Published in final edited form as:
Lupus. 2013 July ; 22(8): . doi:10.1177/0961203313492578.

Erythrocyte sedimentation rate is a predictor of renal and overall SLE disease activity

G. Stojan[1,*], **H. Fang**[1], **L. Magder**[2], and **M. Petri**[1]

[1]Division of Rheumatology, Johns Hopkins University School of Medicine, Baltimore, United States

[2]Department of Epidemiology and Public Health, University of Maryland School of Medicine, Baltimore, United States

Abstract

Objective—To assess whether erythrocyte sedimentation rate levels correlate with the level of disease activity at each visit and whether a change in ESR could be useful in predicting changes in disease activity.

Methods—Thousands of visits in a prospective SLE cohort were analyzed to assess the association of ESR and level of disease activity. We explored whether ESR was cross-sectionally associated with disease activity, whether changes in ESR were associated with changes in disease activity, and whether changes in ESR predicted future changes in disease activity. Visits when patients had cancer, infection, pregnancy or were in renal failure were excluded.

Results—After adjusting for confounding factors, mild (25–50mm/hr), moderate (51–75mm/hr), and marked (> 75mm/hr) elevations in ESR levels at a given visit correlated with the SELENA-SLEDAI, the physician global assessment(PGA), fatigue, renal, joint, rash, serositis, hematological visual analogue scale (VAS), hematuria and proteinuria ($p<0.0001$) levels at that visit. A change in ESR between two visits was highly correlated with a concurrent change in physician global assessment (PGA), renal, fatigue and joint VAS ($p<0.0001$). There was no statistically significant correlation between change in ESR between two visits and change in disease activity at a future visit. The subgroup analysis of patients who do not have anti-dsDNA and low complement levels as a feature of their disease showed ESR to be positively associated with SLEDAI, PGA, renal and joint visual analogue scale at that visit ($p<0.0001$), but there were few significant assocations between changes in ESR and changes in disease activity.

Conclusion—ESR is associated with disease activity in SLE measured by the SELENA-SLEDAI, the physician global assessment (PGA), and with organ specific activity including serositis, rash, joint, renal and hematological visual analogue scales. Grouping baseline ESR into 4 levels does associate with both global and organ specific disease activity. A change in ESR between two visits was highly correlated with a change in physician global assessment (PGA), renal, fatigue and joint visual analogue scale (VAS). In patients without anti-dsDNA and low

Correspondence to: Michelle Petri M.D. M.P.H., Professor of Medicine, Division of Rheumatology, 1830 East Monument Street Suite 7500, Baltimore MD 21205, USA. Telephone: 410-955-3823, Fax: 410-614-0498, mpetri@jhmi.edu.
George Stojan M.D., Division of Rheumatology, Johns Hopkins University School of Medicine, 5200 Eastern Avenue, Mason F. Lord Bldg. Center Tower, Suite 4100, Baltimore MD 21224, USA, gstojan1@jhmi.edu
Hong Fang M.D. M.S., Division of Rheumatology, Johns Hopkins University School of Medicine, 1830 East Monument Street Suite 7500, Baltimore MD 21205, USA, hfang6@jhmi.edu
Laurence S. Magder Ph.D., Department of Epidemiology and Public Health, University of Maryland School of Medicine, 660 West Redwood Street, Room 112, Howard Hall, Baltimore MD 21201, USA, lmagder@epi.umaryland.edu
Michelle Petri M.D. M.P.H., Division of Rheumatology, Johns Hopkins University School of Medicine, 1830 East Monument Street Suite 7500, Baltimore MD 21205, USA. Telephone: 410-955-3823, Fax: 410-614-0498, mpetri@jhmi.edu

complement levels, ESR was positively associated with SLEDAI, PGA, renal and joint visual analogue scale at the same visit. Until more specific biomarkers are validated, serial ESR does have some utility in following disease activity in SLE.

Key Indexing Terms

erythrocyte sedimentation rate; ESR; systemic lupus erythematosus; disease activity

Introduction

The erythrocyte sedimentation rate (ESR) is a simple and inexpensive laboratory test for assessing the inflammatory response. It is an indirect, qualitative measure of fibrinogen and other acute phase protein concentrations in plasma (1). ESR can be greatly influenced by the size, shape, and number of erythrocytes, as well as by other plasma constituents such as immunoglobulins. Erythrocyte aggregation is affected by two major factors: red cell surface charges and frictional forces around the red cell. The erythrocytes normally have net negative charges and, therefore, repel each other. High molecular weight proteins, especially when positively charged, increase viscosity and favor rouleaux formation and thus raise the ESR. Fibrinogen, the most abundant acute phase reactant, has the greatest effect on the elevation of ESR when compared with other acute phase proteins (2, 3). Ultimately, ESR levels are influenced by a wide range of factors, many of them unrelated to inflammation. Hypoalbuminemia, hypercholesterolemia, and hypergammaglobulinemia may increase ESR (4). In anemia, the velocity of the upward flow of plasma is altered when the hematocrit is reduced so that red blood cells sediment faster. However, in strongly direct Coombs positive anemia, the density gradient between plasma and erythrocytes is lost and the ESR is low (5). Normal ESR values increase with age (6). In African Americans, normal values of the ESR are at least 2 mm/hr to 13 mm/hr higher even after correcting for age, hemoglobin concentration, and certain chronic diseases such as malignancies, infections, connective tissue diseases and chronic renal insufficiency (7, 8).

ESR elevation is common in SLE. It was found in 56% of SLE patients in a survey of 570 patients at Cedars Sinai between 1980 and 1989 (9). It is often measured as a potential indicator of disease activity. For this reason, it was included in the Systemic Lupus Activity Measure (SLAM) (10). However, there is significant uncertainty with regard to the utility of this test in the assessment of SLE activity. Previous studies have been limited by inconsistent patient follow up, lack of adjustment for confounding factors and coexistent conditions and use of non-validated SLE activity scales. Here we report on the utility of ESR as a marker and predictor of disease activity in the Hopkins Lupus Cohort.

Patients and methods

As previously described (11), the Hopkins Lupus Cohort is a prospective cohort study of predictors of lupus flare, atherosclerosis, and health status in SLE. The study cohort includes all patients at the Hopkins Lupus Center who have a clinical diagnosis of SLE and give informed consent to participate in the study. Subjects enrolled in the cohort are followed quarterly or more frequently if clinically necessary. The clinical features, laboratory testing, and damage accrual data are recorded at the time of entry into the cohort and are updated at subsequent visits. The Hopkins Lupus Cohort has been approved by the Johns Hopkins University School of Medicine Institutional Review Board and complies with the Health Insurance Portability and Accountability Act.

ESR was measured by an InteRRliner ESR Analyzer automated system. The InteRRliner is a fully automated rack system utilizing the Westergren Method for erythrocyte

sedimentation analysis. Full 3 or 5ml tube of venous blood collected in EDTA was delivered to the laboratory within 4 hours of collection or within 6 hours if specimen was refrigerated. The EDTA specimen was mixed and automatically diluted during aspiration to the next available glass pipette. The pipette travelled around the belt for 60 minutes at which time the measuring sensor determined the sedimentation rate. The result was sent to the printer and host computer for verification. Quality control of the system was performed with every shift, three times daily, by using the SEDRite Plus Controls and verifying them with the Sysmex autoverification program. Normal values for those younger than 50 years of age were 4–25 mm/hr for women and 1–15 mm/hr for men, while for those older than 50, normal values were between 4–30mm/hr for women and 1–20mm/hr for men.

In case the automated system failed or did not pass quality control, a manual ESR measurement based on a modified Westergren method was used as a backup. Four parts of anticoagulated whole blood were added to one part 0.85% saline. The specimen was thoroughly mixed by a minimum of 8 repeated inversions. The Dispette Tube was inserted to the bottom of the reservoir. The full Dispette assembly was placed in the leveled Dispette stand at a 90 degree angle. At the end of the 60 minutes, the result was read by observing the number of millimeters the RBC column has dropped from the zero mark printed on the Dispette2 pipette (12). Normal values were identical to the values used by the automated system.

Patients and Activity Indices

Ninety-five percent of patients fulfilled 4 or more of the American College of Rheumatology (ACR) 1982 revised classification criteria for SLE (13, 14). Disease activity was measured with the Physician Global Assessment, Lupus Activity Index (15), and the SELENA revision of the Safety of Estrogens in Lupus Erythematosus National Assessment–Systemic Lupus Erythematosus Disease Activity Index instrument score (16).

The lupus activity index (LAI) is both a global and organ-specific activity score assessing activity over the previous 2 weeks. The index consists of five sections and includes eight organ systems and three laboratory measures, including anti-dsDNA. The index includes the physician global assessment as well as a score for treatment with glucocorticoids and immunosuppressive drugs. The index allows grading for severity based on physician judgment. The overall score ranges from 0 to 3, and is the mean of the physician global assessment, physician judgment of the severity of clinical manifestations, degree of laboratory manifestations, and treatment (15). We used the organ specific visual analogue scales of the Lupus Activity Index in this study.

The SELENA revision of the Safety of Estrogens in Lupus Erythematosus National Assessment–Systemic Lupus Erythematosus Disease Activity Index (SELENA-SLEDAI) instrument score measures disease activity within the last 10 days. It includes 24 clinical and laboratory variables that are weighted by type of manifestation as well as the physican global assessment and a flare index. Disease activity may, in theory, range from 0 to 105 (16).

Statistical methods

To assess the association between ESR level, and levels of disease activity at the same visit, we analyzed data from all cohort visits, excluding visits in which patients had cancer, infection, pregnancy or were in end stage renal failure. End stage renal failure was defined as renal failure requiring hemodialysis or renal transplantation. This resulted in a cross-sectional analysis of 35,373 visits from 1865 different patients. The number of visits per patient ranged from 1 to 131. 43% of the patients had less than 10 visits, 22% of the patients

had 10–19 visits, and 35% of the patients had more than 20 visits. For this analysis, ESR values were expressed in 4 categories: less than 25 (normal), 25–50 (mild elevation), 51–75 (moderate elevation), and greater than 75 (marked elevation) mm/h. A subgroup analysis of patients who did not have anti-dsDNA and/or low complement as a feature of their disease was performed, including 5703 visits from 418 different patients were included. The number of visits per patient in this subgroup analysis ranged from 1 to 97. Fifty-five percent of the patients had less than 10 visits, 19% had 10–19 visits, and 26% had 20 or more visits.

To assess the relationship between changes in ESR and changes in disease activity, we identified all pairs of cohort visits from the same patient that were separated by 80–100 days. Then we examined the association between changes in ESR between these two visits and concurrent changes in disease activity. This resulted in an analysis of 12,119 pairs of visits from 1386 different patients. The number of paired visits per patient ranged from 1 to 62. Sixty-eight percent contributed to less than 10 pairs, 20% contributed to 10–19 pairs, and 12% contributed to 20 or more pairs. A subgroup analysis of patients who did not have anti-dsDNA and low complement levels as a feature of their disease was performed, based on 2160 pairs of visits from 293 individuals.

To assess the relationship between changes in ESR and changes at a future visit, we identified all sets of 3 consecutive visits from each patient where the consecutive visits were separated by 80–100 days. Then we examined the association between changes in ESR between the first two visits, and changes in disease activity between the second and third visit. This resulted in an analysis of 6141 visit triplets from 987 different patients. The number of triplets contributed per patient ranged from 1 to 45. Seventy-eight percent contributed to less than 10, 17% contributed to 10–19, and 5% contributed 20 or more triplets.

To assess associations we used mixed effects models to account for the fact that the same patients contributed multiple visits to each analysis. To assess associations controlling for other predictors, we included terms in the model to adjust for age, ethnicity, gender, body mass index, cholesterol, complement levels, hematocrit, anti-dsDNA, prednisone use, hydroxychloroquine use, and other immunosuppressant use. To make the results easier to interpret, we provide estimates of the expected difference in disease activity measured per one SD change in ESR. In this sample, the SD was approximately 27 mm/hr.

Results

Table 1 shows the results of the cross-sectional analysis to address the question of whether there is an association between ESR at a visit and the level of disease activity at that same visit. After adjusting for confounding factors, ESR divided into normal, mild, moderate, and severely high categories was positively associated with global measures of disease activity, and all organ-specific measures. Mild, moderate and marked ESR elevations were strongly associated with SELENA-SLEDAI, physician global assessment, rash, renal, joint, hematology, and serositis visual analogue scales, as well as with hematuria and proteinuria. The association with the neurological and pulmonary visual analogue scales was also statistically significant. Table 2 shows the results of the subgroup analysis which included only the patients with no history of anti-dsDNA or low complement levels. In this important clinical subset of patients, mild, moderate and marked ESR elevations were still positively associated with SLEDAI, physician global assessment, renal and joint visual analogue scales. The sensitivity and specificity of ESR elevation (>25mm/hr) for confirming active disease is 56% and 63%, respectively, if high disease activity is defined as SELENA-SLEDAI of 3 or more. For a physician global assessment of 1 or more, ESR elevation (>25mmHg) has a sensitivity of 49% and specificity of 64%.

Table 3 shows the association between changes in ESR and changes in disease activity measures between pairs of consecutive visits separated by 80–100 days. A change in ESR between two visits was highly correlated with a concurrent change in physician global assessment, renal, fatigue and joint visual analogue scales ($p<0.0001$) and with changes in hematuria or proteinuria, but not with changes in other organ activity indices. This correlation remained strong after adjustment for changes in body mass index, complement levels, hematocrit, anti-dsDNA levels, and prednisone, hydroxychloroquine or immunosuppressant use. The magnitude of the associations were small, however. For example, an increase in ESR of one SD was associated with a 0.1 point increase in SELENA-SLEDAI. Table 4 shows the results of the subgroup analysis, which included the patients with no history of anti-dsDNA or low complement levels. In this subgroup, there was no association between changes in ESR and changes in disease activity measures between two consecutive visits.

Table 5 shows the results of visit triplet analysis to address the question of whether changes in ESR between the first two visits predicted changes in disease activity between the second and third visits. There was no statistically significant correlation between change in ESR between the first and second visit and change in disease activity in between the second and third visit.

Discussion

The association between elevated ESR and disease activity in SLE has been a matter of controversy over the years because the available data were contradictory. The ESR, for example, is not a variable in the SLE Disease Activity Index (SLEDAI) (17)or the British Isles Lupus Activity Group (BILAG) activity measures (18), but was included in the Systemic Lupus Activity Measure (SLAM) (10). A longitudinal study of outcome from the multiethnic LUMINA cohort assessed the utility of ESR as a categorical marker of same day disease activity and damage accrual. They showed that mild (25–50mm/hr), moderate (51–75mm/hr), and marked (> 75mm/hr) ESR elevations were strongly associated with global disease activity in SLE measured by SLAM-noESR (19). The limitations of the LUMINA report included, among others, not being able to ascertain other coexistent conditions that might be associated with increased ESR, for example, infections, malignancy, pregnancy and end stage renal failure. We were able to address these limitations in our study design. Similar data were obtained in a cross-sectional study from Iran, in which Nasiri et al described a significant association between increasing ESR and overall BILAG scores in 100 patients with SLE (20). On the other hand, in a prospective study of 120 SLE patients by Mirzayan et al (21), elevation of ESR did not predict an increase in the SLE Disease Activity Index. Chang *et al* found no significant association between ESR and physician-reported improvement based on SLAM-R or SLEDAI, but SLE patients that perceived improvement of their condition were more likely to have lower ESR (22).

In recent years, the continuous search for new biomarkers for assessment of SLE activity yielded indirect data on their relation to ESR. Viallard and colleagues studied HLA–DR expression by subsets of peripheral T lymphocytes in relation to disease activity in 60 SLE patients over a 3-year period, using flow cytometric analysis. Thirty-four patients had “quiescent” disease (SLEDAI scores 1–6 throughout the study) and 26 had active disease (at least a 3-point increase in the SLEDAI score at some point). In univariate analyses, erythrocyte sedimentation rate was significantly higher in the active disease group (23). In a study used to validate the potential utility of serum chemokine levels as biomarkers of disease activity, the chemokine score was significantly associated with disease flare (SLEDAI>3), but none of the common laboratory tests (ESR, complement, anti-dsDNA antibody) were significant predictors of a disease flare, although the ESR showed a positive

trend (P =0.071) (24). In a study in which serum concentrations of neopterin, beta-2-microglobulin, 55 kD-type soluble tumor necrosis factor receptor, soluble interleukin-2 receptor and soluble CD8 were compared to the Index of European Consensus Lupus Activity Measurement (ECLAM), it was found that ESR strongly correlated with ECLAM ($P < 0.001$) (25). In a study from Brazil that evaluated the association of plasma concentrations of terminal complement complex (SC5b-9) with disease activity, it was found that a significant elevation of ESR was present in SLE patients with moderate/severe activity compared to those without active disease or with mild disease activity (26).

Our data show that mild, moderate, and marked ESR elevations are strongly associated with disease activity in SLE at the same visit, as measured by SELENA-SLEDAI, physician global assessment (PGA) and with organ specific activity including SLEDAI, PGA, rash, renal, joint, hematology, neurological, pulmonary, and serositis visual analogue scale, as well as with hematuria and proteinuria. This correlation persisted after adjustment for age, ethnicity, sex, weight, cholesterol, C3, C4, hematocrit, anti-dsDNA, prednisone use, hydroxychloroquine use, and immunosuppressant use. A change in ESR between two visits was also significantly correlated with a change in physician global assessment (PGA), renal, fatigue and joint visual analogue scales (VAS), but not with changes in other organ activity indices. However, the magnitude of the association was small. In the subgroup analysis of patients with no history of anti-dsDNA or low complement levels, ESR categories (normal, mild, moderate, severe) were positively associated with SELENA-SLEDAI, physician global assessment, renal and joint visual analogue scales at the same visit but there was no association with changes in disease activity measures between two consecutive visits. Changes in ESR between two visits also did not predict changes in disease activity at a third visit.

Thus, we conclude that, until more specific biomarkers are validated, categorical levels of ESR (normal, mild, moderate, severe) do associate meaningfully with disease activity, including in patients with no anti-dsDNA or low complement. Changes in ESR between two visits do associate statistically with changes in disease activity, but the magnitude is unlikely to be clinically important.

Acknowledgments

The Hopkins Lupus Cohort is supported by a grant from the National Institute of Health (NIH AR 43727). This publication was also made possible by Grant Number UL1 RR 025005 from the National Center for Research Resources (NCRR), a component of the National Institutes of Health (NIH), and NIH Roadmap for Medical Research.

Dr. George Stojan is supported by NIH Grant T32 AR048522.

References

1. Gabay C, Kushner I. Acute-phase proteins and other systemic responses to inflammation. N Engl J Med. 1999 Feb 11; 340(6):448–54. [PubMed: 9971870]
2. Ballas SK. The erythrocyte sedimentation rate, rouleaux formation and hyperviscosity syndrome. theory and fact. Am J Clin Pathol. 1975 Jan; 63(1):45–8. [PubMed: 803345]
3. Sox HC Jr, Liang MH. The erythrocyte sedimentation rate. guidelines for rational use. Ann Intern Med. 1986 Apr; 104(4):515–23. [PubMed: 3954279]
4. Reinhart WH, Nagy C. Albumin affects erythrocyte aggregation and sedimentation. Eur J Clin Invest. 1995 Jul; 25(7):523–8. [PubMed: 7556371]
5. Brigden ML. Clinical utility of the erythrocyte sedimentation rate. Am Fam Physician. 1999 Oct 1; 60(5):1443–50. [PubMed: 10524488]

6. Smith EM, Samadian S. Use of the erythrocyte sedimentation rate in the elderly. Br J Hosp Med. 1994 Apr-May;51(8):394–7. [PubMed: 8081575]
7. Gillum RF. A racial difference in erythrocyte sedimentation. J Natl Med Assoc. 1993 Jan; 85(1):47–50. [PubMed: 8426384]
8. Bester FC, Weich DJ, Badenhorst PN, de Wet JI. Erythrocyte sedimentation rate in elderly blacks. S Afr Med J. 1993 Jul; 83(7):498–500. [PubMed: 8211489]
9. Pistiner M, Wallace DJ, Nessim S, Metzger AL, Klinenberg JR. Lupus erythematosus in the 1980s: A survey of 570 patients. Semin Arthritis Rheum. 1991 Aug; 21(1):55–64. [PubMed: 1948102]
10. Liang MH, Socher SA, Larson MG, Schur PH. Reliability and validity of six systems for the clinical assessment of disease activity in systemic lupus erythematosus. Arthritis Rheum. 1989 Sep; 32(9):1107–18. [PubMed: 2775320]
11. Petri M. Hopkins lupus cohort. 1999 update. Rheum Dis Clin North Am. 2000 May.26(2):199, 213, v. [PubMed: 10768209]
12. ICSH recommendations for measurement of erythrocyte sedimentation rate. international council for standardization in haematology (expert panel on blood rheology). J Clin Pathol. 1993 Mar; 46(3):198–203. [PubMed: 8463411]
13. Hochberg MC. Updating the american college of rheumatology revised criteria for the classification of systemic lupus erythematosus. Arthritis Rheum. 1997 Sep.40(9):1725. [PubMed: 9324032]
14. Tan EM, Cohen AS, Fries JF, Masi AT, McShane DJ, Rothfield NF, et al. The 1982 revised criteria for the classification of systemic lupus erythematosus. Arthritis Rheum. 1982 Nov; 25(11): 1271–7. [PubMed: 7138600]
15. Petri M, Hellmann D, Hochberg M. Validity and reliability of lupus activity measures in the routine clinic setting. J Rheumatol. 1992 Jan; 19(1):53–9. [PubMed: 1556700]
16. Petri M, Kim MY, Kalunian KC, Grossman J, Hahn BH, Sammaritano LR, et al. Combined oral contraceptives in women with systemic lupus erythematosus. N Engl J Med. 2005 Dec 15; 353(24):2550–8. [PubMed: 16354891]
17. Bombardier C, Gladman DD, Urowitz MB, Caron D, Chang CH. Derivation of the SLEDAI. A disease activity index for lupus patients. the committee on prognosis studies in SLE. Arthritis Rheum. 1992 Jun; 35(6):630–40. [PubMed: 1599520]
18. Yee CS, Farewell V, Isenberg DA, Rahman A, Teh LS, Griffiths B, et al. British isles lupus assessment group 2004 index is valid for assessment of disease activity in systemic lupus erythematosus. Arthritis Rheum. 2007 Dec; 56(12):4113–9. [PubMed: 18050213]
19. Vila LM, Alarcon GS, McGwin G Jr, Bastian HM, Fessler BJ, Reveille JD, et al. Systemic lupus erythematosus in a multiethnic cohort (LUMINA): XXIX. elevation of erythrocyte sedimentation rate is associated with disease activity and damage accrual. J Rheumatol. 2005 Nov; 32(11):2150–5. [PubMed: 16265693]
20. Nasiri S, Karimifar M, Bonakdar ZS, Salesi M. Correlation of ESR, C3, C4, anti-DNA and lupus activity based on british isles lupus assessment group index in patients of rheumatology clinic. Rheumatol Int. 2010 Nov; 30(12):1605–9. [PubMed: 19809816]
21. Mirzayan MJ, Schmidt RE, Witte T. Prognostic parameters for flare in systemic lupus erythematosus. Rheumatology (Oxford). 2000 Dec; 39(12):1316–9. [PubMed: 11136872]
22. Chang ER, Abrahamowicz M, Ferland D, Fortin PR. Organ manifestations influence differently the responsiveness of 2 lupus disease activity measures, according to patients' or physicians' evaluations of recent lupus activity. J Rheumatol. 2002 Nov; 29(11):2350–8. [PubMed: 12415591]
23. Viallard JF, Bloch-Michel C, Neau-Cransac M, Taupin JL, Garrigue S, Miossec V, et al. HLA-DR expression on lymphocyte subsets as a marker of disease activity in patients with systemic lupus erythematosus. Clin Exp Immunol. 2001 Sep; 125(3):485–91. [PubMed: 11531958]
24. Bauer JW, Petri M, Batliwalla FM, Koeuth T, Wilson J, Slattery C, et al. Interferon-regulated chemokines as biomarkers of systemic lupus erythematosus disease activity: A validation study. Arthritis Rheum. 2009 Oct; 60(10):3098–107. [PubMed: 19790071]
25. Samsonov MY, Tilz GP, Egorova O, Reibnegger G, Balabanova RM, Nassonov EL, et al. Serum soluble markers of immune activation and disease activity in systemic lupus erythematosus. Lupus. 1995 Feb; 4(1):29–32. [PubMed: 7767335]

26. Chiu YY, Nisihara RM, Wurzner R, Kirschfink M, de Messias-Reason IJ. SC5b-9 is the most sensitive marker in assessing disease activity in brazilian SLE patients. J Investig Allergol Clin Immunol. 1998 Jul-Aug;8(4):239–44.

Table 1

Mean Disease Activity Measure at a visit, by ESR level at the same visit

Disease Activity Measure	ESR Level				P-value[1]	P-value[2]
	<25 (n=18,021)	25–50 (n=10,495)	51–75 (n=3983)	>75 (n=2874)		
SELENA-SLEDAI	2.22 (2.86)	2.98 (3.26)	3.65 (3.52)	4.26 (3.79)	<0.0001	<0.0001
Physician Global	0.62 (0.63)	0.79 (0.71)	0.89 (0.75)	1.05 (0.81)	<0.0001	<0.0001
Fatigue VAS[3]	0.07 (0.30)	0.08 (0.35)	0.08 (0.33)	0.09 (0.37)	0.0060	0.0083
Neuro VAS[3]	0.04 (0.24)	0.05 (0.26)	0.04 (0.25)	0.03 (0.21)	0.0004	0.0010
Rash VAS[3]	0.16 (0.39)	0.20 (0.46)	0.24 (0.50)	0.25 (0.50)	<0.0001	<0.0001
Renal VAS[3]	0.16 (0.45)	0.30 (0.61)	0.37 (0.69)	0.53 (0.82)	<0.0001	<0.0001
Joints VAS[3]	0.23 (0.43)	0.28 (0.52)	0.29 (0.54)	0.32 (0.57)	<0.0001	<0.0001
Pulmonary VAS[3]	0.01 (0.11)	0.01 (0.14)	0.01 (0.15)	0.02 (0.21)	0.0002	0.0059
Hematology VAS[3]	0.12 (0.34)	0.11 (0.32)	0.13 (0.37)	0.17 (0.44)	<0.0001	0.0011
Serositis VAS[3]	0.02 (0.17)	0.03 (0.19)	0.04 (0.23)	0.07 (0.29)	<0.0001	<0.0001
Hematuria[4]	0.03 (0.16)	0.05 (0.21)	0.06 (0.24)	0.09 (0.29)	<0.0001	<0.0001
Proteinuria[4]	0.04 (0.18)	0.07 (0.26)	0.10 (0.30)	0.12 (0.32)	<0.0001	<0.0001

[1] P-value based on a random effects model to account for repeated measures from the same patients

[2] P-value based on a random effects model, and adjusted for age, race, sex, weight, c3, c4, hematocrit, anti-dsDNA, prednisone use, plaquenil use, and immunosuppressant use

[3] Visual Analogue Scale from 0–3 with 3 representing most disease activity.

[4] Present/absent, so difference in means corresponds to differences in probability of presence.

Table 2

Mean Disease Activity Measure at a visit, by ESR level at the same visit among those with no history of anti-dsDNA or low complement

Disease Activity Measure	ESR Level				P-value[1]	P-value[2]
	<25 (n=3,385)	25–50 (n=1,613)	51–75 (n=435)	>75 (n=270)		
SELENA-SLEDAI	1.08 (1.95)	1.71 (2.48)	2.36 (2.64)	1.69 (2.57)	<0.0001	<0.0001
Physician Global	0.55 (0.56)	0.72 (0.63)	0.86 (0.69)	0.71 (0.71)	<0.0001	<0.0001
Fatigue VAS[3]	0.04 (0.22)	0.04 (0.22)	0.04 (0.23)	0.06 (0.28)	0.75	0.64
Neuro VAS[3]	0.03 (0.22)	0.04 (0.23)	0.05 (0.23)	0.02 (0.15)	0.24	0.73
Rash VAS[3]	0.19 (0.41)	0.26 (0.51)	0.31 (0.55)	0.19 (0.45)	0.56	0.75
Renal VAS[3]	0.06 (0.24)	0.12 (0.38)	0.16 (0.41)	0.17 (0.45)	<0.0001	<0.0001
Joints VAS[3]	0.29 (0.44)	0.34 (0.54)	0.45 (0.67)	0.40 (0.62)	0.0040	0.0001
Pulmonary VAS[3]	0.00 (0.07)	0.00 (0.06)	0.00 (0.05)	0.02 (0.17)	0.21	0.12
Hematology VAS[3]	0.08 (0.15)	0.09 (0.23)	0.10 (0.26)	0.08 (0.28)	0.67	0.26
Serositis VAS[3]	0.02 (0.15)	0.02 (0.16)	0.01 (0.08)	0.02 (0.18)	0.13	0.083
Hematuria[4]	0.01 (0.09)	0.01 (0.12)	0.03 (0.16)	0.03 (0.17)	0.010	0.0035
Proteinuria[4]	0.01 (0.09)	0.03 (0.16)	0.04 (0.20)	0.03 (0.17)	0.10	0.40

[1] P-value based on a random effects model to account for repeated measures from the same patients

[2] P-value based on a random effects model, and adjusted for age, race, sex, weight, c3, c4, hematocrit, anti-dsDNA, prednisone use, plaquenil use, and immunosuppressant use

[3] Visual Analogue Scale from 0–3 with 3 representing most disease activity.

[4] Present/absent, so difference in means corresponds to differences in probability of presence.

Table 3

Association between changes in ESR and changes in disease activity measures between two consecutive visits.

Disease Activity Measure	Difference in mean activity level[1] (95% CI)	P-value	Adjusted[2] Difference in mean activity level[1] (95% CI)	P-value
SELENA-SLEDAI	0.056 (−0.030, 0.014)	0.20	0.110 (0.017, 0.202)	0.020
Physician Global	0.045 (0.026, 0.064)	<0.0001	0.050 (0.030, 0.071)	<0.0001
Fatigue VAS[3]	0.013 (0.006, 0.021)	0.0004	0.016 (0.008, 0.024)	0.0001
Neuro VAS[3]	−0.004 (−0.010, 0.002)	0.23	−0.004 (−0.011, 0.003)	0.28
Rash VAS[3]	0.010 (−0.002, 0.021)	0.096	0.008 (−0.004, 0.020)	0.21
Renal VAS[3]	0.027 (0.015, 0.038)	<0.0001	0.030 (0.018, 0.043)	<0.0001
Joints VAS[3]	0.029 (0.014, 0.044)	0.0002	0.027 (0.011, 0.044)	0.0012
Pulmonary VAS[3]	0.000 (−0.003, 0.003)	0.94	−0.001 (−0.004, 0.002)	0.65
Hematology VAS[3]	0.001 (−0.007, 0.009)	0.83	0.001 (−0.007, 0.010)	0.76
Serositis VAS[3]	0.007 (0.001, 0.013)	0.022	0.005 (−0.002, 0.011)	0.16
Hematuria[4]	0.008 (0.001, 0.014)	0.019	0.009 (0.002, 0.026)	0.015
Proteinuria[4]	0.006 (−0.001, 0.012)	0.076	0.009 (0.003, 0.016)	0.0072

[1] Difference in mean change in activity level per one SD difference in ESR (One SD=27 mm/hr)

[2] Adjusted for age, race, sex, and changes in: weight, c3, c4, hematocrit, andti-dsDNA, prednisone use, plaquenil use, and immunosuppressant use.

[3] Visual Analogue Scale from 0–3 with 3 representing most disease activity.

[4] Present/absent, so difference in means corresponds to differences in probability of presence.

Table 4

Association between changes in ESR and changes in disease activity measures between two consecutive visits among those with no history of anti-dsDNA or low complement.

Disease Activity Measure	Difference in mean activity level[1] (95% CI)	P-value	Adjusted[2] Difference in mean activity level[1] (95% CI)	P-value
SELENA-SLEDAI	−0.070 (−0.279, .139)	0.51	−0.131 (−0.355, 0.094)	0.25
Physician Global	0.004 (−0.047, 0.056)	0.87	−0.006 (−0.061, 0.049)	0.84
Fatigue VAS[3]	0.039 (−0.013, 0.021)	0.65	0.009 (−0.009, 0.027)	0.34
Neuro VAS[3]	−0.006 (−0.023, 0.010)	0.44	0.007 (−0.025, 0.010)	0.41
Rash VAS[3]	−0.032 (−0.063, −0.000)	0.049	−0.036 (−0.069, −0.002)	0.040
Renal VAS[3]	0.025 (−0.000, 0.051)	0.054	0.022 (−0.006, 0.049)	0.12
Joints VAS[3]	−0.016 (−0.063, 0.031)	0.50	−0.018 (−0.068, 0.032)	0.48
Pulmonary VAS[3]	−0.002 (−0.006, 0.002)	0.35	−0.001 (−0.006, 0.003)	0.51
Hematology VAS[3]	0.001 (−0.017, 0.020)	0.88	0.003 (−0.017, 0.023)	0.77
Serositis VAS[3]	0.009 (−0.005, 0.023)	0.19	0.004 (−0.011, 0.019)	0.56
Hematuria[4]	0.010 (−0.005, 0.025)	0.17	0.011 (−0.005, 0.027)	0.18
Proteinuria[4]	0.000 (−0.010, 0.010)	0.96	−0.003 (−0.014, 0.008)	0.63

[1] Difference in mean change in activity level per one SD difference in ESR (One SD=27 mm/hr)

[2] Adjusted for age, race, sex, and changes in: weight, c3, c4, hematocrit, andti-dsDNA, prednisone use, plaquenil use, and immunosuppressant use.

[3] Visual Analogue Scale from 0–3 with 3 representing most disease activity.

[4] Present/absent, so difference in means corresponds to differences in probability of presence.

Table 5

Association between changes in ESR between first and second visit and the changes in disease activity between the second and third visits

Disease Activity Measure	Difference in mean activity level[1] (95% CI)	P-value	Adjusted[2] Difference in mean activity level[1] (95% CI)	P-value
SELENA-SLEDAI	0.099 (−0.021, 0.219)	0.11	0.048 (−0.081, 0.178)	0.46
Physician Global	0.004 (−0.022, 0.031)	0.75	0.002 (−0.027, 0.031)	0.90
Fatigue VAS[3]	−0.002 (−0.011, 0.008)	0.75	0.002 (−0.009, 0.012)	0.76
Neuro VAS[3]	0.003 (−0.005, 0.011)	0.48	0.005 (−0.004, 0.014)	0.25
Rash VAS[3]	0.005 (−0.011, 0.021)	0.55	−0.004 (−0.021, 0.014)	0.69
Renal VAS[3]	−0.003 (−0.019, 0.014)	0.76	−0.006 (−0.022, 0.012)	0.53
Joints VAS[3]	−0.008 (−0.030, 0.014)	0.48	−0.009 (−0.033, 0.014)	0.45
Pulmonary VAS[3]	0.001 (−0.003, 0.005)	0.56	0.003 (−0.001, 0.007)	0.15
Hematology VAS[3]	0.005 (−0.006, 0.016)	0.38	0.009 (−0.003, 0.021)	0.13
Serositis VAS[3]	0.005 (−0.003, 0.012)	0.24	0.005 (−0.003, 0.013)	0.22
Hematuria[4]	0.007 (−0.002, 0.016)	0.14	0.003 (−0.007, 0.013)	0.52
Proteinuria[4]	−0.003 (−0.012, 0.005)	0.45	−0.008 (−0.017, 0.002)	0.12

[1] Difference in mean change in activity level per one SD difference in ESR (One SD=27 mm/hr)

[2] Adjusted for age, race, sex, weight, and previous changes in c3, c4, hematocrit, anti-dsDNA, prednisone use, plaquenil use, and immunosuppressant use.

[3] Visual Analogue Scale from 0–3 with 3 representing most disease activity.

[4] Present/absent, so difference in means corresponds to differences in probability of presence