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Childhood-Onset Disease Predicts Mortality in an Adult Cohort of Patients with Systemic Lupus Erythematosus

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Abstract

Objective—To examine childhood-onset disease as a predictor of mortality in a cohort of adult patients with systemic lupus erythematosus (SLE).

Methods—Data were derived from the University of California Lupus Outcomes Study, a longitudinal cohort of 957 adult subjects with SLE that includes 98 subjects with childhood-onset SLE. Baseline and follow-up data were obtained via telephone interviews conducted between 2002-2007. The number of deaths during 5 years of follow-up was determined and standardized mortality ratios (SMRs) for the cohort, and across age groups, were calculated. Kaplan-Meier life table analysis was used to compare mortality rates between childhood (defined as SLE diagnosis <18 years) and adult-onset SLE. Multivariate Cox proportional hazard models were used to determine predictors of mortality.

Results—During the median follow-up period of 48 months, 72 deaths (7.5% of subjects) occurred, including 9 (12.5%) among those with childhood-onset SLE. The overall SMR was 2.5 (CI 2.0-3.2). In Kaplan-Meier survival analysis, after adjusting for age, childhood-onset subjects were at increased risk for mortality throughout the follow-up period ($p<0.0001$). In a multivariate model adjusting for age, disease duration and other covariates, childhood-onset SLE was independently associated with an increased mortality risk (hazard ratio [HR]: 3.1; 95% confidence interval [CI]: 1.3-7.3), as was low socioeconomic status measured by education (HR: 1.9; 95% CI 1.1-3.2) and end stage renal disease (HR: 2.1; 95% CI 1.1-4.0).

Conclusion—Childhood-onset SLE was a strong predictor of mortality in this cohort. Interventions are needed to prevent early mortality in this population.

Introduction

The long-term survival for adults and children with systemic lupus erythematosus (SLE) has improved dramatically over the last several decades. While once associated with significant early mortality, five-year survival rates for SLE have improved from 64-87% in the 1980's to above 95% today [1-4]. Improvement in survival has been attributed to several important advances in SLE care including more timely diagnosis and treatment, and earlier recognition and more aggressive management of disease-related comorbidities. Despite this

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improvement in short-term survival, a significant percentage of SLE patients still die prematurely. Across studies, the fifteen-year survival rate ranges from 76-85% [1-3]. In addition, the standardized mortality rate for patients with adult-onset SLE is 2 to 5 times higher than that for the general population [5-7], and is almost 20 times higher among young adults with SLE [8].

Approximately 15-20% of patients with SLE are diagnosed in childhood [9]. While the trends in improved survival for childhood-onset SLE appear to be similar to that of adult-onset SLE [10-13], little is known about the long-term outcomes of adults with childhood-onset SLE. Prior studies suggest that childhood-onset SLE has a more aggressive course than adult-onset SLE [14-16], likely leading to increased exposure to potentially toxic immunosuppressive medications, over a longer disease duration [17]. Similarly, some studies suggest that patients with childhood-onset SLE accumulate disease damage more quickly, as compared to adult-onset SLE, and as a result may be at higher risk for early mortality [16].

The primary objective of this study was to determine predictors of mortality in a large, community-based cohort of patients with SLE, with a focus on describing the long-term mortality associated with childhood-onset SLE. Given the known increased risk of morbidity associated with childhood-onset SLE, we hypothesized that these subjects would have a higher risk of mortality in the follow-up period, as compared to their adult counterparts.

Subjects and Methods

Subjects

Between 2002-2003, 957 subjects were enrolled in the University of California, San Francisco Lupus Outcomes Study (LOS), an ongoing longitudinal study of a large cohort of persons with SLE from the United States. Details regarding eligibility and enrollment of participants have been described elsewhere [18]. Briefly, subjects previously enrolled in the UCSF Lupus Genetics Project [19] were invited to enroll in the LOS. Participants were recruited from both clinical and community-based sources: 22% from UCSF-associated clinics, 11% from non-UCSF-rheumatology offices, and 67% from various community-based sources (e.g., lupus support groups, conferences, newsletters, websites). All participants had a confirmed diagnosis of SLE based on review of medical records. The study protocol was approved by the UCSF Committee on Human Research.

Data Collection

LOS data are derived from structured, one-hour telephone interviews conducted by trained interviewers. Validated items from the annual survey pertaining to demographic and socioeconomic characteristics, cumulative disease manifestations and recent SLE activity and general health status were used to determine predictors of mortality in the LOS. The data in this study include results from the first (baseline) interviews which occurred in 2002-2003, and the subsequent four years of annual interviews (2004-2007).

Demographics—At baseline, information regarding various demographic characteristics was collected including age, gender, self-reported ethnicity, education and poverty status. Ethnicity was dichotomized into Caucasian versus non-Caucasian. Highest level of education achieved either before or during the study follow-up period was categorized as 1) graduated high school or less, 2) some college/trade school or 3) a college degree or higher. The percentage of participants living below poverty, defined as household income less than 125% of the Federal poverty guidelines, was also determined.

Disease duration, activity and general health status—Disease duration was calculated as the number of years since diagnosis of SLE. Disease activity was assessed using the Systemic Lupus Activity Questionnaire (SLAQ), a validated, patient-reported assessment of disease activity in SLE [20]. This measure correlates strongly with the Systemic Lupus Activity Measure-Revised (SLAM-R) and with the other self-report measures of SLE activity used in this study [21]. SLAQ scores are not available from the first year (baseline) interviews, leading to missing data for 70 subjects who only completed the baseline interview. In addition to the SLAQ, disease activity was determined by patient assessment of disease activity (reported on a scale of 0-10; 0= 'no activity', 10= 'extremely active'); this measure is available in all years and correlates strongly (r=0.73) with the SLAQ. General health status was assessed by the Short Form-12 Physical Component Score (PCS-12) [22]. The data reported for the SLAQ and PCS-12 reflect the interview results from the year preceding subject death or the most recent interview available prior to the end of the study follow-up period.

Organ involvement and co-morbidities—A history of renal involvement was determined based on whether or not the subject met the ACR SLE criteria for renal disease (from medical records), as well as subject self-report of end stage renal disease (ESRD) either at the baseline interview or at any point during the study follow-up period. Subjects were considered to have a positive history of cardiovascular disease if they reported a history of 'heart disease' or a 'heart attack' at the baseline interview or during the follow-up period.

Childhood-onset SLE—Subjects were classified as having childhood-onset SLE if the age at diagnosis was <18 years.

Outcomes

In this analysis, the primary outcome of interest was mortality over five years of study follow-up from 2003-2008. In the majority of cases, the study coordinators were notified of a subjects' death by family members at the time that the subjects were contacted to participate in the annual survey. To confirm the deaths and to obtain cause of death data, probabilistic linkage to the National Death Index (NDI) was performed for patients deceased or lost to follow-up prior to December 2006, the last month for which NDI data are currently available. The NDI was provided key subject data (name, date of birth, last known address) and previously validated algorithms were used for selecting matches on the basis of the probability of a correct match.

From a combination of study and NDI records, we determined that here were 72 deaths among LOS subjects between 2002-2008. Forty-seven deaths occurred prior to December 2006 (the last month for which NDI data are currently available), and the majority of these deaths (35/47) were also listed in the NDI. Cause of death data, using ICD-10 codes, was provided for 33/35 subjects (cause of death data was not listed for two subjects). In addition, three subjects who had been lost to follow-up were determined by NDI data to be deceased, for a total of 38 NDI listed deaths. Therefore, cause of death data were obtained on 36/72 deceased subjects. In the analysis, subjects lost to follow-up (approximately 3-5% per year) are presumed to be survivors.

Statistical Analysis

The primary outcome variable for this study was mortality. Subjects were classified as "deceased" if they died during the follow-up period; "survivors" included subjects who were alive as of the last contact with the study, or those who were lost to follow-up but not confirmed to be deceased. We compared the demographic and disease characteristics

(disease activity, organ manifestations, general health status) of the two groups. Demographic and disease characteristics were expressed using means, medians, standard deviations (SD) and proportions, as appropriate, and statistical tests (rank sum, t-test, chi squared) of comparison were employed.

Standardized mortality ratios (SMRs) (ratio of the observed number of deaths to the expected number of deaths) were calculated for the overall cohort and for 5 age groups (19-34, 35-49, 50-64, 65-79 and ≥ 80 years). The number of expected deaths was derived from the death records from the National Vital Statistics Reports for 2006 [23].

Kaplan-Meier life table analyses, including calculation of unadjusted and age-adjusted log rank tests, were used to compare mortality rates between subjects with childhood and adult-onset SLE. Individual Cox proportional hazard models, adjusting for age and disease duration categorized as a dichotomous variable (disease duration of < 10 years versus ≥ 10 years) were used to assess predictors of mortality. Covariates for these models were selected a priori and included childhood-onset SLE, male gender, ethnicity (Caucasian versus non-Caucasian), baseline measures of socioeconomic status including education (any college versus not), and insurance status (categorized as employer-based as the referent group, Medicare and Medicaid), history of ESRD, history of cardiovascular disease and SLAQ score as of the most recent interview. A multivariate model was constructed to determine the relative contribution of each predictor to mortality, and included age and disease duration, along with the covariates that were statistically significant ($p<0.05$) in the individual Cox models. Education was chosen as the measure of socioeconomic status in the final multivariate model, however alternative models substituting other measures of socioeconomic status (poverty, insurance source) yielded similar results.

Statistical analyses were performed using SAS version 9.2 (SAS Institute, Cary, NC) and STATA software, version 9.0 (StataCorp, College Station, TX).

Results

Differences between the ‘Survivors’ and the ‘Deceased’

Baseline data were collected on 957 subjects. The mean age of the cohort was 46.8 years, 91% were female, 66% Caucasian, 10% (n=98) had childhood-onset SLE, and median disease duration was 11 years. During the follow-up period, 72 deaths (7.5% of subjects) occurred, including 9 deaths (12.5% of all deaths) among subjects with childhood-onset SLE. The median follow-up time was 48.1 months.

Differences in demographic, SLE-related and general health characteristics between the ‘surviving’ and ‘deceased’ subjects are shown in Table 1. Deceased subjects were older and more likely to be male. There was no difference in mortality with regard to ethnicity. Deceased subjects had less education, were more likely to have incomes below the poverty level and were more likely to have Medicare or Medicaid versus employer-based insurance.

Regarding SLE characteristics, deceased subjects had a longer disease duration (20 versus 16 years, $p=0.0009$), were more likely to meet the ACR criteria for renal disease (40% versus 26%, $p=0.008$) and were more likely to have ESRD (26% versus 8%, $p<0.0001$). Deceased subjects were also more likely to report a history of cardiovascular disease (53% versus 26%, $p=<0.0001$). There was no difference in the frequency of SLE flares in the 3 months prior to interview between the survivors and the deceased; hospitalizations in the past year were much more common in the deceased group (51% versus 23%, $p<0.0001$). The PCS-12 was significantly lower in the deceased group (33 versus 38, $p<0.0001$).

Risk of death compared with the general population

The SMRs for all cause mortality, by age groups, are shown in Table 2. The overall SMR for the cohort was 2.5 (CI 2.0-3.2) The excess mortality risk was strikingly high (20.4 (CI 9.3-38.7) in the youngest age groups, but remained elevated through age 79.

Cause of death

Cause of death data has been obtained so far on 36/72 (50%) deceased subjects. Systemic lupus erythematosus was coded as one of the causes of death in 19/36 (53%) cases. Three deaths were attributed directly to SLE. The most common causes of death not attributable to SLE alone included death due to: 1) circulatory disease (n=12), including heart failure, arterial disease and cerebrovascular disease (stroke); 2) infection (n=7), including pneumonia and septicemia; 3) malignant neoplasm (n=4), including lung and lingual cancer and B cell lymphoma; 4) pulmonary disease (n=5), including pulmonary fibrosis, chronic obstructive respiratory disease and respiratory failure; 5) renal failure (n=2); and 6) other causes not related to SLE (n= 3), including 'muscular dystrophy', 'exposure to uncontrolled fire' and 'poisoning by exposure to drugs and medications.'

Childhood versus Adult-Onset SLE

Differences between the childhood and adult onset subjects are shown in Table 3. As has been demonstrated in a prior study, childhood-onset subjects were younger and were more likely to be male and non-Caucasian [17]. They were also more likely to have obtained a college degree or other higher education, and they were more likely to have employer-based health insurance. With regard to SLE characteristics, childhood-onset SLE subjects had a longer disease duration (19.5 versus 16.5 years, $p<0.0001$), were more likely to meet the ACR criteria for renal disease (56.1% versus 23.6%, $p<0.0001$) and were more likely to have ESRD (21.4% versus 8.4%, $p<0.0001$). Rates of cardiovascular disease were similar between the two groups. Adult-onset SLE subjects were more likely to report an SLE flare in the three months prior to interview and had higher disease activity scores, but childhood-onset SLE subjects were more likely to be on prednisone and other immunosuppressive therapies ([17], data not shown). The PCS-12 was significantly higher in the childhood-onset cohort (44 versus 37, $p<0.0001$).

Mortality among Subjects with Childhood-Onset SLE versus Adult-Onset SLE

Nine of 98 (9%) childhood-onset SLE subjects died in the follow-up period, and are described in more detail in Table 4. The median age of death was 33 (range 19-49) years and the median disease duration was 16 (range 5-33) years.

The Kaplan Meier survival curves for childhood versus adult onset disease are shown in Figure 1. Results from an unadjusted log rank test demonstrated no significant difference in the mortality rates between childhood and adult-onset SLE ($p=0.34$), but after controlling for age, the differences in mortality rates between childhood and adult-onset SLE became statistically significant ($p<0.0001$).

Predictors of Mortality

As shown in the first column of Table 5, in Cox proportional hazards models adjusting for age and disease duration at baseline, childhood-onset SLE, male gender, education, Medicare or Medicaid insurance and a history of ESRD and cardiovascular disease were all associated with a higher risk of death in the follow-up period. Ethnicity and SLE disease activity were not associated with increased mortality risk. In the full multivariate model, childhood-onset SLE, education and ESRD remained significant predictors of mortality.

Discussion

In this study, we examined the causes and predictors of mortality in a large community-based cohort of patients with SLE, which includes a substantial number of subjects with childhood-onset SLE. We found that childhood-onset SLE was a significant predictor of mortality in our population. This finding highlights the importance of identifying modifiable risk factors to prevent early mortality among patients with childhood-onset SLE.

During the first five years of study follow-up, 7.5% of LOS subjects died. This study confirms some of the previously identified predictors of increased mortality in SLE, including demographic characteristics such as male gender, lower educational attainment and income, and disease-related factors, including the presence of cardiovascular disease and ESRD, and poorer general health [5, 24-27].

The SMR for the cohort was 2.5, which is consistent with SMRs calculated from other large SLE cohorts [5, 6]. A 2006 study by Bernatsky et al utilizing the Systemic Lupus International Collaborating Clinics (SLICC) international multi-site cohort, calculated an unadjusted SMR across participating sites of 2.4, and an SMR for the sites in the United States of 2.2 [8]. The SLICC cohort study also noted a particularly high SMR of 19.2 for adolescents and young adults (ages 16-24 years) with SLE. In our cohort, the SMR for subjects in the youngest age category of ages 19-34 years was also strikingly high at 20.4, and this calculation included six deaths among subjects with childhood-onset SLE. Among the subjects for whom cause of death could be determined, approximately half of the deaths were due to cardiovascular disease or infection, which is consistent with other studies describing cause of death in SLE [3, 5, 8, 28-31]. Systemic Lupus Erythematosus was listed as a cause of death in just over half of the subjects for whom cause of death records were available. At least one prior study has demonstrated an under-reporting of SLE as the cause of death on death certificates [32].

There were nine subjects with childhood-onset SLE who died during the follow-up period. It is both striking and disturbing that all of the deaths in the childhood-onset cohort occurred in young patients (age range 19-49 years), with a median disease duration of 16 years. Three of these subjects self-reported a history of a ‘heart attack’, including one subject who died at age 26.

Given the difficulties inherent in conducting longitudinal, long-term follow-up studies of patients with childhood-onset rheumatic disease, little is known about the outcomes of patients with childhood-onset SLE once they reach adulthood. Tucker et al., compared differences in morbidity and mortality among adolescent and adult-onset SLE patients in the Lupus in Minorites: Nature versus Nurture (LUMINA) cohort, who were followed for and average of 6.8 and 5.6 years after diagnosis, respectively [16]. The adolescent-onset cohort, who aged into early adulthood during the period of study follow-up, had increased disease-related damage as measured by an Systemic Lupus International Collaborating Clinics/ American College of Rheumatology (SLICC/ACR) Damage Index (SDI) score of 2.3 (versus 1.6 for the adult-onset group). Unadjusted mortality rates were almost twice as high among patients with adolescent-onset disease, although these differences did not reach statistical significance. The findings from the present study, which compares childhood and adult-onset subjects in the context of a much longer mean disease duration, suggest that childhood-onset SLE patients continue to be at risk for early mortality over the duration of their disease. In addition, after adjusting for several important covariates, childhood-onset SLE was an independent predictor of mortality in our cohort.

Why would childhood-onset SLE subjects be at risk for early mortality, and what factors (eg. differences in demographic or disease-related factors) explain this risk? As compared to

adult-onset SLE, childhood-onset SLE subjects are more likely to be male and non-Caucasian, both previously identified risk factors for mortality in SLE. With regard to disease factors, one could presume that increased disease damage (eg. increased rates of ESRD), earlier development of disease related morbidities (eg. cardiovascular disease) and longer exposure to SLE-related therapies and side effects could all predispose these patients to an increased risk of death at an earlier age, as compared to patients with adult-onset SLE with the same disease duration. However, after controlling for many of these factors in the multivariate model, childhood-onset SLE remained an independent predictor of mortality. This suggests that there must be another explanation for the increased mortality risk among patients with childhood-onset SLE. One hypothesis is that genetic differences, such as increased genetic susceptibility, leads to earlier disease onset and increased disease severity among childhood-onset SLE patients. Another possibility is that pediatric patients are more biologically vulnerable to the effects of SLE and its treatment.

Although this study is the one of the first to examine the long-term mortality associated with childhood-onset SLE, there are several important limitations. First, because this study relies on subject self-reported outcomes, inaccuracies in subject reporting may occur. This limitation was addressed in part by validating a subset of the self-reported outcomes through chart review. Second, the LOS is not an inception cohort, so the conclusions should be interpreted in the context of a potential survival bias, as mortality data are only available over the period of study follow-up, and not from the date of diagnosis. Given the increased risk of early mortality among patients with childhood versus onset-SLE, our sample may underestimate the true differences in long-term mortality of childhood and adult-onset SLE, as the sicker childhood-onset SLE patients were less likely to have survived to enrollment in the LOS. Third, cumulative disease damage was not assessed in this study. The increase in mortality among childhood-onset SLE subjects could be explained by increased disease damage, as prior studies have shown an increase in cumulative disease damage in childhood versus adult-onset SLE [14-16] . However, ESRD is a significant marker of disease damage and mortality in SLE, and this was included as an independent predictor of mortality in the multivariate model [33]. Finally, given the small number of deaths in the childhood-onset cohort, our study was not powered to identify particular risk factors associated with mortality among the childhood-onset group.

In conclusion, our findings indicate that SLE patients with childhood-onset disease were at high risk for mortality at an early age. These results highlight the need for long-term, longitudinal studies of patients with childhood-onset chronic disease that better delineate the modifiable disease-related, behavioral and health care system factors which contribute to less favorable outcomes for patients with childhood-onset SLE. Studies are needed to develop prognostic models to identify patients at high risk for significant morbidity or early mortality for both childhood and adult-onset SLE, and to design interventions to improve the quality of care for this vulnerable group of patients.

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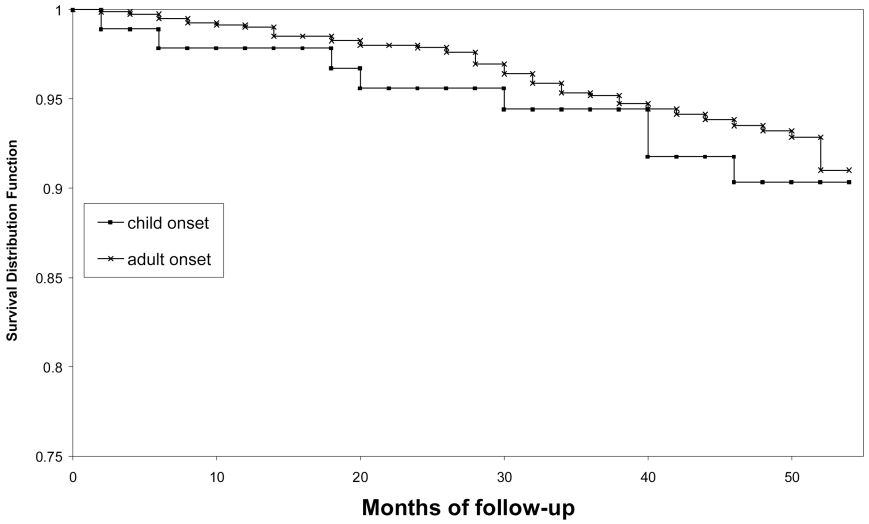

Figure 1.
Comparison of mortality among subjects with childhood versus adult-onset SLE.

Table 1

Characteristics of LOS subjects according to survival status.

	Survivors (n=885)	Deceased (n=72)	*p* value
Demographic Characteristics			
Age, mean (range), y *	49 (19-86)	56 (21-100)	0.0006
Male, %	8	21	0.0002
Ethnicity, %			
Non-Caucasian	34	30	0.57
Education, % *			
Some/Graduated High School	16	32	
Some College/Trade School	45	42	0.0011
College degree or Higher	39	26	
Below Poverty, % §	11.3	25.7	0.0008
Insurance, % §			
Employer-based	72	40	
Medicare	22	45	<0.0001
Medicaid	6	15	
SLE Characteristics *			
Age at diagnosis, median (range), y	33 (2-75)	31 (13-87)	0.32
Disease duration, mean (range), y	16 (1-51)	20 (7-42)	0.0009
Organ Manifestations, %			
ACR Renal Criteria	26	40	0.008
End Stage Renal Disease	8	26	<0.0001
Cardiovascular disease †	26	53	<0.0001
Disease Activity			
SLAQ score (SD) ‡	12.6 (8.0)	14.6 (8.9)	0.09
SLE activity score (SD)	4.2 (2.8)	4.5 (3.3)	0.54
Hospitalization in the past year, %	23	51	<0.0001
Childhood-onset SLE, no (%)	89 (10)	9 (12.5)	0.51
General Health Status *			
PCS-12, mean (SD)	38 (10.8)	33 (8.4)	<0.0001

SLE= Systemic Lupus Erythematosus, ACR= American College of Rheumatology, CESD = Center for Epidemiologic Studies Depression Scale, SLAQ= Systemic Lupus Activity Questionnaire, PCS-12= Short Form-12 Physical Component Score

* Data from most recent interview

§ Data from baseline interview

† Includes history of heart disease or heart attack

‡ Missing data for 70 observations and 22 decedents

Table 2

Standardized Mortality Ratios (SMR) and number of deaths by age group in the LOS.

Age group	Adult-Onset Deaths (n=63)	Childhood-Onset Deaths (n=9)	Total Deaths (n=72)	SMR* (95% CI)
19-34	3	6	9	20.4 (9.3–38.7)
35-49	16	1	17	5.1 (2.9–8.1)
50-64	19	2	21	1.9 (1.2–2.9)
65-79	23	0	23	1.7 (1.1–2.5)
≥ 80	2	0	2	0.7 (0.1–2.4)

*Standardized Mortality Ratio (SMR) comparing total observed deaths to the number of expected deaths, derived from the 2006 National Vital Statistics Reports.

Table 3

Characteristics of LOS subjects according to age of diagnosis.

	Adult-Onset SLE (n= 859)	Childhood-OnsetSLE (n= 98)	*p* value
Demographic Characteristics			
Age, mean (range), y *	52 (23-99)	33 (19-63)	
Male, %	8	15.5	0.018
Ethnicity, %			
Non-Caucasian	32	51	0.0009
Education, % *			0.05
Some/Graduated High School	17	15	
Some College/Trade School	46	36	
College degree or Higher	37	49	
Below Poverty, % §	12.2	13.4	0.7
Insurance §			0.04
Employer-based	69	74	
Medicare	24	16	
Medicaid	7	10	
SLE Characteristics *			
Age at diagnosis, median (range), y	35 (18-87)	15 (2-17)	<0.0001
Disease duration, mean (range), y	16.5 (1-50)	19.5 (4-51)	<0.0001
Organ Manifestations, %			
ACR Renal Criteria	23.6	56.1	<0.0001
End Stage Renal Disease	8.4	21.4	<0.0001
Cardiovascular disease †	28	24	NS
Disease Activity,			
SLAQ score, mean (SD) ‡	13 (8.0)	9 (7.9)	<0.0001
SLE activity score, mean (SD)	4.4 (2.8)	3.0 (2.8)	<0.0001
Hospitalization in the past year, %	25	24	NS
General Health Status *			
PCS-12, mean (SD)	37 (10.7)	44 (9.0)	<0.0001
Mortality			
No of deaths, (%)	63 (7)	9 (9)	NS
Age of death, mean (range), y	52 (23-100)	33 (19-49)	<0.0001

SLE= Systemic Lupus Erythematosus, ACR= American College of Rheumatology, CESD= Center for Epidemiologic Studies Depression Scale, SLAQ= Systemic Lupus Activity Questionnaire, PCS-12= Short Form-12 Physical Component Score

* Data from most recent interview

§ Data from baseline interview

† Includes history of heart disease or heart attack

‡ Missing data for 62 adult-onset and 8 childhood-onset subjects with only baseline data

Table 4

Description of deceased subjects with childhood-onset SLE in the LOS.

Subject Number	Male/Female	Age at Diagnosis (yrs)	Age of Death	Disease Duration (yrs)	History of ESRD	History of a 'Heart Attack'	Cause of death
1	F	14	26	11	Yes	Yes	*
2	F	13	21	8	No	No	*
3	M	16	24	8	No	No	*
4	M	15	51	36	No	No	SLE/Encephalopathy
5	F	17	47	30	Yes	Yes	Acute MI
6	F	15	50	35	Yes	Yes	*
7	F	15	34	19	No	No	SLE/Arteritis
8	M	14	25	11	Yes	No	Muscular dystrophy
9	F	17	32	15	Yes	No	SLE/ESRD

SLE= Systemic Lupus Erythematosus, ESRD= End Stage Renal Disease, MI= Myocardial Infarction

* Data not available from National Death Index

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Table 5

Mortality risk in the LOS, from Cox proportional hazard models.

Variable	Individual models* HR (95% CI)	Full multivariate model† HR (95% CI)
Childhood-Onset SLE	**3.5 (1.5-8.0)**	**3.1 (1.3-7.3)**
Male	**2.2 (1.2-4.0)**	1.6 (0.8-3.0)
Education	**2.1 (1.2-3.4)**	**1.9 (1.1-3.2)**
Insurance		
Employer-based	ref	
Medicare	**2.0 (1.1-3.5)**	
Medicaid	**4.5 (2.1-9.5)**	
Below Poverty	**2.4 (1.4-4.3)**	
End Stage Renal Disease	**2.0 (1.2-3.4)**	**2.1 (1.1-4.0)**
Cardiovascular Disease	**1.9 (1.2-3.1)**	1.6 (0.8-3.1)
SLE activity	1.06 (0.9-1.1)	

*Individual models adjusted for baseline age and disease duration.

†Full multivariate model includes for baseline age and disease duration, in addition to the variables shown.