Quality of life in Japanese female patients with systemic lupus erythematosus: Evaluation using the Short Form 36 Health Survey

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Abstract

Objective. Aspects of health-related quality of life (HRQoL) are important for assessing perceived health status and treatment burden. We evaluated HRQoL using Short Form 36 Health Survey (SF-36) and factors associated with HRQoL.

Methods. We collected basic and lifestyle-related, clinical, and treatment characteristics among 119 female Japanese patients with systemic lupus erythematosus (SLE). Odds ratios (ORs) and their 95% confidence intervals were assessed for associations between HRQoL and selected factors.

Results. Irregularity of sleep was significantly associated with risk of lower role physical (RP) (OR = 8.27), vitality (VT) (OR = 8.45), and role emotional (OR = 10.7) domains. Compared with clerical work, non-clerical work was significantly associated with risk of lower RP (OR = 7.39), and unemployment was significantly associated with risk of lower VT (OR = 41.0). Daily soybean intake was associated with improved General Health or GH (OR = 0.17). Compared with Systemic Lupus Collaborative Clinics Damage Index (SDI) = 0, SDI > 2 was associated with risk of lower PF (OR = 7.88), RP (OR = 4.29), and bodily pain (OR = 3.06) domains.

Conclusion. Reduced HRQoL was observed in our SLE patients. Interventions addressing sleep and work disturbances, as well as daily soybean consumption, could alter the HRQoL of SLE patients.

Introduction

Systemic lupus erythematosus (SLE) is an autoimmune disease in which autoantibodies against a large variety of self-antigens are formed. SLE affects many organs such as the skin, joints, kidney, heart, lungs, and brain. Therefore, clinical symptoms are broad and variable in severity. The cause and cure of this chronic lifelong disease with remissions and exacerbations remain unknown. In the clinical management and research of SLE patients, objective parameters are used to describe disease activity and treatment efficacy. In addition, aspects of subjective quality of life (QOL) are important to determine perceived health status and treatment burden [1]. The disease has a life-long trajectory characterized by day-to-day fatigue, sudden flare-ups, repeated life-threatening infections, mild-to-severe kidney impairments, strokes, and sometimes permanent disability. SLE primarily affects women in their reproductive years, that is, 9 of 10 SLE patients are female [2].

WHO defined QOL as individuals’ perceptions of their position in life in the context of culture and value systems within which they live, as well as the relation to their goals, expectations, standards, and concerns [3]. QOL is a broad-ranging concept that is affected in a complex way by a person’s physical health, psychological state, personal beliefs, and social relationships, as well as their relationship with salient features of their environment. Measures of QOL include the effects of disease or its treatment from the patient’s perspective, and determine the need for social, emotional, and physical support during illness [4].

In recent years, the impact of chronic illnesses, including SLE, on QOL has become an increasing concern to society and health care professionals. Patients with a chronic or critical illness have concerns not only about their chances for survival but also about the quality of that survival [2]. Several Caucasian and Asian studies have demonstrated that the health-related QoL (HRQoL) of adult and adolescent patients with SLE is significantly impaired compared with that of healthy controls [4–9]. In Japan, there have been only 2 reports on the evaluation of QOL in SLE patients using a questionnaire other than Short Form 36 Health Survey (SF-36) (the original questionnaire including the content of SF-36 [10] and the Japanese version of the Skindex-29 [11]). However, whether HRQoL is associated with disease activity and damage scores is controversial because inconsistent results have been reported across different cross-sectional and prospective studies [4–8]. In addition, age, disease duration, renal disorder, fibromyalgia (FM), stress, anxiety, fatigue, and depression have been reported as associated factors of HRQoL in SLE patients [6,12–15].

Keywords

Female, Japanese, Quality of life, SF-36, Systemic lupus erythematosus

History

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The purpose of this study was to investigate the impact of SLE on the HRQoL in terms of physical, psychological, and social well-being, and to identify those domains of the HRQoL most affected by SLE. To evaluate HRQoL and, if possible, to identify risk or protective lifestyle factors associated with domains of HRQoL in female Japanese patients with SLE, we evaluated HRQoL using the SF-36 questionnaire in 119 female Japanese patients with SLE and collected demographic, lifestyle, clinical factors, and treatment data.

Patients and methods

Patients

One hundred nineteen consecutive female patients with SLE who regularly attended the rheumatology clinic at the Kyushu University Hospital (Fukuoka, Japan) were included in this study. All patients fulfilled the 1997 ACR revised criteria for the classification of SLE [16] and were informed of the objectives of the study. Prior to study inclusion, all participants provided written informed consent. This study was approved by the ethical review board of the Kyushu University Hospital, and all study-related procedures were designed and conducted in accordance with the tenets of the Declaration of Helsinki.

Data collection and measurement

All measurements were performed between November 2006 and November 2011. Data were collected by questionnaire survey. Demographic and lifestyle data were obtained regarding age, age at diagnosis, body mass index (BMI), menstrual cycle (presence of regular menstruation and menopause) and obstetric history (number of deliveries), marital status and state of family (number of persons living together), working status (present status, history), occupational type, and educational background. In addition, we inquired about smoking; alcohol intake; exercise; going out; intake of milk, dairy products, fish, small fish, eggs, soybean products, onion, garlic, leek, green vegetable, fruits, fast foods, coffee, tea (black tea, Japanese green tea, or oolong tea); cola; and sleeping status (sleeping schedule, regularity, and sufficiency).

Clinical data such as disease duration, current or ever history of the presence of ACR revised criteria, and current or ever history of any complication (infection, hypertension, thrombosis, femoral neck necrosis, operation of femoral neck, vertebral fracture, osteoporosis, diabetes, hyperlipidemia, gastric ulcer, malignant cancer, interstitial pneumonia, depression, schizophrenia, and other collagen diseases such as Sjogren’s syndrome, rheumatoid arthritis, systemic sclerosis, chronic thyroiditis, and antiphospholipid antibody syndrome). The ACR revised criteria include malar rash; discoid rash; photosensitivity; oral ulcer; arthritis; serositis; renal disorder; neurological disorder; hematological disorders such as leukopenia, hemolytic anemia, thrombopenia, and lymphopenia; and immunological disorders such as raised anti-native DNA antibody levels, positive anti-Sm antibody, positive antinuclear antibody, positive lupus anticoagulant, and positive serologic test for syphilis or STS. Laboratory data were obtained, including complete blood count or CBC, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), albumin, serum creatinine, blood urea nitrogen (BUN), glucose, total cholesterol, triglyceride, anti-nuclear antibody (ANA), double-stranded DNA antibodies, immunoglobulins, and complement components. Disease activity was scored using the Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) [17] by the attending physicians. Disease damage was also similarly scored using the Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index or SLICC/ACR-DI [18]. A history of corticosteroids (CS) and other immunosuppressant use was also noted. We investigated past and current use of CS, duration of use in years, maximal dosage taken orally, current prednisone use, and past intravenous (IV) methylprednisolone use. In addition, we investigated past and current use of cyclosporine, methotrexate, cyclophosphamide, azathioprine, mizoribine, mycophenolate mofetil or MMF, tacrolimus, rituximab, and IV administration of cyclophosphamide. We also inquired about current use of nonsteroidal anti-inflammatory drugs (NSAIDs), major or minor tranquillizers, antipsychotics, warfarin, bisphosphonates (alendronates or risedronates), drugs prescribed in other hospitals, and supplements.

QOL measurement

The QOL measurement was made using the SF-36. It is a standard questionnaire assessing QOL, both in the general healthy population, as well as groups of sick people. We used the SF-36 v2 Japanese version [19]. It consists of 36 questions grouped into 8 domains measuring different aspects of QOL [Physical Functioning (PF), Role Physical (RP), Bodily Pain (BP), General Health (GH), Vitality (VT), Social Functioning (SF), Role Emotional (RE), and Mental Health (MH)]. The obtained results are converted into a scale from 0 to 100, where 0 indicates the lowest quality of life and 100 indicates the highest one. The obtained data are further converted into a normalized scale using norm-based scoring (NBS), where the norm is 50. The SF-36 also allows us to summarize the results into two summary measures: a physical component summary (PCS) and a mental component summary (MCS).

Statistical analysis

We first examined all variables having an association with each value of the 8 domains comprising the SF-36 using univariate tests. The analysis of categorical (dichotomous by median value of each domain) variables included frequency distributions, proportions, and statistical comparisons using Pearson’s tests. We used the Student’s t-test for the analysis of continuous variables. Controllable variables with a level of significance less than or equal to 10% (P = 0.10) for the univariate tests (shown in Supplementary Tables 1A, 1B, 1C, 1D, 1E, 1F, 1G, and 1H available online at http://informahchealthcare.com/doi/abs/10.3109/14397595.2015.1060668) were included as candidate predictors (risk factors) in the multivariable logistic regression model. Variables that were strongly correlated were excluded from the model to avoid multicollinearity problems. Unconditional logistic regression analysis was used to obtain the crude odds ratios (ORs) for the risk of lower domains of the SF-36 and corresponding 95% confidence intervals (CIs), with adjustments for potential confounders. A P value less than or equal to 0.05 (2-sided) was considered statistically significant. All of the calculations were performed using STATA ver. 13.1 (Stata Corporation, College Station, TX, USA) software.

Results

Measures of 8 domains in SF-36

The mean (standard deviation [SD]) score for each domain of the SF-36 was 72.6 (23.6) in PF, 68.9 (27.4) in RP, 60.9 (27.3) in BP, 47.4 (19.5) in GH, 51.3 (20.7) in VT, 71.5 (25.7) in SF, 73.5 (26.7) in RE, and 64.8 (16.9) in MH (data not shown). The SF-36 User Manual recommends that norm-based scores (mean = 50, SD = 10) should be used rather than 0–100 scores to simplify interpretation of the data [20]. As shown in Table 1, the mean (SD) score for each domain of the SF-36 was 38.1 (17.1) in PF, 39.2
Table 1. The mean score data using norm-based scoring (mean = 50, SD = 10) of SF-36 compared with two controls.

| Domain of SF-36 | Mean (SD) | No. of missing | Study patients (n = 119) | Control 1** (n = 199) | P* | Control 2† (n = 949) | P† |
|----------------|-----------|----------------|--------------------------|-----------------------|-----|-----------------------|-----|
| PF             | 38.1 (17.1) | 1              | 50.9 (9.4)               | < 0.001               | 46.2 (13.5)   | < 0.001               | 46.2 (13.5)   | < 0.001 |
| RP             | 39.2 (14.6) | 0              | 51.0 (8.6)               | < 0.001               | 47.2 (12.0)   | < 0.001               | 47.2 (12.0)   | < 0.001 |
| BP             | 44.3 (12.1) | 1              | 47.9 (10.6)              | 0.006                 | 46.3 (10.5)   | 0.055                 | 46.3 (10.5)   | 0.055  |
| GH             | 41.7 (10.4) | 2              | 50.4 (9.5)               | < 0.001               | 46.1 (10.1)   | < 0.001               | 46.1 (10.1)   | < 0.001 |
| VT             | 44.1 (10.6) | 2              | 48.6 (9.4)               | < 0.001               | 48.5 (10.5)   | < 0.001               | 48.5 (10.5)   | < 0.001 |
| SF             | 42.3 (13.3) | 1              | 49.1 (10.6)              | < 0.001               | 48.1 (11.3)   | < 0.001               | 48.1 (11.3)   | < 0.001 |
| RE             | 42.9 (13.4) | 0              | 50.2 (9.8)               | < 0.001               | 47.9 (11.6)   | < 0.001               | 47.9 (11.6)   | < 0.001 |
| MH             | 46.3 (9.1)  | 2              | 49.0 (10.3)              | 0.019                 | 48.8 (10.7)   | 0.015                 | 48.8 (10.7)   | 0.015  |
| PCS            | 38.6 (15.2) | 5              | 50.3 (8.1)               | < 0.001               | 45.9 (10.6)   | < 0.001               | 45.9 (10.6)   | < 0.001 |
| MCS            | 46.9 (9.68) | 5              | 48.9 (10.4)              | 0.075                 | 49.3 (11.0)   | 0.018                 | 49.3 (11.0)   | 0.018  |

*Comparison between study subjects and norm. **Japanese female norm (age matched) [19]. †Comparison between study subjects and control 1. ‡Japanese norm with more than 2 chronic diseases [19]. §Comparison between study subjects and control 2.

Comparison of demographic, lifestyle, clinical, and treatment factors between SLE patients having above the median and below the median for 8 domains of SF-36

Physical Functioning

The average age of SLE patients above the median of PF (45.3 years) was younger than those below (53.2 years) (P = 0.001). A greater number of patients above the median of PF (66.7%) reported regular menstruation than those below the median (35.2%) (P = 0.001). As for complications, ever thrombosis (27.1% vs. 6.9%) (P = 0.004) and hyperlipidemia (55.2% vs. 29.3%) (P = 0.005) were more prevalent in patients below the median of PF than in those above the median, and both ever (33.9% vs. 13.6%) (P = 0.009) and current (18.2% vs. 1.8%) (P = 0.004) femoral neck fractures were more prevalent in patients below the median of PF than those above the median.

Table 2. Characteristics of the SLE patients in this study.

| Variable                          | Value   | No. of missing |
|-----------------------------------|---------|----------------|
| Number of patients                | 119     | 0              |
| Age, mean (SD), years             | 49.1 (13.4) | 1              |
| Disease duration, mean (SD), years| 18.5 (9.2) | 5              |
| Postmenopausal, n (%)             | 53 (44.5) | 9              |
| ACR revised criteria, n (%)       | 84 (70.6) | 1              |
| Malar rash ever                   | 24 (20.2) | 1              |
| Discoid rash ever                 | 60 (50.4) | 1              |
| Photosensitivity ever             | 46 (38.7) | 1              |
| Oral ulcers ever                  | 25 (21.0) | 2              |
| Arthralgia ever                   | 65 (54.6) | 1              |
| Serositis ever                    | 85 (71.4) | 2              |
| Renal disorder ever               | 33 (27.7) | 1              |
| Neurological disorder ever        | 101 (84.9) | 0              |
| Hematological disorder ever       | 111 (93.3) | 2              |
| Ever complication, n (%)          | 18 (15.1) | 0              |
| Sjögren’s syndrome                | 3 (2.5)  | 0              |
| Depression                        | 18 (15.1) | 0              |
| Antiphospholipid antibody syndrome| 3.9 (4.6) | 2              |
| SLEDAI, mean (SD)                 | 1.6 (4.6) | 0              |
| dsDNA Ab, mean (SD)               | 19.9 (16.1) | 18             |
| Current CS treatment, n (%)       | 20.9 (33.5) | 10             |
| Actual PSL dosage, mean (SD) mg/day| 106 (81.9) | 0              |
| Other treatment, n (%)            | 8.9 (3.8) | 13             |

Characteristics of study patients

Table 2 shows the characteristics of the female patients with SLE included in this study. Mean age (SD) was 49.1 (13.4) years, and 44.5% of the study patients were postmenopausal. Mean BMI (SD) was 21.3 (3.4). Mean disease duration (SD) was 18.5 (9.2) years, and mean SLEDAI (SD) was 3.9 (4.6). Mean Systemic Lupus Collaborative Clinics Damage Index (SDI) score (SD) was 1.7 (1.6). Eighty-six patients (72.3%) had a history of arthritis and 33 (27.7%) had neurological involvement. One hundred-six patients (89.1%) were currently using CS with a mean daily dose of 8.9 mg. As for other treatments, 44.5% of patients reported current use of NSAIDs, and 10.9% reported current use of warfarin. Major tranquilizer was currently used in 5.0% of patients, and minor tranquilizer was currently used in 23.5% of patients.
necrosis was more prevalent in patients below the median of PF than in those above. The average value of BUN (18.1 mg/dl vs. 13.5 mg/dl) \( (P = 0.009) \) and triglyceride (149.2 mg/dl vs. 126.1 mg/dl) \( (P = 0.008) \) of SLE patients below the median of PF were higher than those above.

The difference in SDI scores between those above (1.1) and below (2.3) the median of PF was statistically significant \( (P < 0.001) \). Current use of minor tranquilizers was more prevalent in patients below the median of PF (33.9\%) than in those above (13.6\%) \( (P = 0.009) \) (shown in Supplementary Table 1A available online at http://informahealthcare.com/doi/abs/10.3109/14397595.2015.1060668).

### Role Physical

The average age of patients below the median of RP (52.8) was significantly higher than those above the median (46.2) \( (P = 0.008) \). More patients above the median of RP reported regular menstruation (62.9\%) than those below the median (36.2\%) \( (P = 0.006) \). A greater number of patients above the median of RP (60.4\%) listed office work as their occupational type than those below the median (25.6\%) \( (P = 0.006) \). A history of positive anticardiolipin antibodies (49.0\% vs. 24.6\%) \( (P = 0.008) \) and lupus anticoagulant (31.0\% vs. 10.3\%) \( (P = 0.01) \) were more prevalent in patients below the median of RP than in those above. As for complications, history of (51.9\% vs. 27.3\%) \( (P = 0.001) \) and current (45.1\% vs. 17.2\%) \( (P = 0.001) \) hypertension were more prevalent in patients below the median of RP than in those above, and a history of hyperlipidemia was more prevalent in patients below the median of RP (58.8\%) than in those above (28.8\%) \( (P = 0.001) \). The difference in CRP values between patients above the median of RP (0.16) and those below (0.22) was significant \( (P = 0.007) \) (shown in Supplementary Table 1B available online at http://informahealthcare.com/doi/abs/10.3109/14397595.2015.1060668).

### Bodily Pain

Regularity of sleep was associated with BP score \( (P = 0.005) \). A history of leukopenia was more prevalent in patients above the median of BP (72.9\%) than in those below (46.6\%) \( (P = 0.004) \). Current oral ulcer was more prevalent in patients below the median of BP (19.6\%) than in those above (3.4\%) \( (P = 0.006) \). Current positive anticardiolipin antibodies (51.9\% vs. 16.7\%) \( (P = 0.005) \) was more prevalent in patients below the median of BP than in those above the median. The ANA value was associated positively with BP score \( (P = 0.002) \), probably due to the small number of cases. The SDI score was associated negatively with BP \( (P = 0.005) \). Current use of warfarin was more prevalent in patients below the median of BP (19.0\%) than in those above (3.3\%) \( (P = 0.007) \) (shown in Supplementary Table 1C available online at http://informahealthcare.com/doi/abs/10.3109/14397595.2015.1060668).

### General Health

Small fish \( (P = 0.037) \) and soybeans \( (P = 0.044) \) were consumed more among the SLE patients above the median than those below. The sufficiency of sleep was associated with GH score \( (P = 0.018) \). Immunoglobulin M (IgM) value was associated positively with GH \( (P = 0.008) \), probably due to the small number of cases (shown in Supplementary Table 1D available online at http://informahealthcare.com/doi/abs/10.3109/14397595.2015.1060668).

### Vitality

As for treatment variable, the current value of actual prednisone dosage was higher in patients below the median of VT than in those above (10.2 mg/day vs 8.0 mg/day) \( (P = 0.003) \) (shown in Supplementary Table 1E available online at http://informahealthcare.com/doi/abs/10.3109/14397595.2015.1060668).

### Social Functioning

The percentage of patients above the median of SF in an employed position was higher (45.6\%) than in those below the median (17.4\%) \( (P = 0.002) \). The regularity of sleep was associated positively with SF score \( (P = 0.007) \). A history of vertebral fracture was more prevalent in patients below the median of SF (17.0\%) than in those above (3.1\%) \( (P = 0.011) \). Complement titer (CH50) value was associated positively with SF score \( (P = 0.011) \) (shown in Supplementary Table 1F available online at http://informahealthcare.com/doi/abs/10.3109/14397595.2015.1060668).

### Mental Health

Frequency of green vegetable intake was associated positively with MH score \( (P = 0.027) \). A history of CS use was more prevalent in patients below the median of MH (97.8\%) than in those above (85.5\%) \( (P = 0.028) \) (shown in Supplementary Table 1G available online at http://informahealthcare.com/doi/abs/10.3109/14397595.2015.1060668).

### Factors associated with QoL in SLE patients

Table 3 shows the association between selected factors and the risk of being below the median score for each of the SF-36 domains among female SLE patients.

Irregularity of sleep was significantly associated with an increased risk of lower RP (adjusted OR = 8.27, 95\% CI = 1.45–47.2; \( P = 0.017 \)), lower VT (adjusted OR = 8.45, 95\% CI = 1.39–51.3; \( P = 0.020 \)), and lower RE (adjusted OR = 10.7, 95\% CI = 1.88–61.1; \( P = 0.008 \)). Compared with clerical work, occupational type other than clerical work (e.g., service and business industry, professional, or technical job) was significantly associated with an increased risk of lower VT (adjusted OR = 41.0, 95\% CI = 1.94–866; \( P = 0.017 \)). In contrast, daily soybean intake was associated with a decreased risk of lower GH (adjusted OR = 0.17, 95\% CI = 0.03–0.98; \( P = 0.047 \)).

As for SLEDAI and SDI scores, we included both scores in the same model with age and the disease duration, and significant associations between SDI score and lower PF, RP, and BP persisted. When the patients were subdivided into 3 groups, namely SDI score = 0, score = 1, and score ≥2, and assessed using SDI score = 0 as a reference, SDI score ≥2 was significantly associated with an increased risk of lower PF (adjusted OR = 7.88, 95\% CI = 2.61–23.83; \( P < 0.001 \)), lower RP (adjusted OR = 4.29, 95\% CI = 1.47–12.54; \( P = 0.008 \)), and lower BP (adjusted OR = 3.06, 95\% CI = 1.14–8.25; \( P = 0.027 \)) (data not shown).
Table 3. Association between selected factors and risk of being below the median score for each of the SF-36 domains among female SLE patients.

| Factors                                      | PF    | RP    | BP    | GH    | VT    | SF    | RE    | MH    |
|----------------------------------------------|-------|-------|-------|-------|-------|-------|-------|-------|
| Sleep                                        |       |       |       |       |       |       |       |       |
| Irregular vs. regular                        | 4.5 (0.89–23.8) | 8.27** (1.45–47.2) | 2.02 (0.49–8.29) | 3.54 (0.75–16.6) | 8.45*** (1.39–51.3) | 3.27 (0.84–12.8) | 10.7† (1.88–61.1) | 2.43 (0.64–9.28) |
| Current work                                 | 0.92 (0.20–4.32) | 3.88 (0.60–25.0) | 2.99 (0.64–13.9) | 1.40 (0.27–7.14) | 0.92 (0.17–5.06) | 0.40 (0.08–1.86) | 0.48 (0.07–3.33) | 0.54 (0.19–2.44) |
| Occupation                                   | 0.69 (0.15–3.15) | 7.39‡ (1.34–40.9) | 1.46 (0.37–5.81) | 0.47 (0.09–2.50) | 1.56 (0.30–8.06) | 2.96 (0.66–13.4) | 6.50 (0.95–44.6) | 0.86 (0.21–3.53) |
| Others* vs. clerical work                    | 0.50 (0.05–4.97) | 5.20 (0.45–60.7) | 5.90 (0.67–52.1) | 3.63 (0.34–38.9) | 41.0§ (1.94–866) | 0.97 (0.13–18.8) | 2.15 (0.19–24.6) | 1.35 (0.18–10.2) |
| Green and yellow vegetable intake            |       |       |       |       |       |       |       |       |
| Daily vs. non-daily                          | 3.40 (0.73–15.7) | 3.01 (0.53–17.0) | 0.81 (0.20–3.19) | 2.27 (0.49–10.5) | 3.23 (0.57–18.4) | 1.13 (0.31–7.40) | 0.98 (0.15–6.47) | 0.96 (0.25–3.66) |
| Coffee intake                                | 1.41 (0.21–9.69) | 13.5 (0.72–255) | 1.10 (0.19–6.52) | 0.43 (0.07–2.85) | 0.16 (0.02–1.13) | 2.20 (0.33–14.6) | 6.18 (0.34–113)  | 0.24 (0.05–1.24) |
| Drinker vs. non-drinker                      | 1.16 (0.26–5.12) | 1.16 (0.22–6.08) | 1.26 (0.31–8.23) | 2.68 (0.54–13.4) | 1.77 (0.37–8.51) | 0.73 (0.18–2.93) | 1.02 (0.17–5.98) | 1.56 (0.38–6.39) |
| Milk intake (mL/day)                         |       |       |       |       |       |       |       |       |
| 180 ≤ vs. 180>                               | 0.57 (0.12–2.69) | 1.51 (0.15–8.45) | 2.65 (0.64–10.9) | 0.17‡ (0.03–0.98) | 0.21 (0.03–1.26) | 0.73 (0.15–3.47) | 1.60 (0.22–11.4) | 0.81 (0.19–3.45) |
| Soybean intake                               |       |       |       |       |       |       |       |       |
| Daily vs. non-daily                          | 2.94 (0.21–40.8) | 4.79 (0.15–150) | Not calculable | Not calculable | 8.32 (0.19–372) | 3.97 (0.19–81.1) | 1.49 (0.04–52.0) | 2.59 (0.13–51.1) |

*Service and business industry, professional, or technical job.

**p = 0.017.

***p = 0.020.

†p = 0.008.

‡p = 0.022.

§p = 0.017.

#p = 0.047.

Adjusted for age, sleep regularity, current work, occupation, green and yellow vegetable intake, coffee intake, milk intake, soybean intake, and fish intake. Variables that are highly correlated are excluded from the model.
Discussion

SLE is a chronic, multisystem autoimmune disorder that provokes inflammation in various parts of the body [2]. Moreover, levels of daily stress among patients with SLE are generally higher than those experienced by the general population. Such stress is closely linked to depression and anxiety, and the worsening of lupus symptoms [21].

Our study demonstrated that the HRQoL of Japanese female SLE patients was significantly poorer compared with that of age- and gender-matched Japanese norm control [16] both in physical and global health perception, as well as social and emotional status. This is consistent with the findings reported in several Caucasian and Asian studies of SLE patients [4–8]. It showed that PCS was more reduced than MCS in our study. On the contrary, in other studies, PCS and MCS were reduced equivalently [5,6]. In brief, MCS is considered to be more preserved than PCS in our study compared with other studies [6]. This is presumed to be due to the differences in the percentage of patients with neuropsychiatric complication, psychosocial factors, socioeconomic background, and other factors. Compared with Japanese norm control with more than 2 chronic diseases [19], the HRQoL of our SLE patients was demonstrated to be significantly poorer, especially in physical status except bodily pain, and similarly with regard to global health perception, social, and emotional status. The degree of reduction in HRQoL due to SLE is comparable to that observed in severe medical illness, including AIDS, Sjögren’s syndrome, rheumatoid arthritis, congestive heart failure, and post-myocardial infarction [13,22–24].

It was demonstrated that the SDI score was associated with lower PF, lower RP, and lower BP, that is, only physical domains of SF-36, while SLEDAI scores showed no correlation with either domain of the SF-36 in patients with SLE in this study. Regarding disease activity in SLE patients, some studies suggest that it correlates with HRQoL [4–5,14], while other studies provide evidence as to the contrary [6–8,25]. Regarding organ damage in SLE patients, some reports demonstrate an association with HRQoL [5,8,14], while others show no association with HRQoL [6–7,25]. In short, whether HRQoL is associated with both is controversial regardless of the study design (cross-sectional or prospective).

It has previously been demonstrated that the inverse relationship between organ damage and HRQoL is mainly confined to the physical component of the SF-36 [5] and our study outcome is consistent with this. Minor differences were reported that depended on the disease activity measure used [6]. At the least, SLEDAI and SDI do not quantify the social impact of the disease, or measure functioning and well-being from the patient’s perspective, and are therefore poor indicators of HRQoL in patients with SLE [26]. A lack of change in QOL has also been reported which is perhaps due to the patients becoming accustomed to the disease, accepting it, and finding their own way to deal with it [7]. Reportedly, disease activity, cumulative damage, and quality of life had some influence in the overall view of lupus but those parameters are distinct domains of health status [7]. Therefore, all three aspects should be measured in SLE patients in order to obtain a complete clinical picture [6].

Concerning the effect on HRQoL in SLE patients by complication, we could not find any association between complications and HRQoL. In univariate analysis, antiphospholipid antibody syndrome (23.1% vs. 9.0%) (P = 0.033) was more prevalent in patients below the median of RP than in those above, and a history of chronic thyroiditis (12.5% vs. 2.9%) (P = 0.043) was more prevalent in patients below the median of VT than in those above, whereas there were no significant associations in both cases in multivariate analysis. The prevalence of Sjögren’s syndrome, depression, antiphospholipid syndrome, and FM in the study patients was 15.1%, 2.5%, 15.1%, and 0%, respectively. FM is one of most well-known risk factors of HRQoL in SLE patients. In univariate analysis, lower BP was significantly associated with current positive anticardiolipin antibodies and lupus anticoagulant, thrombosis, SDI score, and current use of warfarin. We expected these univariate analysis data to show an association between bodily pain and thrombosis; however, we did not find this association in multivariate analysis. Among our study patients, there was no diagnosis of FM. Reportedly, the prevalence of the concurrence of SLE and FM was high in Caucasians (22–25%), and ethnicity can play an important role in FM manifestation [27]. To the best of our knowledge, there are no published reports on the prevalence of FM in Asian SLE patients. Concerning other factors that influence the occurrence of FM in SLE patients, it was reported that patients with severe lupus did not have FM, whereas a strong family and social support system and the absence of disability compensations, as well as ethnic differences in response to pain threshold have been postulated to account for differences in the prevalence rate [27]. Most (71.4%) of our patients have renal involvement, whereas their PCS was relatively preserved. This might be because our patients received abundant support from family members and other people, which helped them maintain a relatively good mental status despite their disease. In addition, FM would not be major candidate as an associated factor of HRQoL in Asian SLE patients.

Our data demonstrated that irregular sleep was associated with an increased risk of lower RP, VT, and RE scores in SLE patients. Poor sleep is a common complaint in various types of illnesses, especially in pain disorders [28]. Physicians recognize sleep disturbance as a common complaint in SLE patients. The effects of SLE on sleep can be due to direct effects of the disease, or thorough indirect emotional factors from stress, body dysmorpia, and/or a combination of both influences [29]. Previous studies describe the prevalence of sleep disturbance in SLE as ranging from 56% to 80% of patients [28–32]. Factors contributing to sleep disturbances in SLE patients in previous studies include exacerbation of disease symptoms [30,31,33], pain [30,33], physical disability [34], depressive mood (such as depression) [30–31,35], and high doses of corticosteroids [31,36]. One study reported low, moderate, and high risks of sleep disturbances in SLE when using prednisolone at equivalent doses of less than 40 mg/day, 40–80 mg/day, and more than 80 mg/day, respectively [36]. Further studies have pointed out a possible role for cytokines in the regulation of sleep, which provides further reasoning as for exploring sleep patterns in patients with inflammatory systemic disorders such as SLE [37–39]. Valencia-Flores et al. reported SLE patients had problems due to a decrease in sleep efficiency, and that their patients exhibited a delta sleep pattern in their polysomnographic records and sleep fragmentation [40]. Recent research also shows that depression is strongly associated with sleep disturbances, and an awareness of underlying depression, as well as sleep disturbances in SLE patients, and treating them properly could improve treatment outcomes in these patients [29]. It was reported that the MH score is the domain of SF-36 that is most closely related to depression scores [41]. The calculated MH score cutoff value that significantly differentiated depressed from non-depressed SLE patients was 61 (in raw value) [41]. As the mean MH score in raw value is 64.8 in this study, it is considered to be unlikely that sleep disturbance is associated with depression in study patients.

In this study, we identified two work-related risk factors in SLE patients. Work disability (WD), defined as stopped work due to an illness, is multifactorial with profound repercussions for both the individual and society as work loss leads to loss of earnings, loss of ability to accumulate assets, loss of self-esteem, and increased social isolation [42–43]. Compared with clerical work, unemployment was associated with an increased risk of lower VT in the SLE study patients. Previous studies showed that 19%-69% of patients...
with SLE were unable to work because of the disease [42–46]. Moreover, studies on musculoskeletal illness such as arthritis and SLE have indicated that, although measures of disease activity and severity are important predictors of work loss, they have less effects on WD overall than socio-demographic and work-related factors [47]. In the present study, it was demonstrated that occupational type, except clerical work, was significantly associated with an increasing risk of lower RP among female SLE patients. Baker et al. reported that there was a tendency toward more sedentary jobs in women with SLE as compared with those in the general population who are working in Canada [48]. More regular review, aggressive therapy to achieve better control of disease activity, and measures to reduce fatigue are effective in enhancing work capability in SLE patients [49].

In the present study, daily soybean intake was associated with a decreased risk of lower GH. Soy factors can potentiate immunologic function such as lymphocyte proliferation, cellular and humoral immune responses, thymocyte differentiation, and tumor immunity, independently of their estrogenic activity [50,51]. Regarding collagen diseases, animal studies report that soy protein, genistein, and daidzein improve serum paraoxonase activity and lipid profiles in rheumatoid arthritis [52]. It is considered that immune response modulation by soybean factors could have led to decreased health burden and an improved HRQoL in SLE patients of this study; however, this could not be confirmed owing to limitations of the present study design. Due to the small sample size, all potential confounders could not be controlled simultaneously. Therefore, the possibility of a spurious association cannot be ruled out.

In conclusion, the present study demonstrates that the HRQoL of female Japanese SLE patients, based on the SF-36 questionnaire, was significantly poorer than that of age- and gender-matched Japanese controls with regard to physical functioning, global health perception, social functioning, and emotional health. Organ damage also showed a significant association with lower physical and emotional domains of HRQoL in SLE patients, while the disease activity had no association with HRQoL in this study. Additionally, irregularity of sleep was associated with lower physical and emotional domains of HRQoL in SLE patients. Regarding occupation, non-clerical work was associated with lower RP and unemployment was associated with lower vitality compared with SLE patients engaged in clerical work. Therefore, clinicians should pay attention not only to the disease activity and organ damage, but also to HRQoL as an independent domain, including the patients’ perspectives, for a more comprehensive assessment of SLE patients and to detect and cope with masked underlying problems to decrease patients’ health burden. Intervention with regard to improving sleep, adjusting work, as well as dietary interventions with soybean products could lead to improvements in HRQoL of SLE patients. As we could not establish cause and effects in this study, additional studies with prospective designs would undoubtedly lead to a more thorough understanding of factors associated with HRQoL in female patients with SLE.

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Conflict of interest

None.

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Supplementary material available online

Supplementary Figure 1, Tables 1A–1H available online at http://informahealthcare.com/doi/abs/10.3109/14397595.2015.1060668.