Secondary Sjögren's Syndrome in Systemic Lupus Erythematosus Defines a Distinct Disease Subset

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ABSTRACT. ***Objective.*** Sjögren's syndrome (SS) may occur in patients with systemic lupus erythematosus (SLE). We sought to determine whether the presence of SS in a large cohort of patients with SLE defines a subset with distinctive sociodemographic, clinical, and laboratory features.

Methods. The Johns Hopkins Lupus Cohort was divided into 2 groups, based on the presence or absence of SS, defined by the presence of an objective measure of sicca or an abnormal minor salivary gland biopsy in a patient with sicca symptoms. These groups were compared with regard to sociodemographic, clinical, and laboratory features. Multivariable logistic regression was then performed to adjust the findings for potential sociodemographic, clinical, and laboratory confounders.

Results. The 259 patients with SS (14% of the cohort), when compared with the 1531 patients without SS, were older at the time of SLE diagnosis and were more commonly women and white. Photosensitivity, oral ulcers, Raynaud's phenomenon, anti-Ro antibodies, and anti-La antibodies had a significant positive association while renal disease, anti-ribonucleoprotein (RNP) antibodies, and anti-dsDNA antibodies had a negative association with the presence of SS after adjustment for age (at last cohort visit), gender, ethnicity, and anti-Ro antibodies. The older age at diagnosis of SLE among the patients with SS did not remain a significant finding after adjustment for the age of the patient at last cohort visit.

Conclusion. The subset of patients with SLE and SS has a distinct clinical and laboratory phenotype, with a higher frequency of older white women with photosensitivity, oral ulcers, Raynaud's phenomenon, anti-Ro antibodies, and anti-La antibodies and a lower frequency of renal disease, anti-dsDNA antibodies, and anti-RNP antibodies. (First Release April 1 2010; J Rheumatol 2010; 37:1143–9; doi:10.3899/jrheum.090804)

Key Indexing Terms:
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Autoimmune exocrinopathy is manifested by an inadequate production or a diminished quality of tears and saliva, resulting in keratoconjunctivitis sicca and xerostomia. It may occur as a primary disease or in the context of a well established systemic rheumatic disease. The primary disease is known as Sjögren's syndrome (SS) if specific clinical, laboratory, and histopathologic features are present, as specified in a set of diagnostic criteria. The most recent of these are the American-European Consensus Criteria[1]. By these criteria, the diagnosis of primary SS requires the presence of anti-Ro antibodies and/or anti-La antibodies or histopathologic evidence of focal lymphocytic sialoadenitis in a minor salivary gland biopsy. In the presence of systemic lupus erythematosus (SLE), rheumatoid arthritis, scleroderma, or another systemic rheumatic disease, an autoimmune exocrinopathy is known as secondary SS.

The diagnostic boundaries between primary SS and SLE can be difficult to define because they share certain clinical and laboratory features. Prominent examples include photosensitive rash, arthritis, neurologic manifestations, anti-Ro antibodies, and/or anti-La antibodies[2-4]. Additionally, it is not known whether autoimmune exocrinopathy occurring in the setting of SLE defines a specific SLE subset, is simply an organ manifestation of lupus, or reflects an overlap of 2 autoimmune diseases. In previous studies of lupus cohorts, the subset of patients with SS has been found repeatedly to be older[5-10]. This may reflect the increased prevalence of sicca symptoms in older individuals, rather than a unique phenotypic characteristic of this subset.

There has been variability as to the types of clinical or laboratory manifestations of SLE that define patients with SLE who have secondary SS. We hypothesized that there are distinctive sociodemographic, clinical, and laboratory features of patients with SLE and SS in the Hopkins Lupus Cohort, the largest cohort analyzed in this fashion to date.

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MATERIALS AND METHODS

Patient population. The Hopkins Lupus Cohort is a prospective cohort in which patients with SLE are followed quarterly or more frequently if clinically necessary. Patient inclusion in the cohort is based on the clinical diagnosis of SLE by a member of the Rheumatology Division; 94% of the patients satisfied at least 4 of the 1982 American College of Rheumatology revised criteria for the classification of SLE[11,12]. At each patient visit, disease activity is assessed by physician's global assessment [0 to 3 visual analog scale and the SELENA (Safety of Estrogens in Lupus Erythematosus: National Assessment) revision of the SLE Disease Activity Index (SLEDAI)[13]] and laboratory tests (complete blood count, erythrocyte sedimentation rate, serum creatinine, cholesterol, urinalysis, urine protein to creatinine ratio, C3, C4, and anti-dsDNA). Patient visits consist of an interview, a physical examination, and laboratory testing. The Hopkins Lupus Cohort has been approved on an annual basis by the Johns Hopkins University Institutional Review Board, and all patients gave informed consent. Information recorded since cohort entry consists of basic demographic characteristics (date of birth, age at SLE onset, ethnicity, sex, socioeconomic status, years of education, combined annual household income), presenting and cumulative clinical manifestations, SELENA SLEDAI scores[13], the Systemic Lupus International Collaborating Clinics/American College of Rheumatology (SLICC/ACR) Damage Index for systemic lupus erythematosus[14], and immunologic markers [serum C3 and C4 levels, antinuclear antibody, anti-dsDNA, anti-Sm, anti-ribonucleoprotein (RNP), anti-Ro, anti-La, lupus anticoagulant by dilute Russell viper venom time, and anticardiolipin antibody].

All patients were asked at cohort entry about sicca symptoms. Patient complaints of sicca symptoms at any subsequent visit prompted formal ophthalmology testing. In addition, all patients with SLE receiving hydroxychloroquine therapy had at least yearly ophthalmology examinations. SS in this cohort of patients with SLE was defined by sicca symptoms in concert with an abnormal Schirmer's or ocular vital dye staining test, absent sublingual salivary pool, or a minor salivary gland biopsy showing Greenspan grade 3 or higher focal lymphocytic sialoadenitis[15]. These findings were only considered valid in the absence of medication use that might reduce tear or saliva production. The Schirmer's test and/or ocular staining test were coded as abnormal if they were reported as such by an ophthalmologist examining the patient. In many cases, this information was collected on the basis of a chart review of patients entering or enrolled in the cohort. Otherwise, it was coded based on ophthalmology followup notes. Similarly, abnormalities of the minor salivary gland biopsy were determined by the pathologist who read the original biopsy material.

Study design. The Hopkins Lupus Cohort computerized database was queried as of December 2007. The cohort was divided into 2 groups based on the presence or absence of secondary SS. These groups were compared in regard to sociodemographic, clinical, and laboratory features. Multivariable logistic regression was then performed to adjust the findings for features that were potential confounders.

Statistical analysis. Data were analyzed using Stata 10.0 (Stata Corp., College Station, TX, USA). Baseline sociodemographic and clinical features were compared between patients with and without SS. Characteristics were analyzed using Pearson's chi-squared or Fisher's exact test (because of small cell sizes) for categorical variables and t-tests for continuous variables. Categorical data were expressed as proportions and continuous data as mean values with SD.

Univariable analyses were performed using logistic regression to evaluate the unadjusted relationship between SS and clinical risk factors. Bonferroni's correction was used for multiple comparisons. We used multivariable logistic regression to examine relations between SS and clinical variables, adjusting for potential confounders. Models were explored using likelihood ratio testing and forward and backward model selection. The final model selection was based on knowledge of clinically relevant variables and based on variables that were statistically significant in the univariable analysis. Our first model adjusted for age at last cohort visit, age at SLE diagnosis, ethnicity, and sex. Our second model adjusted for these variables, in addition to the presence of anti-Ro antibodies.

Collinearity for the logistic regression analyses was checked by performing a multiple regression analysis instead of the logistic regression analyses to calculate the variance inflation factors, which were all below 5. Model checking was performed with goodness-of-fit tests, including Pearson's chi-squared and Hosmer-Lemeshow chi-squared goodness-of-fit statistics. All of the models showed good fit ($p > 0.05$) or a correction was performed for overdispersion or underdispersion.

RESULTS

Among the cohort of 1859 patients, there were data concerning a diagnosis of SS for 1790 patients. Of these, 259 (14.5%) had secondary SS. Sixty-nine patients (4%) lacked data concerning a diagnosis of SS and were excluded from the analysis. In 98 patients, SS was documented within 1 year of the onset of SLE. The diagnosis of SLE preceded that of SS by more than 1 year in 109 patients (median 7 yrs, range 1–35 yrs) and followed the diagnosis of SS by more than 1 year in 32 patients (median 3 yrs, range 1–17 yrs). The baseline characteristics of the patients are shown in Table 1. Patients with SS were significantly older at SLE diagnosis than patients without SS ($p < 0.001$). The diagnosis of SLE was established at age 40 or older in 45% of the patients with SS and 24% of the patients who did not have SS ($p < 0.001$). The patients with SS were also significantly older than those without SS at the time of enrollment into the Hopkins Lupus Cohort, but had a comparable duration of followup in the cohort. The mean age of the patients with SS at the time of their last cohort visit was 49.5 years, significantly greater than the mean age of 41.4 years among the patients without SS ($p < 0.001$).

The group with SS was 97.7% women, significantly more than the group without SS (91.8% women; $p < 0.001$). There was a striking predominance of white patients among the patients with SS (70.7% vs 53.6%; $p < 0.001$).

The patients with SS had a significantly longer duration of SLE than did the patients without SS (Table 2). As a reflection of this longer disease duration, these patients with SS had a higher average number of cumulative SLE manifestations that form the ACR classification criteria and significantly greater SLICC/ACR Damage Index scores. The musculoskeletal, neuropsychiatric, and ocular components were the leading contributors to the higher damage scores of the patients with SS. Their maximum SLEDAI disease activity scores were comparable.

Univariable analysis. Clinical and laboratory features of the patients are shown in Table 3 and differed in frequency between the groups of patients with and without SS. With the multiple comparisons, a p value < 0.002 was used to define a significant difference (Bonferroni's correction). Features that were more common among the patients with SS at this significance level included photosensitivity, oral ulcers, Raynaud's phenomenon, anti-Ro antibodies, and anti-La antibodies. Features that were more common among

Table 1. Baseline characteristics of patients with SLE with and without secondary Sjögren's syndrome (SS). All numbers are percentages, unless otherwise noted.

Characteristics	Secondary SS Present, N = 259	Secondary SS Absent, N = 1531	p
Age, mean yrs ± SD			
At SLE diagnosis	38.6 ± 12.4	31.6 ± 12.8	< 0.001*
At cohort entry	44.1 ± 12.2	36.5 ± 12.5	< 0.001*
At SS diagnosis	41.4 ± 13.2	—	
At last cohort visit	49.5 ± 12.5	41.4 ± 13.09	< 0.001*
Duration of cohort followup, mean yes ± SD	5.5 ± 4.7	5.0 ± 4.8	NS
Sex			
Women	97.7	91.8	< 0.001
Men	2.3	8.2	
Ethnicity			
White	70.7	53.6	< 0.001
African American	25.5	39.5	
Hispanic	1.9	2.1	
Asian	1.2	3.3	
Insurance type			
Private	81.4	78.7	0.39
Medicaid	16.7	17.7	
None	2.0	3.6	
Past smoking	44.0	37.6	0.05
Past alcohol abuse	4.3	7.0	0.11
Past illicit drug use	3.5	6.2	0.09

* Student t test; other p values by chi-square statistic. SLE: systemic lupus erythematosus; SS: Sjögren's syndrome.

Table 2. Cumulative ACR criteria, disease activity, and damage in patients with SLE with and without Sjögren's syndrome. Values are given as mean ± SD.

Feature	SS Present	SS Absent	p*
Cumulative ACR criteria for SLE	6.4 ± 1.8	6.0 ± 1.8	0.004
Maximum SELENA SLEDAI score	7.9 ± 5.6	7.7 ± 5.1	NS
Disease duration, yrs	19.5 ± 9.8	16.4 ± 9.7	< 0.001
SLICC/ACR Damage Index score	3.8 ± 3.4	2.8 ± 2.9	< 0.001

* p value by Student t test. ACR: American College of Rheumatology; SLE: systemic lupus erythematosus; SELENA: Safety of Estrogens in Lupus Erythematosus: National Assessment; SLEDAI: SLE Disease Activity Index; SLICC: Systemic Lupus International Collaborating Clinics.

the patients who did not have SS at this significance level included proteinuria, nephrotic syndrome, anti-dsDNA antibodies, and anti-RNP antibodies.

Among patients with SS, 38.3% of whites had anti-Ro antibodies compared with 61.7% of nonwhites (p = 0.004). However, SS was more common in whites (18.3%) than in nonwhites (9.7%) in the cohort (p < 0.001). All the patients with both SLE and SS and with anti-La antibodies also had anti-Ro antibodies, while 79.7% of the patients with SLE who did not have SS but had anti-La antibodies also had anti-Ro antibodies (p < 0.001).

Logistic regression. Multivariable logistic regression models were created with secondary SS as the outcome. Separate models were created for photosensitivity, oral ulcers, Raynaud's, proteinuria, nephrotic syndrome, anti-La antibodies, anti-dsDNA antibodies, and anti-RNP antibodies. In the first set of models, we adjusted for age at last cohort visit, age at SLE diagnosis, ethnicity, and sex. In the second set of models we also adjusted for anti-Ro antibodies.

Increasing age, photosensitivity, oral ulcers, Raynaud's phenomenon, and anti-Ro antibodies were associated with the presence of secondary SS. The risk of SS was dramatically higher in whites than African Americans (Table 4). Age at diagnosis of SLE was not significantly different between the 2 groups when adjusted for age at last cohort visit. In both models, the risk of proteinuria was significantly less in the patients with SLE who did not have SS than in those who did have SS. Similarly, there was a statistically significant decrease in the risk of nephrotic syndrome in patients with SS compared to those without SS. When anti-Ro antibodies were added to the model, the results were not significantly different.

DISCUSSION

This is the largest study of the characteristics of patients with secondary SS. These patients were older at the time of SLE diagnosis and were more often white, compared with patients with SLE in the cohort without SS. Multiple differences in the clinical and laboratory features of these patients were evident by univariable analyses. Since the features of SLE are known to vary as a function of age, ethnicity, and specific serologic markers, some differences were expected.

Table 3. Disease manifestations of patients with SLE with and without secondary Sjögren's syndrome. All numbers are percentages, unless otherwise noted.

Manifestation	SS Present, No. (%)	SS Absent, No. (%)	OR	95% CI	p
Cutaneous					
Photosensitivity	177 (68.3)	808 (52.9)	1.92	1.45–2.54	< 0.001
Malar rash	154 (59.5)	798 (52.2)	1.35	1.03–1.76	0.03
Discoid rash	51 (19.7)	322 (21.1)	0.92	0.66–1.28	0.62
Oral ulcers	177 (68.3)	734 (47.9)	2.34	1.77–3.10	< 0.001
SCLE	18 (7.0)	74 (4.8)	1.47	0.86–2.50	0.16
Vascular					
Raynaud's	171 (66.0)	758 (49.5)	1.98	1.50–2.61	< 0.001
Musculoskeletal					
Arthritis	209 (81.3)	1117 (73.2)	1.60	1.14–2.23	0.006
Renal					
Proteinuria	75 (29.0)	658 (43.1)	0.54	0.40–0.71	< 0.001
Hematuria	59 (22.8)	472 (30.9)	0.66	0.48–0.90	0.008
Nephrotic syndrome	23 (8.9)	302 (20.0)	0.39	0.25–0.61	< 0.001
Serositis					
Pleuritis	120 (46.3)	688 (45.0)	1.06	0.81–1.37	0.69
Pericarditis	60 (23.2)	329 (21.5)	1.10	0.80–1.50	0.56
Neurologic					
Psychosis	17 (6.6)	46 (3.0)	2.28	1.28–4.04	0.005
Seizures	30 (11.6)	142 (9.3)	1.28	0.84–1.94	0.25
Hematologic					
Hemolytic anemia	20 (8.1)	166 (11.2)	0.70	0.43–1.14	0.15
Leukopenia	110 (42.6)	678 (44.4)	0.93	0.71–1.22	0.60
Thrombocytopenia	46 (17.8)	333 (21.9)	0.77	0.55–1.08	0.14
Immunologic					
Anti-Ro	115 (45.3)	395 (26.8)	2.25	1.71–2.96	< 0.001
Anti-La	56 (22.1)	148 (10.0)	2.55	1.81–3.59	< 0.001
Anti-Ro and anti-La-positive	56 (22.1)	118 (8.0)	3.26	2.30–4.64	< 0.001
Anti-Ro-positive, anti-La-negative	58 (22.9)	276 (18.7)	1.29	0.94–1.78	0.12
Anti-dsDNA	117 (45.4)	901 (59.1)	0.57	0.44–0.75	< 0.001
Anti-Sm	24 (9.7)	254 (17.3)	0.52	0.33–0.81	0.004
Anti-RNP	33 (13.3)	409 (28.0)	0.39	0.27–0.58	< 0.001
Anticardiolipin	105 (41.7)	721 (49.1)	0.74	0.57–0.97	0.03
Decreased C3 level	117 (45.2)	842 (55.1)	0.67	0.51–0.87	0.003
Decreased C4 level	108 (41.7)	747 (48.9)	0.75	0.57–0.97	0.03

p values by chi-square statistic. The denominator used in calculation of percentages varies due to missing values. SLE: systemic lupus erythematosus; SCLE: subacute cutaneous lupus erythematosus; RNP: ribonucleoprotein.

However, several key differences persisted after logistic regression analysis, with adjustments for known confounders. The patients with SLE and SS had a higher frequency of photosensitivity, oral ulcers, Raynaud's phenomenon, and anti-Ro antibodies, and a lower frequency of renal disease, anti-dsDNA antibodies, and RNP antibodies. The patients with SS were older at the time of diagnosis of their SLE, but this difference was no longer significant when adjusted for the age of the patients at the time of their last cohort visit. Since the sicca syndrome occurs more commonly with advancing age and usually persists once present, its greater prevalence in a cohort of older patients with SLE is expected and does not depend on the presence of SLE.

Our patients with SLE and SS also had higher SLICC/ACR damage scores than the patients with SLE who did not have SS. This most likely reflects their older age at disease onset[16] and longer duration of disease[17,18], known risk factors for organ damage in patients with SLE.

The association of SS and SLE was first highlighted in a case series published by Heaton in 1959[19]. The link between these 2 diseases was strengthened by the recognition that anti-Ro antibodies and anti-La antibodies are common to both diseases[20]. The relationship between the 2 disease processes is debated. SS may be a secondary manifestation of SLE, with autoimmune exocrinopathy being simply one of multiple organ manifestations of SLE. Indeed, sicca manifestations are common in patients with SLE[8,21-23]. Alternatively, SS and SLE may be separate autoimmune diseases and occasionally overlap as a result of shared organ or serologic manifestations. Examples of this have included the occurrence of subacute cutaneous lupus and dsDNA antibodies, both purportedly lupus-specific phenomena, in

Table 4. Multivariable models of the features of secondary Sjögren's syndrome in patients with SLE. Model 1 adjusted for ethnicity, age at last cohort visit, age at SLE diagnosis, and sex. Model 2 adjusted for ethnicity, age at last cohort visit, age at SLE diagnosis, and anti-Ro antibodies.

Feature	Model 1			Model 2		
	OR	95% CI	p	OR	95% CI	p
Age at last cohort visit	1.04	1.03–1.06	< 0.001	1.04	1.02–1.06	< 0.001
Age at SLE diagnosis	1.00	0.99–1.02	0.67	1.00	0.99–1.02	0.64
Ethnicity (African American vs white)	0.49	0.36–0.67	< 0.001	0.44	0.32–0.60	< 0.001
Photosensitivity	1.55	1.15–2.09	0.004	1.52	1.12–2.07	0.008
Oral ulcers	2.19	1.63–2.96	< 0.001	2.35	1.73–3.19	< 0.001
Raynaud's	1.96	1.46–2.63	< 0.001	1.93	1.42–2.61	< 0.001
Proteinuria	0.72	0.53–0.99	0.04	0.70	0.51–0.96	0.03
Nephrotic syndrome	0.56	0.35–0.90	0.02	0.55	0.34–0.88	0.01
Anti-Ro	2.60	1.94–3.48	< 0.001	2.59	1.94–3.48	< 0.001
Anti-La	2.59	1.79–3.73	< 0.001	1.57	1.03–2.40	0.04
Anti-dsDNA	0.65	0.49–0.86	0.002	0.57	0.42–0.76	< 0.001
Anti-RNP	0.53	0.35–0.80	0.003	0.49	0.32–0.74	< 0.001

SLE: systemic lupus erythematosus; RNP: ribonucleoprotein.

patients with well established SS[24,25]. Similarly, the sharing of certain nonspecific organ manifestations by both diseases, such as photosensitive rash, arthritis, demyelinating central nervous system lesions, and leukopenia, makes it difficult to distinguish SS with extraglandular features from SLE[4,26,27].

In prior studies of SLE cohorts, the prevalence of SS as defined by accepted diagnostic criteria ranged from 7% to 33%[5-8,28,29]. These studies differ in regard to the diagnostic criteria for SS, but share the requirement for an objective measure of dry eyes or dry mouth and/or an abnormal labial gland biopsy. Within the Hopkins Lupus Cohort, the largest prospective cohort of patients with SLE, 14.5% had SS, a value that is commensurate with other studies.

The patients with SS in previous SLE cohorts were significantly older at the time of SLE diagnosis than the patients who did not have SS[5-10]. The patients who had both SS and SLE had less frequent renal involvement[5-7,10,29] and a higher prevalence of anti-Ro antibodies[5,6,8,9,23,30]. The prevalence of anti-dsDNA was lower in some studies[7,9] and higher in others[6,23]. Manoussakis, *et al* demonstrated that patients with SLE and SS and patients with primary SS share an increased frequency of the HLA DRB1*0301 allele, in contrast to patients with SLE but without SS[5].

Our study supports and extends previous observations regarding the relationship of SS and SLE. In agreement with prior studies, the patients with SLE and SS were significantly older than those who did not have SS. Our observation of a reduced prevalence of SLE and SS among African American patients compared to white patients supports an earlier study from our group. In a study of 100 patients with anti-Ro antibodies, there were significantly fewer African Americans relative to whites among those with primary SS compared to those with SLE[26]. In our study, anti-Ro antibodies were more common in the nonwhite patients with SLE and SS than in white patients with SLE and SS. Thus, the increased rates of anti-Ro antibodies do not lead to higher rates of SLE and SS in nonwhite patients. In agreement with earlier studies, our patients with SLE and SS were less likely to have proteinuria and nephrotic syndrome, even after adjustment for sociodemographic variables.

Our patients with SS had a significantly higher frequency of both Ro and La antibodies compared to the patients who did not have SS, even though a majority lacked these antibodies. The finding of Ro and La antibodies in only a minority of patients with SLE and secondary SS has also been observed in other series[5,7,8], but not all[6,9,10,22,29], and may reflect differences in cohort size and ethnic composition, case ascertainment, and SS case definition. In our series of patients with SLE, the coincidence of both anti-Ro and anti-La antibodies was significantly more frequent among the patients with SS compared to those without it, a finding not observed for the dyad of anti-Ro antibodies without anti-La antibodies. Patients with primary SS more commonly have both anti-Ro and anti-La antibodies, while patients with SLE more commonly have anti-Ro antibodies without anti-La antibodies[20,31]. However, the presence of both anti-Ro and anti-La antibodies in patients with SLE is a marker for a group of patients with older age at disease onset, sicca complex, less renal disease, and HLA-DR3[31]. Wasicek and Reichlin also demonstrated that patients with SLE with antibodies to anti-Ro and anti-La had a lower incidence of DNA antibodies and a lower incidence of nephritis, compared to patients with anti-Ro antibodies alone[32].

Our patients with SLE and SS also had a higher frequency of oral ulcers and Raynaud's phenomenon. The basis for this is uncertain; it has not been previously described among such patients nor among elderly patients with SLE[33]. Since Raynaud's phenomenon correlates with the presence of anti-RNP antibodies, and anti-RNP antibodies were less

common in the patients with SLE and SS, this finding is unexpected. It may indicate the presence of nonimmunologic mechanisms important to the pathogenesis of these symptoms in older patients with SLE and secondary SS. The decreased frequency of anti-RNP in patients with SLE and SS has not been previously observed. RNP antibodies cluster with Sm antibodies and are less common in patients with SLE with anti-Ro, anti-La, or anti-dsDNA antibodies[34]. However, anti-RNP antibodies were equally common in our patients with SLE and SS and with anti-Ro antibodies as opposed to those without anti-Ro antibodies (data not shown), arguing against autoantibody clustering as the explanation for this finding.

The data in our study were derived from a large longitudinal and observational cohort of patients with SLE. Accordingly, there was no attempt to evaluate all patients prospectively for the presence of sicca symptoms or to screen them for the presence of keratoconjunctivitis sicca or salivary gland hypofunction. The patients had objective evidence of sicca, but did not necessarily meet currently accepted diagnostic criteria for SS[1] because the establishment of the cohort predated these criteria. Thus, the number of patients with SLE and SS in our cohort may have been lower if they had to meet the 2002 American-European consensus criteria. Alternatively, the number might have been higher if every patient with SLE had been formally tested for the presence of sicca. The overall prevalence of SS in our cohort, defined by sicca symptoms and either an objective measure of sicca or a positive labial gland biopsy, was 14.5%, commensurate with values noted in other lupus cohorts[5-8,28,29].

Our findings support the conclusion that patients with SLE with subjective and objective findings of an autoimmune exocrinopathy (i.e., secondary SS) define a distinct subset. They are typically older white women with a lower risk for the development of renal disease. Raynaud's phenomenon, photosensitivity, and oral ulcers are more commonly present than in lupus patients without SS. Although there was a higher frequency of anti-Ro and anti-La antibodies in this subset, the majority did not have either of these antibodies. Similarly, anti-dsDNA antibodies were less common, but were still present in 45%. These patients had cumulative organ damage comparable to the patients who did not have SS, suggesting that their SLE was not necessarily milder in the long term.

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