# Charlson Comorbidity Index Is Related to Organ Damage in Systemic Lupus Erythematosus: Data from KORean lupus Network (KORNET) Registry

Seong-Kyu Kim, Jung-Yoon Choe, and Shin-Seok Lee

*ABSTRACT.* ***Objective.*** The aim of this study was to identify whether comorbidity status is associated with organ damage in patients with systemic lupus erythematosus (SLE).

***Methods.*** A total of 502 patients with SLE enrolled in the KORean lupus Network were consecutively recruited. Data included demographics, age-adjusted Charlson Comorbidity Index (CCIa), disease activity indexes, the Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index (SDI), the Medical Outcomes Study Short Form-36 health survey (SF-36) score, and the Beck Depression Inventory (BDI) score.

***Results.*** Of the total patients, 21.1% (n = 106) experienced organ damage (SDI ≥ 1). Univariate correlation analysis revealed that SDI was not statistically correlated with any clinical variables (correlation coefficient r < 0.3 of all). There were significant differences in the BDI, mental component score of the SF-36, Systemic Lupus Erythematosus Disease Activity Index (SLEDAI), CCIa, C-reactive protein, and mean dose of corticosteroid between non-damage (SDI = 0) and damage (SDI ≥ 1) groups. The presence of damage to at least 1 organ in patients with SLE was found to be closely related with higher CCIa, higher SLEDAI, and mean dose of corticosteroid (OR 1.884, 95% CI 1.372–2.586, p < 0.001; OR 1.114, 95% CI 1.041–1.192, p = 0.002; OR 1.036, 95% CI 1.004–1.068, p = 0.026; respectively) in binary logistic regression analysis.

***Conclusion.*** This study suggests that organ damage as assessed by the SDI in Korean patients with SLE is related to comorbidities together with disease activity and corticosteroid exposure. (First Release March 15 2017; J Rheumatol 2017;44:452–8; doi:10.3899/jrheum.160900)

*Key Indexing Words:*
SYSTEMIC LUPUS ERYTHEMATOSUS COMORBIDITY SLEDAI
SLICC/ACR DAMAGE INDEX CORTICOSTEROID

Systemic lupus erythematosus (SLE) is a multisystem autoimmune disease with a variable spectrum of clinical manifestations and is characterized by fluctuating disease activity and irreversible organ damage[1]. The mortality of patients with SLE has been reduced substantially over the last decades with recent advances in new therapeutic agents and strategies[2,3]. Irreversible damage to affected organs and tissues resulting from both disease activity and therapeutics has been noted to markedly affect health status and mortality in patients with SLE[4,5,6]. The organ damage in patients with SLE gradually accrues during the first 5 years after diagnosis, even with decreasing disease activity[7].

The Systemic Lupus International Collaborating Clinics (SLICC)/American College of Rheumatology (ACR) Damage Index (SDI) is a validated outcome measure for assessing irreversible damage that has developed during the disease process in patients with SLE[8,9]. The SDI has also been recognized as a comprehensive instrument for evaluating the prognosis and longterm effect of SLE. The damage index as assessed by the SDI increases over time and reflects future mortality in patients with early and established SLE[6,10,11]. In addition, several clinical studies examining factors related to the SDI have demonstrated that higher SDI was associated with late onset at the time of diagnosis[12], longer disease duration[13,14], ethnicity[15,16,17], corticosteroid therapy[14,16,18], a higher baseline SLE Disease Activity Index (SLEDAI)[16,19], and comorbidities[20].

To our knowledge, there are no sufficient data on comorbidities related to organ damage in Asian patients with SLE. Here, we identified the relationship between comorbidities

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and organ damage assessed by the SDI in patients registered in a Korean SLE cohort.

## MATERIALS AND METHODS

*Patients*. The KORean lupus Network registry is a prospective, multicenter cohort of patients with SLE recruited from 4 university-based medical centers in 3 metropolitan cities (Daegu, Gwangju, and Seoul) in Korea. The patients in this cohort fulfilled the ACR classification criteria for SLE (1982 revised and 1997 updated) and were recruited between January 2014 and December 2015[21,22]. Patients provided written informed consent at the time of enrollment. The protocol of this study was reviewed and approved by the Institutional Review Board (IRB) of the Daegu Catholic Medical Center (IRB No. CR-14-123-L) and the Chonnam National University Hospital (IRB No. CNUH-2015-250).

*Data collection*. The baseline demographic characteristics included age, sex, disease duration, education duration, smoking status, alcohol consumption, family history of other autoimmune rheumatic diseases such as rheumatoid arthritis (RA) and primary Sjögren syndrome (pSS), marital status, and employment status. These data were obtained by individual interviews with each patient. In addition, at the time of enrollment, these characteristics were measured: height, body weight, waist and hip circumferences, systolic blood pressure, and diastolic blood pressure. Laboratory data were collected at the time of enrollment, such as erythrocyte sediment rate (ESR), C-reactive protein (CRP), anti-dsDNA antibody, complement factor 3, complement factor 4, and CH50.

We assessed whether the patients were treated with steroids such as methylprednisolone and triamcinolone and immunosuppressants including methotrexate, hydroxychloroquine, tacrolimus, azathioprine, and mycophenolate mofetil. All steroids such as methylprednisolone and triamcinolone were reported as the equivalent dose of oral prednisone per day. For the corticosteroids, the mean dose of prednisone per day was described.

For the evaluation of health status, the Becker Depression Inventory (BDI) and the Medical Outcomes Study Short Form-36 health survey (SF-36) were used. Disease activity and damage were measured by a well-trained rheumatologist at each medical center using the SLEDAI score[23] and the SDI[8,9], respectively. We classified the patients into non-damage (SDI = 0) and damage (SDI ≥ 1) groups. The Charlson Comorbidity Index (CCI) score is the sum of the comorbidity scores for each morbidity item and was determined by including the age component (CCIa)[24]. The CCI score can be transformed into a survival/mortality percentage with the following formula:

$$\text{Charlson probability (10-yr survival)} = 0.983^{e(\text{CCI} \times 0.9)}$$

Electronic development of the case report form and data management for our study were performed using iCReaT (internet-based Clinical Research and Trial management system; icreat.nih.go.kr/cdc/webapps/com/hismainweb/jsp/cdc_n2.live), a data management system established by the Centers for Disease Control and Prevention, Ministry of Health and Welfare, Republic of Korea (iCReaT Study No. C140018).

*Statistical analysis*. The data are described as median with interquartile range (IQR) for continuous variables or number (%) for categorical variables. Both Kolmogorov-Smirnov and Shapiro-Wilk analyses were used for the assessment of the normality of the data distribution, which revealed a non-normal distribution. Univariate correlation analysis was first performed to identify the correlation of the SDI with demographic and clinical variables through Spearman correlation method for quantitative variables. The differences in demographic and clinical variables, laboratory variables, SLEDAI, comorbidity index, and corticosteroid between the non-damage (SDI = 0) and damage (SDI ≥ 1) groups were evaluated by the Mann-Whitney U test. Logistic regression analysis was applied to identify the risk of damage (SDI ≥ 1). The result was described as the OR and 95% CI. For the evaluation of statistical significance, a 2-sided significance level of 0.05 was applied. All statistical analyses were performed by IBM SPSS Statistics 19.0 (IBM Corp.).

## RESULTS

*Characteristics of the study population*. The baseline demographic and clinical characteristics of a total of 502 patients with SLE are shown in Table 1. The median age of

*Table 1*. Baseline characteristics of enrolled patients. Values are median (interquartile range) unless otherwise specified.

| Characteristics | Values |
|---|---|
| Age, yrs | 38.0 (31.0–47.0) |
| Disease onset age, yrs | 29.1 (20.4–38.1) |
| Female, n (%) | 469 (93.4) |
| Disease duration, yrs | 7.9 (3.7–14.0) |
| Education duration, yrs | 14.0 (12.0–16.0) |
| SBP, mmHg | 117.0 (110.0–127.0) |
| DBP, mmHg | 71.0 (65.0–79.0) |
| Height, cm | 160.0 (156.0–164.0) |
| Weight, kg | 55 (50.0–60.2) |
| BMI, kg/m$^2$ | 21.4 (19.5–23.6) |
| Waist circumference, cm | 73.0 (67.0–81.0) |
| Hip circumference, cm | 90.0 (85.0–96.0) |
| Marital status, n (%) | |
| Single | 149 (29.7) |
| Married | 314 (62.5) |
| Divorced | 26 (5.2) |
| Bereaved | 13 (2.6) |
| Employment, n (%) | 235 (46.8) |
| Family history of rheumatic diseases, n (%) | 53 (10.6) |
| Alcohol consumption, n (%) | 142 (28.3) |
| Smoking status, n (%) | |
| Never | 447 (89.0) |
| Current | 36 (7.2) |
| Ex-smoker | 19 (3.8) |
| ESR, mm/h | 19.5 (10.0–32.0) |
| CRP, mg/dl | 0.09 (0.06–0.30) |
| Anti-dsDNA positivity, n (%) | 269 (53.7) |
| Complement 3, mg/dl | 79.2 (67.0–95.5) |
| Complement 4, mg/dl | 15.3 (10.4–20.4) |
| CH50, U/ml | 47.7 (37.0–56.7) |
| BDI | 7.0 (3.8–13.0) |
| SF-36 health survey | |
| PCS | 48.7 (42.6–53.8) |
| MCS | 49.6 (40.6–55.9) |
| PGA | 1.0 (0.5–1.0) |
| SLEDAI | 4.0 (2.0–6.0) |
| CCIa | 1.0 (1.0–2.0) |
| Charlson probability, 10-yr survival | 95.9 (90.1–95.9) |
| SDI ≥ 1, n (%) | 106 (21.1) |
| Medications, n (%) | |
| Hydroxychloroquine | 490 (97.6) |
| Methotrexate | 58 (11.6) |
| Corticosteroid | 480 (95.6) |
| Azathioprine | 154 (30.7) |
| Mycophenolate mofetil | 111 (22.1) |
| Tacrolimus | 49 (9.8) |

SBP: systolic blood pressure; DBP: diastolic blood pressure; BMI: body mass index; ESR: erythrocyte sedimentation rate; CRP: C-reactive protein; BDI: Becker Depression Inventory; SF-36: Medical Outcomes Study Short Form-36; PCS: physical component score; MCS: mental component score; PGA: physician's global assessment; SLEDAI: The Systemic Lupus Erythematosus Disease Activity Index; CCIa: age-adjusted Charlson Comorbidity Index; SDI: Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index.

the patients was 38.0 years (IQR 31.0–47.0), and women were 93.4% (n = 469) of the patient population. The median onset age and disease duration were 29.1 years (IQR 20.4–38.1) and 7.9 years (IQR 3.7–14.0), respectively. The median values of the ESR and CRP were 19.5 mm/h (IQR 10.0–32.0) and 0.09 mg/dl (IQR 0.06–0.30), respectively. At the time of enrollment, the BDI score and the SLEDAI score were 7.0 (IQR 3.8–13.0) and 4.0 (IQR 2.0–6.0), respectively. There were 106 patients (21.1%) who were categorized into the damage group (SDI ≥ 1); 76 patients (15.1%) had an SDI score of 1 point, 18 patients (3.6%) had an SDI score of 2 points, 4 patients (1.2%) had an SDI score of 3 points, and 6 patients (1.2%) had an SDI score of 4 points. The median CCIa score was 1.0 (IQR 1.0–2.0). Current medications at the time of enrollment were also described.

*Distribution of comorbid conditions*. Table 2 shows the distribution of each comorbid condition in the CCI. With the exception of the presence of connective tissue disease, solid tumor without metastasis was the most frequently identified condition (n = 15, 3%), followed by cerebrovascular disease (n = 10, 2%) and diabetes mellitus (DM) without end-organ damage (n = 9, 1.8%).

*Correlation of SDI with clinical variables, disease activity, and comorbidities*. Univariate correlation analysis revealed that the SDI score was found to be associated with disease duration (r = –0.092, p = 0.040), education duration (r = –0.097, p = 0.030), body mass index (r = 0.106, p = 0.017), CRP (r = 0.092, p = 0.049), BDI score (r = 0.168, p < 0.001), physical and mental component scores of the SF-36 (r = –0.119, p = 0.007 and r = –0.141, p = 0.002, respectively), SLEDAI score (r = 0.123, p = 0.006), CCIa score (r = 0.273, p < 0.001), and the dose of corticosteroid (r = 0.115, p = 0.012; Table 3). Correlation coefficients of those variables were < 0.3, which indicated statistically weak correlation.

*Identification of determinants for the presence of organ damage*. Table 4 shows a comparison of the clinical variables, disease activity, and organ damage between the non-damage group (SDI = 0) and the damage group (SDI ≥ 1). Values of BDI score, SLEDAI score, CCIa, CRP, and corticosteroid therapy were higher in the damage group than in the non-damage group (p = 0.004, p = 0.002, p = 0.012, p = 0.002, and p < 0.001, respectively). In addition, the mental component score of the SF-36 was significantly different between the 2 groups (p = 0.041).

To identify factors associated with damage (SDI ≥ 1), logistic regression analysis revealed that the presence of organ damage was associated with higher CCIa score (OR 1.884, 95% CI 1.372–2.586, p < 0.001), higher SLEDAI score (OR 1.114, 95% CI 1.041–1.192, p = 0.002), and increasing mean dose of corticosteroid (OR 1.036, 95% CI 1.004–1.068, p = 0.026; Table 5).

*Table 2*. Distribution of Carlson Comorbidity Index scores in enrolled subjects. Values are n (%).

| Weighted Score | Conditions | Values |
|---|---|---|
| 1 | Myocardial infarction | 3 (0.6) |
| | Congestive heart failure | 1 (0.2) |
| | Peripheral vascular disease | 4 (0.8) |
| | Cerebrovascular disease | 10 (2.0) |
| | Dementia | 0 (0.0) |
| | Chronic pulmonary disease | 0 (0.0) |
| | Connective tissue disease | 502 (100.0) |
| | Peptic ulcer disease | 7 (1.4) |
| | Mild liver disease, without portal hypertension | 6 (1.2) |
| | Diabetes mellitus without end-organ damage | 9 (1.8) |
| 2 | Hemiplegia | 3 (0.6) |
| | Moderate or severe renal disease | 6 (1.2) |
| | Diabetes mellitus with end-organ damage | 1 (0.2) |
| | Solid tumor without metastasis, exclude if > 5 yrs from diagnosis | 15 (3.0) |
| | Leukemia | 2 (0.4) |
| | Lymphoma | 0 (0.0) |
| 3 | Moderate or severe liver disease | 5 (1.0) |
| 6 | Metastatic solid tumor | 0 (0.0) |
| | AIDS | 0 (0.0) |

## DISCUSSION

The crucial finding of our study is that comorbidities, disease activity, and corticosteroid therapy were significantly associated with the SDI, a validated instrument developed by

*Table 3*. Correlation of SDI with clinical variables by univariate correlation analysis.

| Characteristics | Univariate Correlation Coefficient | p |
|---|---|---|
| Age, yrs | 0.071 | 0.112 |
| Disease onset age, yrs | 0.016 | 0.713 |
| Disease duration, yrs | –0.092 | 0.040 |
| Education duration, yrs | –0.097 | 0.030 |
| BMI, kg/m$^2$ | 0.106 | 0.017 |
| ESR, mm/h | 0.038 | 0.417 |
| CRP, mg/dl | 0.092 | 0.049 |
| Complement 3, mg/dl | –0.007 | 0.871 |
| Complement 4, mg/dl | 0.000 | 0.992 |
| CH50, U/ml | 0.008 | 0.872 |
| BDI | 0.168 | < 0.001 |
| SF-36 health survey | | |
| PCS | –0.119 | 0.007 |
| MCS | –0.141 | 0.002 |
| PGA | 0.069 | 0.120 |
| SLEDAI | 0.123 | 0.006 |
| CCIa | 0.273 | < 0.001 |
| Corticosteroid, mg/day | 0.115 | 0.012 |

SDI: Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index; BMI: body mass index; ESR: erythrocyte sedimentation rate; CRP: C-reactive protein; BDI: Becker Depression Inventory; SF-36: Medical Outcomes Study Short Form-36; PCS: physical component score; MCS: mental component score; PGA: physician's global assessment; SLEDAI: Systemic Lupus Erythematosus Disease Activity Index; CCIa, age-adjusted Charlson Comorbidity Index.

*Table 4*. Comparison of clinical variables according to SDI scores. Values are median (interquartile range) unless otherwise specified.

| Characteristics | SDI = 0, n = 396 | SDI ≥ 1, n = 106 | p |
|---|---|---|---|
| Age, yrs | 38.5 (31.0–46.8) | 40.5 (33.0–48.0) | 0.127 |
| Disease onset age, yrs | 29.2 (20.4–38.1) | 28.7 (19.5–37.9) | 0.739 |
| Female, n (%) | 374 (94.4) | 95 (89.6) | 0.075 |
| Disease duration, yrs | 7.5 (3.5–13.4) | 9.7 (4.6–14.6) | 0.072 |
| Education duration, yrs | 14.0 (12.0–16.0) | 12.0 (12.0–16.0) | 0.054 |
| Employed, n (%) | 188 (47.5) | 47 (44.3) | 0.566 |
| Family history of rheumatic diseases, n (%) | 43 (10.9) | 10 (9.4) | 0.672 |
| Alcohol consumption, n (%) | 112 (28.3) | 30 (28.3) | 0.997 |
| Smoking status, n (%) | | | 0.182 |
| Never smoker | 357 (90.2) | 90 (84.9) | |
| Current smoker | 27 (6.8) | 9 (8.5) | |
| Ex-smoker | 12 (3.0) | 7 (6.6) | |
| Height, cm | 160.0 (156.0–164.0) | 160.0 (155.0–164.0) | 0.424 |
| Weight, kg | 55.0 (50.0–60.0) | 55.0 (50.0–64.0) | 0.332 |
| BMI, kg/m$^2$ | 21.2 (19.4–23.5) | 22.0 (19.7–24.6) | 0.084 |
| Waist circumference, cm | 73.0 (66.0–80.0) | 74.5 (68.0–84.0) | 0.072 |
| Hip circumference, cm | 90.5 (85.0–96.0) | 90.0 (85.0–96.0) | 0.910 |
| SBP, mmHg | 117.0 (109.0–126.0) | 120.0 (110.0–129.5) | 0.091 |
| DBP, mmHg | 70.0 (65.0–79.0) | 72.0 (65.5–80.0) | 0.542 |
| BDI | 7.0 (3.0–12.0) | 9.0 (5.0–16.0) | 0.004 |
| SF-36 health survey | | | |
| PCS | 49.1 (42.9–53.8) | 47.2 (39.7–53.9) | 0.116 |
| MCS | 50.4 (41.5–56.1) | 47.9 (37.6–55.2) | 0.041 |
| PGA | 1.0 (0.5–1.0) | 1.0 (0.5–1.2) | 0.093 |
| SLEDAI | 2.0 (1.0–4.8) | 4.0 (2.0–8.0) | 0.002 |
| CCIa | 1.0 (1.0–1.8) | 1.0 (1.0–3.0) | 0.012 |
| ESR, mm/h | 20.0 (10.0–31.0) | 19.0 (9.8–36.0) | 0.507 |
| CRP, mg/dl | 0.08 (0.06–0.30) | 0.18 (0.06–0.50) | 0.002 |
| Anti-dsDNA positivity, n (%) | 208 (52.5) | 61 (58.1) | 0.309 |
| Complement 3, mg/dl | 79.3 (67.0–95.1) | 78.2 (65.4–97.6) | 0.746 |
| Complement 4, mg/dl | 15.4 (10.4–20.3) | 14.1 (10.1–21.8) | 0.726 |
| CH50, U/ml | 47.6 (36.9–56.7) | 48.8 (38.2–56.7) | 0.921 |
| Corticosteroid, mg/day | 5.8 (5.0–8.8) | 8.1 (5.0–10.2) | < 0.001 |

SDI: Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index; BMI: body mass index; SBP: systolic blood pressure; DBP: diastolic blood pressure; BDI: Becker Depression Inventory; SF-36: Medical Outcomes Study Short Form-36; PCS: physical component score; MCS: mental component score; PGA: physician's global assessment; SLEDAI: The Systemic Lupus Erythematosus Disease Activity Index; CCIa: age-adjusted Charlson Comorbidity Index; ESR: erythrocyte sedimentation rate; CRP: C-reactive protein.

*Table 5*. Identification of determinants for the presence of disease damage (SDI ≥ 1) by binary logistic regression analysis.

| Characteristics | OR 95% | CI | p |
|---|---|---|---|
| Age, yrs | 0.989 | 0.962–1.017 | 0.454 |
| Male sex | 0.754 | 0.294–1.929 | 0.555 |
| Disease duration, yrs | 1.034 | 0.996–1.073 | 0.081 |
| CRP, mg/dl | 1.020 | 0.852–1.220 | 0.831 |
| BDI | 1.019 | 0.976–1.064 | 0.398 |
| MCS | 0.990 | 0.956–1.025 | 0.562 |
| CCIa | 1.884 | 1.372–2.586 | < 0.001 |
| SLEDAI | 1.114 | 1.041–1.192 | 0.002 |
| Corticosteroid, mg/day | 1.036 | 1.004–1.068 | 0.026 |

SDI: Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index; CRP: C-reactive protein; BDI: Becker Depression Inventory; MCS: mental component score; CCIa: age-adjusted Charlson Comorbidity Index; SLEDAI: The Systemic Lupus Erythematosus Disease Activity Index.

consensus by an international group of rheumatology experts[8,9], in a multicenter SLE cohort in Korea. Organ damage in patients with SLE might be caused by disease progression, therapeutics, or underlying comorbid conditions. Especially, data from cohorts with longterm followup periods have shown that comorbidities at the time of diagnosis were associated with decreased survival in patients with SLE[20].

Over the last several decades, earlier diagnosis, improved disease recognition, and emerging new therapeutics have significantly benefited mortality and progression in SLE[1,2,3]. However, the mortality rates of patients with SLE still remain more than 3× greater than those of the general population, which is likely because of the irreversible organ damage[4,25]. The need to predict disease damage or mortality has increased in the clinical field of SLE. The SDI is currently used for the assessment of permanent and irreversible organ damage in patients with SLE[8,9]. In the Lupus in Minority:

NAture vs Nurture (LUMINA) cohort, a higher SDI score at the time of enrollment was associated with early mortality within 5 years of diagnosis, suggesting that organ damage was already present in some patients[16]. In addition, the SDI has been shown to increase over time in patients with SLE, although this is not always the case[14]. Overall, the SDI effectively reflects current and future organ damage in SLE.

Many investigators have tried to identify factors related to the development or progression of damage based on the SDI. Some studies have focused on ethnic variations as a crucial determinant of organ damage in SLE. The LUMINA study assessed differences in damage accrual among 3 ethnic groups and found that Hispanics with higher SDI score at the last visit were more susceptible to organ damage compared with African Americans and whites[16]. Another study reported that Chinese patients with SLE were more likely to develop major organ involvement over the course of the disease than were whites, ultimately resulting in increased mortality[17]. However, in an analysis of factors associated with the development of new damage (transition from SDI 0 to ≥ 1) and progression of damage (transition from SDI ≥ 1 to a higher score) in 1722 patients with SLE from the SLICC Inception Cohort, Bruce, *et al* demonstrated that ethnicity, with the exception of African American ethnicity, did not influence the SDI in patients with SLE[6]. Interestingly, Asian ethnicity, including Korean ethnicity, showed a protective effect on the development of new damage in patients with SLE. In our study, even though the median disease duration was 7.9 years, only 21.1% of patients showed accrual of organ damage (Table 1). This finding is not consistent with data from earlier studies suggesting that about 50% of patients with organ damage develop it within 5 years of diagnosis[16,26]. There are several reasons why the proportion of patients with organ damage in our study was lower than that reported for other ethnic groups, including whites, African Americans, and Hispanics. First, earlier diagnosis and the emergence of novel therapeutics through more advanced understanding of the pathogenesis of SLE have led to decreases in disease- and treatment-related injuries. Second, it was hypothesized that Asian ethnicity might be protective against the occurrence of organ involvement and mortality in SLE.

Several studies have reported on the effects of therapeutics, including corticosteroids, on SLE-related organ damage. The use of corticosteroids is an important therapy for controlling disease activity in SLE. However, it is also recognized to be closely associated with the development of osteoporosis and DM. In the Hopkins Lupus Cohort study, patients with SLE exposed to cumulative and high-dose prednisone showed an increased risk of morbidity related to permanent organ damage[18]. In an inception cohort study, Gladman, *et al* identified that a higher proportion of organ damage could be attributed to corticosteroid exposure during both the early and late followup period[14]. In particular, 58% of the damage accrual occurred within 1 year after diagnosis, including both definite (e.g., cataract) and possible (e.g., diabetes) corticosteroid-related organ system involvement. In the multiethnic LUMINA cohort of patients with SLE with disease duration ≤ 5 years, the maximum dose of corticosteroid at the time of enrollment was an independent predictor of the SDI at the last visit[16]. In the logistic regression analysis of our study, higher daily mean dose of corticosteroid therapy significantly increased the risk of organ damage (OR 1.036, 95% CI 1.004–1.068), a finding consistent with data from previous studies[14,18]. In addition, the effects of different characteristics of corticosteroid exposure, such as maximum dose, cumulative dose, and duration of exposure, on SLE-related damage remain unclear.

The CCI is a well-established and validated tool to evaluate comorbidities and was first developed to predict 1-year patient mortality using clinical comorbidities obtained from hospital medical review[24]. The comorbidity index has been applied to assess the mortality or burden of illness in a variety of rheumatic diseases such RA[27], pSS[28], and SLE[20]. One study demonstrated that the CCI was closely associated with decreased survival in 2 independent prospective Sweden SLE cohorts, the Montreal (HR 1.57, 95% CI 1.18–2.09) and Lund (HR 1.35, 95% CI 1.13–1.60) cohorts[20]. However, data on the association between the CCI and disease damage has not been studied in an Asian SLE population. Here, we identified a significant relationship between the CCI and organ damage as assessed by SDI, revealing that the development of organ damage was largely related to the CCI score (OR 1.884 per unit increase in the CCI, 95% CI 1.372–2.586). A correlation coefficient of the CCIa in univariate correlation analysis was shown to be < 0.3 (r = 0.273), indicating weak correlation between the SDI and CCIa in patients with SLE. This suggests, in part, an interaction between current comorbidities and organ damage in patients with SLE.

The CCI score of our study is relatively lower than that of the Western population published by Jönsen, *et al*[20]. This lower comorbidity could be explained by multiple factors. First, in a study for the effect of the CCI on longterm survival outcome in 336 Korean men with prostate cancer after radical prostatectomy, the mean CCI was shown to be 0.28 (0–4), and only 70 patients (20.8%) showed more than 1 point of the CCI[29]. Another study reported that about 50% of Korean elderly patients with cancer receiving chemotherapy had a CCI score of 0[30]. The authors excluded corresponding in the assessment of the CCI. These might indicate that the Korean population had a lower comorbidity. Second, the median age of the study population in a previous study[20] was older than those in our study. Therefore, their risk of comorbidity was higher than in our study population.

Becker-Merok and Nossent demonstrated that weighted average SLEDAI > 3 was the only independent predictor of development of severe damage (SDI ≥ 3; HR 2.34, 95% CI 1.1–4.9), in addition to age > 40 years at diagnosis[19]. Another

study showed significant positive correlations between the SDI at last visit and the mean and maximal SLEDAI scores ($p = 0.05$ and $p < 0.001$, respectively)[31]. Similarly, we also observed that both the SDI score and the presence of damage (SDI ≥ 1) were significantly related to the SLEDAI score. This suggests that organ damage in the early and late phases of the disease might be partially responsible for the inflammatory responses.

There are some limitations to the interpretation of our findings. First, cross-sectional analysis cannot determine the definite causal relationship between factors such as the SDI, SLEDAI, and CCIa, although the SDI was shown to be related with comorbid conditions, disease activity, and corticosteroid use in our study. Second, our study did not include SLE-specific health-related quality-of-life measures such as the SLE-specific Quality of Life (SLEQOL) questionnaire and SLE Quality of Life questionnaire, although SF-36 has been used at clinical studies assessing the quality of life in patients with SLE. Third, although our cohort included specific laboratory biomarkers of organ damage and disease activity such as anti-Sm antibody and urinalysis, quantitative analysis could not be sufficiently performed because of missing data and different normal ranges for each marker. To overcome these limitations, followup data on the changes in the SDI and biomarkers over time should be assessed in addition to SLEQOL measurements. Fourth, the contents or items of the CCI and SDI may be overlapped, such as renal disease and cerebrovascular/peripheral vascular diseases. Therefore, it is somewhat possible to lead to bias to explain the effect of CCIa on SDI in patients with SLE.

Our study showed that the SDI is closely related to current comorbidities, together with corticosteroid therapy and SLEDAI of disease activity in a Korean SLE cohort, which implicates medical therapeutics, disease activity, and underlying comorbid conditions as contributing factors to the development of organ damage in SLE. The involvement of these factors in predicting organ damage and mortality should be confirmed in future prospective studies.

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