Published in final edited form as:
Arthritis Care Res (Hoboken). 2013 March ; 65(3): 441–447. doi:10.1002/acr.21841.

High sensitivity C-reactive protein, disease activity and cardiovascular risk factors in systemic lupus erythematosus

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Abstract

Objectives—To study the level of high-sensitivity C-reactive protein (hsCRP) and its relationship with disease activity, damage and cardiovascular risk factors in patients with systemic lupus erythematosus (SLE).

Method—Consecutive patients who fulfilled ≥4 ACR criteria for SLE but did not have concurrent infection were recruited. Blood was assayed for hsCRP and disease activity, organ damage of SLE and cardiovascular risk factors were assessed. Linear regression was performed for the relationship among hsCRP, SLE activity, damage and cardiovascular risk factors.

Results—289 patients were studied (94% women; age 39.0±13.1 years; SLE duration 7.8±6.7 years). The mean SLEDAI score was 4.9±5.6 and clinically active SLE was present in 122(42%) patients. The mean hsCRP level was 4.87±12.7mg/L, and 28(23%) patients with active SLE had undetectable hsCRP (<0.3mg/L). Linear regression revealed a significant correlation between hsCRP and musculoskeletal (Beta=0.21), hematological (Beta=0.19), serosal (Beta=0.46) and clinical SLEDAI score (Beta=0.24), adjusting for age, sex, body mass index, creatinine and the use of various medications ($p<0.005$ in all). Levels of hsCRP correlated significantly with anti-dsDNA titer (Beta=0.33;$p<0.001$) but not with complement C3 (Beta=0.07;$p=0.26$). Significantly more patients with hsCRP >3.0mg/L were men and chronic smokers, and had diabetes mellitus, higher atherogenic index and history of arterial thrombosis. hsCRP levels correlated significantly with pulmonary and endocrine damage score.

Conclusions—hsCRP is detectable in 77% of SLE patients with clinically active disease and correlates with SLEDAI scores, particularly serositis and in the musculoskeletal and hematological systems. Elevated hsCRP in SLE is associated with certain cardiovascular risk factors and history of arterial thromboembolism.

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Keywords

C-reactive protein; acute phase; disease activity; cardiovascular; damage; outcome

Introduction

C-reactive protein (CRP) is an acute phase reactant synthesized mainly by hepatocytes in response to cytokines such as IL-6, IL1β and TNFα. Elevation of CRP is an essential component of the acute phase response to a variety of cellular insults such as infection, inflammation, tissue trauma and malignancies (1). The genes coding for CRP have been mapped to the long arm of chromosome 1 (2). Basal levels of CRP are independently influenced by two polymorphisms at the CRP locus, namely CRP 2 and CRP 4 alleles (3). CRP binds to polysaccharides of micro-organisms and plays a role in the activation of the classical complement pathway, as well as clearance of apoptotic cells (4).

In chronic rheumatic diseases such as rheumatoid arthritis and systemic vasculitis, CRP level correlates with disease activity. CRP is in fact one of the components of many disease activity indices used for disease activity assessment of inflammatory arthritis (5). However, in patients with systemic lupus erythematosus (SLE), the CRP response to disease activity is intriguing. It is well recognized that CRP is either normal or only modestly elevated in patients with active SLE (6,7). The explanation for this phenomenon is still unclear, although there are postulations such as the presence of anti-CRP that enhances clearance of serum CRP (8), genetic polymorphisms that lead to altered CRP production (9), and the altered hepatic response of CRP production to IL-6 and TNFα (10). However, these hypotheses cannot explain the appropriate CRP response of SLE patients to other situations such as the presence of intercurrent infections.

Conventional CRP assay typically measures levels above 3mg/L. Novel high-sensitivity CRP assay can now detect CRP at a level as low as 0.3mg/L. Several recent studies of hsCRP in SLE patients have yielded conflicting results (11-13). Barnes et al. (11) reported that hsCRP levels were significantly higher in SLE patients than controls. However, hsCRP level did not correlate with SLE disease activity scores. Two other studies demonstrated that hsCRP levels correlated significantly with SLE activity (12,13). Adding to this complexity, a longitudinal study of risk factors and markers of lupus flare did not find an independent relationship between hsCRP levels and onset of lupus nephritis flare (14). Although hsCRP level has been demonstrated to be an independent risk factor of cardiovascular disease in the general population (15), there is paucity of data regarding hsCRP level and cardiovascular risk in SLE. Three studies have reported an association of hsCRP with certain factors such as age, blood pressure, body weight, smoking, menopause and apolipoprotein A1 in SLE patients (11,12,16) but the results were not consistent. Moreover, in one of these studies (12), hsCRP levels were found to be higher in the African-Americans than other racial groups, suggesting that racial differences may confound the relationship between hsCRP and cardiovascular risk. Racial differences in other cardiovascular risk factors in SLE would further complicate this relationship, such as the increased frequency of arterial thrombosis in Chinese and African American SLE patients, compared to Caucasian SLE patients (17).

In view of the controversy in the relationship among hsCRP, disease activity and cardiovascular risk in patients with SLE, and the relative lack of data in Chinese patients, we conducted this study in an attempt to bridge the knowledge gap regarding the role of hsCRP in SLE.

Patients and methods

Study population

Consecutive adult patients fulfilling ≥4 of the American College of Rheumatology (ACR) criteria for the classification of SLE (18) who attended our out-patient rheumatology clinics or admitted to the medical wards within a 3-month period from April to June 2008 were recruited for this study. The exclusion criteria were: (1) Patients having evidence of active infection at the time of venepuncture, as confirmed by culture, viral antigen test or serological tests, or judged to be infection by the attending physicians with or without the use of antibiotics or anti-viral agents for treatment; (2) Serum creatinine level >200umol/L. Informed consent was obtained from the participants and the study was approved by the Research and Ethics Committee of our hospital.

Blood was taken from the participants at 9am in the morning for the assay of high sensitivity C-reactive protein (hsCRP) and other markers of disease activity which included anti-dsDNA titer and complement C3 level. Clinical activity and organ damage of SLE was assessed by standard tools. Cardiovascular risk factors were also assessed in the same setting. These included body mass index (BMI), lipid profile, smoking status, and the presence of diabetes mellitus and hypertension. Diabetes mellitus was defined as a fasting blood glucose level of ≥7.0mmol/L or that required drug therapy. Patients were regarded as having hypertension when the blood pressure was ≥140/90mmHg on two occasions or anti-hypertensive therapy was initiated. The antiphospholipid antibodies (lupus anticoagulant and anti-cardiolipin antibodies) were obtained and data on the regular medications received by the participants at the time of venepuncture were also collected. Blood was taken before any modification of drug dosages or addition of new drugs.

Regression analyses were performed among hsCRP, anti-dsDNA titers, complement levels, disease activity and damage scores of SLE. Cardiovascular risk factors and history of arterial thrombosis were also compared between those patients with different levels of the hsCRP.

Assay of hsCRP, anti-dsDNA and complement levels

Levels of hsCRP were measured in serum samples using a solid phase chemilluminescence immunometric assay with the Immulite 1000 (Siemens Healthcare Diagnostics, Inc., 1717 Deerfield Rd., Deerfield, Il., USA). Analytical sensitivity for this assay is 0.01mg/L, with a reportable range of 0.3 to 100mg/L. Intra-assay coefficient of variation is 3.1% and inter-assay coefficient variation is 7.3%. For the purpose of statistical analyses, a value of 0.15mg/L was taken for samples with an hsCRP level of <0.3mg/L. Anti-dsDNA was measured by a commercially available ELISA kit (Euro-diagnostica, Arnhem, Netherlands) and complement levels were measured by immunonephelometry (Siemens, Germany). An anti-dsDNA titer of ≥50IU/mL was regarded as a positive test.

Assessment of SLE activity and damage

Disease activity of SLE was assessed by the Safety of Estrogens in Lupus Erythematosus National Assessment (SELENA)-SLE Disease Ac tivity Index (SLEDAI), a validated instrument employed in the SELENA trials (19). The SELENA-SLEDAI (SS) scores were obtained from all the patients at the time of venepuncture. For the correlation studies, clinical SLEDAI score referred to that after deduction of points due to depressed complements (C3<0.75g/L and/or C4<0.14g/L) or elevated anti-dsDNA titers (≥50IU/ml) from the total SLEDAI score. The physician's global assessment (PGA) of disease activity (score 0-3) was also performed by the attending physicians to grade their impression on the disease activity of the patients (20).

Damage of SLE was measured by the Systemic Lupus International Collaborating Clinics Damage Index (SDI) (21), a validated instrument consisting of 41 items that measure irreversible organ damage unrelated to active inflammation in 12 organ systems. Each item should be present for at least six consecutive months in order to be scored.

Statistical analyses

Unless otherwise stated, values in this study were expressed as mean ± standard deviation (SD). Comparison of hsCRP levels between patients with and without disease activity in different systems was performed by the non-parametric Mann Whitney U test. Linear regression models were established to study the correlation between hsCRP level and disease activity score in different systems with adjustment for age, sex, body mass index (BMI), serum creatinine and the use of concomitant medications such as corticosteroids, hydroxychloroquine, mycophenolate mofetil, azathioprine, calcineurin inhibitors and the statins. Comparison of cardiovascular risk factors (both continuous and categorical variables) between patients with hsCRP level of >3.0 and ≤3.0mg/L was performed by linear regression, with adjustment for serum creatinine level and SLEDAI scores. Correlation between hsCRP and SDI damage score was also studied by linear regression, with adjustment for age, sex, BMI, serum creatinine and concomitant SLEDAI scores.

The sensitivity and specificity of positive anti-dsDNA (≥50 IU/ml) and hsCRP (>3mg/L) for the detection of concurrent lupus activity was calculated by using 2×2 contingency tables. A positive outcome referred to the presence of clinical SLE activity whilst a positive test referred to a positive anti-dsDNA or hsCRP (>3mg/L). Sensitivity was calculated by the ratio of true positive (TP) to TP plus false negative (FN). Specificity was equal to true negative (TN) divided by the sum of TN and false positive (FP).

Statistical significance was defined as a two-tailed P value of less than 0.05. All statistical analyses were performed using the SPSS program, version 11.5 (SPSS, Chicago, IL) for Windows Vista.

Results

Characteristics of the participants

Three hundred and thirty-two adult SLE patients (74% of patients in our cohort) were invited for this study. Twenty-seven patients refused to participate and 16 patients were excluded (evidence of active infection in 14 and renal impairment in 2). Two hundred and eight-nine SLE patients (including 28 hospitalized patients) were finally studied (94% women). The mean age of these patients was 39.0±13.1 years and the mean duration of SLE at the time of recruitment was 7.8±6.7 years. Table 1 shows the cumulative clinical manifestations and autoantibody profile of the participants. One hundred and twenty five (43%) patients had organ damage, as defined by a SDI score of ≥1 point. The mean SDI score of the patients was 0.81±1.18 (median 0; IQR=1). Medications being received by the participants at the time of blood taking were as follows: prednisolone (73%), hydroxychloroquine (51%), azathioprine (37%), mycophenolate mofetil (8%), cyclophosphamide (3%), calcineurin inhibitors (8%), statins (9%) and angiotensin converting enzyme inhibitors (29%).

Disease activity and hsCRP level

One hundred and twenty two (42%) of the patients studied had clinical SLE activity, with and without elevated anti-dsDNA or depressed complement levels. The mean total SLEDAI score of the patients was 4.88±5.55 (median 4; IQR = 4). The mean PGA score was 0.74±0.75 (median 0.5; IQR = 1.2). The clinical disease activity of the patients in various

systems within the domains of the SLEDAI is shown in Table 2. Renal activity was most frequent, followed by dermatological, hematological and musculoskeletal activity. Active SLE serology (either elevated anti-dsDNA or depressed complements) was present in 72% of the participants.

The mean levels of hsCRP in the participants was 4.87±12.7 mg/L (median 0.99; IQR = 3.17). Twenty-eight (23%) patients with clinically active SLE (N=122) did not have detectable hsCRP levels (<0.3mg/L). In contrast, 51 patients (of 64; 80%) who did not have clinical or serological activity (SLEDAI score = 0) had undetectable hsCRP levels.

Table 3 shows the linear regression results of the correlation of hsCRP levels and SLEDAI scores (total, clinical, individual system) after adjustment for age, sex, BMI, serum creatinine and the use of concurrent medications such as corticosteroids, hydroxychloroquine, other immunosuppressive agents such as mycophenolate mofetil, azathioprine and the calcineurin inhibitors (cyclosporin A or tacrolimus), statins and angiotensin converting enzyme inhibitors (ACEI). None of the participants were using hormonal replacement therapy or oral contraceptives at the time of recruitment.

The levels of hsCRP significantly correlated with the SLEDAI scores related to active serositis (Beta 0.46; p<0.001), musculoskeletal disease (Beta 0.21; p=0.001) and hematological disease (Beta 0.19; p=0.002), with the highest R^2 value for serositis (R^2=0.21, ie. 21% of the hsCRP values explained by serositis in the regression model). A significant association between hsCRP and PGA score was also observed (Beta 0.32; p<0.001). Anti-dsDNA titers correlated significantly with hsCRP levels (Beta 0.33; p<0.001) but not with complement C3 levels (Beta -0.07; p=0.26) after adjustment for the same covariates.

Table 4 compares the hsCRP levels of patients with and without disease activity in various organ systems. The hsCRP levels were the highest in patients with active serositis, followed by musculoskeletal disease (mainly arthritis), hematological disease (80% leucopenia; 20% thrombocytopenia), dermatological disease (60% skin rash, 21% mucosal ulceration, 19% alopecia), cutaneous vasculitis and renal disease. Significantly higher hsCRP levels were observed in patients having active musculoskeletal disease, serositis, dermatological disease, renal disease and cutaneous vasculitis compared with those who were not.

Performance of anti-dsDNA and hsCRP in detecting concurrent SLE activity

The sensitivity and specificity of positive anti-dsDNA (≥50IU/mL) and hsCRP (>3mg/L) in the detection of clinical SLE activity was calculated. hsCRP at a cut-off of 3mg/L was less sensitive (0.35 vs 0.76) but more specific (0.77 vs 0.51) than anti-dsDNA in detecting concurrent clinical SLE activity.

Levels of hsCRP and cardiovascular risk factors

Eight-two (28%) of the 289 SLE patients had hsCRP levels of >3mg/L. Table 5 shows the prevalence of cardiovascular factors in patients with hsCRP levels of >3mg/L and ≤3mg/L. A higher level of hsCRP (>3mg/L) was significantly associated with the male sex, chronic smoking >3 years, a history of diabetes mellitus requiring treatment and arterial thrombosis (p<0.05 in all, after adjustment for serum creatinine level and total SLEDAI scores). Moreover, the atherogenic index and ratio of total to HDL cholesterol was significantly higher in patients with hsCRP >3mg/L than those ≤3mg/L (p<0.05 in all).

Levels of hsCRP and organ damage in SLE

Levels of hsCRP did not significantly correlate with the total SDI damage score (Beta 0.09; p=0.12) adjusting for age, sex, serum creatinine, BMI and SLEDAI score (data not shown).

Regarding SDI score in individual systems, hsCRP correlated significantly with pulmonary damage (Beta 0.14; p=0.01) and endocrine damage (Beta 0.17; p=0.005) after adjustment for the same covariates. Pulmonary damage occurred in 13 patients and was contributed by interstitial lung fibrosis in 9 patients (69%), pulmonary hypertension in 3 patients (23%) and pleural fibrosis in 1 patient (8%). All patients with endocrine damage suffered from diabetes mellitus.

Discussion

The exact biologic role of CRP in inflammation and atherosclerosis is controversial. CRP binds to complements and activates the classical complement pathway, thus contributing to host defense to microbes by promoting an inflammatory response (1,4). On the other hand, CRP exhibits anti-inflammatory actions by contributing to complement regulation through the binding of factor H (22), and by binding to apoptotic materials which enhances their phagocytosis and clearance (4). CRP is present in atherosclerotic plaques and is capable of binding to lipid fractions such as low-density lipoprotein (LDL) and very low-density lipoprotein (VLDL) and platelet activation factor (23,24). However, whether or not CRP is an innocent bystander of inflammation or plays a critical role in the inflammatory process that leads to the development of atherosclerosis remains an unresolved issue.

Studies several decades ago have reported that CRP level by conventional assay was not elevated in active SLE except for the presence of serositis, polyarthritis and nephritis (25,26). With the availability of the high sensitivity assay, CRP level was more frequently detectable in SLE patients even in the absence of infection (27). In a study conducted in 2005 (11), hsCRP was not found to be correlated with disease activity or damage in 213 patients with SLE. However, more recent works have reported a significantly association between hsCRP levels and disease activity in cohorts of SLE patients (12,13), particularly with the constitutional, eye, pulmonary, gastrointestinal, neuromotor, and laboratory domains of the activity indices, after adjustment for covariates that might influence the hsCRP level. This is consistent with our results which demonstrated that hsCRP was detectable in 77% of SLE patients with active disease and was significantly associated with disease activity in certain systems.

hsCRP has also been associated with damage in SLE. Lee et al (28) reported that hsCRP was associated with total SLE damage scores and scores in the musculoskeletal and pulmonary systems after adjustment for confounding variables. In the LUMINA study (13), hsCRP was associated with damage scores of the renal, cardiovascular, pulmonary, musculoskeletal and endocrine systems on univariate analysis but did not correlate with the total damage scores in the multivariate model. Our results showed that hsCRP levels correlated with pulmonary and endocrine damage on multivariate analysis. While the association between hsCRP and pulmonary damage (mainly contributed by interstitial fibrosis) is intriguing, the correlation between hsCRP and endocrine damage is attributed by diabetes mellitus, which is a cardiovascular risk factor. Other factors that have been shown by previous studies to influence hsCRP level were age, menopause, renal insufficiency, body mass index, and use of medications such as glucocorticoids, estrogens, statins and the antimalarials (11,12,16), which have been adjusted in the regression models of our study.

hsCRP has emerged to be an important independent risk factor for cardiovascular events in the general population (15). hsCRP is one of the components of the Reynolds cardiovascular risk score (29). In the Justification for the Use of Statins in Prevention: An Intervention Trial Evaluating Rosuvastatin (JUPITER) trial (30), it was demonstrated that statin use in healthy men aged >50 years and women aged >60 years with an LDL cholesterol level of <130mg/dL and an hsCRP level of >2mg/L reduced the incidence of a major cardiovascular event by

44%. The best cardiovascular outcomes occurred in patients who attained an LDL cholesterol level of <70mg/dL and an hsCRP level of <1mg/L with statin treatment (31).

Previous studies have reported a significant association between hsCRP and certain cardiovascular risk factors in patients with SLE (11,12,16). One study that excluded patients with cardiovascular risk factors revealed an association between higher hsCRP levels and vascular stiffness as assessed by flow-mediated dilatation (32). However, no significant association between hsCRP and carotid atherosclerosis could be demonstrated in three recent studies (33-35), despite an older cohort study showing a significant relationship between higher CRP levels at baseline and vascular events (36).

The demonstration of an association between elevated hsCRP level and certain cardiovascular risk factors in our study suggests that hsCRP may be a surrogate marker for cardiovascular risk in SLE patients. However, caution must be exhibited because the level of hsCRP often fluctuates with time because of disease activity and intercurrent infection (16). A spot value of hsCRP, especially during active SLE or infection, may not accurately reflect cardiovascular risk. This might have contributed to the negative relationship between hsCRP and subclinical atherosclerosis in previous studies (33-35). Summating serial hsCRP values over time (area under the curve analysis) obtained during periods of disease quiescence and absence of clinical infection may prove to be more useful in the assessment of cardiovascular risk in SLE patients.

The major limitation of the current study is its cross-sectional design, which prevented us from determining if hsCRP levels could predict changes in SLEDAI or lupus flares in different systems. Another limitation is that the number of patients with active neuropsychiatric manifestations was too small to evaluate the correlation between hsCRP and neuropsychiatric disease activity. Moreover, we did not enroll matched control subjects for the comparison of the hsCRP level and cardiovascular risk factors with the SLE patients.

In conclusion, this study demonstrated that CRP, assayed by a high sensitivity method which was capable of picking up lower levels, was detectable in 77% of SLE patients with active disease but no intercurrent infection. Levels of hsCRP correlated significantly with SLE disease activity score, especially in the musculoskeletal system, hematological system and serositis. A cut-off of 3mg/L of hsCRP level was more specific but less sensitive than anti-dsDNA positivity in the detection of concurrent clinical SLE activity. Higher hsCRP levels were associated with pulmonary damage and certain cardiovascular risk factors in SLE patients such as smoking, male sex, diabetes mellitus, higher atherogenic index and past history of arterial thrombosis. Further studies are necessary to delineate the usefulness of serial hsCRP monitoring in estimating cardiovascular risk in SLE patients so that early preventive strategies can be instituted.

Acknowledgments

The project described was supported by Award Number Grant 8KL2TR000112-05, 8UL1TR000090-05, 8TL1TR000091-05 from the National Center For Advancing Translational Sciences. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Center For Advancing Translational Sciences or the National Institutes of Health.

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Significance and innovation

1. Using a high sensitivity assay, CRP is detectable in 77% of SLE patients with clinically active SLE.
2. hsCRP levels correlate significantly with SLEDAI scores, particularly those related to active serositis, musculoskeletal and hematological disease, as well as pulmonary and endocrine damage.
3. Elevated hsCRP (>3mg/L) is associated with the male sex, chronic smoking, diabetes mellitus, higher atherogenic index and a history of arterial thrombosis.
4. hsCRP is potentially useful marker for disease activity and cardiovascular risk in patients with SLE.

Table 1

Clinical manifestations of the SLE patients studied (N=289)

Clinical manifestations (cumulative since SLE diagnosis)	Number (%)
Arthritis	205 (71)
Myositis	4 (1)
Facial rash	140 (48)
Raynaud's phenomenon	51 (18)
Discoid lupus	25 (9)
Mucosal ulceration	45 (16)
Photosensitivity	82 (28)
Alopecia	87 (30)
Hemolytic anemia	53 (18)
Leukopenia ($<4 \times 10^9$/L)	115 (40)
Thrombocytopenia ($<100 \times 10^9$/L)	74 (26)
Lymphopenia ($<1.5 \times 10^9$/L)	206 (71)
Lymphadenopathy	46 (16)
Seizure	15 (5)
Psychosis	11 (4)
Myelopathy	4 (1)
Acute confusional state	3 (1)
Neuropathy (peripheral or cranial)	5 (2)
Optic neuritis	2 (1)
Renal	169 (58)
Serositis	40 (14)
Autoantibodies	
Anti-dsDNA	218 (75)
Anti-Sm	44 (15)
Anti-Ro	162 (56)
Anti-La	49 (17)
Anti-nRNP	82 (28)
Anti-aCL-IgG	93 (32)

Clinical manifestations (cumulative since SLE diagnosis)	Number (%)
LAC	57 (20)

SLE = systemic lupus erythematosus; aCL = anti-cardiolipin; LAC = lupus anticoagulant

Table 2

Clinical disease activity at the time of venepuncture

Clinical disease activity	Number (%)
Renal	
Proteinuria >0.5g/day or new increase of 0.5g/day	63 (21.8)
Hematuria (RBC >5/HPF)±active casts	26 (9.0)
Pyuria (WBC >5/HPF)±active casts	7 (2.4)
Any	63 (21.8)
Hematological	
WBC count $<3.0 \times 10^9$/L	38 (13.1)
Platelet count $<100 \times 10^9$/L	6 (2.1)
Any	41 (14.2)
Musculoskeletal	
Arthritis >2 joints	25 (8.7)
Myositis	1 (0.4)
Any	26 (9.0)
Dermatological	
Lupus skin rash (including discoid rash)	34 (11.8)
Alopecia	12 (4.2)
Mucosal ulceration (oral / nasal)	22 (3.8)
Any	47 (16.3)
Neuropsychiatric	2 (0.7)
Serositis	9 (3.1)
Cutaneous vasculitis	8 (2.8)
Fever >38°C	9 (3.1)

RBC = red blood cells; HPF = high power field; WBC = white blood cell

Table 3

Linear regression analyses of the correlation between hsCRP and disease activity of SLE

SLEDAI score	Slope (SE)	Beta	*Adjusted P
Renal	0.55 (0.29)	0.12	0.06
Hematological	5.98 (1.88)	0.19	0.002
Musculoskeletal	2.25 (0.64)	0.21	0.001
Dermatological	1.24 (0.78)	0.10	0.11
Neuropsychiatric	−0.66 (1.12)	−0.04	0.56
Serositis	11.6 (1.33)	0.46	<0.001
Cutaneous vasculitis	0.44 (0.57)	0.05	0.44
Serology	1.10 (0.48)	0.14	0.02
Total SLEDAI	0.57 (0.14)	0.25	<0.001
**Clinical SLEDAI	0.64 (0.17)	0.24	<0.001
PGA score	5.40 (1.01)	0.32	<0.001
Anti-dsDNA titer	0.03 (0.005)	0.33	<0.001
Complement C3 level	−3.46 (3.06)	−0.07	0.26

Beta is the regression coefficient in the linear regression models

* adjusted for age, sex, serum creatinine, body mass index and the use of medications (prednisolone, hydroxychloroquine, mycophenolate mofetil, azathioprine, calcineurin inhibitors, statins and angiotensin converting enzyme inhibitors)

** Clinical SLEDAI score = total SLEDAI score minus SLEDAI score due to elevated anti-dsDNA or depressed complements

SLEDAI = systemic lupus erythematosus disease activity index; PGA = physician's global assessment

Table 4

hsCRP level and clinical disease activity in various systems

hsCRP level (mg/L)			
Systems	**Active disease**	**Inactive disease**	**P**
Renal	7.53±16.0	4.13±11.6	0.02
Hematological	9.9±19.7	4.03±11.0	0.92
Musculoskeletal	13.5±22.0	4.02±11.1	<0.001
Dermatological	9.64±18.4	3.95±11.1	0.01
Neuropsychiatric	4.42±0.65	4.88±12.7	0.16
Serositis	34.5±40.9	3.92±9.43	0.005
Cutaneous vasculitis	9.51±6.98	4.74±12.8	0.001

*P values (Mann Whitney U test)

hsCRP = high sensitivity C-reactive protein

Table 5

HsCRP level and cardiovascular risk factors in patients studied

Risk factors	**hsCRP ≤3.0mg/L (N=207)**	**hsCRP >3.0mg/L (N=82)**	***P**
Age, years	39.3±15	38.9±13	0.09
Women	201 (97%)	72 (88%)	0.001
Smoking ≥3 years	19 (9%)	14 (17%)	0.04
Diabetes mellitus	3 (1%)	5 (6%)	0.02
Hypertension	39 (19%)	20 (24%)	0.28
LDL/HDL-chol	1.72±0.69	2.22±2.0	0.06
Total Chol/HDL-chol	3.10±0.87	3.82±2.80	0.03
TG/HDL-chol	0.90±0.60	1.41±2.3	0.045
***Atherogenic index	−0.123±0.26	−0.004±0.32	0.01
BMI, mg/m^2	21.8±3.7	22.2±3.8	0.17
BMI >$27mg/m^2$	19 (9%)	9 (11%)	0.38
History of arterial thrombosis	12 (6%)	11 (13%)	0.01

* P values adjusted for SLE disease activity scores and serum creatinine by regression

** Atherogenic index = Log(triglyceride/HDL-cholesterol)

CRP = C-reactive protein; LDL = low density lipoprotein; HDL = high density lipoprotein; Chol = cholesterol; TG = triglyceride; BMI = body mass index