Results: CD14⁺ cells were the most abundant cells in the urine of LN patients. The mean numbers of urinary CD8⁺, CD4⁺ and CD14⁺ cells/ml were significantly higher in patients with LN (405.6 ± 200.0, 281.1 ± 195.3, and 1554.7 ± 606.8 respectively) than in those without (39.30 ± 17.56, 34.33 ± 16.41, and 161.17 ± 90.91 respectively). AUC for ROC = 1.0 for all 3 markers with CD8⁺ >85 cells/ml, CD4⁺ >80 cells/ml, and CD14⁺ >400 cells/ml being observed exclusively in LN. The cell counts correlated significantly with the protein:creatinine ratio, but not with other markers of disease activity. The CD4:CD8 ratio was significantly lower in LN patients (0.69 ± 0.21) than in those without (0.91 ± 0.31). Urinary CD14⁺ cells seem to occur in much higher counts in Class IV (1736.7 ± 522.0) than Class III LN (898.5 ± 17.68) p=0.084. Figure 1 shows a dot plot of flow cytometric analysis of urinary T cells and monocytes in a patient with lupus nephritis showing increased both CD4⁺ and CD8⁺ T cells and monocytes (dim CD4 expression and CD14 positive (not shown)).

Conclusion: Urinary CD8⁺, CD4⁺ and CD14⁺ cells are highly sensitive and specific markers for detecting proliferative LN. A low CD4:CD8 ratio provides a further clue. The cell counts correlate with proteinuria. CD14 cell counts may be a potential biomarker to differentiate between the different classes of proliferative LN.

REFERENCE:

- [1] Kopetschke K, Klocke J, Griebbach A-S, Humrich JY, Biesen R, Dragun D, et al. The cellular signature of urinary immune cells in Lupus nephritis: new insights into potential biomarkers. *Arthritis research & therapy*. 2015;17(1):94.

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THU0262

FATIGUE IN PRIMARY SJÖGREN'S SYNDROME AS A DISEASE MANIFESTATION REFLECTING THE DEGREE OF MUCOSA-ASSOCIATED LYMPHOID TISSUE (MALT) INVOLVEMENT

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Background: fatigue in primary Sjögren's syndrome (pSS) is a very common and complex symptom, heavily impairing a wide range of patient functions, quality of life and health policies. To date, measures of fatigue and other patient-reported symptoms/outcomes (PROs) poorly correlate with pSS disease activity assessed by ESSDAI. On the other hand, therapeutic interventions reducing pSS disease activity proved useful to improve fatigue burden in pSS.

Objectives: to evaluate if fatigue correlates to other pSS disease manifestations which may also reflect disease activity, by investigating if: a) higher levels of fatigue shows a higher frequency of a heavier involvement of mucosa-associated lymphoid tissue (MALT) documented by histopathology, persistent glandular swelling, or cryoglobulinemia (1); and b) if fatigue correlates to other pSS-related somatic symptoms, such as dryness and arthralgias.

Methods: among pSS patients undergoing clinical evaluation in our Sjögren's Clinic in a six-months period, 86 consecutive unselected patients, fulfilling the latest ACR/EULAR pSS classification criteria, accepted to report their degree of fatigue, general dryness, ocular dryness, oral dryness and pain on 10-cm VAS (range 0-100), and to complete the ESSPRI (range 0-10), the PROFAD-SSI-SF (range 0-28) and the EQ-5D-scale (0-100) questionnaires. Four subgroups of fatigue severity were preliminary defined (2), presenting, as previously described (3): no fatigue (VAS=0): 12.8% (n=11); low fatigue (VAS=1-24): 25.3% (n=19); moderate fatigue (VAS=25-74): 58.7% (n=44); high fatigue (VAS=75-100): 16% (n=12). As previously reported (3) no significant age or sex difference was present between subgroups, and potential contributors to fatigue, such as autoimmune thyroiditis, anemia and fibromyalgia did not play a role.

The frequencies of peculiar manifestations related to an increased activity in MALT involvement in pSS, such as persistent salivary gland swelling, cryoglobulinemia and biopsy-proven diagnosis of myoepithelial sialadenitis (MESA) or of pSS-related MALT lymphoma, at any time in the clinical history of patients, were evaluated for each subgroup.

Secondly, the correlations between fatigue VAS and PROs reflecting somatic symptoms were performed.

Results: pSS patients reporting moderate or high fatigue VAS showed significantly higher frequencies of salivary gland swelling (p=0.0274), of MESA or lymphoma proven by histological diagnosis (p=0.0397), if

compared to pSS patients with no or low levels of fatigue. Cryoglobulinemia was not significantly increased, although more frequent, in patients with moderate or high fatigue (10.7%) compared to patients with no or low fatigue (6.6%).

Fatigue VAS score did not correlate with ESSDAI.

Patients with higher levels of fatigue showed significant (p<0.0001) higher scores in total ESSPRI, dryness-ESSPRI, pain-ESSPRI, ocular dryness VAS, oral dryness VAS, pain VAS, somatic fatigue domain of PROFAD, arthralgia domain of PROFAD, total SSI and PROFAD-SSI-SF.

Finally, patients with higher levels of fatigue reported worst scores in quality of life EQ-5D-scale.

Conclusion: The severity of fatigue appears to mirror the degree of MALT involvement, and this involvement is the biological substrate of pSS itself. This represents a demonstration that fatigue is biologically related to pSS, and supports the notion that fatigue should be treated by disease-modifying drugs rather than only with symptomatic therapies in pSS. In addition, dedicated scores of pSS activity can be developed for pSS patients where fatigue is one of the dominant symptoms. Since fatigue may also correlate with pSS somatic symptoms, such as dryness and arthralgia, they could also be included.

REFERENCES:

- [1] De Vita S et al, *Clin Exp Rheumatol* 2018
- [2] James K et al, *PLoS one* 2015
- [3] Gandolfo S et al, *Ann Rheum Dis* 2018

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THU0263

NOVEL SUBSETS OF SLE PATIENTS ENRICHED FOR RENAL MANIFESTATIONS IDENTIFIED BY CLUSTERING WITH EXPANDED AUTOANTIBODY PROFILES OF NATIVE AMERICAN (NA), AFRICAN AMERICAN (AA), AND EUROPEAN AMERICAN (EA) SLE PATIENTS

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Background: Autoantibodies (AABs) are a hallmark of systemic lupus erythematosus (SLE). Common SLE AABs show differences in specificities, levels and associations with clinical characteristics of disease which may be influenced by ethnicity.(1-2) NA SLE patients do not always exhibit classical AAB profiles.(2) Understanding how AAB profiles associate with clinical disease, including in NA patients, is important to better inform disease management.

Objectives: To identify patient subsets enriched for renal disease by clustering NA, AA and EA SLE patients into more homogeneous disease subsets based on expanded AAB profiles.

Methods: Serum samples from 49 NA, 49 AA, and 49 EA age, sex and ANA titer-matched SLE patients who met ACR classification and 10 sex and age matched controls from each ethnicity were tested for AAB reactivity by autoantigen microarray. Normalized fluorescence intensity (NFI) for AAB binding was determined for each individual for all autoantigens. Ratios of NFIs to total IgG were calculated and converted to Z-scores. Kruskal-Wallis analysis of Z-score transformed AAB ratios were used to identify AABs that differed significantly between patients and controls for each ethnicity; these AABs were used for hierarchical clustering of SLE subjects within each ethnicity. The enrichment of SLE clinical criteria within each cluster was determined by Fisher's exact test.

Results: AABs to nucleic acids and Ro52 were present in SLE patients of all three ethnicities. On average, NA SLE patients, but not EA or AA SLE patients, had lower levels of AABs against extracellular matrix (ECM) antigens compared to controls. AA and EA, but not NA, SLE patients had significantly higher levels of AABs to Sm, RNP and histones compared to matched controls. In each ethnicity four clusters of SLE subjects were identified by ethnicity-specific AABs. All three groups had a cluster of subjects enriched in nucleic acid-specific AABs and a cluster of subjects enriched in Ro52 AABs. The NA group also had two clusters enriched in ECM AABs. The AA group had an Sm/RNP AAB enriched cluster and a nucleolin/histone AAB enriched cluster. Two additional EA

SLE clusters had similar levels of nucleic acid-specific AABs and Ro52 AABs, but were distinguished by significant differences in histone 2A (H2A) AAB levels. Renal manifestations were significantly enriched in the NA Ro52 cluster and the AA nucleolin/histone cluster compared to other SLE patient clusters of the same ethnicity.

Abstract THU0263 – Figure 1

Conclusion: Expanded AAb profiles can be used to identify SLE subsets that are more likely to have renal manifestations of disease.

REFERENCES:

- Sánchez E, et al. Impact of genetic ancestry and sociodemographic status on the clinical expression of systemic lupus erythematosus in American Indian-European populations. *Arthritis Rheum.* 2012;64(11):3687-94.
- Khair JM, et al. Unique clinical characteristics, autoantibodies and medication use in Native American patients with systemic lupus erythematosus. *Lupus Sci. & Med.* 2018;5:e000247.

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THU0264

ANALYSIS OF SURVIVAL ASSOCIATED WITH PULMONARY ARTERIAL HYPERTENSION IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Identifying clinical variables that predict outcome of Systemic lupus erythematosus (SLE)-pulmonary arterial hypertension (PAH) is important.[1] Data focusing on SLE-PAH is lacking as previous studies were based on connective tissue disease (CTD)-PAH patients.

Objectives: To examine clinical, serological and echocardiographic features that are 1) associated with SLE-PAH at baseline and 2) predictors of mortality in SLE-PAH.

Methods: Data on SLE-PAH patients (SLE-PAH group, n=67) attending the Prince of Wales Hospital, from 2008 to 2018 was retrieved. Diagnosis of PAH was based on echocardiogram showing pulmonary artery systolic pressure (PASP) > 30mmHg. Age-, sex- and disease duration-matched SLE patients with PASP < 30mm Hg were selected from the same database as control (SLE-non PAH group, n=154). Clinical, serological, echocardiographic features and medication at baseline (PAH diagnosis) were collected. Censor date was death or last visit on or before 31st December 2018. PAH targeted therapy and immunosuppressant used for PAH were recorded after diagnosis of PAH. Hazard ratio were analysed by cox regression model, and adjusted by age-, sex-, disease-duration, comorbidities and baseline medication.

Results: The cohort (n=221) mean age was 42.7 +/- 12.6 with 96.3% female, and a disease duration of 8.26 +/- 7.61 years. At baseline, the SLE-PAH group had higher anti-ds DNA titre; lower haemoglobin level; higher prevalence of renal impairment; but a lower prevalence of arthritis and thrombocytopenia/neutropenia and anti-phospholipid antibodies compared to the control (Table 1). SLE-PAH group's echocardiogram had a higher prevalence of reduced left ventricular ejection fractions, moderate-

severe tricuspid regurgitation and pericardial effusion compared to the control (Table 1). Amongst the SLE-PAH group, 11/67 had a right heart catheterization done and all were confirmed to have PAH. 8/11 patients received PAH specific treatment and 23/67 received escalated immunosuppressive therapy for presumed PAH, within 1 years of PAH diagnosis. The mortality rate of the SLE-PAH group was 3.82 (95% confident interval 1.50-9.83; p=0.005) compared to the control after adjusting for baseline parameters and medication used after the diagnosis of PAH. Poor prognostic factors at baseline are summarized in table 2.

Table 1. Comparison between SLE-PAH and control at baseline

	SLE non-PAH (N=154)	SLE-PAH (N=67)	p-value
Female	149 (96.8%)	64 (95.5%)	0.701
Age, Mean (SD)	41.84 (11.76)	44.78 (14.18)	0.111
Follow up time (year) [Median (IQR)]	9.78 (4.39-12.42)	8.24 (4.54-12.07)	0.835
Disease duration (year), Median (IQR)	6.85 (1.29-11.77)	7.33 (0.94-15.06)	0.681
Death at end of follow up (%)	8/154 (0.05%)	14/67 (20.1%)	0.001
Renal impairment	25/154 [16.3%]	19/67 [29.7%]	0.026
Arthritis	91/154 [59.9%]	29/67 [43.3%]	0.023
Thrombocytopenia/neutropenia	78/154 [51.3%]	24/67 [35.8%]	0.047
Anti-ds DNA titre (median [IQR])	52 IU/ml [IQR 0-292.5]	160 IU/ml [IQR 0-789.5]	0.036
Haemoglobin (median [IQR])	11.7 g/dL [IQR 10.5-12.9]	10.8 g/dL [IQR 10-10.2]	0.009
Anti-phospholipid antibodies	38/154 [25.5%]	8/67 [12.1%]	0.027
Reduced left ventricular ejection fractions	1/154 [0.6%]	6/67 [9%]	0.003
Moderate-severe tricuspid regurgitation	2/154 [1.3%]	20/67 [29.9%]	<0.001
Pericardial effusion	22/154 [14.3%]	17/67 [25.4%]	0.047

Table 2. Predictors of mortality in SLE-PAH at baseline

	Alive (N=53)	Death (N=14)	p-value
Hyponatremia	7/49 [14%]	4/12 [30.8%]	p=0.011*
Renal impairment	11/51 [21.6%]	8/13 [61.5%]	p=0.007*
Severe tricuspid regurgitation	2/53 [3.8%]	2/14 [14.3%]	p=0.071

Conclusion: SLE-PAH had 3.8-fold increase in mortality despite treatment with PAH specific therapy and immunosuppressants. Hyponatremia and renal disease were associated with poor survival outcome in SLE-PAH patients.

REFERENCE:

- Raina, A, et al. *European Respiratory Review*, 2016

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THU0265

IDENTIFYING COMORBID FIBROMYALGIA IN SYSTEMIC LUPUS ERYTHEMATOSUS USING PATIENT-REPORTED OUTCOMES

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Background: Fibromyalgia (FM) is disproportionately common in patients with systemic lupus erythematosus (SLE) and difficult to diagnose on a background of classical SLE symptoms [1]. The Multi-Dimensional Health Assessment Questionnaire (MDHAQ) has been shown to be useful to recognise improvement over 2 months in a variety of rheumatic conditions including SLE [2] but has not previously been shown to be useful to alert the clinician to comorbid FM in the latter condition. Conversely, the 2011 FM self-report questionnaire is disease-specific and available for use in clinical and epidemiological studies. Administration of multiple forms may be difficult in a busy clinical setting.

Objectives: To identify comorbid FM in patients with SLE using patient-reported outcomes (PROs) from the routinely distributed MDHAQ, in comparison to the 2016 revision of the 2010/2011 FM criteria.

Methods: Patients with SLE completed an MDHAQ and the 2011 FM Criteria questionnaire. FM status was assigned using the 2016 revision of the 2010/2011 FM criteria as the gold standard. The MDHAQ features