.3	0.61 – 2.7	0.5
Current smoking (yes, no) †	1.3	0.49 – 3.4	0.5
Lifetime prednisone dose of >20 g (yes, no)	0.88	0.45 – 1.7	0.7
SLEDAI disease activity score‡	0.97	0.90 – 1.0	0.4
SLICC/ACR damage score§	1.1	0.91 – 1.3	0.3

*CI denotes confidence interval

†Smoking was present if subjects had smoked any cigarettes within the last 3 months.

‡Systemic Lupus Erythematosus Disease Activity Index.

§Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index.

Table 5

Differences in lipid levels and inflammatory biomarkers in SLE patients with low versus medium and high exercise activity*

	Low Exercise† (*n* = 81)	Medium & High Exercise† (*n* = 161)	*P*-value
piHDL (yes, no) % (n)	58.0 (47)	43.8 (71)	0.04
Total Cholesterol (mg/dL)	191.6 ± 45.1	183.2 ± 39.6	0.2
High-Density Lipoprotein (mg/dL)	56.4 ± 16.1	57.2 ± 17.9	0.7
Low-Density Lipoprotein (mg/dL)	110.6 ± 34.5	103.96 ± 32.7	0.2
Triglycerides (mg/dL)	123.0 ± 80.5	107.1 ± 69.8	0.1
High-sensitivity CRP (mg/L)	2.8 ± 4.4	2.7 ± 7.9	0.9
Erythrocyte Sedimentation Rate (mm/h)	24.5 ± 24.5	20.2 ± 17.7	0.1

*Except where indicated otherwise, values are mean, plus or minus the standard deviation.

†Low exercise was defined as <225 METs per week; Medium exercise was defined as 225-945 METs per week; and High exercise was defined as >945 METs per week.