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Adipocytokines in Systemic Lupus Erythematosus: Relationship to Inflammation, Insulin Resistance and Coronary Atherosclerosis

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Abstract

We tested the hypothesis that concentrations of adipocytokines are altered in SLE and associated with coronary atherosclerosis, insulin resistance and inflammation. Concentrations of resistin, leptin, adiponectin, and visfatin were measured in 109 patients with SLE and in 78 control subjects. Coronary calcification was measured by electron beam computed tomography and insulin resistance was defined by the homeostasis (HOMA) index. Concentrations of adiponectin (28.7 $\pm$ 17.9 vs. 22.0 $\pm$ 15.3 μ g/mL, $p=0.003$), leptin (41.1 $\pm$ 49.9 vs. 19.8 $\pm$ 24.6 ng/mL, $p<0.001$) and visfatin (7.5 $\pm$ 10.5 vs. 4.5 $\pm$ 2.8 ng/mL, $p<0.001$) were higher in patients with SLE than controls. These differences remained significant after adjustment for age, race, sex and BMI, (all p -values <0.02). Concentrations of resistin (10.7 $\pm$ 7.6 vs. 9.1 $\pm$ 5.1 ng/mL, $p=0.41$) did not differ in patients and controls. In patients with SLE, leptin was positively associated with BMI ($\rho=0.80$, $p<0.001$), insulin resistance ($\rho=0.46$, $p<0.001$), and CRP ($\rho=0.30$, $p=0.002$), while adiponectin was negatively associated with the same factors ($\rho=-0.40$, $p<0.001$; $\rho=-0.38$, $p<0.001$, $\rho=-0.22$, $p=0.02$, respectively). None of the adipocytokines were associated with coronary atherosclerosis in SLE. In conclusion, patients with SLE have increased concentrations of adiponectin, leptin and visfatin. Lower concentrations of adiponectin and higher concentrations of leptin are associated with insulin resistance, BMI and CRP in patients with SLE.

Keywords

systemic lupus erythematosus; adipocytokines; atherosclerosis; insulin resistance; inflammation

Adipose tissue has endocrine functions and is the main source of several mediators, termed adipocytokines, which include leptin, resistin, visfatin and adiponectin. These adipocytokines have profound effects on glucose homeostasis, appetite regulation, inflammation and atherosclerosis.¹

Leptin, resistin and visfatin have pro-inflammatory and atherogenic effects and are associated with insulin resistance.^{1,2} For example, increased concentrations of these three adipocytokines are found in animal models of obesity and in individuals with diabetes,¹ and higher

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concentrations of resistin and leptin are associated with coronary atherosclerosis and coronary events.^{3, 4} Adiponectin, in contrast, has anti-diabetic, anti-inflammatory and anti-atherogenic effects.^{1, 5} Lower concentrations of adiponectin are found in patients with diabetes or the metabolic syndrome⁶ and are associated with the presence and progression of coronary atherosclerosis, independent of traditional cardiovascular risk factors.⁵

Thus, adipocytokines may provide a mechanistic link between impaired insulin sensitivity, obesity, chronic inflammation, and atherosclerosis. We have reported that patients with systemic lupus erythematosus (SLE) frequently meet the criteria for the metabolic syndrome⁷, and have accelerated atherosclerosis⁸ and a higher prevalence of insulin resistance.⁷ Little is known about adipocytokines in SLE.⁹ We therefore examined the hypothesis that concentrations of adipocytokines are altered in SLE and associated with coronary atherosclerosis, insulin resistance and inflammation.

Methods

We studied 109 patients with SLE and 78 control subjects who are participating in ongoing clinical investigations into the prevalence and mechanisms of atherosclerosis.^{7, 8, 10–12} Eligible SLE patients included individuals who met the criteria for SLE,¹³ were over 18 years of age, and had a disease duration of one year or greater. The controls did not meet the criteria for SLE or any other autoimmune disease, and were frequency-matched to the SLE patients for age, sex, and race. Patients were recruited from local rheumatologists in Nashville, Tennessee, USA, from advertisements, and from a Lupus Foundation newsletter. Six subjects with SLE were excluded because of a history of myocardial infarction, angina or stroke. Controls were recruited from advertisements, patients' acquaintances, and a database maintained by the General Clinical Research Center at Vanderbilt University School of Medicine, Nashville, Tennessee, USA. Subjects were excluded if they had a history of myocardial infarction, angina, or stroke. All subjects provided a written informed consent, and the Institutional Review Board of Vanderbilt University Hospital approved the study.

Patient assessment included a standardized interview, physical examination, laboratory tests, and, in patients, a review of medical records. The use of current and cumulative medications was determined both through chart review and the standardized interview. BMI was calculated using the attained height and weight measurements and waist circumference measured. Blood pressure was determined as the average of two measurements recorded 5 minutes apart after subjects had rested supine for 10 minutes. Subjects were considered to be hypertensive if they were taking anti-hypertensive medications, if their systolic blood pressure was 140 mmHg or higher, or if their diastolic blood pressure was 90 mmHg or higher. After an overnight fast, a blood sample was taken to measure high-density lipoprotein (HDL), total cholesterol, triglycerides, glucose, and insulin. Subjects were considered to be diabetic if they were taking anti-diabetic medications or if their glucose levels were above 126 mg/dl. Low-density lipoprotein (LDL) was calculated. Insulin, leptin, adiponectin, resistin, tumor necrosis factor (TNF) α , interleukin (IL)-6, IL-1 α (Linco/Millipore Corp.) and visfatin (Phoenix Pharmaceuticals, Inc.) concentrations were measured using ELISA. In patients with SLE, C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) were determined. Additionally, for SLE patients, disease activity and damage were measured using the Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) and the Systemic Lupus International Collaborating Clinics Damage Index (SLICC), respectively.^{14, 15}

To measure coronary atherosclerosis, subjects underwent chest computed tomography imaging with an Imatron C-150 scanner (GE/Imatron, South San Francisco, CA) as described previously.^{8, 16} Briefly, imaging was performed with a 100-msec scanning time and a single-slice thickness of 3 mm. Forty slices were obtained during a single breath-holding period

starting at the aortic arch and proceeding to the level of the diaphragm. All scans were scored, as described by Agatston et al,¹⁷ by a single experienced investigator (PR), unaware of the subjects' clinical status.

Patient and control subjects were classified as having the metabolic syndrome based on the definition set forth by the World Health Organization (WHO). The modified WHO definition requires the presence of insulin resistance, which is defined by any of the following: a homeostasis model assessment (HOMA) index (fasting glucose [mmol/l] * fasting insulin [μ U/ml]/22.5) in the top quartile of a non-diabetic population, impaired fasting glucose (≥ 110 mg/dl), or diabetes. In addition to insulin resistance, the WHO definition also requires two of the three following criteria: central obesity (waist >94 cm in men and >88 cm in women), elevated triglycerides (≥ 150 mg/dl or HDL <35 mg/dl in men and <40 mg/dl in women), and high blood pressure, defined as $\geq 140/90$ mmHg or the use of hypertensive medications. Based on the Study of Inherited Risk of Coronary Atherosclerosis (SIRCA) data,¹⁸ a HOMA index of >2.114 was defined as representative of the top quartile of a non-diabetic population.

Demographic characteristics are presented as mean and standard deviation for continuous variables, or as frequencies and percentages for categorical variables. The differences among cases and controls were determined by Wilcoxon rank sum test or Fisher's exact test, as appropriate. Adipocytokine concentrations are presented as mean ($\pm$ SD) and compared in patients with lupus and control subjects by Wilcoxon rank sum tests. To further assess if these differences were independent of age, race, sex, and BMI, linear regressions with adipocytokines (after logarithmic transformation to achieve normal distribution of the residuals) as the dependent variable and disease status (either SLE or control) as the independent variable were modeled. We used Spearman correlations to examine the association between adipocytokines and clinical variables, markers of inflammation and disease characteristics. We used logistic regression to examine the association between the metabolic syndrome and adipocytokines in patients with SLE. Adipocytokines were logarithmically transformed and results are expressed as odds ratios and 95% confidence interval and are further adjusted for CRP and BMI (*except for the model including obesity that was only adjusted for CRP). Logistic regressions were modeled to examine the association between adipocytokines as independent, and coronary artery atherosclerosis as dependent variable. To assess if the association between adipocytokines and coronary atherosclerosis was independent of traditional risk factors, multivariable regressions were modeled using prespecified covariates that are known to be strongly associated with the outcomes of interest (age, race, sex, BMI and Framingham risk score). All analyses used a two-sided significance level of 5 percent and were performed with STATA 9.1.

Results

Patients and control subjects

Patients with lupus and control subjects were of similar age (40.2 ± 11.5 years, and 40.5 ± 12.0 years, respectively, $P=0.86$) and sex (91.7 and 85.9 percent female, respectively, $P=0.24$). Seventy-four (68%) patients with lupus and 57 (73%) control subjects were Caucasian. There was a trend toward higher BMI in patients with lupus (29.2 ± 7.5 kg/m²) than in controls (27.0 ± 6.0 kg/m², $P=0.05$), and the HOMA index was significantly higher in patients (2.0 ± 1.8 units) than controls (1.5 ± 1.0 units, $P=0.04$). (Table 1) The mean disease duration of SLE was 8.2 ± 7.3 years, the mean SLEDAI was 4.1 ± 4.0 , and the mean SLICC 0.9 ± 1.3 . Patients with SLE had a mean ESR of 26.9 ± 27.5 mm/hr and CRP of 6.3 ± 9.1 mg/L.

Adipocytokines in SLE patients and controls

As shown in Figure 1, concentrations of adiponectin (28.7 ± 17.9 versus 22.0 ± 15.3 $\mu\text{g/mL}$, $p=0.003$), leptin (41.1 ± 49.9 versus 19.8 ± 24.6 ng/mL , $p<0.001$) and visfatin (7.5 ± 10.5 versus 4.5 ± 2.8 ng/mL , $p<0.001$) were higher in patients with SLE than controls. These differences between patients with lupus and control subjects remained significant after adjustment for age, race, sex and BMI (all p values < 0.02). There were no significant differences in concentrations of resistin between patients and control subjects (10.7 ± 7.6 and 9.1 ± 5.1 ng/mL respectively, $p=0.41$).

Cardiovascular risk factors and adipocytokines

In patients with SLE, adiponectin was significantly negatively correlated with BMI ($\rho=-0.40$) and positively correlated with HDL cholesterol ($\rho=0.38$) (Table 2). Leptin correlated significantly with BMI ($\rho=0.80$), total ($\rho=0.25$) and LDL cholesterol ($\rho=0.21$) and triglycerides ($\rho=0.22$) (Table 2). Visfatin was not significantly associated with any cardiovascular risk factor. Similar results were found in control subjects; adiponectin was significantly negatively correlated with BMI ($\rho=-0.54$) and leptin was significantly positively correlated with it ($\rho=0.70$).

Disease characteristics and adipocytokines in SLE

Among patients with SLE, adiponectin ($\rho=-0.22$) and leptin ($\rho=0.30$) were significantly associated with CRP; resistin ($\rho=0.23$) and leptin ($\rho=0.20$) were associated with ESR. Neither SLEDAI nor SLICC scores were associated with adipocytokine concentrations. (Table 3)

There were 27 (24.8%) patients receiving hormone replacement therapy (HTR), 8 (7.4%) taking statins and 64 (59%) taking corticosteroids. Concentrations of leptin were higher in patients on HTR (50.5 ± 47.8 compared to 38.1 ± 50.5 ng/mL , $p=0.03$). Adipocytokine concentrations were not related to current use of immunosuppressive therapy (defined as use of cyclophosphamide, azathioprine, mycophenolate, or methotrexate). Concentrations of adiponectin ($p=0.85$), resistin ($p=0.40$), leptin ($p=0.12$) and visfatin ($p=0.82$) were not significantly different in patients with SLE receiving immunosuppressive therapy and those who were not. There were no other statistically significant differences in adipocytokine concentrations related to current use of HRT, corticosteroids or statins. Furthermore, cumulative exposure to corticosteroids was not significantly correlated with adipocytokine concentrations (Table 3).

Insulin resistance, the metabolic syndrome, and coronary atherosclerosis and adipocytokines in SLE

Lower adiponectin concentrations were significantly associated with the presence of insulin resistance ($p=0.001$) (Table 4). This association was not significant after adjusting for BMI ($p=0.14$) and BMI and CRP ($p=0.13$). Higher concentrations of leptin were also significantly associated with insulin resistance ($p<0.001$), but were not significant after adjusting for BMI ($p=0.77$) and BMI and CRP ($p=0.47$). Neither resistin nor visfatin was associated with insulin resistance. (Table 4) Higher leptin concentrations were associated with the presence of the metabolic syndrome and several individual components of it (obesity, insulin resistance, and hypertension). In contrast, higher adiponectin concentrations were inversely related to the presence of the metabolic syndrome and to the components of obesity, insulin resistance and dyslipidemia.

There was no association between coronary calcification and adipocytokines. (Table 5) After statistical adjustment for age and sex the association between resistin and coronary artery

calcification was of borderline significance ($p=0.06$) but not after adjustment for Framingham risk score ($p=0.20$).

Discussion

The main findings of this study are that patients with SLE have increased concentrations of adiponectin, leptin and visfatin, independent of BMI. Lower concentrations of adiponectin and higher concentrations of leptin are associated with insulin resistance. Furthermore, none of the adipocytokines studied was associated with coronary atherosclerosis in SLE.

Mutations resulting in loss of function of the leptin receptor are associated with increased appetite, obesity and hyperglycemia, but leptin concentrations are increased in obesity – a paradox thought to reflect “leptin resistance”.¹⁹ Recent information that C-reactive protein binds to leptin, impairs signaling and mediates leptin resistance,²⁰ suggests that leptin resistance may be more likely in the setting of chronic inflammation. Indeed, leptin and CRP concentrations were independently associated in healthy volunteers.²¹ Leptin also induces CRP expression in vitro²² and is both pro-inflammatory²¹ and atherogenic;²³ increased concentrations are associated with insulin resistance and are an independent risk factor for coronary heart disease.⁴

There is little information about leptin in SLE. Leptin concentrations were higher in patients than in controls,^{9, 24} suggesting a relationship between leptin and lupus disease related factors. We found that leptin concentrations were increased in SLE, and as would be expected, leptin was strongly associated with BMI. We also showed, for the first time in SLE, an association between leptin and insulin resistance, the metabolic syndrome, CRP, ESR, LDL cholesterol and triglycerides. Although leptin was strongly associated with obesity in SLE, the difference in leptin concentrations between patients with lupus and controls was independent of age, race, sex and BMI, suggesting that additional factors drive leptin production or alter the relationship between obesity and leptin in lupus.

Visfatin is a recently discovered adipocytokine that binds to the insulin receptor and is thought to be secreted to compensate for insulin resistance.²⁵ It is also pro-inflammatory and associated with unstable atherosclerotic lesions.²⁶ In addition to its potential role in glucose metabolism and atherosclerosis, visfatin has been linked with inflammation and concentrations are increased in patients with rheumatoid arthritis.²⁷ To the best of our knowledge there is no information about visfatin in SLE. Visfatin concentrations were significantly higher in patients with SLE than controls but were not associated with metabolic or inflammatory measures. This is concordant with some recent population studies, including the Framingham Offspring Cohort, that found no relationship between visfatin concentrations and metabolic variables.²⁸ Visfatin, previously known as pre-B-cell colony enhancing factor, activates human leukocytes and stimulates the production of cytokines such as IL-6.²⁵ Thus, although not associated with the inflammatory mediators and markers we measured, the elevated concentrations of visfatin observed could reflect inflammation in SLE.

Resistin mediates obesity-induced insulin resistance in a mouse model of obesity.²⁹ The administration of anti-resistin antibodies improved blood glucose and insulin action, and rosiglitazone, an antidiabetic drug, decreased resistin concentrations in an animal model.³⁰ In humans, resistin has been associated with obesity, diabetes and inflammation in some studies.^{3, 31} However, its role in SLE is poorly defined. We did not find a statistically significant difference in resistin concentrations among patients with SLE and control subjects. Consistent with our data, in patients with RA, concentrations of resistin were not higher than in controls, although there were differences in leptin, adiponectin and visfatin.²⁷ We found a relatively weak association between resistin and ESR but no association with CRP, IL-6, TNF and

HOMA. These findings are largely compatible with those of the SIRCA study that found no relationship between resistin and HOMA and only a weak association with CRP and IL-6 ($\rho=0.10$ and 0.16 , respectively) in a community-based sample of asymptomatic subjects from the general population.³

Adiponectin is secreted by adipose tissue, but in contrast to leptin, resistin and visfatin, has anti-diabetic, anti-inflammatory and anti-atherogenic effects.^{1,5} Adiponectin acts as an insulin sensitizer¹ and decreases the inflammatory response induced by TNF- α .³² Thus, low concentrations of adiponectin are associated with obesity, insulin resistance and dyslipidemia.^{32, 33} Patients with SLE have higher concentrations of adiponectin than controls,⁹ and we show that despite this increase, the inverse relationship between adiponectin and BMI, HOMA, metabolic syndrome, systolic blood pressure and dyslipidemia persist in SLE. Thus, the increase in adiponectin concentrations in SLE might reflect a partial compensatory response to these metabolic perturbations.

In addition to their role in mediating the metabolic and inflammatory changes associated with obesity, adipocytokines may play a role in atherogenesis. Leptin concentrations are associated with risk of coronary events,⁴ and in type 2 diabetics, with coronary calcification.³⁴ Similarly, resistin concentrations are associated with coronary calcification³ and carotid intima-media thickness.³⁵ Conversely, low concentrations of adiponectin are associated with increased risk of myocardial infarction and progression of coronary calcification.^{5, 36} In our patients with SLE, although concentrations of leptin were elevated, and in this same cohort of subjects atherosclerosis was accelerated,⁸ we found no relationship between concentrations of adipocytokines and coronary calcification. There are several possible explanations. First, other unidentified risk factors may drive atherosclerosis in SLE and obscure the effect of adipocytokines. Second, the increased concentrations of adiponectin could offset the adverse cardiovascular effects of increased concentrations of leptin. This appears to be unlikely since we also examined the leptin:adiponectin ratio - a parameter that may provide a better measure of atherogenic risk than either adipocytokine alone³⁷ and found no relationship to coronary calcification.

Our data suggest that adipocytokines are associated with inflammatory markers but not with disease activity, as measured with the SLEDAI score. Although perhaps counterintuitive, the correlation between the SLEDAI score and laboratory markers of inflammation is relatively weak, for example in our population the correlation between SLEDAI and ESR and CRP ($r=0.21$ for both) explained only approximately 4% of the variance.

This study has some limitations. First, our observations are based on a cross-sectional rather than a longitudinal analysis, and thus the analysis only includes a single measurement of adipocytokines. Multiple measurements of adipocytokines over time are likely to provide additional information. Second, this is a population with relatively low disease activity, and therefore our findings may not be applicable to patients with very active disease.

In conclusion, patients with SLE have higher concentrations of adiponectin, leptin and resistin. Leptin (positively) and adiponectin (negatively) were associated with BMI, insulin resistance, CRP and the metabolic syndrome. Coronary calcification was not related to adipocytokines. Adipocytokines may provide a link between insulin resistance and inflammation in SLE.

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Figure 1. Concentrations of adipocytokines in patients with SLE and control subjects
Horizontal lines represent the mean and whiskers represent the 95% confidence interval

Table 1
Characteristics of patients and controls

Characteristics:	Patients with SLE (n=109)	Control subjects (n=78)	P Value
Demographic characteristics			
Age: years	40.2 +/- 11.5	40.5 +/- 12.0	0.86
Sex: n (% female)	100 (91.7%)	67 (85.9%)	0.24
Race: n (% Caucasian)	74 (67.9%)	57 (73.1%)	0.52
Diabetes: n (%)	4 (3.67%)	1 (1.28%)	0.40
Body Mass Index (kg/m ²)	29.2 +/- 7.5	27.0 +/- 6.0	0.05
Hypertension: n (%)	49 (45.0%)	13 (16.7%)	<0.001
Current smoking	29 (27%)	14 (18%)	0.22
Current antihypertensive drugs	37 (33%)	8 (10%)	<0.001
Current antidiabetic drugs	4 (4%)	1 (1%)	0.40
Current statin therapy	8 (7%)	5 (6%)	1.0
Current oral contraceptive therapy	9 (8%)	10 (13%)	0.33
Current immunosuppressive therapy *	23 (21%)	NA	NA
Past immunosuppressive therapy *	48 (44%)	NA	NA
Current corticosteroid therapy	64 (59%)	NA	NA
Past corticosteroid therapy	105 (97%)	NA	NA
Glucose (mg/dl)	86.9 +/- 26.0	85.8 +/- 9.5	0.21
Insulin (mg/dl)	373.7 +/- 271.0	283.8 +/- 185.7	0.03
HOMA-IR	2.0 +/- 1.8	1.5 +/- 1.0	0.04
Total Cholesterol (mg/dl)	175.1 +/- 47.1	179.5 +/- 42.0	0.18
High Density Lipoprotein (mg/dl)	47.2 +/- 14.8	49.1 +/- 15.6	0.56
Low Density Lipoprotein (mg/dl)	104.0 +/- 38.2	111.1 +/- 34.9	0.06
Lipoprotein a (mg/dl)	24.6 +/- 27.6	21.7 +/- 23.4	0.78
Triglycerides (mg/dl)	119.1 +/- 58.6	97.1 +/- 55.9	0.004
Metabolic Syndrome (WHO)	33 (30.3%)	7 (9.5%)	0.003

* immunosuppressive therapy is defined as use of cyclophosphamide, azathioprine, methotrexate or mycophenolate mofetil

NA represents not applicable

Table 2Correlation (ρ) between adipocytokines and cardiovascular risk factors in patients with SLE

	Adiponectin	Resistin	Leptin	Visfatin
Age	-0.11	-0.14	0.05	-0.09
BMI	-0.40 ^b	0.13	0.80 ^b	-0.05
Systolic blood pressure	-0.11	0.09	0.15	-0.08
Diastolic blood pressure	-0.03	0.08	-0.03	-0.11
Total Cholesterol (mg/dl)	0.11	0.14	0.25 ^a	-0.06
High Density Lipoprotein (mg/dl)	0.38 ^b	-0.12	-0.03	0.03
Low Density Lipoprotein (mg/dl)	0.02	0.15	0.21 ^a	-0.10
Triglycerides (mg/dl)	-0.18	0.19	0.22 ^a	-0.07
Framingham score	-0.07	-0.04	0.18	-0.07

^aP<0.05^bP<0.001

Table 3

Correlations (ρ) between adipocytokines and markers of inflammation, disease activity, accrual damage, coronary calcium, insulin resistance and cumulative corticosteroid exposure in patients with SLE

	Adiponectin	Resistin	Leptin	Visfatin
ESR	-0.07	0.23 ^a	0.20 ^a	0.01
CRP	-0.22 ^a	0.16	0.30 ^a	-0.08
SLEDAI	-0.002	0.02	0.02	-0.05
SLICC	0.14	0.05	0.03	0.01
IL-6	-0.05	0.09	-0.08	0.11
TNF- α	0.05	0.13	-0.09	-0.04
IL-1a	-0.02	0.11	-0.12	0.03
Agatston score	-0.04	0.15	0.01	-0.02
HOMA	-0.38 ^b	0.18	0.46 ^b	0.15
Cumulative corticosteroids	0.03	0.13	0.04	0.02

^aP<0.05

^bP<0.001

Table 4
Association between adipocytokines and the metabolic syndrome and its components in SLE

		Adiponectin		Resistin		Leptin		Visfatin	
		OR (95% CI)	p	OR (95% CI)	p	OR (95% CI)	p	OR (95% CI)	p
Metabolic syndrome	Unadjusted	0.33 (0.16–0.68)	0.002	1.54 (0.79–3.0)	0.21	4.09 (2.21–7.57)	<0.001	1.29 (0.64–2.57)	0.48
	Adjusted ^a	0.62 (0.27–1.44)	0.26	1.38 (0.59–3.20)	0.46	1.68 (0.74–3.85)	0.22	1.26 (0.45–3.53)	0.65
Insulin resistance	Unadjusted	0.31 (0.15–0.61)	0.001	1.63 (0.87–3.07)	0.13	2.81 (1.74–4.54)	<0.001	1.44 (0.76–2.72)	0.26
	Adjusted ^a	0.52 (0.22–1.22)	0.13	1.59 (0.72–3.49)	0.25	1.27 (0.66–2.48)	0.47	1.86 (0.70–4.92)	0.21
Obesity	Unadjusted	0.34 (0.18–0.67)	0.002	1.73 (0.92–3.26)	0.09	6.19 (3.01–12.73)	<0.001	1.09 (0.57–2.09)	0.80
	Adjusted ^a	0.37 (0.19–0.75)	0.005	1.73 (0.90–3.32)	0.10	6.16 (2.97–12.80)	<0.001	1.09 (0.56–2.11)	0.80
Dyslipidemia	Unadjusted	0.41 (0.22–0.78)	0.006	1.13 (0.62–2.07)	0.69	1.36 (0.98–1.89)	0.07	1.16 (0.63–2.13)	0.64
	Adjusted ^a	0.45 (0.23–0.89)	0.02	1.09 (0.59–2.03)	0.78	1.47 (0.86–2.52)	0.16	1.11 (0.60–2.08)	0.74
Hypertension	Unadjusted	0.77 (0.43–1.39)	0.39	1.96 (1.03–3.73)	0.04	1.50 (1.06–2.13)	0.02	0.91 (0.49–1.70)	0.77
	Adjusted ^a	1.13 (0.58–2.20)	0.73	1.72 (0.88–3.37)	0.12	0.89 (0.51–1.56)	0.69	0.80 (0.41–1.57)	0.51

Adipocytokines were logarithmic transformed.

^aResults are adjusted for CRP and BMI (*except for the model including obesity that was only adjusted for CRP).

Table 5
Association between adipocytokines^a and presence or absence of coronary calcification in patients with SLE

	Leptin	Adiponectin	Leptin: Adiponectin ratio	Resistin	Visfatin
Unadjusted	1.05 (0.72–1.55)	0.76 (0.38–1.49)	1.10 (0.80–1.51)	1.51 (0.73–3.13)	0.80 (0.38–1.68)
Adjusted for age and sex	1.15 (0.73–1.81)	0.95 (0.45–2.0)	1.10 (0.78–1.56)	2.43 (0.98–6.03)	1.11 (0.49–2.54)
Adjusted for Framingham risk score	0.94 (0.62–1.41)	0.91 (0.45–1.83)	0.98 (0.70–1.36)	1.68 (0.76–3.71)	0.81 (0.39–1.69)

^a Adipocytokines were logarithmically transformed. Results are expressed as odds ratios and 95% confidence interval