The risk of end-stage renal disease in systemic lupus erythematosus
A nationwide population-based study in Korea

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Abstract

Systemic lupus erythematosus (SLE) is known to be one of the leading causes of end-stage renal disease (ESRD). The aim of this study was to estimate the incidence rate of ESRD and the risk for progression to ESRD in SLE patients compared to the general population.

A total of 21,253 SLE patients were extracted from the Korean National Health Insurance Service database between 2008 and 2013. Age-and sex-matched controls (n = 106,265) were randomly sampled in a 5:1 ratio from non-SLE individuals. Both cohorts were followed up for development of ESRD until 2015.

During the median 7.53 years of follow-up, 533 (2.51%) cases of ESRD were newly developed in SLE patients and 145 (0.14%) cases in matched controls (incidence rate: 4.075 and 0.219 per 1000 person-year, respectively). SLE patients were at higher risk for ESRD development compared to matched controls (hazard ratio [HR], 9.84; 95% confidence interval [CI] 8.10–11.96) after multivariate adjustment. In subgroup analysis, the risk for ESRD was higher in male (HR, 7.76; 95% CI 5.07–11.90) and female patients with SLE (HR, 10.48; 95% CI 8.41–13.07) than in matched controls. When analyzed by age group, the younger the age, the higher the risk of ESRD versus non-SLE matched controls; this result was also significant after adjustment. In subgroup analysis according to comorbidities, the SLE group had a significantly higher risk of ESRD than the non-SLE group in almost all subgroups.

SLE was associated with an increased incidence of ESRD.

Abbreviations: CHF = congestive heart failure, CI = confidence interval, CKD = chronic kidney disease, COPD = chronic obstructive pulmonary disease, eGFR = estimated glomerular filtration rate, ESRD = end-stage renal disease, HR = hazard ratio, ICD-10 = International Classification of Diseases, 10th revision, MI = myocardial infarction, NHIS = National Health Insurance System, SLE = systemic lupus erythematosus, USRDS = United States Renal Data System.

Keywords: end-stage renal disease, risk, systemic lupus erythematosus

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1. Introduction

Systemic lupus erythematosus (SLE) is a chronic autoimmune disease that is typically characterized by the formation of autoantibodies such as antinuclear antibodies and anti-double-stranded DNA antibodies. SLE has diverse clinical presentations involving multiple organs including the kidney. Renal involvement is one of the most frequent and serious complications of SLE, and the presentation varies from subclinical laboratory abnormalities to overt nephritis or nephrotic syndrome. Further, SLE is one of the major causes of chronic kidney disease (CKD) and end-stage renal disease (ESRD). It is known that renal involvement occurs in approximately 60% of SLE patients,[1] and 10% to 20% of them progress to ESRD.[2] CKD and ESRD caused by lupus nephritis are major causes of mortality in SLE patients.[1] Although there have been recent advances in immunosuppressive treatment, progression to ESRD and mortality has not declined in the last decades.[1,3]

The prevalence and incidence of SLE are known to vary by race, and renal involvement tends to be more common in Asian patients.[4,5] Therefore, it is very important to evaluate the characteristics, risk factors, and prognosis of diseases that are specific to a race or country and to apply them in therapy. The aim of this nationwide cohort study was to investigate the

incidence rate of ESRD and risk factors for progression to ESRD in Korean SLE patients compared to the general population.

2. Materials and methods

2.1. Data source and study population

The Korean National Health Insurance System (NHIS), which includes an eligibility database (age, sex, socioeconomic variables, type of eligibility, income level, etc), a medical treatment database (based on the accounts that were submitted by medical service providers for their medical expenses), a health examination database (results of general health examinations and question-naires on lifestyle and behavior), and a medical care institution database (types of medical care institutions, location, equipment, and number of physicians), comprises a complete set of health information pertaining to 50 million Koreans.[6–8] In Korea, the NHIS is the only insurer, is managed by the government, and is subscribed to by approximately 97% of the Korean population. The remaining 3% of the population is covered by the Medical Aid program. In addition, the total claim rate for medical expenses is 100%. Therefore, it can be said that there are few people missing in the NHIS cohort among the Korean population.

Diagnosis statements were defined by the International Classification of Diseases, tenth revision (ICD-10). All patients in whom SLE was diagnosed (International Classification of Diseases, 10th revision [ICD-10] codes M32 and special medical aid code V136) between 2008 and 2013 were extracted from the database. New patients for whom the SLE code had not been previously entered were included. Of these, patients younger than 20 years or those with a history of ESRD during a washout period from 2002 to 2007 were excluded. For the non-SLE control cohort, age- and sex-matched controls (n=106,265) were randomly sampled from non-SLE individuals in 2008~2013 at a 5:1 ratio of controls to cases. Randomization was done using an algorithm within the SAS version 9.3 program (SAS Institute, Cary, NC).

2.2. Definitions of comorbidities

Income level was dichotomized at the lowest 20%. The presence of diabetes mellitus was defined according to the following criteria: at least 1 claim per year under ICD-10 codes E11–14 and at least 1 claim per year for the prescription of antidiabetic medication. The presence of hypertension was defined according to the presence of at least 1 claim per year under ICD-10 codes I10~I13 and I15 and at least one claim per year for the prescription of an antihypertensive agent. The presence of dyslipidemia was defined according to the presence of at least 1 claim per year under ICD-10 code E78 and at least 1 claim per year for the prescription of a lipid-lowering agent. The presence of myocardial infarction (MI) was defined as at least one claim under ICD-10 codes I21, I22, Congestive heart failure (CHF) as at least 1 claim under ICD-10 code I50, and chronic obstructive pulmonary disease (COPD) as at least 1 claim code J41~J44 during the 3 years before the entry year. The presence of stroke was defined as at least 1 claim under ICD-10 codes I63 and I64, and prescription of brain computed tomography or magnetic resonance imaging during the 3 years before the entry year. Blood samples for the measurement of serum creatinine were drawn from patients after an overnight fast. The estimated glomerular filtration rate (eGFR) was calculated using the modification of diet in renal disease study formula, and CKD was defined as eGFR <60 mL/min/1.73 m^2.

2.3. Study outcomes and follow-up

The study population was followed from baseline to the date of ESRD diagnosis or until December 31, 2015, whichever came first. The primary endpoint was incident ESRD, which was defined using the combination of ICD-10 codes (N18 and N19) and special medical aid codes for renal replacement therapy (V001 for hemodialysis, V003 for peritoneal dialysis, and V005 for kidney transplantation). All medical care expenses for dialysis are reimbursed using the Korean Health Insurance Review and Assessment Service database. These patients are also registered as special medical aid beneficiaries. Therefore, we were able to identify every ESRD patient in the whole of the South Korean population and to analyze the data for all ESRD patients who had started dialysis. Codes for treatment or medical expense claims included R3280 for kidney transplantation, O7011-O7020 or V001 for hemodialysis, and O7071-O7075 or V003 for peritoneal dialysis. We excluded individuals with previous ESRD who had a transplant or dialysis code on the same date as an acute renal failure code. Subjects on continuous renal replacement therapy or acute peritoneal dialysis were also excluded.

2.4. Statistical analysis

The participants' baseline characteristics are presented as means ±standard deviation or n (%). The incidence rates of primary outcomes were calculated by dividing the number of incident cases by the total follow-up period. The incidence rates of the primary outcomes are presented as per 1000 person-years. The disease-free probability of a primary outcome according to the presence of SLE was calculated using Kaplan-Meier curves, and the log-rank test was used to analyze differences between groups. Hazard ratios (HRs) and 95% confidence interval (CI) values for ESRD among groups were analyzed using Cox proportional hazard models. Multivariable-adjusted proportional hazard models were applied as follows: model 1 was not adjusted; model 2 was adjusted for age and sex; model 3 was further adjusted for lower income status, diabetes mellitus, hypertension, dyslipidemia, MI, stroke, and CHF. In model 2 and 3, we performed an adjustment for age and sex in consideration of their effect over time on the survival analysis and its relevance to other factors. Statistical analyses were performed using SAS version 9.3 (SAS Institute, Cary, NC), and a P value <.05 was considered to indicate significance.

2.5. Ethics statement

This study was approved by the Institutional Review Board of the Chonnam National University Hospital of Korea (CNUH-EXP-2018–026) and Institutional Review Board of the Republic of Korea National Institute for Bioethics Policy (NHIS-2018–1–128). Anonymized and deidentified information were used for the analyses, and thus, the need for informed consent was waived.

3. Results

3.1. Baseline characteristics of the study population

The characteristics of participants classified by the presence of SLE are described in Table 1. A total of 21,253 patients were recruited for the SLE cohort: 19,213 (90.4%) were women, the mean age was 41.9±13.2 years, and 106,265 age and sex-matched non-SLE cohort individuals were selected as the control.

Table 1

Baseline characteristics of SLE patients and matched controls.

	Control (n=106265)	SLE (n=21253)	*P* value
Sex, female	96065 (90.4)	19213 (90.4)	–
Age, years	41.9±13.2	41.9±13.2	–
20–39 years	50610 (47.63)	10122 (47.63)	
40–64 years	48745 (45.87)	9749 (45.87)	
≥65 years	6910 (6.5)	1382 (6.5)	
Low income status	25923 (24.39)	5409 (25.45)	<.001
Diabetes mellitus	3827 (3.6)	911 (4.29)	<.001
Hypertension	10568 (9.94)	5670 (26.68)	<.001
Dyslipidemia	6239 (5.87)	2951 (13.89)	<.001
COPD	10545 (9.92)	4600 (21.64)	<.001
Myocardial infarction	541 (0.51)	577 (2.71)	<.001
Stroke	1798 (1.69)	1058 (4.98)	<.001
Congestive heart failure	948 (0.89)	784 (3.69)	<.001
ESRD	145 (0.14)	533 (2.51)	<.001
Duration to ESRD, years	6.24±2.19	6.15±2.24	<.001

COPD = chronic obstructive pulmonary disease, ESRD = end-stage renal disease, SLE = systemic lupus nephritis.

Compared to the control group, the SLE group had lower income distributions and a significantly higher prevalence of comorbidities related to ESRD, such as diabetes mellitus (4.29%), hypertension (26.68%), dyslipidemia (13.89%), COPD (21.64%), MI (2.71%), stroke (4.98%), and CHF (3.69%).

3.2. Incidence risk of ESRD in SLE patients

During a median 7.53 years of follow-up after the diagnosis of SLE, 533 (2.51%) participants developed ESRD, while 145 (0.14%) non-SLE participants developed ESRD (Table 1). In addition, the mean duration of progression to ESRD was significantly shorter in the SLE group than in the non-SLE group (6.15±2.24 years and 6.24±2.19 years, respectively, $P<.001$) (Table 1). The incidence probability of ESRD according to the presence of SLE is shown in Figure 1. The SLE group had a significantly higher incidence of ESRD than the non-SLE group (P of log-rank test <.001).

3.3. Subgroup analysis of risk of ESRD in SLE patients

The incidence rate of ESRD was higher in the SLE group (4.075/ 1000 person-years) than in the non-SLE group (0.219/1000 person-years) (Table 2). The crude hazard ratio (HR) for ESRD was higher for the SLE group (HR 18.64; 95%, confidence interval [CI], 15.56–22.47) than for the non-SLE group (Table 2, Model 1). After multivariate adjustment for age, sex, income, diabetes mellitus, hypertension, dyslipidemia, MI, stroke, and CHF, there was still a significant difference in ESRD risk between the 2 groups (HR, 9.84; 95% CI, 8.10–11.97) (Table 2, Model 3). In the subgroup analysis, male (HR, 7.76; 95% CI, 5.07–11.90) and female patients (HR, 10.479; 95% CI, 8.405–13.066) with SLE had a higher risk of ESRD than the non-SLE matched controls. When analyzed by age group, the younger the age, the higher the risk of ESRD versus non-SLE matched control, which was also significant after adjustment. The risk for ESRD was higher in 20 to 39-year-old patients with SLE (HR, 22.41; 95% CI 14.20–35.36), 40–64-year-old patients with SLE (HR, 8.46; 95% CI 6.42–11.13), and ≥65-year-old patients with SLE (HR, 5.01; 95% CI 3.34–7.53) than in matched controls. In subgroup analysis according to income status and comorbidities, the SLE

group had a significantly higher risk of ESRD than the non-SLE group in almost all subgroups (the only exception was the MI subgroup).

We further performed adjustment for CKD status and subgroup analysis according to the presence of CKD. Only patients who had a serum creatinine value from a health examination performed within 1 year after diagnosis of SLE were analyzed. Even after full adjustment for comorbidities, the population with SLE had a higher risk for ESRD than the matched controls (Fig. 2 and supplementary Table 1, http://links. lww.com/MD/D110). The risk of incident ESRD was higher in both the non-CKD and CKD subgroups than in the population without SLE.

4. Discussion

ESRD is not an uncommon complication in SLE. Despite active chemotherapy in patients with lupus nephritis, a significant proportion of SLE patients progress to ESRD.[9,10] In this population-based cohort study, we investigated the incidence rate of ESRD and risk factors for progression to ESRD in Korean SLE patients compared to the general population. Our results showed that SLE was associated with a higher risk of ESRD development and shorter duration of progression to ESRD during the follow-up period. In subgroup analyses by age or sex, SLE was still a risk factor for ESRD, even after the adjustment for comorbidities. The present study is the first attempt to investigate the incidence and risk factors for ESRD in SLE patients from a nationwide cohort in Korea.

Several previous studies have analyzed the incidence and risk factors of ESRD in patients with SLE. Croca et al[1] observed the incidence of ESRD in a British lupus nephritis cohort for 30 years, and 30 out of 154 lupus nephritis patients (19.5%) developed ESRD, with an average time to progression to ESRD of 7.5 years. The rate of progression to ESRD 5 years after the diagnosis of lupus nephritis was not statistically significant among the first to third decades of life, indicating no difference in the risk of developing ESRD over time.[1] Studies on the occurrence of ESRD in SLE patients using United States Renal Data System (USRDS) data have been conducted since the 1980s.[3,11–13] Recently, Sexton et al[11] reported the standardized incidence ratio of ESRD
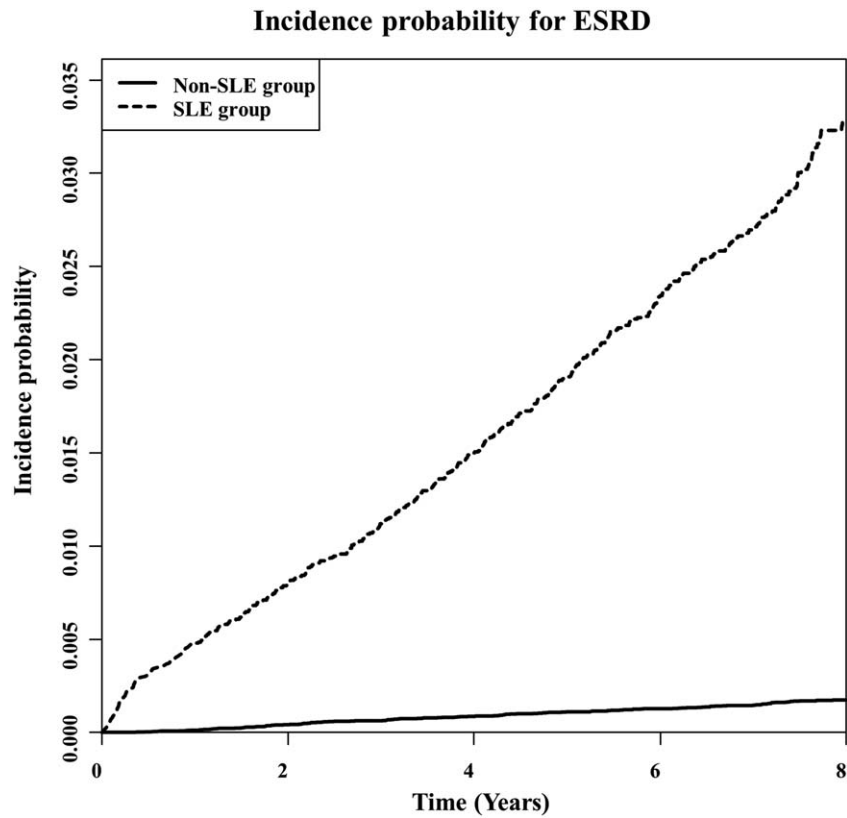
Incidence probability for ESRD

Figure 1. Kaplan–Meier curve for 8-year crude cumulative incidence of ESRD between SLE and non-SLE patients. (*P* of log-rank <.001). ESRD=end-stage renal disease, SLE=systemic lupus nephritis.

Table 2

Association of SLE and incident ESRD.

Subgroup			Total No.	ESRD cases	Duration	IR*	Model 1[†]	Model 2[‡]	Model 3[§]	P for interaction
Total		Control	106265	145	662846.34	0.219	1 (Ref.)	1 (Ref.)	1 (Ref.)	
		SLE	21253	533	130795.93	4.075	18.64 (15.56,22.47)	18.67 (15.58,22.50)	9.84 (8.10,11.97)	
Sex	Male	Control	10200	33	60096.96	0.549	1 (Ref.)	1 (Ref.)	1 (Ref.)	.032
		SLE	2040	98	11685.3	8.387	15.28 (10.42,22.99)	15.27 (10.41,22.98)	7.76 (5.07,11.90)	
	Female	Control	96065	112	602749.38	0.186	1 (Ref.)	1 (Ref.)	1 (Ref.)	
		SLE	19213	435	119110.64	3.652	19.67 (16.04,24.32)	19.66 (16.04,24.31)	10.48 (8.41,13.07)	
Age	20-39	Control	50610	23	322798.59	0.071	1 (Ref.)	1 (Ref.)	1 (Ref.)	<.001
		SLE	10122	269	63611.77	4.229	59.42 (39.75,93.51)	59.51 (39.81,93.65)	22.41 (14.20,35.36)	
	40-64	Control	48745	74	302992.04	0.244	1 (Ref.)	1 (Ref.)	1 (Ref.)	
		SLE	9749	215	59894.31	3.590	14.70 (11.35,19.26)	14.73 (11.37,19.30)	8.46 (6.42,11.13)	
	≥65	Control	6910	48	37055.7	1.295	1 (Ref.)	1 (Ref.)	1 (Ref.)	
		SLE	1382	49	7289.85	6.722	5.19 (3.48,7.74)	5.20 (3.49,7.75)	5.01 (3.34,7.53)	
Income status	Other	Control	80342	99	500576.84	0.19777	1 (Ref.)	1 (Ref.)	1 (Ref.)	.528
		SLE	15844	374	98026.27	3.8153	19.31 (15.54,24.21)	19.33 (15.56,24.25)	10.86 (8.63,13.77)	
	Low 20%	Control	25923	46	162269.5	0.28348	1 (Ref.)	1 (Ref.)	1 (Ref.)	
	20%	SLE	5409	159	32769.66	4.85205	17.10 (12.43,24.00)	17.18 (12.49,24.12)	8.73 (6.18,12.52)	
Diabetes mellitus	No	Control	102438	72	640887.7	0.1123	1 (Ref.)	1 (Ref.)	1 (Ref.)	<.001
		SLE	20342	469	125690.38	3.7314	33.24 (26.18,42.94)	33.37 (26.23,43.11)	16.40 (12.72,21.43)	
	Yes	Control	3827	73	21958.64	3.3244	1 (Ref.)	1 (Ref.)	1 (Ref.)	
		SLE	911	64	5105.56	12.5354	3.77 (2.69,5.26)	3.55 (2.52,4.98)	3.34 (2.36,4.72)	
Hypertension	No	Control	95697	51	601117.8	0.0848	1 (Ref.)	1 (Ref.)	1 (Ref.)	<.001
		SLE	15583	134	96261.16	1.392	16.48 (12.02,22.94)	16.72 (12.19,23.28)	14.43 (10.49,20.17)	
	Yes	Control	10568	94	61728.54	1.5228	1 (Ref.)	1 (Ref.)	1 (Ref.)	
		SLE	5670	399	34534.78	11.5536	7.58 (6.08,9.54)	6.81 (5.37,8.70)	7.44 (5.86,9.52)	
Dyslipidemia	No	Control	100026	86	628663.16	0.1368	1 (Ref.)	1 (Ref.)	1 (Ref.)	.006
		SLE	18302	314	113814.47	2.7589	20.19 (15.99,25.77)	20.28 (16.05,25.89)	11.92 (9.32,15.39)	

(*continued*)

Table 2
(continued).

Subgroup			Total No.	ESRD cases	Duration	IR*	Model 1†	Model 2‡	Model 3§	P for interaction
	Yes	Control	6239	59	34183.18	1.726	1 (Ref.)	1 (Ref.)	1 (Ref.)	
		SLE	2951	219	16981.47	12.8964	7.45 (5.63,10.03)	6.61 (4.88,9.06)	6.49 (4.76,8.95)	
COPD	No	Control	95720	108	597976.68	0.18061	1 (Ref.)	1 (Ref.)	1 (Ref.)	<.001
		SLE	16653	405	102451.08	3.95311	21.92 (17.80,27.22)	22.27 (18.08,27.66)	11.90 (9.53,14.96)	
	Yes	Control	10545	37	64869.66	0.57037	1 (Ref.)	1 (Ref.)	1 (Ref.)	
		SLE	4600	128	28344.85	4.51581	7.91 (5.55,11.56)	7.85 (5.50,11.48)	5.36 (3.68,7.97)	
Myocardial infarction	No	Control	105724	137	659542.21	0.20772	1 (Ref.)	1 (Ref.)	1 (Ref.)	<.001
		SLE	20676	506	127091.5	3.98138	19.18 (15.93,23.25)	19.290 (16.02,23.37)	10.79 (8.87,13.21)	
	Yes	Control	541	8	3304.13	2.42122	1 (Ref.)	1 (Ref.)	1 (Ref.)	
		SLE	577	27	3704.44	7.28855	2.99 (1.42,7.06)	2.58 (1.19,6.20)	2.21 (0.98,5.47)	
Stroke	No	Control	104467	117	652464.39	0.17932	1 (Ref.)	1 (Ref.)	1 (Ref.)	<.001
		SLE	20195	503	124378.7	4.0441	22.57 (18.53,27.72)	22.80 (18.72,28.01)	12.27 (9.96,15.23)	
	Yes	Control	1798	28	10381.94	2.69699	1 (Ref.)	1 (Ref.)	1 (Ref.)	
		SLE	1058	30	6417.23	4.67491	1.74 (1.04,2.92)	1.83 (1.06,3.16)	2.07 (1.18,3.62)	
Congestive Heart failure	No	Control	105317	127	657461.28	0.1932	1 (Ref.)	1 (Ref.)	1 (Ref.)	<.001
		SLE	20469	478	126578.07	3.7763	19.56 (16.14,23.88)	19.65 (16.21,23.98)	10.56 (8.60,13.03)	
	Yes	Control	948	18	5385.05	3.3426	1 (Ref.)	1 (Ref.)	1 (Ref.)	
		SLE	784	55	4217.87	13.0398	3.89 (2.33,6.81)	3.85 (2.25,6.87)	3.71 (2.15,6.68)	

* Incidence rate per 1000 person-years.
† No adjusted.
‡ Adjusted for age and sex.
§ Adjusted for age, sex, income level, diabetes mellitus, hypertension, dyslipidemia, myocardial infarction, stroke, and congestive heart failure.
COPD = chronic obstructive pulmonary disease, ESRD = end-stage renal disease, SLE = systemic lupus nephritis.

in lupus nephritis patients of approximately 1.05 cases per million patient-years during the biennium period from 2009 to 2010 using the USRDS data.

It is well known from previous studies that the epidemiology, course, disease pattern and activity, complications, and prognosis of SLE are largely different depending on race or ethnicity.[4,14–18] Asian patients have been reported to have higher rates of lupus nephritis and more active glomerulonephritis compared to Caucasian patients.[19] Renal outcome and the level of

immunosuppressant use in Asians were comparable to African-American Blacks in some studies. Joo et al[20] reported the clinical features and organ damage in 996 Korean patients with SLE compared with other Asian SLE patients. Compared to other Asian cohorts, disease activity was lower and organ damage was less in Korean SLE patients. During the follow-up period of 10 years, lupus nephritis increased over time, and eventually, 50% of the patients developed lupus nephritis and 3% of patients required dialysis. However, considering that most of the above
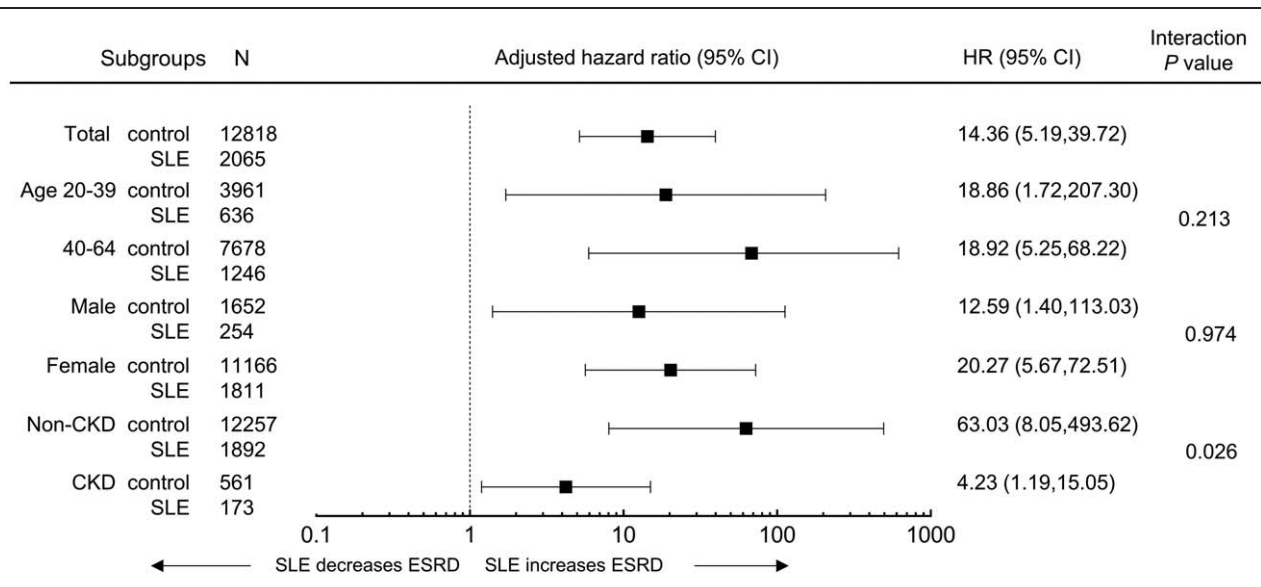

Figure 2. Analysis of end-stage renal disease in subgroups of patients with SLE. HRs and 95% CIs of end-stage renal disease in the SLE group vs control in subgroups. Adjusted for age, sex, income, diabetes mellitus, hypertension, dyslipidemia, myocardial infarction, stroke, congestive heart failure, and CKD. CI = confidence interval, CKD = chronic kidney disease, HR = hazard ratios.

previous studies were cohort studies, direct comparisons with our results are not appropriate. Although nationwide population-based studies of SLE patients have been conducted in Korea, there have been no studies focused on ESRD.[21,22] Based on the largest population ever studied, we analyzed the risk of incident ESRD in a Korean population with SLE. SLE was associated with a significant increase in the risk of ESRD even after adjustment for comorbidities. In the subgroup analysis, SLE increased the risk of ESRD regardless of the presence of various diseases. Especially in the subgroup analysis according to CKD, SLE significantly increased the incidence of ESRD not only in patients without baseline CKD, but also in patients with CKD.

A nationwide population-based study similar to ours was conducted in Taiwan.[23] Taiwan's national health insurance system is similar to that of Korea. Yu et al[23] used Taiwan's Longitudinal Health Insurance Database to analyze the risk of ESRD in SLE patients. The incidence rates of ESRD were 612.8 and 29.3 cases per 100,000 patient-years in the SLE and non-SLE groups, respectively. The incidence of ESRD occurred more frequently in male patients than in female patients, and the HR for ESRD was 18.2 times higher in the SLE group than in the non-SLE group. Our results showed that the incidence rate of ESRD in Korean SLE patients (4.075/1000 person-year) was lower than that of Taiwanese patients. This is consistent with the findings reported in previous studies.[20]

This study was the first nationwide population-based study in Korea for the incidence and risk factors of ESRD in SLE patients. Due to the special nature of the Korean health insurance system, in which the insured are covered by a single compulsory insurance with a 100% claim rate, the number of patients who are missing is small, because information on all SLE and ESRD patients being treated in the hospital is collected by the insurer. However, the present study has some limitations. First, patients not treated in the hospital were not included in the study because they are not recorded in the claim data. Therefore, the prevalence or incidence of SLE may be underestimated rather than actual. Second, claim data does not include laboratory results and detailed history including information on serum creatinine and proteinuria of patients that may affect the outcome of the study. To overcome this, history of major diseases such as hypertension, diabetes, and cardiovascular disease were also analyzed by ICD-10 code of the claim data. Third, lupus nephritis could not be validated because the claim data do not include the results of renal biopsy or the presence of proteinuria.

In summary, this study showed a high incidence rate of ESRD in SLE patients. SLE patients had a 10-fold greater risk of ESRD when compared to non-SLE patients. Despite some limitations, this is the first study of the incidence and the risk of ESRD in Korean patients with SLE, which was performed using Korean National Health Insurance Service database. The results of this study would be helpful in establishing a national health policy for the management of SLE patients.

Author contributions

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