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ORIGINAL RESEARCH

Number of Attending Physicians and Accumulated Organ Damage in Patients with Systemic Lupus Erythematosus: LUNA Registry Cross-Sectional Study

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ABSTRACT

Introduction: Patients with systemic lupus erythematosus (SLE) frequently change attending physicians. The number of changes in attending physicians is related to the accumulated organ damage in patients with diabetes mellitus and inflammatory bowel disease, although similar results are not known for patients with SLE. This study investigated whether the number of attending physicians after the onset of SLE is associated with organ damage.

Methods: Patients with SLE were enrolled in a multicenter registry of 14 institutions (the Lupus Registry of Nationwide Institutions). Patients with a disease duration of 6 months to 10 years were included. Exposure was defined as the number of attending physicians. The primary outcome was the Systemic Lupus International Collaborating Clinics/American

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College of Rheumatology damage index (SDI). The secondary outcomes were corticosteroid- and non-corticosteroid-related damage. Multiple logistic regression analysis was used to estimate the association between the number of attending physicians and SDI, adjusting for potential confounders, including age, sex, disease duration, number of hospitalizations due to SLE, disease activity at diagnosis, and emotional health.

Results: Of the 702 patients, 86.5% were women (median age 46 years, interquartile range 35–58). The disease duration was 7.3 years (4.3–11.3), the number of hospitalizations due to SLE was 1 (1–3), the number of attending physicians was 3 (2–4), and SDI was 0 points (0–1). The number of attending physicians was significantly associated with SDI [odds ratio (OR) 1.14, 95% confidence interval (CI) 1.03–1.26]. In the secondary outcome, the number of attending physicians was significantly associated with corticosteroid-related damage (OR 1.22, 95% CI 1.09–1.38). The number of attending physicians was not significantly associated with non-corticosteroid-related damage (OR 1.08, 95% CI 0.99–1.19).

Conclusions: This study showed that SDI could increase as the number of attending physicians increases. The impact of changing attending physicians warrants greater attention for SLE and other diseases.

Keywords: Attending physicians; Organ damage; Systemic lupus erythematosus; Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index

Key Summary Points

Why carry out this study?

Patients with chronic diseases such as systemic lupus erythematosus (SLE) require long-term hospital visits and are treated by many attending physicians.

We hypothesized that, in patients with SLE, a higher number of attending physicians is associated with an accumulation of organ damage, as inadequate data transfer on handover and missing changes in disease activity can lead to organ damage.

What was learned from the study?

The number of attending physicians was significantly associated with the Systemic Lupus International Collaborating Clinics/American College of Rheumatology damage index (SDI) (odds ratio 1.14, 95% confidence interval 1.03–1.26, $P = 0.01$).

This study showed that SDI could increase as the number of attending physicians increases.

Changing attending physicians is an issue that requires more attention for SLE and other diseases.

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INTRODUCTION

Systemic lupus erythematosus (SLE) is a chronic systemic autoimmune disease characterized by persistent inflammation in several organs, including the skin, joints, kidneys, lungs, blood, and central nervous system. The highest incidence is observed in women aged 20–40 years. Repeated relapses, high disease activity, and the use of immunosuppressants, such as glucocorticoids, cause organ damage and worsen the patient's quality of life [1]. Organ damage can predict mortality in SLE [2]. Therefore, prevention of damage accumulation is crucial for the practice of SLE [3].

Patients with chronic diseases such as SLE require long-term hospital visits. Inevitably, they are treated by many attending physicians. Reasons for changing attending physicians vary. Causes of changes in primary care physicians have been reported in Spain and Denmark [4, 5]. Reasons for changing attending physicians include deterioration of the doctor–patient relationship, discrepancies in outpatient schedules, long waiting times, short consultation times, and insufficient skills of attending physicians.

There have been some reports on the association between change in attending physicians and prognosis. Excessive changes in attending physicians, known as "doctor shopping," have been identified as a potential health hazard for patients [6]. A report of patients with diabetes mellitus in Taiwan showed a correlation between the number of changes in attending physicians and comorbidity assessed by the Charlson comorbidity index [6]. A report from Australia found that for patients with inflammatory bowel disease, an autoimmune disease similar to SLE, changing attending physicians was associated with a greater likelihood of having Crohn's disease, current active disease, a history of bowel resection, and recent hospitalization [odds ratio (OR) 2.6, 95% confidence interval (CI) (1.3–5.4), 2.2 (1.0–4.7), 5.56 (1.92–16.67), and 2.0 (1.3–3.0), $P < 0.05$ respectively] [7]. In summary, patients who change their attending physicians for various reasons tend to have increased disease activity and severity. It is not known how the number of changes in attending physicians is related to accumulated organ damage in patients with SLE.

We hypothesized that a higher number of attending physicians in patients with SLE is associated with an accumulation of organ damage, as inadequate data transfer on handover and missing changes in disease activity can lead to organ damage. Therefore, this study aimed to evaluate the association between the number of attending physicians and the accumulation of organ damage in patients with SLE.

METHODS

Study Design and Setting

This cross-sectional study used data from a multicenter cohort (Lupus Registry of Nationwide Institutions, LUNA) established in 2016 to examine clinical manifestations, social background, and outcomes in patients with SLE from 15 institutions across Japan, ranging from the Tohoku region to the Kyushu region. LUNA provides data on patients aged $\geq$ 20 years diagnosed with SLE according to the revised 1997 American College of Rheumatology (ACR) classification criteria [8]. Patients deemed ineligible by the investigator and those who found it difficult to complete the questionnaire, such as patients with dementia, were excluded. Approximately 1700 cases (2.5% of Japanese patients with SLE) have been registered in LUNA.

Data Collection

This analysis used data obtained from medical records from July 2019 to March 2021. The data included laboratory tests, medications, activity scores, and comorbidities. Quality of life and comorbidity were collected from self-administered questionnaires. Data were collected annually for each patient through the LUNA. Although multiple surveys were conducted during the course of the study for a patient, only the most recent data were included.

Patients

Patients who provided the number of attending physicians enrolled in LUNA were eligible to participate in this study. Patients with a missing Systemic Lupus International Collaborating Clinics/ACR damage index (SDI) were excluded from the study. Patients with a disease duration of less than 6 months were excluded, since the primary outcome, SDI, required a minimum of 6 months for irreversible manifestation. Patients with more than 10 years of disease were also excluded because of recall bias. The disease duration was evaluated using patient questionnaires, which may have differed from the true disease duration.

Exposures

Exposure was defined as the number of attending physicians. The patients provided this item using a questionnaire. The questionnaire item was "Is your SLE disease duration less than 10 years? If yes, please answer the following questions. How many attending physicians have treated you in an outpatient visit since you were diagnosed with SLE? Please include the attending physician at the hospital prior to transfer."

Outcomes

The primary outcome was SDI, which measures cumulative damage since the onset of SLE. SDI reflects irreversible damage lasting more than 6 months in various systems [9]. The total score is 47 points. We divided SDI into two categories: 0 and 1 or more points, in accordance with a previous study [10]. The secondary outcomes were corticosteroid-related damage and non-corticosteroid-related damage. Corticosteroid-related damage consists of ocular cataract, osteoporosis with fracture or vertebral collapse, avascular necrosis, or diabetes [9, 11]. Non-corticosteroid-related damage consists of SDI items other than corticosteroid-related damage. We also divided both types of damage into two categories: 0 and 1 or more points, in accordance with a previous study [10].

Confounders

The following factors were used as potential confounders: age, sex, number of hospitalizations due to SLE, systemic lupus erythematosus disease activity index (SLEDAI) at diagnosis, disease duration, and emotional health. Emotional health is one of the domains of Lupus PRO, a disease-specific quality of life measurement [12, 13]. These variables were selected based on those previously reported for SDI and changes in attending physicians [1, 4, 5, 7]. Furthermore, a directed acyclic graph was constructed to show the relationships between these variables (Supplementary Fig. S1).

Statistical Analysis

Descriptive statistics are presented as median [interquartile range (IQR)] for continuous variables and as absolute numbers (percentage) for categorical variables. Subsequently, we performed multiple logistic regression analysis to assess the associations between exposure and outcome variables (primary and secondary) to adjust for the potential confounders mentioned above. We also performed a sensitivity analysis that excluded patients with a large number of attending physicians (30 or 50). We performed multiple imputations on the assumption of missing values at random to deal with the missing values of potential confounders. The results of 100 imputed datasets were averaged, and the standard error was adjusted to account for variability within and between imputations. The estimates and their standard errors were combined using Rubin's rules. A two-sided p value of less than 0.05 was considered to indicate a statistically significant difference. All statistical analyses were conducted using STATA 16 software (StataCorp).

Ethics

The study was approved by the Ethics Committee of the Showa University School of Medicine (authorization number 22–082-A) and the institutional review boards or ethics committees of each participating hospital. Written

informed consent was obtained from all patients. Before analysis, patient data were anonymized and deidentified. The procedures for this study were conducted in accordance with the Declaration of Helsinki and the Ethics Guidelines for Medical and Health Research Involving Human Subjects in Japan. Ethics committee names and reference numbers are listed in Supplementary Table S3.

RESULTS

Patient Flow Chart

A total of 724 patients from 14 institutions who provided the number of attending physicians were enrolled. There were no missing data for SDI. Of those, 22 patients with a disease duration of less than 6 months were excluded. Ultimately, 702 patients were included in this study.

Patient Characteristics

The median age of the 702 patients was 46 years (IQR 35–58), and 86.5% were women. The median SLEDAI score was 11 (IQR 7–18). The median disease duration was 7.3 years (4.3–11.3), and the median number of hospitalizations for SLE was 1 (IQR 1–3). Many patients had low disease activity; the SLEDAI at the investigation median was 3 (IQR 1–6). Furthermore, 54.3% of the patients met the definition of a lupus low disease activity state (LLDAS) [15]. The immunosuppressants used the most frequently were tacrolimus (35.2%) and mycophenolate mofetil (24.5%). Furthermore, 54.1% of the patients took antimalarials. Table 1 presents the characteristics of the patients.

Distribution of the Number of Attending Physicians

The median number of attending physicians was three (IQR 2–4). Figure 1 shows the number of attending physicians. The maximum number of attending physicians was 50.

Distribution of SDI

The median SDI score was 0 [IQR 0–1]. Corticosteroid-related damage was scored as 0 [IQR 0–0]. Non-corticosteroid-related damage was also observed at 0 points (IQR 0–1). Figure 1 shows the number of attending physicians. Figure 2 shows the number of attending physicians and SDI. A total of 372 patients (53.0%) had an SDI score of 0, and 330 patients (47.0%) had an SDI score of 1 or more.

Association Between the Number of Attending Physicians and SDI Scores

In the primary outcome, the number of attending physicians was significantly associated with SDI (OR 1.14, 95% CI 1.03–1.26, $P = 0.01$) (Table 2). In the secondary outcome, the number of attending physicians was significantly associated with corticosteroid-related damage (OR 1.22, 95% CI 1.09–1.38, $P = 0.001$) (Supplementary Table S1). The number of attending physicians was not significantly associated with non-corticosteroid-related damage (OR 1.08, 95% CI 0.99–1.19, $P = 0.08$) (Supplementary Table S2). We also performed a sensitivity analysis that excluded patients with a large number of attending physicians (30 or 50). In the primary outcome, the number of attending physicians was significantly associated with SDI (OR 1.14, 95% CI 1.03–1.26, $P = 0.01$). In the secondary outcome, the number of attending physicians was significantly associated with corticosteroid-related damage (OR 1.21, 95% CI 1.07–1.37, $P = 0.002$). The number of attending physicians was not significantly associated with corticosteroid-related damage (OR 1.08, 95% CI 0.98–1.18, $P = 0.11$). Sensitivity analysis revealed that the results were robust.

DISCUSSION

No previous studies have reported the number of attending physicians and the accumulation of organ damage in patients with SLE. This study determined the association between the

Table 1 Characteristics of the patients

	***n* = 702**	**Missing (*n*)**
Demographic characteristics		
Age median [IQR]	46 (35–58)	4
Female, *n* (%)	613 (86.5)	0
Clinical characteristics		
Number of attending physicians, median [IQR]	3 (2–4])	0
Number of hospitalizations due to SLE, median [IQR]	1 (1–3)	14
Disease duration (years), median [IQR]	7.3 (4.3–11.3)	12
Manifestation at diagnosis (SLEDAI)		
Neurological	16(9.4)	531
Vasculitis	3(1.8)	531
Musculoskeletal	66(38.6)	531
Renal	64(37.4)	531
Skin	92(54.4)	531
Hematological	90(19.1)	531
SLEDAI median [IQR] at investigation	3 (1–6)	11
SLEDAI median [IQR] at diagnosis	11 (7–18)	532
LLDAS, *n* (%)	381 (54.3)	0
Emotional health (Lupus PRO), median [IQR]	33 (25–42)	113
Total SDI score, median [IQR]	0 (0–1)	0
Corticosteroid-related damage, median [IQR]	0 (0–0)	0
Non-corticosteroid-related damage, median [IQR]	0 (0–1)	0
Medications		
PSL, *n* (%)	454 (64.7)	173
PSL dose (mg/day), median [IQR]	5 (2–7)	3
Immunosuppressants	460 (65.5)	3
Biological agents	61 (8.7)	3
Antimalarials, *n* (%)	380 (54.1)	5

SLE systemic lupus erythematosus, *IQR* interquartile range, *SLEDAI* Systemic Lupus Erythematosus Disease Activity Index [14], *PGA* Physician Global Assessment of Disease Activity, *LLDAS* lupus low-disease activity state [15], *PSL* prednisolone, *SDI* Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index, *PRO* patient-reported outcome

Corticosteroid-related damage: ocular cataract, osteoporosis with fracture or vertebral collapse, aortic necrosis, or diabetes

Immunosuppressants include cyclophosphamide, mycophenolate mofetil, mizoribine, methotrexate, azathioprine, tacrolimus, and cyclosporin

Biological agents include rituximab and belimumab

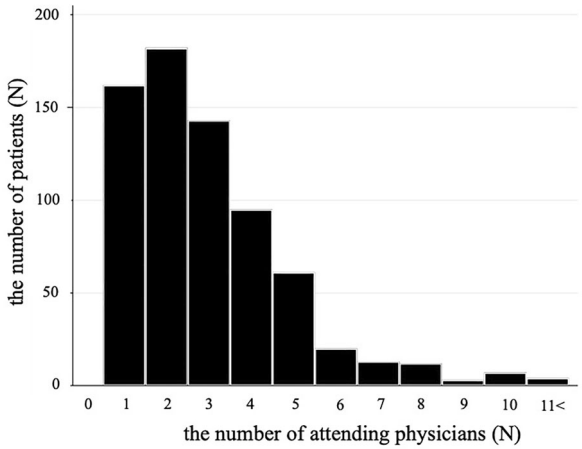

Fig. 1 Number of attending physicians. Four patients each had 15, 20, 30, and 50 attending physicians, respectively

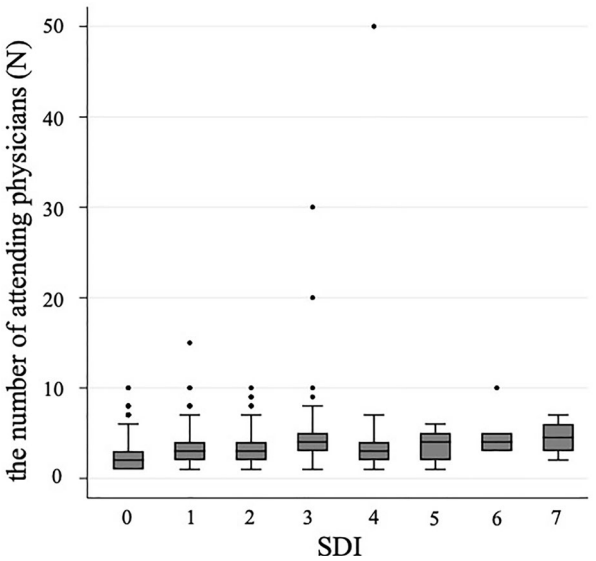

Fig. 2 Association between the number of attending physicians and accumulated organ damage. *SDI* Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index

number of attending physicians and the cumulative organ damage in patients with SLE.

There are several possible reasons for this phenomenon. First, there may be inadequate handovers at the time of change in attending physicians. Although not for SLE, some reports have pointed out problems with inaccurate and illegible handover information provided by attending physicians [16]. The quality of the handover of the anesthesiologist in patients who have undergone surgery has been reported to be related to the incidence of postoperative complications [17]. In SLE patients, if handover is not sufficient, a change in attending physicians can cause problems when new attending physicians miss minor symptoms suggestive of relapse or continue inappropriate steroid reduction. Furthermore, a change in attending physicians can cause a continued prescription of steroids without a dosage reduction because it is difficult to have a treatment plan that considers the patient's long-term prognosis. In fact, in our study, the number of attending physicians was also significantly associated with glucocorticoid-related damage (OR 1.22, 95% CI 1.09–1.38, $P = 0.001$), and the non-corticosteroid-related damage tended to increase as the number of attending physicians increased (OR 1.08, 95% CI 0.99–1.19). Second, patients may not develop a trusting relationship with their new attending physicians. This can result in increased emotional stress and worsened adherence, which can further worsen the activity of lupus disease. Trust in attending physicians has been reported to be associated with disease outcomes, supporting this mechanism of action [18, 19].

This study has several strengths. First, we investigated the associations between institutions across multiple sites and regions. The rules and reasons for changing attending physicians may differ between institutions. This study was able to reduce selection bias. Second, the confounding adjustment was based not only on the disease duration but also on emotional health and the number of hospitalizations due to SLE. These factors are strongly associated with changes in attending physicians. Emotional health is correlated with SDI through adherence to SLE medications, and the number of hospitalizations due to SLE is correlated with SDI. Therefore, the present study strengthened the internal validity by making appropriate adjustments.

This study has several clinical implications for rheumatologists and researchers. First, this study suggests that frequent changes in attending physicians should be avoided. When

Table 2 Association between the number of attending physicians and SDI scores

	Adjusted OR	95% CI	*P* value
Number of attending physicians	1.14	1.03–1.26	0.01
Age	1.04	1.02–1.05	0.00
Female	0.58	0.35–0.96	0.03
Disease duration	1.05	1.03–1.08	0.00
SLEDAI at diagnosis	1.02	0.96–1.07	0.39
Number of hospitalizations due to SLE	1.00	1.00–1.00	0.99
Emotional health	1.08	0.75–1.55	0.68

OR odds ratio, *CI* confidence interval, *SLE* systemic lupus erythematosus, *SDI* Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index, *SLEDAI* Systemic Lupus Erythematosus Disease Activity Index

a change in attending physicians is inevitable, it is important to create a sufficient transfer so that there is no disadvantage to the patient. Although not in the field of collagen disease, handover tools have been actively developed, and it may be useful to use such tools when changing attending physicians [20, 21]. Second, in the field of collagen disease, there has been no discussion on the impact of changing attending physicians, and we believe that this study is important for drawing attention to this issue.

This study has several limitations. First, causality can be reversed. Because the study did not measure when the attending physicians were changed or the damage progressed, the progression of the damage could have reduced patient satisfaction and made them more likely to change attending physicians, or hospitalization could have triggered a change in the attending physicians. A prospective longitudinal study that measures patient satisfaction at the time of change in attending physicians should be conducted for further investigation. Second, there was an essential unmeasured confounding factor (Supplementary Fig. S1). Data on the number of years of clinical experience (attending physician competence) of the attending physicians at the time of change in attending physicians and patient adherence were not available and could not be adjusted. The inability to adequately adjust for both factors led to an overestimation, which may have changed the results of this study. Bias due to unmeasured patient adherence was partially addressed by adjusting for emotional health. Third, there was recall bias. Patients who had been ill for a prolonged period of time and whose SDI tended to increase may have forgotten their past attending physicians and may have rated them lower. Checking for consistency across different survey responses for each patient was challenging because attending physicians often change throughout the year. This study addressed these biases by limiting the analysis to patients who had been ill for less than 10 years. Fourth, we could not distinguish whether the patient received care from a rheumatologist only or from a rheumatologist along with a general practitioner, since a patient may receive care from both a rheumatologist and a general practitioner. In the latter case, the patient may have reported the number of attending physicians as two, and so the progression of damage may have been caused by poor communication with the general practitioner.

CONCLUSIONS

This study showed that SDI could increase as the number of attending physicians increases. Changing attending physicians is an issue that

requires more attention for SLE and other diseases.

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Compliance with Ethics Guidelines. The study was approved by the Ethics Committee of the Showa University School of Medicine (authorization number 22–082-A) and the institutional review boards or ethics committees of each participating hospital. Written informed consent was obtained from all patients. Before analysis, patient data were anonymized and deidentified. The procedures for this study were conducted in accordance with the Declaration of Helsinki and the Ethics Guidelines for Medical and Health Research Involving Human Subjects in Japan. Ethics committee names and reference numbers are listed in Supplementary Table S3.

Prior Presentation. The authors confirm that these data have not been previously presented or publicly shared.

Data Availability. The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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