

Disease Course in Systemic Lupus Erythematosus: Changes in Health Status, Disease Activity, and Organ Damage After 2 Years

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ABSTRACT. Objective. To examine changes in health status, disease activity, and organ damage after 2 years and to study possible disease variables predicting change in health status, disease activity, and organ damage at followup in systemic lupus erythematosus (SLE). Second, to compare changes in health status in patients with SLE to that of matched patients with rheumatoid arthritis (RA) and matched healthy controls.

Methods. A 2 year longitudinal observational study, measuring health status (Short-Form 36, visual analog scale for pain and fatigue, modified Health Assessment Questionnaire, patient global assessment of disease activity), disease activity, and organ damage in 87 patients with SLE. Health status measures in SLE were compared to 65 matched RA patients selected from the Oslo RA register and to 77 matched healthy controls from the population register.

Results. On a group level the SLE patients showed stable health status measures and disease activity scores 2 years after baseline, but organ damage scores increased significantly. Increase in organ damage was significantly and independently predicted by baseline scores of disease activity and organ damage, health status, and disease activity by the respective baseline scores. Changes in health status measures over 2 years were similar in SLE, RA, and healthy controls.

Conclusion. Our 2 year longitudinal observational SLE study showed a stable course of health status and disease activity, whereas organ damage increased. Disease activity and organ damage at baseline predicted the latter. Our results indicate the value of careful monitoring of disease activity over time in SLE and individually tailored treatment guided by the predictors of course and outcome. (J Rheumatol 2001;28:266–74)

Key Indexing Terms:

SYSTEMIC LUPUS ERYTHEMATOSUS RHEUMATOID ARTHRITIS HEALTH STATUS
DISEASE ACTIVITY ORGAN DAMAGE LONGITUDINAL STUDY

Survival of patients with systemic lupus erythematosus (SLE) has improved considerably in recent years, partly due to recognition of milder cases of the disease and probably also due to better treatments. The improved prognosis requires use of outcome measures other than mortality. Health status, disease activity, and accumulated organ damage are accepted as important independent outcome measures of the course of SLE^{1,2}, and are recommended for use in longitudinal followup studies³.

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To evaluate all patient-relevant dimensions of health status, including physical, psychological, and social functioning in SLE, the Medical Outcome Survey Short-Form-36 (SF-36)⁴ is considered the preferable instrument². SF-36 is a comprehensive generic instrument allowing comparison with other patient groups. Several instruments capturing disease activity in SLE are available. For example the SLE Disease Activity Index (SLEDAI)¹ has been validated and shown to be sensitive to change over time⁵. To assess organ damage in SLE, the Systemic Lupus International Collaborating Clinics/ American College of Rheumatology Damage Index (SLICC/ACR-DI)⁶ has been introduced; it describes accumulation of organ damage since disease onset, caused by the inflammatory process, the disease therapy, or intercurrent events without attribution. It has been used to assess damage in a large number of patients with SLE in different centers⁷, and shown to be sensitive to change over time⁸.

Several dimensions of outcome measures in SLE (health status, disease activity, and organ damage) have until now only been simultaneously examined by cross sectional studies⁹⁻¹², with one exception¹³. This latter prospective

study had a short followup time, studying especially the correlation between health status and disease activity¹³. No prospective study has examined all 3 dimensions of outcome in the same study, and none has simultaneously compared health status in SLE to patients with rheumatoid arthritis (RA) and healthy controls in a longitudinal design.

Our objectives were to examine changes in health status, disease activity, and organ damage after 2 years, and to search for disease variables predicting changes in organ damage, health status, and disease activity at followup in SLE. We particularly wished to compare changes in health status measures in patients with SLE to those of age, sex, and residential area matched healthy controls, and age, sex, and disease duration matched patients with RA.

MATERIALS AND METHODS

Setting. The study was performed at Diakonhjemmet Hospital, Oslo City Department of Rheumatology, which offers rheumatological service for the community of Oslo, the capital city of Norway, with roughly 500,000 inhabitants. Studies on reactive arthritis and RA¹⁴ have shown that the community of Oslo serves as a reliable setting for the performance of epidemiological studies in rheumatology.

Patients and controls. This SLE cohort consisted of 93 SLE patients fulfilling the ARA/ACR classification criteria¹⁵ (Table 1). The patients were partly recruited from our retrospective study in 1995¹⁶, partly from new SLE referrals in 1995 and 1996. The patients were invited by mail to a cross sectional examination in 1995-96 (baseline), with a followup examination after 2 years. Eighty-seven of the 93 patients (94%) completed the followup examination after 2 years (1997-98) (Table 1).

Individuals included as healthy controls were selected from the population register of Oslo, each matched to one of the SLE patients with regard to age, sex, and zone of residence within Oslo. The controls received an invitation by mail and the initial nonrespondents a reminder after 2 weeks. We succeeded in obtaining data from 85 healthy controls at baseline, and 77 (91%) at followup. The 85 SLE patients with and the 8 without matched controls at baseline did not differ in demographic and disease variables.

Eighty-two patients with RA¹⁷ matched to the SLE patients for sex, age (± 2 yrs), and disease duration (± 2 yrs) were identified from the RA register at Diakonhjemmet Hospital and served as disease controls at baseline. We succeeded in collecting data from 70 (85%) after 2 years, of whom 65 were matched to the 87 patients with SLE.

Data collection. The SLE patients consenting to participate attended a cross sectional and a followup outpatient examination in 1995-96 and 1997-98, respectively. One rheumatologist (IMG) examined the patients, using a standardized interview to obtain a detailed history, followed by a clinical examination, laboratory analyses, radiographs, and electrocardiographs. Disease activity was assessed by SLEDAI¹, accumulated organ damage by SLICC/ACR-DI⁶, and presence of fibromyalgia according to the classification criteria¹⁸. A self-report health status questionnaire was filled in the day before or during the visits, including the SF-36⁴, the Modified Health Assessment Questionnaire (MHAQ)¹⁹, joint pain and fatigue on 100 mm visual analog scale (VAS), and patient global assessment of disease activity.

The healthy controls and patients with RA completed the same self-report health status measures as the patients with SLE, collected by mail from healthy controls in 1995-96 and 1997-98, and from RA patients in 1994 and 1996.

Instruments. The SF-36 is a generic instrument measuring 8 of the most commonly used dimensions in health surveys. It is suitable for self-administration. The version covering the last 4 weeks was used. The SF-36 scales were scored according to published scoring procedures, each expressed with values from 0 to 100, with higher value representing better func-

tion/health⁴. The SF-36 has been translated into Norwegian and validated in Norwegian patients with RA²⁰.

The MHAQ examines disability in 8 dimensions of activities of daily living (one item in each dimension)¹⁹. Four responses were available for each item, 1 to 4. The total difficulty MHAQ score is expressed as the mean score and requires a minimum of 6 responses to be computed.

Two 100 mm VAS were completed, to assess the degree of joint pain and fatigue during the last 4 weeks, by placing a mark between the anchoring points designated "no pain/no fatigue" and "pain/fatigue as bad as it could be." Patients' global assessment of disease activity was assessed on a categorical scale, from 1 = no activity to 5 = very severe activity.

The SLEDAI is a validated SLE disease activity measure index¹. The version covering the last 10 days was used. It contains 24 descriptors in 9 organ systems, including clinical and laboratory measures of SLE activity, and is weighted to reflect the degree of activity. The maximum possible score is 105. Cognitive impairment is part of the central nervous system SLEDAI assessment. Change in individual SLEDAI scores was defined as SLEDAI followup scores minus baseline scores. Decrease in SLEDAI score > 3 indicates significant improvement, change of -3 to $+3$ persistent activity, increase > 3 flare, and SLEDAI score = 0 at followup indicates remission²¹.

The SLICC/ACR-DI is designed to assess accumulated damage in the patient with SLE since onset of disease and damage must be present continuously for at least 6 months⁶. Damage is defined for 12 organ systems: ocular, neuropsychiatric, renal, pulmonary, cardiovascular, peripheral vascular, gastrointestinal, musculoskeletal, skin, gonadal, endocrine, and malignancy. Damage index score can only increase over time, theoretically to a maximum of 47.

Disease onset was defined as the time the patient fulfilled the ARA/ACR criteria for SLE¹⁵ and RA¹⁷. Disease duration was defined as the period from disease onset to the time of the baseline examination. SLE disease manifestations were obtained from the patient's hospital records and the cross sectional and followup examinations.

Data analyses and statistics. All statistical analyses were performed by SPSS, version 8.0. Descriptive statistics for continuous variables are presented as means with range and standard deviation (SD) or 95% confidence interval (CI). Comparisons between patients with SLE or RA and healthy controls were examined by matched pair 2 way ANOVA. Because we only had data from 77 matched healthy controls and 65 matched patients with RA, the number of patients with SLE was reduced to 77 and 65, respectively, for the analyses. T tests for independent samples were used to compare the means of 2 independent groups and T test for paired samples to compare the means in paired groups (SLEDAI and SLICC/ACR-DI at baseline and followup in SLE). Chi-squared test was used when comparing categorical variables in 2 independent groups and McNemar test when comparing categorical variables in paired groups. The differences were regarded as statistically significant when $p < 0.05$ and highly significant when $p < 0.01$. For prediction of health status, disease activity, and change in organ damage (no change vs deterioration) at followup, demographic and disease variables at baseline were used as independent variables. Possible predictors to be used in the multivariate analyses were identified in univariate analyses if $p < 0.15$. Linear regression was used to assess prediction of health status and disease activity after 2 years (continuous dependent variables), logistic regression for prediction of increase in organ damage (categorical dependent variable). Patients who died were classified as having deterioration in organ damage. The assumed linear relationship of the odds to the continuous explanatory variables in the logistic regression model shown by scatterplots was reasonable.

The local ethical committee approved the study and the Data Inspectorate the register of patients with SLE and RA in Oslo.

RESULTS

Demographic data and clinical features. Table 1 shows descriptive characteristics of patients with SLE at baseline

Table 1. Characteristics of the patients with SLE. Mean (range) for continuous variables, number (%) for categorical.

	Baseline, n = 93	2 year Followup, n = 87
Women	84 (90)	78 (90)
Age, yrs	45.5 (18–82)	47.0 (20–84)
Disease duration, yrs	6.1 (0–31)	7.7 (2–27)
Married	53 (57)	53 (60)
Full or part time work	41 (44)	32 (36)
ACR criteria	5.05 (4–8)	
Fibromyalgia	15 (16)	24 (27)
Antirheumatic medication		
NSAID current users	14 (15)	16 (18)
Corticosteroids		
Ever users	79 (85)	74 (84)
Current users	55 (59)	54 (61)
Mean current dose, mg	10.1 (2.5–40)	7.1 (2.5–20)
Cumulative dose, g	17.8 (0.2–124.5)	21.8 (0.2–113.4)
Duration, mo	57.3 (1–360)	73.5 (1–364)
DMARD		
Ever users	59 (63)	63 (72)
Current users	26 (28)	33 (38)
Cytotoxic drugs		
Ever users	37 (40)	37 (42)
Current users	15 (16)	15 (17)

No significant changes (paired sample T test for continuous variables, McNemar test for categorical).

and at 2 year followup, comprising 93 and 87 patients, respectively. Ninety percent were women and all were Caucasian. The 6 patients lost to followup were either dead (n = 4) or reluctant to participate further in the study (n = 2) and had a significantly longer disease duration than the patients completing the study (p = 0.02). The use of antirheumatic medication was similar at baseline and at followup, except for a trend of increasing use of disease modifying antirheumatic drugs (DMARD) at followup (Table 1), especially the use of antimalarials.

Application of the 1982 revised criteria for SLE¹⁵ at baseline showed that the cohort was characterized by mild disease, with a high proportion of patients with musculoskeletal and/or skin involvement and a low proportion of patients with severe internal organ manifestations (data not shown), with a mean number of fulfilled ACR criteria of 5.05 (Table 1).

Both at baseline and at followup the patients with RA used more nonsteroidal antiinflammatory drugs (NSAID) and less corticosteroid than patients with SLE, whereas use of DMARD and cytotoxic drugs was similar. At baseline, 48% of RA patients used NSAID, 35% corticosteroids, 23% DMARD, and 19% cytotoxic drugs (data not shown).

Health status measures: Comparison between patients with SLE and RA and healthy controls. Table 2 displays scores of health status at baseline and changes at 2 year followup for 77 patients with SLE and 77 matched healthy controls and

65 SLE and 65 matched RA patients, respectively. At baseline patients with SLE had significantly lower scores in SF-36 subscales for all dimensions of health (except for role limitation due to emotional problems), and significantly higher scores for VAS pain, VAS fatigue, and MHAQ compared to healthy controls, consistent with worse health status in the SLE patients. The SLE and RA patients had similar scores for most dimensions of health status (Table 2B), except for less affect on physical function (SF-36 physical functioning and MHAQ), joint pain (VAS pain), and patient global assessment in SLE.

Health status measures remained unchanged (followup minus baseline) in patients with SLE after 2 years and changes in health status measures showed no significant difference between SLE, RA, and healthy controls after 2 years in the SF-36 subscales, VAS pain and fatigue, and the MHAQ, except for change in patient global assessment of disease activity showing differences between SLE and RA (Table 2A, 2B).

Disease activity. The proportions of the 87 SLE patients with disease activity in the 9 organ systems and the mean SLEDAI scores at baseline and followup are displayed in Table 3. Similar scores were recorded at baseline and at followup. At both baseline and followup the immune system was the organ most frequently affected, in 44 and 55% of the patients, respectively, followed by the dermal and musculoskeletal organ systems (Table 3). Although the mean SLEDAI score remained stable, changes in individual SLEDAI scores indicated flare in 25% of the patients at followup compared to baseline, persistent activity in 46%, significant improvement in 17%, and remission in 12% (data not shown).

No difference in SLEDAI scores was observed between men and women, but men had a higher renal score, whereas women had higher vasculitis and musculoskeletal and skin SLEDAI scores. The 4 patients who died had similar SLEDAI scores at baseline compared to the others. Patients with antibodies to dsDNA at baseline and followup had a significantly higher SLEDAI score than those without. SLEDAI at baseline and followup was weakly inversely correlated to age, but not to disease duration (data not shown).

Organ damage. The proportions of the 87 SLE patients with organ damage in the 12 organ systems and the mean SLICC/ACR-DI scores at baseline and at followup are shown in Table 4. Both at baseline and at followup, musculoskeletal damage was most frequently observed, followed by neuropsychiatric and cardiovascular damage. As shown, the mean SLICC/ACR-DI score was significantly higher at followup than at baseline, indicating increase in organ damage over 2 years. Increase in organ damage occurred in 24 patients (26%), including the 4 who died. Only the neuropsychiatric damage score increased significantly after 2 years (p = 0.03), including 3 patients developing new

Table 2A. Mean baseline and 2 year change scores (1998 minus 1996) of SF-36 subscales, VAS pain and fatigue, and MHAQ in 77 patients with SLE and 77 matched healthy controls.

	SLE, n = 77	Baseline Controls, n = 77	p*	SLE, n = 77	2 Year change Controls, n = 77	p*
SF-36						
Physical	65.2	87.1	< 0.001	0.73	-0.33	0.67
Role physical	36.3	73.4	< 0.001	2.96	7.89	0.28
Bodily pain	49.6	72.9	< 0.001	2.41	2.96	0.85
General	44.2	73.4	< 0.001	1.42	2.33	0.68
Social	63.3	80.2	< 0.001	4.93	1.62	0.39
Vitality	37.9	57.4	< 0.001	0.74	1.67	0.96
Mental	70.1	79.1	0.004	1.86	-1.81	0.16
Role emotional	67.5	75.9	0.178	3.93	4.67	0.77
VAS						
Pain	34.6	14.8	< 0.001	-1.38	-1.19	0.76
Fatigue	53.2	27.4	< 0.001	-1.30	-1.59	0.85
MHAQ (range 1-4)	1.33	1.10	0.001	0.03	0.02	0.46

*Paired analyses (difference between SLE and healthy controls in baseline and change scores).

Table 2B. Mean baseline and 2 year change scores (1998 minus 1996) of SF-36 subscales, VAS pain and fatigue, MHAQ and patient global assessment of disease activity in 65 SLE and 65 matched RA patients.

	SLE, n = 65	Baseline RA, n = 65	p*	SLE, n = 65	2 Year change RA, n = 65	p*
SF-36						
Physical	64.2	54.9	0.04	0.17	0.09	0.98
Role physical	39.6	33.6	0.43	-5.77	4.56	0.13
Bodily pain	51.2	45.4	0.19	-0.58	1.83	0.55
General	45.1	45.8	0.87	-1.06	-2.70	0.62
Social	64.8	68.9	0.40	2.12	-0.54	0.63
Vitality	38.2	40.7	0.38	-1.15	-1.83	0.53
Mental	70.3	71.5	0.70	0.59	-3.67	0.08
Role emotional	67.7	58.5	0.15	1.88	-3.34	0.51
VAS						
Pain	35.7	45.2	0.04	-0.73	-10.5	0.08
Fatigue	51.2	54.4	0.68	1.16	-6.84	0.19
MHAQ range (1-4)	1.33	1.49	0.02	0.01	0.05	0.46
Patient global assessment	2.49	2.87	0.02	0.25	-0.23	0.01

*Paired analyses (difference between SLE and RA in baseline and change scores).

cognitive impairments, one cerebrovascular accident, and one peripheral neuropathy. The pattern of the increase in damage scores is displayed in Figure 1. Bivariate analyses revealed that patients with change in the SLICC/ACR-DI score had significantly higher disease activity, organ damage, erythrocyte sedimentation rate (ESR), and SF-36 bodily pain at baseline compared to those without. Furthermore, a higher proportion of them had discoid lupus and a lower proportion arthritis. They had used more corticosteroids and over a somewhat longer time, and a lower proportion of them had used antimalarial drugs (Table 5). The 4 patients who died during followup had significantly

higher organ damage scores at baseline than the others (mean SLICC/ACR-DI score 4.5; $p < 0.01$).

Predictors of change in health status, disease activity, and organ damage at followup. Multivariate analyses were performed to identify independent baseline predictors of 2 year change in health status (SF-36 physical, SF-36 mental), disease activity (SLEDAI), and organ damage (SLICC/ACR-DI) (Tables 6 and 7). Age and baseline score of SF-36 physical were significant predictors of SF-36 physical at followup, and together explained 72% of the variance of the variable. SF-36 mental score at baseline was the only significant predictor of this domain at followup. Disease activity

Table 3. SLEDAI and disease activity in the 9 organ systems: proportion of 87 patients with SLE (%) with disease activity and mean scores (SD) at baseline and at 2 year followup.

	Baseline		2 Year Followup	
	% of patients, with scores > 0	Mean (SD)	% of patients, with scores > 0	Mean (SD)
SLEDAI	86	6.51 (5.66)	88	6.70 (5.56)
CNS	12	1.32 (2.94)	6	0.46 (1.88)
Vascular	12	0.94 (2.60)	16	1.29 (2.96)
Renal	14	0.90 (2.51)	22	1.06 (2.24)
Musculoskeletal	33	1.33 (1.89)	32	1.29 (1.88)
Serosal	2	0.04 (0.29)	0	0
Skin	34	0.84 (1.23)	40	1.06 (1.46)
Immunologic	44	1.27 (1.59)	52	1.36 (1.48)
Constitutional	3	0.03 (0.18)	10	0.10 (0.31)
Hematologic	10	0.10 (0.33)	8	0.09 (0.33)

No significant changes (paired sample T test). CNS: central nervous system.

Table 4. SLICC/ACR-DI and damage in the 12 organ systems: proportion of 87 patients with SLE (%) with organ damage and mean damage scores (SD) at baseline and at 2 year followup.

	Baseline		2 Year Followup	
	% of patients with score > 0	Mean (SD)	% of patients with score > 0	Mean (SD)
SLICC/ACR-DI	70	1.82 (1.99)	75	2.09 (2.21)*
Ocular	10	0.11 (0.35)	11	0.12 (0.36)
Neuropsychiatric	23	0.33 (0.67)	28	0.40 (0.75)*
Renal	8	0.10 (0.37)	10	0.13 (0.51)
Pulmonary	18	0.20 (0.46)	20	0.22 (0.47)
Cardiovascular	20	0.28 (0.68)	23	0.31 (0.68)
Peripheral vascular	7	0.07 (0.25)	8	0.08 (0.27)
Gastrointestinal	3	0.03 (0.18)	5	0.05 (0.21)
Musculoskeletal	34	0.42 (0.64)	37	0.45 (0.66)
Skin	11	0.15 (0.44)	11	0.15 (0.44)
Premature gonadal failure	4	0.05 (0.21)	4	0.05 (0.21)
Diabetes mellitus	1	0.01 (0.11)	2	0.02 (0.15)
Malignancy	3	0.03 (0.18)	5	0.05 (0.21)

*p < 0.05 paired sample T test.

was predicted by SLEDAI score at baseline, number of ACR criteria, ESR, and VAS pain score (Table 6). The baseline values contributed more than the other variables to the explained variability of the SF-36 physical and SLEDAI score at followup (Table 6). Increase in organ damage was significantly predicted by disease activity and organ damage scores at baseline, whereas presence of arthritis reduced the risk (Table 7).

We also explored the multivariate relationships between change in health status (SF-36, MHAQ, VAS pain and fatigue — dependent variables) and change in individual disease activity according to Gladman²¹ and change in organ damage (independent variables). No significant relationships were found except between VAS fatigue score and improvement in SLEDAI (data not shown).

DISCUSSION

On a group level, our 2 year longitudinal study of SLE showed a stable disease course with reference to health status and disease activity, whereas organ damage progressed. Explorative analyses showed that current disease activity and severity might be helpful for the prediction of future damage. The stability of health status in SLE included all dimensions of health, and the findings were evident from both generic and disease-specific instruments. Health status remained stable, although organ damage increased, supporting health status as an independent outcome measure²² and that it is part of the core domains to be assessed in longitudinal studies of SLE³. Health status may reflect the presence of comorbidity (e.g., fibromyalgia), as observed in a high proportion of patients in this study as

Table 5. Comparison of baseline demographic and disease variables between patients with and without 2 year increase in organ damage. Mean (SD) for continuous, number (%) for categorical variables.

	Increased Damage, n = 24	No Change, n = 67	p*
Women	22 (92)	60 (90)	0.77
Age	46.6 (15.5)	45.5 (15.5)	0.78
Disease variables			
Disease duration, yrs	7.9 (7.9)	5.5 (4.9)	0.17
Disease activity (SLEDAI)	9.1 (6.3)	5.5 (5.1)	0.02
Organ damage (SDI)	3.4 (2.9)	1.5 (1.7)	0.01
Number of ARA/ACR criteria	5.03 (1.09)	5.00 (1.02)	0.91
Discoid lupus	8 (33)	7 (10)	0.01
Arthritis	18 (75)	62 (92)	0.02
Serositis	6 (25)	23 (34)	0.40
Renal disorder	6 (25)	9 (13)	0.19
Neurologic disorder	3 (13)	8 (12)	0.94
Hematologic disorder	17 (71)	48 (72)	0.94
Immunologic disorder	16 (67)	36 (54)	0.27
ESR, mm/h	35.2 (28.7)	22.9 (19.2)	0.02
C3, g/l	0.99 (0.31)	0.94 (0.22)	0.30
C4, g/l	0.169 (0.07)	0.16 (0.07)	0.93
Anti ds-DNA	8 (33)	18 (26)	0.55
Medication			
Current corticosteroid users	14 (58)	39 (58)	0.99
Current corticosteroid dose, mg	7.0 (11.2)	5.5 (7.5)	0.48
Cumulative corticosteroid dose, mg	24.2 (34.2)	12.2 (17.8)	0.03
Corticosteroid duration, mo	71.9 (93.7)	41.3 (60.9)	0.15
Current antimalarial drug users	3 (13)	22 (33)	0.05
Current cytotoxic drug users	3 (13)	11 (16)	0.65
Health status			
SF-36 Physical	50.5 (26.9)	69.0 (29.5)	0.08
SF-36 Bodily pain	38.8 (27.5)	52.6 (23.6)	0.02
SF-36 Vitality	36.9 (21.8)	38.2 (21.9)	0.70
SF-36 General health	35.9 (25.2)	45.5 (26.3)	0.13
SF-36 Mental	68.9 (19.2)	70.2 (16.7)	0.79
SF-36 Social	61.9 (31.4)	64.9 (26.9)	0.66
MHAQ	1.37 (0.41)	1.29 (0.35)	0.41
VAS pain	33.5 (21.1)	35.4 (25.8)	0.75
VAS fatigue	53.9 (29.6)	53.3 (31.9)	0.94
Patient global assessment	2.66 (0.92)	2.58 (1.07)	0.73

*Independent sample T test for continuous and chi-square for categorical variables.

Table 6. Significant predictors of health status (SF-36 physical, SF-36 mental) and disease activity (SLEDAI) after 2 years (multiple linear regression analyses).

	Regression Coefficient	Standard Error	p*	R ²
SF-36 physical				0.72*
SF-36 physical at baseline	0.82	0.07	< 0.001	
Age	-0.30	0.12	0.01	0.04**
SF-36 mental				0.37*
SF-36 mental at baseline	0.60	0.09	< 0.001	
SLEDAI				0.40*
SLEDAI at baseline	0.29	0.10	0.004	
Number of ACR criteria	1.80	0.50	0.001	0.16**
ESR	0.01	0.02	0.005	
Pain VAS	0.01	0.02	0.03	

R² for respective final model after forward stepwise analyses. *Explained variance full model, **explained variance without baseline values of the dependent variable.

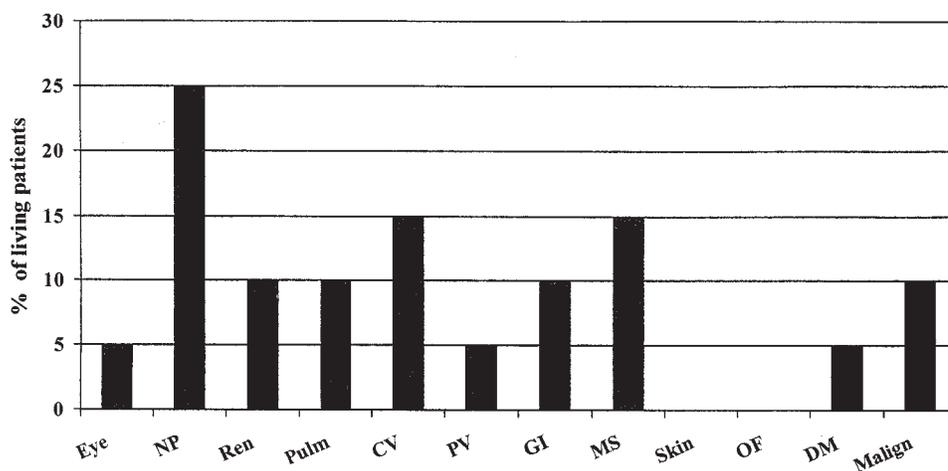


Figure 1. The pattern of the increase in damage scores for the 20 living patients with increase in damage after 2 years. Eye: ocular, NP: neuropsychiatric, Ren: renal, Pulm: pulmonary, CV: cardiovascular, PV: peripheral vascular, GI: gastrointestinal, MS: musculoskeletal, OF: premature gonadal failure, DM: diabetes mellitus, malign: malignancy.

Table 7. Demographic and clinical predictors of change in organ damage using multiple logistic regression analysis. Odds ratio (OR) with 95% confidence intervals (CI).

	OR	95% CI	p
Age	0.97	0.92, 1.02	0.20
Sex			
Female	1.0		
Male	1.17	0.14, 19.2	0.67
Disease duration	1.07	0.96, 1.20	0.20
Discoid lupus	2.82	0.59, 13.3	0.19
Arthritis	0.10	0.02, 0.63	0.01
SLEDAI	1.14	1.00, 1.28	0.04
SDI	1.52	1.02, 2.27	0.04
ESR	1.02	0.99, 1.05	0.09
SF-36 pain	0.99	0.96, 1.02	0.39

well as in other studies^{23,24}. To our knowledge this is the first study simultaneously comparing change in health status in SLE to that of both matched healthy controls and matched RA patients in a longitudinal design. The stability of health status in patients with SLE was comparable to that of RA as well as healthy controls, although the latter group had a much better status at baseline. Longitudinal health status data are abundant in RA²⁵⁻²⁷, but have been collected only to a limited extent in SLE¹³. In this perspective it is of interest that SLE and RA patients had similar change. Presence of fibromyalgia may explain the higher level of pain in patients with SLE.

Like health status, no significant change in mean SLE disease activity was observed over the 2 years, whereas individual activity changed. Mean SLEDAI scores were comparable with observations in other studies^{9-11,13,22}, as well as the most frequently observed activity in the immune system⁹. Similarities to other studies were also found for the magni-

tude of the organ damage scores and the proportion of patients with damage in at least one organ system after 2 years^{7,8,28}, as well as the most frequently observed damage in the musculoskeletal system, followed by the central nervous system^{11,23,29,30}. However, we observed a higher proportion of patients with muscular weakness and osteoporosis as part of damage in the musculoskeletal system compared to the findings of Petri, *et al*³¹ and Zonana-Nacach, *et al*²⁹, who reported avascular bone necrosis was the most frequent musculoskeletal damage. Although a low proportion of our patients had neurologic disorder according to the ACR criteria, increase in damage occurred most frequently in the neuropsychiatric system. Probably the damage may be associated with subclinical neurologic or psychiatric disorders, as described by Urowitz, *et al*³².

Our study reveals the progression of organ damage in spite of stable health status. This dissociation may be related to the different metric properties of the instruments in question. Changes in health status may occur both in the directions of improvement and/or deterioration, whereas the SLICC/ACR-DI scores may either be stable or increase⁶. Stable measures of self-reported health status may reflect the adjustment of patients to daily life despite their chronic disease. In contrast, rheumatologists assessing organ damage may be more concerned with damage over time, which may contribute to an over-reporting. Similar findings are evident from RA, showing preserved functional health status in contrast to progression in structural damage in the joints³³⁻³⁵.

The progression of organ damage may also be due to side effects of the treatment⁶, in particular corticosteroids and to a lesser extent cytotoxic drugs. We found a possible role of cumulative corticosteroid dose in the development of organ damage, as shown in bivariate analysis (Table 5). The higher

dose probably reflects the active disease in these patients, which may indicate that the antimalarial and cytotoxic drugs should have been used more rigorously. Petri, *et al*²³ had shown that corticosteroids contributed to damage even more than SLE itself, whereas Nossent, *et al*²⁸ found no clear correlation between corticosteroids and damage.

One major challenge for the clinician is to predict disease course when facing a patient with SLE. This study showed that the best predictors of increase in organ damage were disease activity and organ damage at baseline. Our data support that use of a SLEDAI score is clinically important, not only at diagnosis³⁶ but also during the disease course. Disease activity and high levels of organ damage have also been identified as prognostic factors for adverse outcome in other studies^{28,37-40}.

Arthritis was found to reduce the risk of further damage. This observation could not be explained by interaction between arthritis and antimalarial therapy. On the other hand we did not find decreased risk of nephritis in the patients with arthritis, in contrast to Kaplan, *et al*⁴¹.

The best predictors of health status after 2 years (SF-36 physical and SF-36 mental) were the respective baseline scores (Table 6). Similar observations have been made in RA³⁵. Longitudinal health status data have been lacking in SLE, and this is the first study trying to predict outcome in terms of health status. As expected, no significant relationships were found when exploring change in health status scores, change in individual SLEDAI scores, and change in organ damage scores in multivariate analysis, in agreement with results from a previous cross sectional study²².

Selection bias must always be considered a possible limitation of clinical studies. The relatively high proportion of skin and musculoskeletal involvement among our patients with SLE may indicate a somewhat selective patient population in the direction of less internal organ involvement. Other possible study limitations include the relatively small study sample of SLE patients, lack of prospective data from their disease onset, and lack of clinical data for the patients with RA in terms of disease activity and joint damage. The strength of this study is the prospective followup design, the comprehensive data collection capturing all domains that were recently proposed for longitudinal observation studies in SLE³, the high response rates, and the successful matches of the study populations regarding health status measures. The patient data from the Oslo RA register have been considered representative for the true RA population in the county⁴², which should also be the case for RA patients sampled for this study.

Our 2 year longitudinal observational study showed a stable course of SLE with reference to health status and disease activity, in contrast to worsening of organ damage. Our data highlight the role of disease activity and previous organ damage as predictors of damage. Clinical conclusions arising from our study include careful monitoring of disease

activity over time and individually tailored treatment guided by the predictors of course and outcome.

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