Increased risk of acute myocardial infarction and mortality in patients with systemic lupus erythematosus: two nationwide retrospective cohort studies

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ABSTRACT

Background: This study evaluated the risk of acute myocardial infarction (AMI) and mortality among patients with systemic lupus erythematosus (SLE) in two nationwide retrospective cohort studies.

Methods: Using Taiwan's National Health Insurance Research Database, we conducted a retrospective cohort study and identified 1207 adults newly diagnosed with SLE in 2000-2004. Non-SLE cohort consisted of 9656 adults without SLE, frequency-matched for age and sex and randomly selected from the same data set. Events of AMI were considered as outcome during the follow-up period between 2000 and 2008. Another nested cohort study of 6900 patients with AMI receiving cardiac surgeries was conducted to analyze the impact of SLE on post-AMI mortality.

Results: During the follow-up period, there were 52 newly diagnosed AMI cases. The incidences of AMI for SLE cohort and non-SLE cohort were 2.10 and 0.49 per 1000 person-years, respectively, with an adjusted hazard ratio (HR) of 5.11 (95% confidence interval [CI] 2.63-9.92). For females, the adjusted HR of AMI associated with SLE was as high as 6.28 (95% CI 2.67-14.7). Further analyses in the nested cohort showed SLE was significantly associated with post-AMI mortality (odds ratio, 2.60; 95% CI 1.09-6.19).

Conclusion: Patients with SLE had higher risk of AMI compared with non-SLE

control, and this risk was more significant in females. In addition, SLE is an independent risk factor for post-AMI mortality.

Keywords: Myocardial infarction, Mortality, Systemic lupus erythematosus

Introduction

Systemic lupus erythematosus (SLE) is a chronic autoimmune connective tissue disorder with a broad range of clinical presentations that mainly affects women of childbearing age [1]. It represents a substantial global disease burden, with one United States estimate of prevalence finding 143.7 cases per 100,000 people [2]. Although the epidemiology, complications and treatment of SLE are well studied [1-3], poor quality of life and increased mortality from SLE are serious problems of global concern [4].

Over the past thirty years, many studies have provided clinical evidence regarding management of acute myocardial infarction (AMI) [5]. Although reductions in incidence and mortality of AMI have been investigated [6,7], the high cost and social burden associated with this condition remain important issues [8,9]. Epidemiological studies have documented that more than 90% of AMI cases are attributable to modifiable risk factors such as smoking, dyslipidemia, hypertension, abdominal obesity, and diabetes [10]. However, specific risk factors for AMI still need to be validated.

People with SLE have shown a higher prevalence of atherosclerosis, which is a traditional risk factor for cardiovascular diseases [11]. The significantly increased risk of cardiovascular diseases in patients with SLE also has been investigated [12-20].

Previous studies reported that people with SLE had higher risk of AMI compared with those without SLE [12-16]. However, these studies were limited by small sample size [15], focusing on specific populations [12,14,16], poor study design [13,14], and inadequate adjustment for potential confounding factors [12,15].

Using Taiwan's National Health Insurance Research Database, we conducted a retrospective cohort study to investigate the association between SLE and AMI with longitudinal design, a nationwide sample, and multivariate adjustment. We also performed a nested retrospective cohort study to verify the potentially higher risk of post-AMI adverse outcomes in patients with SLE when receiving cardiac surgery.

Methods

Data sources

The research data used in this study was obtained from reimbursement claims of Taiwan's National Health Insurance Program, which was implemented in 1995 and which covers more than 99% of 22.6 million Taiwan residents. The National Health Research Institutes established a National Health Insurance Research Database recording all beneficiaries' medical services, including inpatient and outpatient demographics, primary and secondary diagnoses, procedures, prescriptions and medical expenditures. The validity of this database has been favorably evaluated, and research articles based on it have been accepted in prominent scientific journals worldwide [21-24].

Ethical approval

Insurance reimbursement claims from Taiwan's National Health Insurance Research Database are available for public access. To protect personal privacy, the electronic database with patient identifications was decoded and scrambled for further research access. Although informed consent is not required because of this decoding and scrambling to prevent patient identification, the study was evaluated and approved by Taiwan's National Health Research Institutes [21-24].

Study design

Using insurance claims, we conducted a retrospective cohort study between 2000 and 2004 and identified 1207 adults (after excluding 2125 people with previous SLE) over 20 years of age newly diagnosed with SLE (no previous history of SLE since the implementation of Taiwan's National Health Insurance Research Database in 1996) with 9656 age- and sex-matched non-SLE adults as control. Both SLE and non-SLE cohorts were either followed-up from the index date until 31 December 2008 or were censored. Follow-up time in person-years was calculated for each subject until the diagnosis of AMI or until being censored because of death, withdrawal from the insurance system or loss to follow-up. The non-SLE group included the remaining people who did not have a history of SLE throughout the following period.

A nested retrospective cohort study consisted of 6900 patients with AMI receiving cardiac surgeries with general anesthesia between 2004 and 2010. This cohort analysis was designed to investigate whether pre-AMI history of SLE is associated with 30-day in-hospital mortality after AMI with cardiac surgery. History of SLE was identified by physicians' primary diagnosis before the AMI within 24 months.

Definition and criteria

We identified patients' income status by defining low-income patients as those qualifying for waived medical copayment, as this status is verified by the Taiwan Bureau of National Health Insurance. The calculation of population density (persons

per square kilometer) was described in a previous study and categorizes quartiles as low, moderate, high and very high urbanization areas. In this retrospective cohort study, we evaluated the coexisting medical conditions throughout the follow-up period (from the 24 months before the diagnosis of SLE to the end of 2008). In the nested cohort study, we evaluated the coexisting medical conditions within 24 months before the admission of AMI. We used the *International Classification of Diseases, 9th Revision, Clinical Modification* (ICD-9-CM) to define SLE (ICD-9-CM 710.0), AMI (ICD-9-CM 410), and coexisting medical conditions including trauma (ICD-9-CM 800-904), mental disorders (ICD-9-CM 290-319), hypertension (ICD-9-CM 401-405), hyperlipidemia (ICD-9-CM 272.9), atherosclerosis (ICD-9-CM 440), liver cirrhosis (ICD-9-CM 571), diabetes (ICD-9-CM 250), and stroke (ICD-9-CM 430-438). Renal dialysis was identified by administrative code (D8, D9). Use of corticosteroid (prednisolone, betamethasone, hydrocortisone, methylprednisone, dexamethasone, cortisone, and budesonide), immunosuppressant (azathioprine, mycophenolate, cyclophosphamide, and methotrexate), anti-hypertensive (captopril, enalapril, lisinopril, fosinopril, irbesartan, valsartan, acebutolol, atenolol, carvedilol, propranolol, labetalol, metoprolol, bisoprolol, diltiazem, nicardipine, verapamil, felodipine, nifedipine, acetazolamide, metolazone, hydrochlorothiazide, and indapamide), anti-hyperlipidemic, and anti-diabetic

(included insulin, chlorpropamide, metformin, glimepiride, bromocriptine, glipizide, miglitol, glyburide, acarbose, tolazamide, rosiglitazone, tolbutamide, pioglitazone, and repaglinide) medications were also noted.

Statistical analysis

We used chi-square tests and t-tests to compare sociodemographic characteristics, coexisting medical conditions and events of AMI between cohorts with and without SLE. The adjusted hazard ratios (HRs) with 95% confidence intervals (CIs) of AMI associated with SLE were calculated in the multivariate Cox proportional hazard regression models with the adjustment of age, sex, urbanization, low income, coexisting medical conditions (such as trauma, mental disorders, hypertension, hyperlipidemia, atherosclerosis, liver cirrhosis, diabetes, renal dialysis, and stroke) and medication use (such as corticosteroid, immunosuppressants, beta-blocker, diuretics, anti-diabetes, calcium channel blocker, and angiotensin-converting-enzyme inhibitor). The sex-stratified analysis for the adjusted HRs of AMI associated with SLE was calculated in the multivariate Cox proportional hazard models. We also estimated adjusted HRs of emergency care and hospitalization for SLE on the risk of AMI. Chi-square tests were used to compare sociodemographics and coexisting medical conditions in patients having AMI with and without history of SLE. Multivariate logistic regression analysis was performed to calculate adjusted odds

ratios (ORs) and 95% CIs of post-AMI adverse events and mortality associated with history of SLE. Statistical Analysis System software version 9.1 (SAS Institute Inc., Cary, North Carolina, USA) was used for data analyses; differences between groups were considered significant if two-sided p were less than 0.05.

Results

Compared with non-SLE cohort (Table 1), cohort with SLE had higher proportions of living in very urbanized areas (27.9% vs. 23.5%, $p = 0.0004$), low income (3.3% vs. 2.1%, $p = 0.0093$), trauma (74.2% vs. 66.9%, $p < 0.0001$), mental disorders (34.1% vs. 24.8%, $p < 0.0001$), hyperlipidemia (12.7% vs. 10.2%, $p = 0.0073$), atherosclerosis (6.9% vs. 3.6%, $p < 0.0001$), liver cirrhosis (5.6% vs. 4.2%, $p = 0.0293$), and renal dialysis (2.7% vs. 0.5%, $p < 0.0001$). Patients with SLE had used more medication than non-SLE cohort, such as corticosteroid (32.8% vs. 9.1%, $p < 0.0001$), immunosuppressants (25.4% vs. 1.0%, $p < 0.0001$), beta-blocker (15.6% vs. 8.9%, $p < 0.0001$), and diuretics (3.8% vs. 1.4%, $p < 0.0001$). AMI incidence was higher in SLE cohort patients than in people without SLE (1.6% vs. 0.3%, $p < 0.0001$).

Table 2 shows that cohort with SLE had higher incidence of AMI compared with non-SLE cohort (0.49 vs. 2.10 events per 1000 person-years). After adjustment for age, sex, urbanization, low income and coexisting medical conditions, SLE was associated with AMI in the Cox proportional hazard model (HR 5.11 [95% CI 2.63-9.92]). The corresponding HRs of AMI associated with SLE for women and men were 6.28 (95% CI 2.67-14.7) and 6.00 (95% CI 1.75-20.5), respectively. In further severity analysis, emergency visits (HR 5.66 [95% CI 1.08-29.7]) and hospitalization (HR 8.77 [95% CI 2.40-32.0]) with the primary diagnosis of SLE were significant factors associated with risk of AMI (Table 3).

In the cohort of 6900 patients receiving cardiac surgeries with AMI, 24 had a history of

SLE (Table 4). There were significant differences in age, sex, low income, and renal dialysis between patients having AMI with and without history of SLE. Table 5 shows that patients with SLE had higher post-AMI mortality compared with those without SLE after adjusting for age, sex, urbanization, low income, hypertension, diabetes, stroke, mental disorders, renal dialysis, hyperlipidemia and liver cirrhosis with the multivariate regressions (OR 2.60 [95% CI 1.09-6.19]).

Discussion

This nationwide retrospective cohort study reported increased risk of AMI among SLE patients compared with non-SLE cohort. The association was more significant in women than in men. We further investigated the impacts of emergency visit and hospital inpatient services among SLE patients having higher risk for AMI. A further retrospective cohort study found SLE patients after AMI had higher 30-day in-hospital postoperative mortality than non-SLE cohort when undergoing cardiac surgeries.

In the United States, SLE prevalence has been shown to be 6 times higher among women than in men; the same study shows that SLE prevalence also varies with age and geographic region [2]. Lower household income was independently associated with organ damage for patients with SLE [24]. The risk of AMI was also associated with older age, male gender, lower socioeconomic status, and greater urbanization [26-28]. In this study, age, sex, urbanization, and low income were identified as potential factors associated with SLE; these factors were adjusted in the multivariate regressions when investigating the association between SLE and AMI.

Stroke [29], hypertension [27,28], diabetes [27,28], hyperlipidemia [28], renal dialysis [30], and mental disorders [31] are considered as risk factors for AMI. Although other researchers have shown a lower rate of myocardial infarction in patients with liver cirrhosis [32], recent studies showed an increased risk of cardiovascular disease in patients with non-alcoholic fatty liver disease [33,34]. Patients with SLE have higher prevalence of hypertension,

hyperlipidemia, and neuropsychiatric disorders, and they often relapse with kidney diseases [35]. To eliminate the potential confounding effects of coexisting medical conditions such as hypertension, diabetes, stroke, mental disorders, renal dialysis, hyperlipidemia, and liver cirrhosis on the association between SLE and AMI and on post-AMI mortality, we used multivariate regression to control these potential confounders.

The results of present study showed increased risk of AMI in patients with SLE, particularly for male patients [12-16]. The pathophysiology of premature accelerated atherosclerosis is incompletely understood but is likely to be multifactorial, particularly when considering disease-related factors [11]. SLE has marked female predominance after puberty, and onset of SLE after postmenopausal age is uncommon [36]. While there is lower incidence of cardiovascular disease in premenopausal women, such disease increases sharply after menopause [37]. Although female hormones seem likely to have cardiac protection [38], the present study investigated the association between SLE and AMI was more significant in women than in men. Higher incidence of SLE and use of medication for treating SLE may explain why female patients with SLE had higher risk of AMI. However, this hypothesis needs further investigations to provide much more evidence.

There are various clinical presentations of SLE involving multiple organ systems. Although several indices have been developed to measure inflammatory disease activity, no consensus has been reached regarding which index is best [39-41]. In this study, history of pre-AMI emergency and inpatient care may be considered as SLE severity. Our results suggested that

patients with history of emergency and inpatient treatment for SLE had significant risk of AMI afterward.

Another aim of this study was to investigate outcomes among SLE patients after AMI and receiving cardiac surgeries, and we found that their 30-day in-hospital mortality was significantly higher compared to non-SLE patients. The possible causes for this may be associated with active inflammatory status, corticosteroids or immunosuppressant treatments, and progressive organ damage. This information can help physicians to determine whether patients with SLE should be more aggressively treated for cardiovascular disease in daily clinical practice.

Because the pathogenesis of cardiovascular disease in lupus is likely multifactorial, we proposed some possible explanations for clarifying the increased risk of AMI and post-AMI mortality in SLE patients. First, SLE was considered as persistent systemic inflammation that is one of risk factor for cardiovascular events. Vascular inflammation may be a major contributor for cardiovascular events, although it is not the sole etiology in patients with SLE [12,13]. Second, corticosteroid treatment with resulting hypertension may accelerate the atherosclerotic process in people with SLE [12]. Third, parts of patients with SLE had renal problems, such as nephritis and ESRD that may contribute to cardiovascular events [43]. In addition to the traditional risk factors for atherosclerosis, patients with SLE may have other proatherogenic or prothrombotic risk factors, including dyslipidemia and antiphospholipid antibodies, that further increase their risk for AMI [14,44,45]”

Several studies have shown correlations between SLE and risk of AMI [12-16]. The risk of developing cardiovascular disease among SLE patients is variously reported to be two to fifty times greater; these variations are possibly due to smaller sample size, focusing on specific populations, inadequate adjustment for potential confounding factors and poor study design [12-16]. The strength of this investigation included large population-based samples, retrospective cohort design, multivariate adjustment, and age- and sex-matched selection of non-SLE control group. Because this nationwide cohort study analyzed the risk of developing AMI among SLE patients, it provides more information in different clinical scenarios such as various severity levels and postoperative mortality.

Some limitations of this study need to be addressed. First, this study used retrospective reimbursement claims, which lack data on the first major organ involvement or severity of SLE, as well as data on lifestyles and personal characteristics. Several types of biochemical data, such as fibrinogen or C-reactive protein, also were unavailable for analysis from this database. Second, since the patients were based on the diagnosis from hospital inpatient care registers, there is a limitation of the true number of cases due to silent incidence cases missed. Third, this study enrolled adults aged older than 20 years with new-onset SLE only. Although AMI rarely occurs during childhood, patients with pediatric SLE have a higher risk of premature atherosclerosis [42]. Therefore, the risk of AMI in patients with SLE may be underestimated. In addition, the detailed information on the severity of AMI and treatments, such as the New York Heart Association class, culprit lesion, maximal creatinine kinase level,

diseased vessel number, and the time (hours) to receive surgery after onset of AMI, were not available in the Taiwan National Health Insurance Research Database. In conclusion, this population-based cohort study reported that patients with SLE have increased risk of AMI, particularly those with experience of emergency visits and inpatient care for SLE. The 30-day in-hospital mortality after AMI with cardiac surgery is significantly higher in patients with SLE than in those without SLE. These findings may provide a more comprehensive understanding of risks and outcomes of AMI in this susceptible population.

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Author contribution: All authors were involved in drafting the article, interpretation of data or revising it critically for important intellectual content, and all authors approved the final version to be published. Dr. Chen had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Study conception and design: Bruderer, Bodmer, Meier. Acquisition of data: Chen. Analysis and interpretation of data: Chou, Liao.

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Table 1

Sociodemographics, coexisting medical conditions, and acute myocardial infarction in patients with and without systemic lupus erythematosus.

	Non-SLE cohort (N=9656)		SLE cohort (N=1207)		p
	n	(%)	n	(%)	
Age, years					1.00
20-29	2544	(26.4)	318	(26.4)	
30-39	2624	(27.2)	328	(27.2)	
40-49	2472	(25.6)	309	(25.6)	
50-59	1000	(10.4)	125	(10.4)	
60-69	712	(7.4)	89	(7.4)	
≥70	304	(3.2)	38	(3.2)	
Sex					1.00
Female	7912	(81.9)	989	(81.9)	
Male	1744	(18.1)	218	(18.1)	
Urbanization					0.0004
Low	2504	(25.9)	267	(22.1)	
Moderate	2508	(26.0)	286	(23.7)	
High	2375	(24.6)	317	(26.3)	
Very high	2269	(23.5)	337	(27.9)	
Low income					0.0093
No	9450	(97.9)	1167	(96.7)	
Yes	206	(2.1)	40	(3.3)	
Coexisting medical conditions					
Trauma	6464	(66.9)	895	(74.2)	<0.0001
Mental disorders	2398	(24.8)	411	(34.1)	<0.0001
Hypertension	1512	(15.7)	215	(17.8)	0.0537
Hyperlipidemia	982	(10.2)	153	(12.7)	0.0073
Atherosclerosis	347	(3.6)	83	(6.9)	<0.0001
Liver cirrhosis	405	(4.2)	67	(5.6)	0.0293
Diabetes	607	(6.3)	64	(5.3)	0.1807
Renal dialysis	47	(0.5)	32	(2.7)	<0.0001
Stroke	192	(2.0)	31	(2.6)	0.1804
Medication use					
Corticosteroid	883	(9.1)	396	(32.8)	<0.0001
Immunosuppressants	94	(1.0)	307	(25.4)	<0.0001
Beta-blocker	862	(8.9)	188	(15.6)	<0.0001
Diuretics	139	(1.4)	46	(3.8)	<0.0001
Anti-diabetes	371	(3.8)	44	(3.7)	0.7367

Calcium channel blocker	174	(1.8)	31	(2.6)	0.0651
ACEI	112	(1.2)	15	(1.2)	0.8007
New-onset AMI					<0.0001
No	9623	(99.7)	1188	(98.4)	
Yes	33	(0.3)	19	(1.6)	

AMI = acute myocardial infarction; ACEI = angiotensin converting enzyme inhibitors; SLE = systemic lupus erythematosus.

Table 2

Incidence and adjusted risk of acute myocardial infarction associated with systemic lupus erythematosus.

	n	Person-years§	AMI events	Incidence*	IRR	HR (95% CI)
SLE†						
No	9656	67407	33	0.49	1.00	1.00 (reference)
Yes	1207	9065	19	2.10	4.29	5.11 (2.63-9.92)
Sex stratification‡						
Female						
No SLE	7912	55250	22	0.40	1.00	1.00 (reference)
SLE	989	7465	12	1.61	4.03	6.28 (2.67-14.7)
Male						
No SLE	1744	12158	11	0.90	1.00	1.00 (reference)
SLE	218	1600	7	4.38	4.87	6.00 (1.75-20.5)

AMI = acute myocardial infarction; CI = confidence interval; HR = hazard ratio; IRR = incidence rate ratio; SLE, systemic lupus erythematosus.

*Per 1000 person-years.

†Adjusted for age, sex, urbanization, low income, coexisting medical conditions and medication use.

‡Adjusted for age, urbanization, low income, coexisting medical conditions and medication use.

§Person-years for SLE (Mean±SD=7.51±1.36; Median [interquartile range]=7.70 [2.18]) and non-SLE people (Mean±SD=6.98±0.29; Median [interquartile range]=7.01 [0.02]).

Table 3

Risk of acute myocardial infarction associated with severity of systemic lupus erythematosus.

	n	Person-years	Acute myocardial infarction		
			Events	Incidence*	HR (95% CI)†
Emergency care for SLE					
No SLE	9656	67407	33	0.49	1.00 (reference)
SLE without emergency care	1056	7845	17	2.17	5.08 (2.61-9.92)
SLE with emergency care	151	1219	2	1.64	5.66 (1.08-29.7)
Inpatient care for SLE					
No SLE	9656	67407	33	0.49	1.00 (reference)
SLE without inpatient care	1022	7592	15	1.98	4.81 (2.43-9.53)
SLE with inpatient care	185	1473	4	2.72	8.77 (2.40-32.0)

CI = confidence interval; HR = hazard ratio; SLE = systemic lupus erythematosus.

*Per 1000 person-years.

†Adjusted for age, sex, urbanization, low income and coexisting medical conditions.

Table 4

Baseline characteristics for patients receiving cardiac surgeries after acute myocardial infarction with and without systemic lupus erythematosus.

	Without SLE (N=6876)		SLE (N=24)		p
	n	(%)	n	(%)	
Sex					0.0002
Female	1945	(28.3)	15	(62.5)	
Male	4931	(71.7)	9	(37.5)	
Age, years					0.0012
20-29	9	(0.1)	0	(0.0)	
30-39	100	(1.5)	3	(12.5)	
40-49	485	(7.1)	1	(4.2)	
50-59	1306	(19.0)	4	(16.7)	
60-69	1673	(24.3)	6	(25.0)	
≥70	3303	(48.0)	10	(41.7)	
Urbanization					0.3427
Low	1878	(27.3)	3	(12.5)	
Moderate	1214	(17.7)	6	(25.0)	
High	2223	(32.3)	10	(41.7)	
Very high	1561	(22.7)	5	(20.8)	
Low income					<0.0001
No	6640	(96.6)	19	(79.2)	
Yes	236	(3.4)	5	(20.8)	
Coexisting medical conditions					
Trauma	3751	(54.6)	17	(70.8)	0.1098
Hypertension	3577	(52.0)	15	(62.5)	0.3050
Diabetes	2878	(41.9)	11	(45.8)	0.6934
Stroke	899	(13.1)	6	(25.0)	0.0840
Mental disorders	1480	(21.5)	5	(20.8)	0.9345
Renal dialysis	436	(6.3)	5	(20.8)	0.0038
Atherosclerosis	2068	(30.1)	3	(12.5)	0.0607
Hyperlipidemia	1021	(14.9)	3	(12.5)	0.7466
Liver cirrhosis	252	(3.7)	1	(4.2)	0.8961
Surgical procedure					
Pericardiotomy	126	(1.8)	2	(8.3)	0.0185
ECMO	968	(14.1)	2	(8.3)	0.4189
Insertion of pacemaker	11	(0.2)	1	(4.2)	<0.0001
Cardiopulmonary bypass	518	(7.5)	2	(8.3)	0.8822
CABG	1692	(24.6)	3	(12.5)	0.1690

Cardiac catheterization	5592	(81.3)	15	(62.5)	0.0183
Medication use					
Beta-blocker	1615	(23.5)	12	(50.0)	0.0023
Anti-diabetes	2011	(29.3)	10	(41.7)	0.1820
Immunosuppressants	182	(2.7)	4	(16.7)	<0.0001
Corticosteroid	462	(6.7)	3	(12.5)	0.2594
ACEI	660	(9.6)	2	(8.3)	0.8336
Diuretics	378	(5.5)	2	(8.3)	0.5432
Calcium channel blocker	340	(4.9)	0	(0.0)	0.2639

ACEI = angiotensin converting enzyme inhibitors; CABG = coronary artery bypass graft;
ECMO = Extra-Corporeal Membrane Oxygenation; SLE = systemic lupus erythematosus.

Table 5

Adverse events after cardiac surgeries in patients receiving cardiac surgeries after acute myocardial infarction associated with systemic lupus erythematosus.

	Non-SLE		SLE		OR (95% CI)*
	n	(%)	n	(%)	
30-day in-hospital mortality	1215	(17.7)	10	(41.7)	2.60 (1.09-6.19)
ICU stay	6653	(96.8)	23	(95.8)	1.15 (0.14-9.39)
Prolonged length of stay	1351	(19.7)	9	(37.5)	1.54 (0.60-3.97)
Increased ME	1371	(19.9)	9	(37.5)	2.22 (0.92-5.34)

CI = confidence interval; ICU = intensive care unit; ME = medical expenditure; OR = odds ratio; SLE = systemic lupus erythematosus.

*Adjusted for age, sex, urbanization, low income, coexisting medical conditions, surgical procedure, and medication use.