

SLE, Sjögren's and APS - clinical aspects (other than treatment)

POS0705

BILAG-2004 INDEX ACTIVE DISEASE PREDICTS DEVELOPMENT OF DAMAGE

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Background: BILAG-2004 Index (BILAG-2004) has undergone construct and criterion validity and is used to assess disease activity in SLE. However, its predictive validity has yet to be established.

Objectives: This study was to determine if disease activity according to BILAG-2004 was predictive of development of damage in an inception cohort.

Methods: This was a prospective multi-centre longitudinal study in the UK of an inception cohort of SLE patients (recruited within 12 months of achieving 1997 ACR revised criteria for SLE). Data were collected on disease activity (BILAG-2004 and BILAG2004-Pregnancy Index during pregnancy), SLICC/ACR DI (SDI), cumulative drug exposure and death at every visit. Information on cardiovascular risk factors (hypertension, diabetes mellitus, hypercholesterolaemia and smoking status) and antiphospholipid syndrome status were also collected. This study ran from 1st January 2005 to 31st December 2017. Longitudinal analysis using Poisson regression with random effects model was used to determine predictors of development of new damage. Death was not included in the analysis due to small numbers.

Results: 273 patients were recruited (91.2% female, 59.3% Caucasian, 17.2% African/Caribbean, 17.2% South Asian) with mean age at recruitment of 38.5 years (SD 14.8). 97.8% had no damage at recruitment (2.2% had SDI score of 1). Median follow-up was 73.4 months (range: 1.8, 153.8) with total follow-up of 1767 patient-years. Prevalence of risk factors during follow-up were: hypertension 23.1%, hypercholesterolaemia 35.5%, diabetes mellitus 5.5%, smoker or ex-smoker 44% and antiphospholipid syndrome 7%. There were 13 deaths and 114 new damage items occurred during follow-up.

There were 6674 assessments with disease activity score: 293 assessments with Grade A activity in 95 patients (92.4% had only 1 system with grade A, range: 1 - 4) and 1704 assessments with Grade A or B activity in 239 patients (78.7% had only 1 system with Grade A or B, range: 1 - 5).

Univariate analysis showed that gender, cardiovascular risk factors, antiphospholipid syndrome and most drug exposure (except hydroxychloroquine, glucocorticoids, mycophenolate and cyclophosphamide) were not associated with new damage (they were not included in the multivariate analysis).

Table 1 summarises multivariate analysis. Similar results were obtained when the disease activity variable was changed to Number of Systems with Grade A per assessment (RR 2.04 with 95% CI: 1.05, 3.94). Analysis using BILAG-2004 systems tally showed that persistent minimal disease was protective of development of damage (RR 0.74 with 95% CI: 0.57, 0.95). Cumulative drug exposure since recruitment for mycophenolate was protective against new damage (RR 0.99 with 95% CI 0.99, 0.99) but not cumulative drug exposure since last visit.

Variable	Risk Ratio (95% CI) for New Damage
Ethnicity	
Afro-Caribbean	1.21 (0.68, 2.17)
South Asian	1.81 (0.97, 3.36)
Others	2.37 (0.68, 8.20)
Age at diagnosis	1.06 (1.04, 1.08)
Prior SDI score	0.69 (0.44, 1.08)
Constitutional A or B	unreliable estimate due to low numbers
Mucocutaneous A or B	1.80 (1.04, 3.14)
Neuropsychiatric A or B	4.68 (1.68, 13.05)
Musculoskeletal A or B	0.76 (0.33, 1.73)
Cardiorespiratory A or B	0.35 (0.05, 2.59)
GIT A or B	unreliable estimate due to low numbers
Ophthalmic A or B	unreliable estimate due to low numbers
Renal A or B	2.08 (0.99, 4.40)
Haematological A or B	4.37 (1.15, 16.65)
Hydroxychloroquine since last visit (per g)	0.99 (0.98, 0.99)
Prednisolone since last visit (per 100mg)	1.01 (1.00, 1.02)
Cyclophosphamide since last visit (per g)	1.42 (0.94, 2.14)

Conclusion: Active disease (Grade A or B) according to BILAG-2004 index is predictive of development of new damage in SLE patients.

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PERFORMANCES OF DIFFERENT CLASSIFICATION CRITERIA FOR SYSTEMIC LUPUS ERYTHEMATOSUS IN A SINGLE CENTER COHORT FROM TURKEY

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Background: Recently developed EULAR/ACR classification criteria for systemic lupus erythematosus (SLE) have important differences compared to the 2012 Systemic Lupus International Collaborating Clinics (SLICC) SLE classification criteria and the revised 1997 American College of Rheumatology (ACR) criteria: The obligatory entry criterion of antinuclear antibody (ANA) positivity is introduced and a "weighted" approach is used¹. Sensitivity and specificity of these three criteria have been debated and may vary in different populations and clinical settings.

Objectives: We aim to compare the performances of three criteria sets/rules in a large cohort of patients and relevant diseased controls from a reference center with dedicated clinics for SLE and other autoimmune/inflammatory connective tissue diseases from Turkey.

Methods: We reviewed the medical records of SLE patients and diseased controls for clinical and laboratory features relevant to all sets of criteria. Criteria sets/rules were analysed based on sensitivity, positive predictive value, specificity and negative predictive value, using clinical diagnosis with at least 6 months of follow-up as the gold standard. A subgroup analysis was performed in ANA positive patients for both SLE patients and diseased controls. SLE patients that did not fulfil 2012 SLICC criteria and 2019 EULAR/ACR criteria and diseased controls that fulfilled these criteria were evaluated.

Results: A total of 392 SLE patients and 294 non-SLE diseased controls (48 undifferentiated connective tissue disease, 51 Sjögren's syndrome, 43 idiopathic inflammatory myopathy, 50 systemic sclerosis, 52 primary antiphospholipid syndrome, 15 rheumatoid arthritis, 15 psoriatic arthritis and 20 ANCA associated

vasculitis) were included into the study. Hundred and fourteen patients (16.6%) were ANA negative.

Sensitivity was more than 90% for 2012 SLICC criteria and 2019 EULAR/ACR criteria and positive predictive value was more than 90% for all three criteria (Table 1). Specificity was the highest for 1997 ACR criteria. Negative predictive value was 76.9% for ACR criteria, 88.4% for SLICC criteria and 91.7% for EULAR/ACR criteria.

In only ANA positive patients, sensitivity was 79.6% for 1997 ACR criteria, 92.2% for 2012 SLICC criteria and 96.1% for 2019 EULAR/ACR criteria. Specificity was 92.6% for ACR criteria, 87.8% for SLICC criteria 85.2% for EULAR/ACR criteria.

Eleven clinically diagnosed SLE patients had insufficient number of items for both 2012 SLICC and 2019 EULAR/ACR criteria. Both criteria were fulfilled by 16 diseased controls: 9 with Sjögren's syndrome, 5 with antiphospholipid syndrome, one with dermatomyositis and one with systemic sclerosis.

Table 1. Sensitivity, positive predictive value, specificity and negative predictive value of 1997 ACR, 2012 SLICC and 2019 EULAR/ACR classification criteria

	SLE (+)	SLE (-)	Sensitivity (%)	Positive Predictive Value (%)	Specificity (%)	Negative Predictive Value (%)
1997 ACR	(+) 308 (-) 84	15 279	78.6	95.4	94.9	76.9
2012 SLICC	(+) 357 (-) 35	26 268	91.1	93.2	91.2	88.4
2019 EULAR/ACR	(+) 368 (-) 24	28 266	93.8	92.9	90.5	91.7

Conclusion: In this cohort, although all three criteria have sufficient specificity, sensitivity and negative predictive value of 1997 ACR criteria are the lowest. Overall, 2019 EULAR/ACR and 2012 SLICC criteria have a comparable performance, but if only ANA positive cases and controls are analysed, the specificity of both criteria decrease to less than 90%. Some SLE patients with a clinical diagnosis lacked sufficient number of criteria. Mostly, patients with Sjögren's syndrome or antiphospholipid syndrome are prone to misclassification by both recent criteria.

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SALIVARY GLAND ULTRASONOGRAPHY AND THE CLINICAL FEATURES USING ESSDAI IN PATIENTS OF EARLY-ONSET VERSUS LATE-ONSET WITH PRIMARY SJÖGREN'S SYNDROME

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Background: Primary Sjögren's syndrome (pSS) is a chronic inflammatory autoimmune disease characterized by lymphocyte infiltration in salivary and lacrimal glands. pSS affects primarily middle-aged and elderly patients, although younger age groups may also be involved. However, differences of etiology and pathogenesis between early-onset pSS (EOpSS) and late-onset pSS (LOpSS) are unknown. Recently, standardized outcome tools for measuring disease-specific activity and patients' reported symptoms have been formulated by the European League Against Rheumatism (EULAR) SS study group: the EULAR SS Disease Activity Index (ESSDAI) for systemic features of pSS [1]. Also, as the new imaging techniques, salivary gland ultrasonography (SGUS) proved valuable for assessing salivary gland involvement in SS and seemed to exhibit good diagnostic properties. In addition, previous studies have demonstrated usefulness of SGUS for the prognostic stratification of patients with pSS [2], [3], [4].

Objectives: The aim of this study was to examine the differences of etiology and pathogenesis between EOpSS and LOpSS using ESSDAI and SGUS.

Methods: Fifty-six pSS patients who fulfilled the American College of Rheumatology (ACR) / European League Against Rheumatism (EULAR) classification criteria for SS were studied. Based on the disease onset age, all pSS patients were divided into two groups as those with the onset age of 40 years old or younger (EOpSS: n=26) and those with the onset age of older than 65 years old (LOpSS: n=30). The clinical findings were evaluated ESSDAI and OMERACT SGUS score at the first visit to our hospital. The ESSDAI (0–123) proposes the evaluation of 12 domains or organ systems (constitutional, lymphadenopathy,

glandular, articular, cutaneous, pulmonary, renal, peripheral nervous system, central nervous system, muscular, hematological and biology). All patients were examined SGUS by a single investigator who was blinded to device (TUS-A300; Canon Medical Systems, Tokyo, Japan) with a linear transducer (7.5-10MHz). The OMERACT SGUS score was used for graded changes in the parenchymal homogeneity of salivary glands: grade 0, normal-appearing salivary gland parenchyma; grade 1, minimal change: mild inhomogeneity without hypo/anechoic areas; grade 2, moderate change: moderate inhomogeneity with focal hypo/anechoic areas; grade 3, severe change: diffuse inhomogeneity with hypo/anechoic areas occupying the entire gland surface [5].

Results: The proportions of positive sera of RF, anti-SS-A and anti-SS-B antibodies were not different in the two groups, but the disease activities were higher in the EOpSS than in the LOpSS patients by measuring ESSDAI (7.30 vs 4.23, p=0.008), especially in constitutional domain (1.50 vs 0.60, p=0.03), articular domain (1.54 vs 0.40, p=0.0002) and biological domain (1.35 vs 0.90, p=0.04). No difference in salivary secretion was found between two groups (EOpSS: 8.02 vs LOpSS: 6.31 mL/10min.), but the OMERACT SGUS score was higher in LOpSS than in EOpSS patients (2.00 vs 2.70, p=0.0002).

Conclusion: Although serological findings were not different, EOpSS patients had higher disease activity but less severe salivary gland degeneration than that in LOpSS patients, suggesting the pathogenesis of these two groups was different.

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PSYCHIATRIC DISORDERS IN PATIENTS WITH DIFFERENT PHENOTYPES OF NEUROPSYCHIATRIC SYSTEMIC LUPUS ERYTHEMATOSUS (NPSLE)

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Background: Patients with systemic lupus erythematosus (SLE) may present with psychiatric disorders. These are important to recognize, as they influence quality of life and treatment outcomes and strategies.

Objectives: We aimed to study the frequency of psychiatric morbidity as classified by the Diagnostic and Statistical Manual of Mental Disorders (DSM-V) in patients with SLE and neuropsychiatric symptoms of different origins.

Methods: In the neuropsychiatric SLE (NPSLE) clinic of the Leiden University Medical Center, patients undergo a standardized multidisciplinary assessment by a neurologist, neuropsychologist, vascular internal medicine, rheumatologist, physician assistant and psychiatrist. After two weeks, a multidisciplinary consensus meeting takes place, in which the symptoms are attributed to SLE requiring treatment (major NPSLE) or to minor involvement of SLE or other causes (minor/non-NPSLE). Consecutive patients visiting the NPSLE clinic between 2007-2019 were included. Data of psychiatric evaluation and current medication use were extracted from medical records. The presence of cognitive dysfunction was established during formal neuropsychological assessment.

Results: 371 consecutive SLE patients were included, of which 110 patients had major NPSLE (30%). Mean age was 44 ± 14 years and 87% was female.

The most frequently diagnosed psychiatric disorders in the total group were cognitive dysfunction (42%) and depression (23%), as shown in Table 1. Furthermore, anxiety was present in 5% and psychotic disorders in 4% of patients. In patients with minor/non-NPSLE, especially depression (26% vs 15%) and anxiety (6% vs 2%) were more common than in major NPSLE. Cognitive dysfunction (54% vs 36%) and psychotic disorders (6% vs 4%) were more common in patients with major NPSLE than minor/non-NPSLE.

Psychiatric medication was used in 33% of patients, of which antidepressants and benzodiazepines the most frequently (both: 18% in both subgroups). Antipsychotics were more often used in patients with NPSLE (10% vs 7%) and benzodiazepines more often in minor/non-NPSLE (20% vs 14%).

In addition, 17 patients (5%) had a history of suicide attempt, which was more common in patients with minor/non-NPSLE than major NPSLE (6% vs 2%).

Conclusion: Psychiatric morbidity, especially cognitive dysfunction and depression, are common in patients with lupus and differ between underlying cause of the neuropsychiatric symptoms (minor/non-NPSLE vs major NPSLE).