Background: Primary Sjögren syndrome (pSS) is a systemic autoimmune disease that may complicate with pulmonary manifestations in up to 16% of patients [1], including interstitial lung disease (SS-ILD) and airway disease (SS-AD).
Objectives: To assess the associated factors with SS-ILD and SS-AD.
Secondary objectives: to describe these manifestations and to investigate their prognosis.
Methods: We performed a retrospective multicentric study involving 9 French centers. We included pSS patients fulfilling the ACR/EULAR 2016 criteria and having a pulmonary disease associated with pSS evidenced by at least one clinician and one computed tomography (CT) report. We collected clinical and biological data at the visit giving access to the most exhaustive collection, pulmonary function test (PFT) and CT scans of the patients. CT scans were reviewed by a radiologist specialist in thoracic diseases. SS-ILD were considered progressive if there were at least a 10% decrease of the forced vital capacity (FVC) between 2 consecutive measurements. SS-ILD and SS-AD were compared to pSS controls with no history of pulmonary involvement, matched on age and disease duration with a 2/1 ratio.
Results: We included 56 SS-ILD, 31 SS-AD and 174 pSS controls. Comparison of SS-ILD, SS-AD and pSS controls is shown in **Table 1**. We found that SS-ILD and SS-AD had higher disease activity (ESSDAI) and B cell biological markers at visit time. Incident lymphomas were more prevalent in SS-ILD. SS-ILD were mostly nonspecific interstitial pneumonia (NSIP, n=16, 36%), usual or probable usual interstitial pneumonia (UIP, n=8, 18%), indeterminate for UIP (n=8, 18%) and lymphoid interstitial pneumonia (LIP, n=4, 9%). Fibrosis features were observed in 43% of cases. 44% of SS-ILD were progressive, independently of pSS characteristics and CT pattern, despite any significant evolution of PFT parameters of overall SS-ILD within 7 years follow-up (**Figure 1A**). We indirectly assessed the impact of the first line of systemic treatments in SS-ILD comparing PFT evolution of treated (43%) and untreated patients. We found that treated SS-ILD tended to have reduce PFT deterioration than non-treated patients with a 6 years follow-up [especially FVC and total lung capacity (TLC)], with a trend to improved FVC and forced expiratory volume (FEV1) with cyclophosphamide and rituximab (**Figure 1C-D**). SS-AD were mostly diffuse, associating bronchiolitis and bronchiectasis in 60% of cases. Here again, we did not find a significant worsening of PFT parameters with 9 years follow-up in SS-AD (**Figure 1B**), despite CT abnormalities worsening in 41% of cases at 6 years.

Table 1. Comparison between SS-ILD, SS-AD and pSS control

	SS-ILD, n=56	pSS control, n=112	SS-AD, n=31	pSS control, n=62
Clinical feature:				
Age, mean	56	56	56	56
Women	49 (87)	103 (92)	30 (97)	58 (93)
Death	7 (13)	7 (6)	2 (7)	3 (5)
Muscular	7 (13)*	3 (3)	3(10)	3 (5)
Splenomegaly	5 (9)*	1 (1)	2 (6)	2 (3)
ESSDAI, mean	16*	4	10*	4
ESSDAI (pulmonary excluded), mean	9*	4	7*	4
Incident lymphoma	5 (9)*	0	1(3)	0
Biology:				
Anti-SSA	41 (76)*	66 (59)	21 (70)	38 (65)
Anti-RNP	11 (22)*	2 (2)	0	1 (2)
Gammaglobulinemia, mean	23*	18	19	18
Beta2-microglobulinemia, mean	3*	2	3*	2

Data are n (%) unless otherwise indicated. Stars indicate significant comparisons to pSS control. Mann-Whitney and Fisher's exact test were used. *: p<0.05.

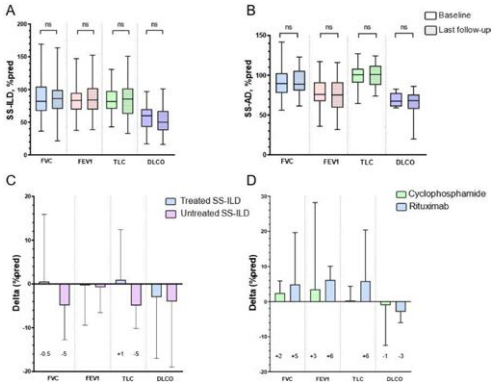

Figure 1. PFT evolution of SS-ILD and SS-AD Comparison of baseline and last follow-up PFT of SS-ILD (A) and SS-AD (B). Delta between last follow-up and baseline PFT of treated compared to untreated SS-ILD (C). Delta between post-therapeutical and pre-therapeutical PFT for cyclophosphamide and rituximab (D). Wilcoxon test was used. *: p<0.05.

Conclusion: SS-ILD are usually fibrosing and progressive manifestations of pSS, associated with disease activity, incident lymphoma and B cell biological markers. Despite the absence of randomized trials in SS-ILD, our results suggest an effect of the therapeutics. SS-AD are also associated with the disease activity and seems to progress slowly.
REFERENCE:
[1] Ramos-Casals et al., Rheumatology. 2015;54(12):2230-8.
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POS0165

DETERMINATION OF DISTINCT PHENOTYPES OF PRIMARY SJÖGREN'S DISEASE USING CLUSTER ANALYSIS BASED ON CLINICAL AND BIOLOGICAL MANIFESTATIONS: DATA FROM 458 PATIENTS FROM THE PARIS SACLAY SJÖGREN'S SYNDROME COHORT

Keywords: Sjögren syndrome

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Background: Primary Sjögren's syndrome (pSS) is a systemic autoimmune disease, with heterogenous manifestations. Main symptoms included dryness features due to the exocrinopathy, fatigue, and joint pain. In addition, systemic manifestations occur in approximately 30 to 40% of the patients with pSS. Previous attempts made to determine distinct pSS phenotypes used only symptom-based classifications, neglecting the B-cell biological activity and the systemic manifestations, which are clearly linked with disease prognosis.
Objectives: We aimed to identify distinct phenotypes among pSS patients, based on all disease features, including symptoms, systemic manifestations, and biological features, using a non-supervised hierarchical cluster analysis.
Methods: We included pSS patients enrolled in the prospective French Paris-Saclay cohort, if satisfying the ACR/EULAR criteria. We performed an unsupervised multiple correspondence analysis using 26 selected variables to widely cover pSS manifestations: VAS for pain, fatigue, ocular and oral dryness; systemic manifestations as defined by ESSDAI domains; biological parameters such as rheumatoid factor (RF), anti-SSA, -SSB, -RNP, -centromere, -DNA antibodies, high IgG levels, monoclonal component, cryoglobulinemia, low C4 levels; and abnormal Schirmer's test and presence of focal sialadenitis. The first axes were then considered to perform hierarchical clustering based on the Ward method. The number of clusters was determined visually on the plotted dendrogram and with the gain in inertia.
Results: We included 458 pSS patients in the analyses (95% women, median age 49 yrs). Cluster hierarchical classification yield in three homogenous groups of patients.

1. Cluster 1 (n=121) included patients with high symptom burden (median [IQR] ESSPRI 6.6 [5.6–7.7]), but low systemic activity (ESSDAI 1; [0-2])
2. Cluster 2 (n=110) included a higher proportion of men (15%) and of patients from African ancestry (19%), with high level of dryness (overall dryness VAS 66 [46–81]) and fatigue (VAS 70 [45–84] but low level of pain (pain VAS 53 [20–77]; high systemic activity (ESSDAI 5 [2–8]): lymphadenopathy (11%), cutaneous (7%), pulmonary (12%), PNS (11%), and articular (40%) involvements; frequent other auto-antibodies: anti-RNP (9.2%), anti-centromere (12%), anti-DNA (16%) and cryoglobulinemia (3.5%).
3. Cluster 3 (n=195) included younger patients (median age 44 yrs), with low symptom burden (ESSPRI 4.9 [3.3–6.2]), low systemic activity (ESSDAI 2 [1–4]), but with frequent B-cell activation signs: biological ESSDAI domain (58%), high IgG levels (52%), rheumatoid factors (58%), low C4 levels (22%); and higher rates of anti-SSA (86%) and -SSB (46%) antibodies.

Patients with history of lymphoma were identified in cluster 2 (n=8, 5.6%) and 3 (n=7, 3.6%).
Conclusion: Using an unsupervised clustering method, and including parameter that encompass all disease features, we identified three distinct subgroups of pSS patients that were 1/ high symptom burden without systemic features; 2/ Systemic features 3/ B-cell biologically active with low-symptom burden. Our study highlights the underlying idea of heterogeneous pathophysiological mechanisms and could help further stratifications among pSS patients. Further studies are needed to assess whether disease evolution is different across these subgroups.
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Disclosure of Interests: None Declared.

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POS0166

OUTCOME OF PREGNANCY IN WOMEN WITH PRIMARY SJÖGREN'S SYNDROME COMPARED TO THE GENERAL POPULATION: THE FRENCH MULTICENTER PROSPECTIVE GR2 STUDY

Keywords: Prognostic factors, Pregnancy and reproduction, Sjögren syndrome

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Background: In the context of primary Sjögren's syndrome (pSS), only retrospective studies have investigated pregnancy outcomes with heterogeneous methods and contradictory results. An increased adverse pregnancy outcome (APO) frequency was found in most case-control studies, including more miscarriage and intrauterine fetal death (IUFD), preterm delivery, small for gestational age and intra-uterine growth retardation, as well as an elevated number of cesarean sections. Moreover, these studies rarely analyzed the impact of pregnancy on the course of pSS.
Objectives: To describe outcome of pregnancies, identify predictive factors for disease flares and APO in pSS patients and compare their risk of adverse pregnancy, delivery and birth outcomes to those of the general population.
Methods: The GR2 study is a French multicentric prospective cohort of pregnancies in women affected with auto-immune diseases. The ENP 2016 is a French national perinatal survey on a sample of around 14.000 births. We included GR2 pSS women fulfilling ACR/EULAR 2016 criteria with an ongoing pregnancy at 12 weeks' gestation. EULAR Sjögren's Syndrome Disease Activity Index and Patient Reported Index (ESSDAI and ESSPRI) were recorded at the first trimester of each pregnancy (baseline or bESSDAI), each trimester and at delivery, and a cumulative ESSDAI (cESSDAI) was calculated, defined as the sum of each domain maximum score during follow-up before pregnancy. A pSS flare was defined as an increase ≥3 points of the ESSDAI. APO were defined as the occurrence of any of the following events: unexplained IUFD ≥12 weeks, neonatal death, placental insufficiency (intrauterine growth restriction, preeclampsia/eclampsia, HELLP syndrome, and/or placental abruption) leading to a premature delivery <37 weeks or small for gestational age birth weight. To determine predictive factors for pSS flares we excluded pregnancies included after 18 weeks and for APO also excluded twin pregnancies and aborted pregnancies. We compared the risk of adverse pregnancy, delivery and birth outcomes occurring ≥ 20 weeks in pSS pregnancies (including those with congenital atrioventricular block) to general population pregnancies from the ENP 2016, after matching (ratio 1:4) on age, parity, residential area and on the type of pregnancy (singleton vs multiple pregnancy).
Results: 106 pregnancies occurred in 96 pSS women. A history of pSS systemic activity was found in 92/102 (90.2%) patients and a systemic activity at inclusion in 48/106 (45.3%). pSS flares occurred in 12/93 (12.9%) pregnancies. Analyses did not identify any baseline parameter associated with the risk of pSS flare, in particular no association with ethnicity, cESSDAI, bESSDAI, or bESSPRI, biological markers of activity or type of autoantibodies. APO occurred in 6/88 (6.8%) [APO-BLOCK in 13/106 (12.3%)] pregnancies including only one with a pSS flare (Table 1). Women with and without APO had comparable age, weight, smoking status, cESSDAI, bESSDAI or bESSPRI at inclusion. However, women with APO had more often antiphospholipid (aPL) antibodies (n available=55, 50% vs 3.9%, p=0.02) and a trend for more frequent RNP antibodies was found (33.3% vs 5.7%, p=0.07). Treatment exposure did not differ between groups. APO frequency in pSS did not differ from that of the ENP population (8.6% vs. 6.7%, OR= 1.31, 95% IC [0.53-2.98], p=0.52). No difference was found in cesarian section rates (21.9% vs 22.9%, p=0.94) and birth outcomes (including APGAR5 and newborns ICU hospitalizations) between both groups.
Conclusion: pSS flares and APO were observed respectively in 12.9% and 6.8% of pregnancies but rarely occurred together. aPL antibodies were associated with a higher risk of APO and a trend for anti-RNP antibodies was found. Adverse pregnancy, delivery and birth outcomes in pSS women were comparable to those of the general population.
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POS0167

THE ANTIMALARIAL PROTECTIVE EFFECT AND A CLEAR CUT-OFF POINT FOR STEROID CUMULATIVE DOSE ASSOCIATED WITH DAMAGE ACCRUAL ON A 10-YEAR FOLLOW-UP SYSTEMIC LUPUS ERYTHEMATOSUS COHORT

Keywords: Organ damage, Systemic lupus erythematosus

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Background: Assessing damage accrual (DA) in patients with systemic lupus erythematosus (SLE) is complex but mandatory. Damage might be caused by the disease itself, comorbidities, and/or its pharmacological treatment or both. Among the pharmacological agents used to treat SLE, glucocorticoids (GC) are arguably the main cause of damage followed by lupus flares [1,2].
Objectives: This study aims to identify precise values of damage accrual related to damage in the long-term, the predictive positive and negative values for damage accrual of different steroid burden cut-offs points and the influence of other drugs, socioeconomic, ethnical and clinical aspects with damage in lupus patients.
Methods: A 10-years follow-up cohort of initially 190 patients, 147 alive at the end, with data regarding SLICC/ACR damage index (SDI) [3], clinical, social, economic and ethnical characteristics were recorded. SDI and medications accrual including GC were analyzed yearly both by patients interviews and chart reviews. A receiver operator characteristic (ROC) curve was developed to better comprehend relations among GC and damage, non-parametric data was analyzed by Mann-Whitney test and regression analyses was performed with Pearson test to evaluate factors related to DA over 10 years.
Results: Patients already with damage at baseline (SDI > 0) needed lesser GC accrual to develop new damage (4.2 g x 7.0 g, $p = 0.022$). Mean annual accrual of GC over a cut-off determined by the ROC curve analyses of 3.0 g (mean 8.22 mg per day) was independently associated with damage enhancement by SDI during the 10 years follow-up period compared to less than 3.0 g per year (OR=