In univariate analysis, SLE participants with fatigue (FACIT-Fatigue<34) were more likely to be women (p=0.01), perceived their disease as more active (p<0.0001), had higher levels of pain (p<0.0001), anxiety (p<0.0001), depression (p<0.0001), insomnia (p<0.0001), stress (p<0.0001), and were more likely to have fibromyalgia (p<0.0001), compared to patients without significant fatigue. In multivariable analysis, the parameters independently associated with fatigue were insomnia (p=0.0003), significant pain (p=0.002), fibromyalgia (p=0.008), self-reported active SLE (p=0.02), and high level of stress (p=0.045).
Following LEAF feedback, 93.2% of the participants found LEAF helpful (NRS ≥ 3/5) and 92.3% would recommend it to another SLE patient (NRS ≥ 3/5).
Conclusion: In SLE patients, fatigue was frequent, commonly severe, and associated with a significant reduction of activities and motivation. This further confirms the urgent need to develop new tools to assess and treat fatigue in SLE. Our study demonstrates the usefulness of an innovative digital tool to manage fatigue in SLE.
Acknowledgements: We would like to thank all patients who have participated to the LEAF study, and in particular the patient association Lupus Europe.
Disclosure of Interests: Lou Kawka: None declared, Juan Camilo Sarmiento-Monroy: None declared, Manuel Ugarte-Gil: None declared, Sophie Geneton: None declared, Matteo Piga: None declared, Laurent Arnaud Consultant of: Abbvie, Alexion, Alpine, Amgen, Astra-Zeneca, Biogen, BMS, Boehringer-Ingelheim, GSK, Grifols, Janssen, LFB, Lilly, Kezar, Medac, Novartis, Oséus, Pfizer, Roche-Chugaï, Sêmeia, UCB.
DOI: 10.1136/annrheumdis-2023-eular.1059

OP0231 EVALUATION OF NON-CRITERIA MANIFESTATIONS OF ANTIPHOSPHOLIPID SYNDROME IN PATIENTS WITH SYSTEMIC LUPUSERYTHEMATOSUS ACCORDING TO ANTI-PHOSPHOLIPID ANTIBODY PROFILE

Keywords: Organ damage, Anti-phospholipid syndrome, Registries

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Background: 30% of patients with SLE have APS, so clinical thromboembolic, obstetric and laboratory manifestations have been extensively studied in this population. The association between antiphospholipid antibodies (aPL) and non-thrombotic manifestations that are not part of the Sydney classification criteria for APS are particularly important in patients with SLE.
Objectives: To compare the presence of non-criteria non-thrombotic manifestations of APS in patients with SLE and APS, SLE with positive aPL, SLE with negative antibodies and different outcomes such as mortality, hospitalizations and damage score.
Methods: Observational, analytical and cross-sectional multicenter study. Data were obtained from the review of the RELESSAR database. We included patients ≥ 18 years with diagnosis of SLE according to modified ACR 1984 criteria. The diagnosis of APS was made according to the Sidney Criteria 2006. The sample was classified into three groups based on the presence of established APS (Group 1), aPL carrier (Group 2) and aPL negative (Group 3). Non-criteria manifestations were described and compared in the three groups. Continuous variables were compared by Student's or Mann Whitney's T test, and categorical variables by Chi[2] test or Fisher's exact test. In cases where a significant difference was found between the groups, multiple post hoc comparisons were made.
Results: One thousand two hundred and two patients were included, 1,110 (92.3%) were women. One hundred and sixty patients (13.3%) had APS (group 1), 241 (20.04%) were aPL carrier (group 2) and 801 (66.6%) were negative for aPL (group 3). Patients with APS were older than patients in group 2 [42.6 (SD 13.5) vs 38 (SD 14.2), p 0.001] and 3 [42.6 (SD 13.5) vs 39.5 (SD 14.1) p 0.004]. The disease duration was longer in patients with APS compared to patients with SLE and negative aPL (138 months (SD 113) vs 101 (SD 113) (p <0.001). Table 1 shows non-thrombotic manifestations in the three groups. A higher percentage of patients with hemolytic anemia was observed in the APS group (p=0.001) and in the aPL carrier group (p=0.018) compared to negative aPL group. Patients with APS showed a higher proportion of thrombocytopenia when compared to patients with negative aPL (p=0.039). Acute cranial/peripheral neuropathy was more frequently observed in APS group compared to aPL-negative group (p=0.006). APS group was significantly associated with hospitalizations due SLE flares, morbidity and damage index (Table 2). A higher proportion of patients in the APS group had thrombotic events compared to aPL carrier and aPL negative groups (p<0.05).

Table 1. Non-criteria non-thrombotic manifestations

	APS (group 1)	aPL + (group 2)	aPL – (group 3)	*p*
Hemolytic anemia	31 (19.9%)	37 (15.4%)	75 (9.47%)	<0.001
Thrombocytopenia	41 (26.6%)	56 (23.4%)	138 (17.6%)	0.011
Depression	23 (14.8%)	17 (7.05%)	92 (11.6%)	0.041
Acute Neuropathy	10 (6.62%)	9 (3.73%)	14 (1.77%)	0.002

Table 2. Patient prognostic measures

	APS (group 1)	aPL + (group 2)	aPL – (group 3)	*p*
Hospitalizations	96 (62.3%)	119 (49.8%)	401 (50.4%)	0.02
Charlson Score	2.43 (1.92)	2.01 (1.51)	1.95 (1.46)	0.009
SLICC	1.53 (1.66)	1.04 (1.32)	0.960 (1.34)	<0.001

Conclusion: In this nation-wide SLE cohort, neurological and hematological manifestations were frequently observed in patients with secondary APS. Moreover, these patients had higher rate of hospitalization, damage score and comorbidities.
REFERENCES: NIL.
Acknowledgements: NIL.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.1792

OP0232 DEEP LEARNING ACCURATELY PREDICTS FOCUS SCORE AND DIAGNOSIS OF PRIMARY SJÖGREN SYNDROME USING LABIAL SALIVARY GLAND BIOPSIES

Keywords: Artificial intelligence, Sjögren syndrome

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Background: The Focus Score (FS) ≥ 1 in minor labial salivary gland (LSG) biopsies is one of the 2 main items (with anti-SSA positivity) to establish the diagnosis of Primary Sjögren Syndrome's (pSS). As such, correctly assessing the FS is crucial for the diagnosis of pSS. However, the histological interpretation of LSG tissue requires specific expertise and poses a challenge to non-specialized centers. Vivino et al. [1] show up to 53% of reclassification after expert center rescoring. Deep learning algorithms using artificial neural networks are increasingly used to assist pathologists and can be designed to provide explainable predictions using heatmaps. Heatmaps show which part of the sample section is used to perform the prediction, thus reducing the black box effect. This is important to allow adoption of accurate FS scoring using machine learning in clinical practice.
Objectives: Based on minor LSG specimen, we developed two deep learning models, the first one to predict the FS (≥ 1 or < 1) and the other to predict pSS diagnosis.
Methods: LSG slides used for the diagnosis of patients suspected of pSS were included in the study from 3 European centers which are part of the NECESSITY consortium, a European H2020 IMI2 project. Three groups were included: patients with sicca symptoms but without pSS (Sicca group), pSS patients with ≥ 1 FS, and pSS patients with <1 FS. All pSS diagnoses were confirmed by rheumatologists from expert centers. Clinical data regarding demographics, disease duration, FS, autoantibodies, and dryness were also collected. All LSG sections used for the pathologic diagnosis were scanned. Two deep learning models were used: one for FS prediction and the other for diagnosis prediction from the biopsies. The models provided a prediction and scored each sub-region of the tissue slides with a risk score. The risk score was used to interpret the algorithm's result and find which areas of the tissue were most significant for the classification (whether FS or diagnosis). For each model, 70% of patients were used for training and 30% for validation. For the FS task, both the validation and test sets include 54% of ≥ 1 FS patients. Similarly, for the pSS task, both the validation and test sets include 67% of pSS+ patients. The algorithm's performance was measured using the area under the ROC curve (AUROC).
Results: The dataset included 327 patients: 145 from Paris-Saclay university (Bicêtre Hospital), 73 from Queen Mary University London and 109 from the University of Birmingham. For binary FS prediction the AUROC was 0.87, and for the pSS diagnosis prediction, the AUROC was 0.84. When areas used to make the prediction were analyzed, the model unsurprisingly identified lymphocyte foci for the FS prediction task (Figure 1). This provides explainability and allows the pathologist to visually confirm the results of the prediction. Results on the validation sets for the two tasks are available in Table 1.

Table 1. Results on the Validation Sets.

Task	AUROC	Positive Predicted Value (PPV)	Negative Predictive Value (NPV)	Specificity	Sensitivity
FS ≥ 1/ FS < 1 Prediction	0.87	0.76	0.83	0.78	0.81
pSS+/- Prediction	0.84	0.83	0.67	0.64	0.84

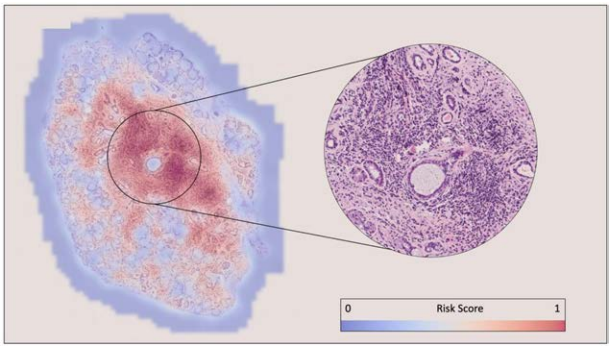

Figure 1. Heatmap Computed from FS Prediction Highlights Lymphocytes.

Conclusion: Deep learning can predict the diagnosis of FS>1 and the diagnosis of pSS with good accuracy. The FS model could represent a valuable help for assisting pathologists who are not experts in oral medicine pathology and reduce their reliance on reference centers. Comprehensive analysis of the tissue areas highlighted by the pSS model paves the way for a better understanding of the disease's physiopathology.

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Acknowledgements: We thank the NECESSITY consortium participants as well as the anonymous patients from the NECESSITY Patient Advisory Group for their valuable contributions.
Disclosure of Interests: None Declared.
DOI: 10.1136/annrheumdis-2023-eular.418

OP0233 IMPACT OF LYMPHOMA TREATMENT STRATEGY ON HEMATOLOGIC RESPONSE AND AUTOIMMUNE DISEASE ACTIVITY IN SJOGREN PATIENTS DEVELOPING LYMPHOMA

Keywords: Sjögren syndrome, Outcome measures

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Background: Primary Sjögren Syndrome (pSS) patients have an increased risk of Non-Hodgkin lymphoma (NHL). There is no consensus on the therapeutic management of low-grade NHL. Two strategies can be proposed; either a "wait and see" strategy or an active therapeutic strategy.
Objectives: To describe characteristics of NHL in pSS, therapeutic strategies and impact of these strategies on prognosis of lymphoma and of pSS.
Methods: This multicentric retrospective study included all lymphoma patients of the ASSESS cohort, enriched with patients recruited in Rheumatology and Internal Medicine departments. For each patient, we collected biological and clinical manifestations of pSS, lymphoma's characteristics, and treatment strategy. Progression free survival (PFS) (lymphoma-PFS and pSS relapse free survival) and overall survival (OS) were analyzed.
Results: A total of 106 pSS patients who presented a B cell lymphoma between 1985 and 2019 were included. Among them 14 (13%) had diffuse large B cell lymphoma (DLBCL) and 82 pSS patients presented a low-grade B cell-NHL, mucosa-associated lymphoid tissue (MALT) lymphomas being the most frequent histologic subtype occurring in 68/82 (83%) patients.
Among these 82 patients, a "wait and watch strategy" was chosen in 19 (23%) patients; 63 patients received a specific treatment for lymphoma at lymphoma diagnosis including systemic treatment (chemotherapy and/or immunotherapy) in 49 (60%) patients and local therapy (surgery or radiotherapy) in 14 (17%) patients; 10 patients further received rituximab (RTX) maintenance therapy.
Comparison of treated versus not treated patients is presented in the Table 1. Untreated patients were older and had less pulmonary lymphoma location.
We then analyzed the prognosis after a mean follow up of 6.5 years. Nine patients (11%) died during the follow-up. In multivariate analysis, age (HR= 1.16 [1.06-1.27], p = 0.001) and pulmonary location (HR= 8.15 [1.57-42.3], p = 0.013) were associated with death.
Last, we compared OS, lymphoma PFS and pSS relapse PFS in treated versus not treated patients after propensity score weighting We observed that starting an active treatment for NHL at lymphoma diagnosis did not impact OS and lymphoma PFS (HR= 4.81 [0.48-47.9], p=0.2 and HR=1.12 l0.50- 2.48], p=0.8, respectively). Conversely, treating lymphoma had a protective effect on the risk of pSS relapse (HR 0.4 [0.17-0.95], p = 0.038). Last, among patients treated for lymphoma, we observed that no lymphoma relapse occurred in patients who received maintenance therapy with RTX (0/10 events vs 18/53, p = 0.04).
Conclusion: This study based on a large number of pSS patients with lymphoma shows that age and pulmonary location are independently associated with the risk of death. The choice of treating lymphoma at its diagnosis or not does not affect OS and PFS for lymphoma. However treatment of lymphoma reduced the risk of pSS relapse. This should be taken into account when deciding therapeutic strategy in our pSS patients with lymphoma.