کارگاه‌های آموزشی مرکز اطلاعات علمی

مقاله نویسی علوم انسانی

اصول تنظیم قراردادها

آموزش مهارت های کاربردی در تدوین و چاپ مقاله
Evaluation of damage index and its association with risk factors in patients with systemic lupus erythematosus

Zahra Sayed Bonakdar\textsuperscript{a}, Negin Mohtasham\textsuperscript{b}, Mansoor Karimifar\textsuperscript{a}

Abstract

BACKGROUND: This study aimed to determine the value of damage index in patients with systemic lupus erythematosus (SLE) and the association between damage index and disease severity, flare-up numbers, disease duration, and anti-phospholipid antibodies.

METHODS: Eighty patients with systemic lupus erythematosus were included. The damage was measured using the SLICC (Systemic Lupus International Collaborating Clinics)/ACR damage index (SDI). The disease flare was defined by the increase in the Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2K). The disease severity surrogates were the presence of class III/IV glomerulonephritis, the presence of severe central nervous system (CNS) involvement, and cyclophosphamide administration. Analysis was performed by independent Student-t and chi-square tests via SPSS\textsuperscript{16} software.

RESULTS: There were significant association between the damage accrual and the disease severity, flare-up, and anti-phospholipid antibodies (p = 0.001, p = 0.004, and p = 0.05, respectively).

CONCLUSIONS: The disease severity, frequency of flares, and positive antiphospholipid antibodies are associated with damage accrual in patients with systemic lupus erythematosus.

KEYWORDS: Systemic Lupus Erythematosus, Damage Index, Antiphospholipid Antibody.
We tried to apply the most important risk factors in one study in our population and ethnicity. This study was performed to determine the association of damage index and severe disease, flare-up, duration, age of onset, gender, and antiphospholipid antibodies among patients with SLE in Isfahan, Iran.

**Methods**

This analytic cross-sectional study was performed on 80 patients with SLE. The patients were enrolled by simple sampling method from Outpatient Clinic of Alzahrah Hospital in Isfahan, Iran. They all met American College of Rheumatology (ACR) criteria for SLE. The patients were excluded if their disease duration was less than 6 months. Information such as age, sex, disease duration, time of disease onset, antibody markers, and organ involvement were obtained by reviewing the clinic files of all patients and through face-to-face interviews by a rheumatologist.

Systemic Lupus International Collaborative Clinics/ACR Damage Index (SLICC/ACR-DI), which Gladman et al determined it as a valid measure in SLE, was used to document each patient. A flare of SLE was defined as an increase of more than 3 points compared to previous assessments in the SLEDAI-2K. SLE disease activity index was defined as the reversible manifestation of the underlying inflammatory process which evaluated the disease activity at the time of a patient’s visit. The severity index does not look at the effects of treatment, but rather scores the effects of active disease over time and is a record of these events (not necessarily irreversible) over the course of a patient’s illness.

Surrogates for severe disease were as: 1. The presence of class III/IV glomerulonephritis (GN); 2. The presence of severe central nervous system (CNS) involvement (psychosis, seizure, altered conscious state); and 3. Intravenous Cyclophosphamide pulse administration. Anti-phospholipid antibodies (aPL) were lupus anticoagulant (LA), anticardiolipin IgG or IgM isotype antibodies (aCL), and anti-Beta2 glycoprotein I antibodies (anti-B2GPI) present in medium or high titer on two or more occasions, 12 weeks or more apart. The time of disease onset was defined as the time at which patients met 4 components of the ACR criteria for SLE. The disease duration was defined as the interval between time of diagnosis and the time.

Data were expressed as mean ± SD and percentiles. We performed bivariate analyses by chi-square for qualitative variables and independent sample t-test for quantitative variables. The significant level was set on 0.05 in all statistical analyzes. Data analyzes were performed with SPSS software (version 16, Chicago, IL).

**Results**

The demographic and clinical characteristics of subjects with and without damage are presented in Table 1 and 2. Of the patients, 67 (83.8%) were women and 13 (16.3%) were men. The mean age of the patients was 28.8 years (SD = 9.36, range: 16-60). 55% of the patients were in the 20-35 years age group. The mean age at disease onset was 23.8 years (SD = 8.84, range: 8-53). The mean disease duration was 60.6 months (SD = 3.35, range: 6-180 months). Approximately 38% of our patients had at least one item of damage index. The mean SDI was 0.59 (SD = 1.002, range: 0-5). The mean flare-up numbers was 2.7 (SD = 5.7, range: 0-10).

The frequency of organ damages among our patients were skin damage (31.8%), neuropsychiatric damage (27%), cardiovascular (14%),...

---

**Table 1.** Demographic and clinical quantitative characteristic of 80 SLE patients with and without damage

| Variable                | Damage index (Mean ± SD) | P value |
|-------------------------|--------------------------|---------|
|                         | Positive (No = 30)       | Negative (No = 50) |
| Age (year)              | 30.23 ± 12.3             | 28.02 ± 7.06 | 0.3 |
| Duration                | 5.97 ± 4.24              | 4.49 ± 2.59  | 0.056 |
| Age at disease onset    | 11.4 ± 24.3              | 7 ± 23.5    | 0.7 |
Evaluation of Damage index and its Association with Clinical, Demographic, and Laboratory Characteristics of 80 Systemic Lupus Erythematosus Patients

Bonakdar et al.

JRMS/ March 2011; Vol 16, No 3.

Flare up numbers

| Flare up numbers | 9 ± 4.23 | 1.28 ± 1.8 | 0.004 |
|------------------|----------|------------|-------|
| Data expressed as mean ± SD p-value: obtained from independent sample t-test. |

**Table 2.** Demographic and clinical qualitative characteristic of 80 SLE patients with and without damage

| Variable      | Damage index | P value | OR     | 95% Confidence Interval |
|---------------|--------------|---------|--------|-------------------------|
|               | Positive (n = 30) | Negative (n = 50) |               |                         |
| Sex           | Male          | 6        | 7      | 0.48                    | 1.5                     |
|               | Female        | 24       | 43     |                         |                         |
| APA           | Positive      | 12       | 10     | 0.046                   | 2.67                    |
|               | Negative      | 18       | 40     |                         |                         |
| Severity      | Positive      | 16       | 9      | 0.001                   | 5.2                     |
|               | Negative      | 14       | 41     |                         |                         |

P value: obtained from chi-Square test. Significant level: p < 0.05.

*Antiphospholipid antibody

**Table 3.** Frequency of damage index in 80 SLE patients

| System damage                | No. | %  |
|------------------------------|-----|-----|
| Ocular                       | 3   | 7   |
| Neuropsychiatric              | 12  | 27  |
| Renal                        | 1   | 2   |
| Pulmonary                    | 3   | 7   |
| Cardiovascular               | 6   | 14  |
| Peripheral vascular          | 2   | 4.5 |
| Gastrointestinal             | 0   | 0   |
| Skin                         | 14  | 31.8|
| Musculoskeletal              | 2   | 14  |
| Premature gonadal failure    | 1   | 2   |
| Diabetes mellitus            | 0   | 0   |
| Malignancy                   | 0   | 0   |

ocular (7%), pulmonary (7%), musculoskeletal (4.5%), peripheral vascular (4.5%), renal (2%), and gonadal failure (2%). The results are shown in Table 3.

Among the patients, 25 (31.3%) had severe disease, and 22 (27.5%) were antiphospholipid antibody positive. There was a significant association between SDI and severe disease (p = 0.001) and there was a significant association between the damage accrual and numbers of flares (p = 0.004). No statistically significant association was observed between the damage index, the gender, the disease duration, the age, and the age at disease onset.

**Discussion**

In our study, damage was detected in 38% of the patients that was in agreement with results of the previous studies. The range of the damage score in our patients was 0-5, similar to the findings of research conducted by Hanly et al.25 While the overall accrual of damage is gradual, the specific systems demonstrate varying patterns of damage accrual between ethnic groups, and damage in different organ systems in SLE does not follow a common pattern.26-29 For example, some investigators have reported kidney and musculoskeletal system as the most involved organs and some of them reported neuropsychiatric damage as the most frequent.30,31 However, similarly to other studies, skin was the most frequent damaged organ in our patients.34,35

While several studies have investigated the relationship between disease activity and damage index, there are few studies evaluating
the association between disease flare-up and severity with damage index. While the disease severity and flare are terms that reflect the cumulative disease activity over time, as expected, our study showed significant association between damage and frequency of disease flares that was similar to the results of Bandeiria et al study which showed that patients who accrued new damage had a significantly greater frequency of disease flares in the 0-3 year follow-up period,\textsuperscript{16} and also the study of Nossent who found a significant association between damage and disease exacerbations.\textsuperscript{34}

Previous studies revealed divergent results on the association between damage and gender, age, age at disease onset, and sex, some conducted by Marx et al,\textsuperscript{37} Sayarlioglu et al,\textsuperscript{38} and Yee et al\textsuperscript{39} which showed no significant association between damage and age, damage and age at disease onset, and damage and sex respectively, although the latter found significant association between the damage with age.

The search for a relationship between damage and disease duration in patients with SLE has yielded diverging results. Although several studies have found significant association between damage and disease duration (p < 0.001),\textsuperscript{16,33,40-42} we found no significant association between them (p = 0.056), which was like some other studies.\textsuperscript{37,43} This could be explained by the fact that in our study, only five out of eighty patients had the disease duration more than 10 years and the mean disease duration of our patients was low (5 years), on the other hand as Bridget et al reported that it is important to include only patients with short duration disease in assessing damage trials, as it is hard to evaluate differences in damage accrual if patients had varying periods of disease activity and therapy before the clinical trial.\textsuperscript{44}

A few studies have evaluated correlation between damage and antibodies, and some of them reported that although auto antibodies are useful in diagnosis and predicting disease activity in SLE, they do not appear to be predictive of damage (p < 0.001).\textsuperscript{40,45} Our study found good association between damage index and antiphospholipid antibodies (p = 0.046) that comply with the finding of other researches (p < 0.001).\textsuperscript{46-48} Also, one study reported that aPL can predict early damage in patients with SLE (p = 0.03).\textsuperscript{49}

Although the results of this research is encouraging and promising, additional researches are needed and there are limitations as the absence of a comparison group, and its cross-sectional design. Nevertheless, it could be concluded that damage index in Iranian patients is relatively high and disease severity, flares, and antiphospholipid antibodies are associated with it. To reduce the occurrence of chronic damage, more attention should be given to the individual clinical and therapeutic decisions in SLE patients.\textsuperscript{50} So, prompt treatment of disease flares, more attention to antiphospholipid antibody positive patients and prevention of severity is mandatory for reducing damage accrual.

**Acknowledgment**

We would like to thank the Office of Vice Chancellor for Research of Isfahan University of Medical Sciences for financial supports.

**Conflict of Interests**

Authors have no conflict of interests.

**Authors’ Contributions**

ZSB has planned the study, collected the data, and finalized the manuscript. NM did the laboratory procedures and statistical analysis and prepared the first version of manuscript. MK supervised the project and help in the laboratory analysis. All authors read and approved the final manuscript.
The association of damage index to risk factors in SLE

Sayed Bonakdar et al

References

1. Thumboo J. Measuring functional status in patients with systemic lupus erythematosus. APLAR Journal of Rheumatology 2003; 6(2): 184-7.
2. Chambers SA, Allen E, Rahman A, Isenberg D. Damage and mortality in a group of British patients with systemic lupus erythematosus followed up for over 10 years. Rheumatology (Oxford) 2009; 48(6): 673-5.
3. Cardoso CR, Signorelli FV, Papi JA, Salles GF. Initial and accrued damage as predictors of mortality in Brazilian patients with systemic lupus erythematosus: a cohort study. Lupus 2008; 17(11): 1042-8.
4. José Santos M, Vinagre F, Nero P, Barcelos F, Barcelos A, Rodrigues AM et al. Predictors of Damage Progression in Portuguese Patients with Systemic Lupus Erythematosus. Annals of the New York Academy of Sciences 2009; 1173: 822-8.
5. Gonzalez LA, Pons-Estel GI, Zhang JS, McGwin G, Jr., Roseman J, Reville JD et al. Effect of age, menopause and cyclophosphamide use on damage accrual in systemic lupus erythematosus patients from LUMINA, a multiethnic US cohort (LUMINA LXIII). Lupus 2009; 18(2):184-186.
6. American College of Rheumatology. Development in classification and Response Criteria for Rheumatic Diseases. Arthritis & Rheumatism (Arthritis Care & Research) 2006; 55(3): 348-52.
7. Nossent J, Cikes N, Kiss E, Marchesoni A, Nassonova V, Mosca M et al. Current causes of death in systemic lupus erythematosus in Europe, 2000--2004: relation to disease activity and damage accrual. Lupus 2007; 16(5): 309-17.
8. Wong M, Lau CS. Management of systemic lupus erythematosus: a brief update on recent advances. APLAR Journal of Rheumatology 2006; 9(4): 387-91.
9. Sundaramurthy S, Bush TM, Neuwelt CM, Ward MM. Time perspective predicts the progression of permanent organ damage in patients with systemic lupus erythematosus. Lupus 2003; 12(6):443-448.
10. Bernatsky S, Clarke A, Abrahamowicz M, Neville C, Karp I, Pineau CA. A comparison of prospective and retrospective evaluations of the Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index for systemic lupus erythematosus. J Rheumatol 2005; 32(5): 820-3.
11. Becker-Merok A, Nossent HC. Damage accumulation in systemic lupus erythematosus and its relation to disease activity and mortality. J Rheumatol 2006; 33(8): 1570-7.
12. Pineau CA, Bernatsky S, Abrahamowicz M, Neville C, Karp I, Clarke AE. A comparison of damage accrual across different calendar periods in systemic lupus erythematosus patients. Lupus 2006; 15(9): 590-4.
13. Bertoli AM, Alarcon GS, McGwin G, Jr., Fernandez M, Bastian HM, Fessler BJ et al. Systemic lupus erythematosus in a multiethnic U.S. cohort (LUMINA) XXVII: factors predictive of a decline to low levels of disease activity. Lupus 2006; 15(1): 13-8.
14. Alarcon GS, Roseman JM, McGwin G, Jr., Uribe A, Bastian HM, Fessler BJ et al. Systemic lupus erythematosus in three ethnic groups. XX. Damage as a predictor of further damage. Rheumatology (Oxford) 2004; 43(2): 202-5.
15. Gladman DD, Goldsmith CH, Urowitz MB, Bacon P, Fortin P, Ginzler E et al. The Systemic Lupus International Collaborating Clinics/American College of Rheumatology (SLICC/ACR) Damage Index for Systemic Lupus Erythematosus International Comparison. J Rheumatol 2000; 27(2): 373-6.
16. Bandeira M, Buratti S, Bartoli M, Gasparini C, Breda L, Pistorio A et al. Relationship between damage accrual, disease flares and cumulative drug therapies in juvenile-onset systemic lupus erythematosus. Lupus 2006; 15(8): 515-20.
17. Nery FG, Borba EF, Hatch JP, Soares JC, Bonfa E, Neto PL. Major depressive disorder and disease activity in systemic lupus erythematosus. Compr Psychiatry 2007; 48(1): 14-9.
18. Ibanez D, Gladman DD, Urowitz MB. Adjusted mean Systemic Lupus Erythematosus Disease Activity Index-2K is a predictor of outcome in SLE. J Rheumatol 2005; 32(5): 824-7.
19. Aranow C, Del Guidice J, Barland P, Weinstein A. Systemic lupus erythematosus disease severity in men and women: a case-control study. J Rheumatol 2002; 29(8): 1674-7.
20. Boers A, Li Q, Wong M, Miller M, Littlejohn G. Differences in SLE disease activity between patients of Caucasian and South-East Asian/Chinese background in an Australian hospital. APLAR Journal of Rheumatology 2006; 9(1): 43-8.
21. Erkan D, Lockshin MD. New treatments for antiphospholipid syndrome. Rheum Dis Clin North Am 2006; 32(1): 129-48, x.
22. Fernandez M, Calvo-Alen J, Alarcon GS, Roseman JM, Bastian HM, Fessler BJ, et al. Systemic lupus erythematosus in a multiethnic US cohort (LUMINA): XXI. Disease activity, damage accrual, and vascular events in pre- and postmenopausal women. Arthritis Rheum 2005; 52(6): 1655-64.
23. Mok CC, Ho CT, Wong RW, Lau CS. Damage accrual in southern Chinese patients with systemic lupus erythematosus. J Rheumatol 2003; 30(7): 1513-9.
24. Thumboo J, Lee HY, Fong KY, Chan SP, Chapman CA, Leong KH, et al. Accuracy of medical record scoring of the SLICC/ACR damage index for systemic lupus erythematosus. Lupus 2000; 9(5): 358-62.
The association of damage index to risk factors in SLE

Sayed Bonakdar et al

25. Hanly JG. Disease activity, cumulative damage and quality of life in systemic lupus erythematosus: results of a cross-sectional study. Lupus 1997; 6(3): 243-7.
26. Stoll T, Stucki G, Malik J, Pyke S, Isenberg DA. Association of the Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index with measures of disease activity and health status in patients with systemic lupus erythematosus. J Rheumatol 1997; 24(2): 309-13.
27. Gladman DD, Urowitz MB, Rahman P, Ibanez D, Tam LS. Accrual of organ damage over time in patients with systemic lupus erythematosus. J Rheumatol 2003; 30(9): 1955-9.
28. Maddison P, Farewell V, Isenberg D, Aranow C, Bae SC, Barr S, et al. The rate and pattern of organ damage in late onset systemic lupus erythematosus. J Rheumatol 2002; 29(5): 913-7.
29. Cooper GS, Treadwell EL, St Clair EW, Gilkeson GS, Dooley MA. Sociodemographic associations with early disease damage in patients with systemic lupus erythematosus. Arthritis Rheum 2007; 57(6): 993-9.
30. Ravelli A, Duarte-Salazar C, Buratti S, Reiff A, Bernstein B, Maldonado-Velazquez MR et al. Assessment of damage in juvenile-onset systemic lupus erythematosus: a multicenter cohort study. Arthritis Rheum 2003; 49(4): 501-7.
31. Sung YK, Hur NW, Sinskey JL, Park D, Bae SC. Assessment of damage in Korean patients with systemic lupus erythematosus. J Rheumatol 2007; 34(5): 987-91.
32. Alarcon GS, McGwin G, Jr., Bartolucci AA, Roseman J, Lisse J, Fessler BJ, et al. Systemic lupus erythematosus in three ethnic groups. IX. Differences in damage accrual. Arthritis Rheum 2001; 44(12): 2797-806.
33. Rivest C, Lew RA, Welsing PM, Sangha O, Wright EA, Roberts WN, et al. Association between clinical factors, socioeconomic status, and organ damage in recent onset systemic lupus erythematosus. J Rheumatol 2000; 27(3): 680-4.
34. Vilar MJ, Bezerra EL, Sato EI. Skin is the most frequently damaged system in recent-onset systemic lupus erythematosus in a tropical region. Clin Rheumatol 2005; 24(4): 377-80.
35. Guarize J, Appenzeller S, Costallat LT. Skin damage occurs early in systemic lupus erythematosus and independently of disease duration in Brazilian patients. Rheumatol Int 2007; 27(5): 483-7.
36. Soares M, Reis L, Papi JA, Cardoso CR. Rate, pattern and factors related to damage in Brazilian systemic lupus erythematosus patients. Lupus 2003; 12(10): 788-94.
37. Noscent JC. SLICC/ACR Damage Index in Afro-Caribbean patients with systemic lupus erythematosus: changes in and relationship to disease activity, corticosteroid therapy, and prognosis. J Rheumatol 1998; 25(4): 654-9.
38. Marx C, Mørgel HP, Büchi S, Stoll T. Are there associations of health status, disease activity and damage in SLE patients?- Results of a study of a cohort of a Swiss specialized outpatient clinic. Psychiatrische Poliklinik, Universitätsspital Zürich 2007; 30(96): 895-9. [German].
39. Sayarlioglu M, Cefle A, Kamali S, Gul A, Inanc M, Ocal L, et al. Characteristics of patients with late onset systemic lupus erythematosus in Turkey. Int J Clin Pract 2005; 59(2): 183-7.
40. Yee CS, Hussein H, Skan J, Bowman S, Situnayake D, Gordon C. Association of damage with autoantibody profile, age, race, sex and disease duration in systemic lupus erythematosus. Rheumatology (Oxford) 2003; 42(2): 276-9.
41. Zonana-Nacach A, Camargo-Coronel A, Yanez P, de Lourdes SM, Jimenez-Balderas FJ, Aceves-Avila J et al. Measurement of damage in 210 Mexican patients with systemic lupus erythematosus: relationship with disease duration. Lupus 1998; 7(2): 119-23.
42. Lilleby V, Flato B, Forre O. Disease duration, hypertension and medication requirements are associated with organ damage in childhood-onset systemic lupus erythematosus. Clin Exp Rheumatol 2005; 23(2): 261-9.
43. Swaak AJ, van den Brink HG, Smeenk RJ, Manger K, Kalden JR, Tosi S, et al. Systemic lupus erythematosus: clinical features in patients with a disease duration of over 10 years, first evaluation. Rheumatology (Oxford) 1999; 38(10): 953-8.
44. Griffiths B, Mosca M, Gordon C. Assessment of patients with systemic lupus erythematosus and the use of lupus disease activity indices. Best Pract Res Clin Rheumatol 2005; 19(5): 685-708.
45. Prasad R, Ibanez D, Gladman D, Urowitz M. Anti-dsDNA and anti-Sm antibodies do not predict damage in systemic lupus erythematosus. Lupus 2006; 15(5): 285-91.
46. To CH, Petri M. Is antibody clustering predictive of clinical subsets and damage in systemic lupus erythematosus? Arthritis Rheum 2005; 52(12): 4003-10.
47. Amigo MC. Prognosis in antiphospholipid syndrome. Rheumatic Disease Clinics of North America 2001; 27(3): 661-9.
48. Brunner HI, Silverman ED, To T, Bombardier C, Feldman BM. Risk factors for damage in childhood-onset systemic lupus erythematosus: cumulative disease activity and medication use predict disease damage. Arthritis Rheum 2002; 46(2): 436-44.
49. Ruiz-Irastorza G, Egebride MV, Martinez-Berriotxoa A, Ugalde J, Aguirre C. Antiphospholipid antibodies predict early damage in patients with systemic lupus erythematosus. Lupus 2004; 13(12): 900-5.

www.SID.ir
50. Freire EA, Maia IO, Nepomuceno JC, Ciconelli RM. Damage index assessment and quality of life in systemic lupus erythematosus patients (with long-term disease) in Northeastern Brazil. Clin Rheumatol 2007; 26(3): 423-8.
کارگاه‌های آموزشی مرکز اطلاعات علمی

مقاله نویسی علوم انسانی

اصول تنظیم قراردادها

آموزش مهارت های کاربردی در تدوین و چاپ مقاله