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Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6752

AB0475 CHANGES IN HEART RATE VARIABILITY REFLECT CHANGES IN CLINICAL STATUS AND PATIENT REPORTED OUTCOMES IN SYSTEMIC LUPUS ERYTHEMATOSUS: A LONGITUDINAL ANALYSIS

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Background: We previously observed an association between systemic lupus erythematosus (SLE) disease activity and heart rate variability (HRV) with a preliminary observation of consistency between these two measures when disease activity changed between two timepoints (1).
Objectives: To prospectively test the hypothesis that HRV reflect longitudinal changes in clinical status and patient reported outcomes.
Methods: The current project evaluated HRV measurements using a 5 min ECG in SLE patients who completed a minimum of 2 visits in an ongoing clinical trial. HRV parameters were calculated in the time domain (RMSSD and pNN50) and the frequency domain [high frequency (HF) as well as low frequency to high frequency (LF/HF) ratio]. A mixed effects linear model, with generalized estimating equations to account for clustering of visits for each patient, was used to compare changes in HRV between paired visits and to examine linear associations between HRV parameters and clinical scores. All models were adjusted for baseline values of each HRV parameter.
Results: Forty nine patients (age 44.9±11.7, 46 female), followed in a total of 413 paired visits (median time between visits 1 month), were included. Global BILAG score was inversely associated with RMSSD (regression coefficient β=-1.39±0.01; $p<0.0001$). BILAG, SLEDAI and PGA were directly associated with the LF/HF ratio (β=0.96±0.02; $p<0.0001$, 0.42±0.10; $p<0.0001$ and 0.83±0.09; $p<0.0001$, respectively). Changes in BILAG were inversely associated with changes in RMSSD and pNN50 (β=-7.0±1.9; p=0.003 and -1.6±0.04; $p<0.0001$, respectively). BILAG changes were also directly associated with changes in the LF/HF ratio (β=0.78±0.05; $p<0.0001$). Categorical improvement, defined as $\geq$1 letter grade improvement in BILAG and no new BILAG A or B scores, occurred in 77 (19%) visit pairs (group 1) and either no improvement or worsening in 335 (81%) group 2. RMSSD and HF increased in group 1 compared to group 2 (group difference=-33.3±10.1; p=0.001 and -30.9±4.1; $p<0.0001$, respectively), and the LF/HF ratio decreased in group 1 compared to group 2 (group difference=3.1±0.8; p=0.002). Changes in Physical Component Summary (PCS) of SF36v2 were inversely related to changes in SLEDAI and PGA (β=-0.39±0.14; p=0.006 and -0.19±0.02; $p<0.0001$, respectively). Changes in Mental Component Summary (MCS) were inversely related to changes in BILAG, SLEDAI and PGA (β=-0.23±0.07; p=0.0001, -0.31±0.10; p=0.002 and -0.08±0.03; p=0.008, respectively). PCS was related to HF (β=0.67±0.28, p=0.01) whereas MCS was inversely related to the LF/HF ratio (β=-0.11±0.03, p=0.0001). Changes in PCS were related to changes in pNN50 (β=0.21±0.05, p=0.0001) and changes in MCS were related to changes in HF (β=1.57±0.18; $p<0.0001$).
Conclusions: Changes in HRV reflect changes in clinical status and patient reported outcomes in patients with SLE. These data suggest that HRV may be a simple non-invasive tool used to gage or predict clinical improvement in SLE. Further studies are warranted.
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Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5425

AB0476 INNER EAR INVOLVEMENT IN SYSTEMIC RHEUMATIC DISEASES

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Background: Patients with systemic rheumatic diseases have increased prevalence of sensorineural hearing loss (SNHL). Detection of cochlin specific antibodies has been reported in patients with idiopatic sensorineural hearing loss. Interestingly, cochlin has been shown a stronger link to autoimmune hearing loss.
Objectives: Objective of this cross-sectional study was to calculate the prevalence of SNHL in patients with systemic rheumatic diseases and to detect human cochlin antibodies in their sera.
Methods: This was a prospective study. Patients older that 18 year old who gave informed consent and fulfilled the criteria of American College of Rheumatology for rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), Sjogren's syndrome (SS) and systemic sclerosis (SSc) were included. Complete head and neck clinical examination was performed, including otoscopy, nasendoscopy and hearing investigation with pure tone audiometry (250Hz -8000Hz). All medical treatments as well as Disease activity score (DAS) 28 for RA and SLE disease activity index (SLEDAI) for SLE were documented. An average tone loss was calculated, taking as a starting point the loss in dB at various frequencies according the American Committee on Hearing and Equilibrium Guidelines for Meniere's disease and also recommendation 02/1 of "Bureau International d' Audiophonologie" (BIAP). Blood samples of the patients were tested for the presence of IgG anti-cochline antibodies (COCH-IgG). The results were compared with those of sex and age-matched healthy subjects.
Results: We studied 133 patients (60 with RA, 41 with SLE, 24 with SS and 8 with SSc) and 133 healthy subjects.61.4% of patients reported vertigo, 41% hyperacousis, 39% hearing loss, 38% tinnitus, 37.9% headache and 2.1% sensation of ear pressure with unremarkable otoscopy. The prevalence of SNL was increased in patients affected by RA, SLE, SS and SSc in comparison to healthy controls (66.6%, 31.71%, 54.17% and 75% respectively). The average hearing thresholds (AHT) calculated using BIAP recommendation 02/1 were significantly increased in RA compared to SLE. AHT were also increased in patients with RA and secondary SS but without statistical significance compared to RA patients. There was a statistically significant correlation between AHT and DAS28 in RA. No correlation observed between AHT and SLEDAI. COCH-IgG were detected in two samples (one patient with RA and one with RA and SS).
Conclusions: Cochlin has been shown to have a stronger link to autoimmune hearing loss, but our study concluded no correlation of hearing loss with human cochlin IgG (COCH). Additional prospective studies are needed to elucidate its pathogenesis.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4805

AB0477 VITAMIN D STATUS, SYSTEMIC LUPUS ERYTHEMATOSUS ACTIVITY AND ENDOTHELIAL DYSFUNCTION

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Background: Systemic lupus erythematosus (SLE) is an autoimmune inflammatory disease, in which cardiovascular complications due to premature and accelerated atherosclerosis represent a serious problem. Endothelial dysfunction is the first step in the atherosclerosis development. Low levels of vitamin D have a high prevalence in lupus patients, correlating with high prevalence of cardiovascular diseases in these patients.
Objectives: The aim of this study was represented by the assessment of endothelial dysfunction in patients with active systemic lupus erythematosus, and correlations of this with SLE activity and vitamin D status.
Methods: The study was performed on a group of 35 female patients with active systemic lupus erythematosus. In all the patients were assessed: SLE activity using SLEDAI (SLE Disease Activity Index), vitamin D status and endothelial dysfunction by means of flow-mediated dilation (FMD). Data were presented as mean ± standard deviation. The statistically analysis was performed using Pearson's test, $p<0.05$ was considered statistically significant.
Results: The mean age of the studied patients was 33.68±8.55 years, and the average duration of SLE was 8.91±5.29 years. The assessed parameters had the values: SLEDAI 9.02±4.51, vitamin D 12.79±2.45 μg/l (4 patients had vitamin D deficiency, and 31 patients had vitamin D insufficiency), and FMD 9.26±2.34%. There were significant correlations between vitamin D levels and FMD (r =0.4517, p=0.003), and between vitamin D levels and SLEDAI (r = -0.6297, p=0.00025).
Conclusions: Low values of vitamin D levels were present in all the studied patients, correlating with the systemic lupus erythematosus activity, and endothelial dysfunction.
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Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3282

AB0478 COMPARATIVE STUDY BETWEEN PATIENTS WITH NORMAL AND OVERWEIGHT IN A COHORT OF SYSTEMIC LUPUS ERITEMATHOSUS FROM ARGENTINA

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Background: Systemic lupus erythematous (SLE) have an increase cardiovascular risk, worsened by overweight and obesity. Increased BMI is associated with other severe complications and comorbidities as lupus nephritis, hypertension, insulin resistance and dyslipemia. Body weight is a modifiable risk factor.
Objectives: To determine the frequency of overweight and obesity in patients with SLE and their impact on this disease

Methods: Descriptive, cross-sectional study. We reviewed the medical records of outpatients with SLE (ACR 1997) who were seen since 2014 to 2016 in the Clinical Hospital of Buenos Aires, Argentina.
We evaluated sex, age, disease duration, obstetric history, use and doses of oral corticosteroids, BMI, 25 OH vitamin D and educational level. Disease activity was scored by SLEDAI. Scores ≥4 were classified as active.
The patients were classified into 2 groups, according to BMI: normal weight (NW) (19–25), overweight and obesity (≥25).
Results: One hundred and sixty two of 230 were evaluated. Sixty-eight patients were excluded due to lack of data. 157 (97%) were women. Mean age for both sexes was 40.6±14.3 years (p 0.70). Means of: SLEDAI 4.3±4.47 (54.9% had SLEDAI ≥4), IMC: 27.04±5.22 (56% had a BMI ≥25) and 25-hidroxivitamin D was 25.15±9.0.
Relation between 2 groups, according to BMI: 84.5% whom were in NW group have received steroids at some point vs 95.6% in BMI≥25 group (p 0.02). Mean steroids doses: BMI ≥25: 9.53±10.98 vs 5.0±7.2 in NW group (p 0.04). Multivariate analysis showed that BMI ≥25 continued significantly associated with SLE duration, independently of the steroids use and other variables.
25 OH vitamin D tended to be lower in BMI ≥25 vs NW, but no significant differences (24.53±9.91 vs 25.50±9.85) (p=0.071)

Table 1. In the multivariate analysis, Number of pregnancies was the only one variable remained significant (OR: 0.78, IC 95%: 0.63–0.98) (p=0.03)

Variable	IMC ? 25 (n: 71)	IMC ≥25 (n: 91)	P
Duration (months) Median (rank)	60 (1–384)	84 (2–480)	0,02
Pregnancies mean (SD)	1,20±1,62	2,64±2,84	0,0
Menopause (%)	27 (38,5)	51 (58,6)	0,009
Abdominal perimeter mean (SD)	88±8,3	99±11,9	0,0
Depression (%)	9 (12,5)	24 (26,6)	0,02
Chronic renal failure (%)	2 (2,7)	9 (10)	0,03
SLEDAI ≥4 (%)	33 (45,8)	56 (62,2)	0,02
SLICC mean (SD)	0,30±0.55	1,3±1,3	0,0
SLICC ≥1 (%)	18 (25)	64 (71,1)	0,0
Arterial hypertension (%)	12 (16,6)	32 (35,5)	0,003
Grade and University Studies (%)	32 (45)	19 (20)	0,004

Conclusions: Over a half of our cohort had BMI ≥25 and was characterized by older age, more frequent menopause, longer course of the disease, increased steroid use and lower educational level. Depression and hypertension were the statistically more frequent comorbidities found. Obesity was associated with more activity and accrual damage including chronic renal disease.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2766

AB0479 THE ROLE OF ANTIBODIES TO XANTHINE OXIDASE AND ADENOSINE DEAMINASE IN THE DEVELOPMENT OF ANTI-PHOSPHOLIPID SYNDROME IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Objectives: The aim of the research was to study the processes of formation of antibodies to the enzyme purine metabolism (PM) - xanthine oxidase (XO) and adenosine deaminase (ADA) - in patients with systemic lupus erythematosus (SLE) with laboratory indicants of secondary antiphospholipid syndrome (APS).
Methods: 30 healthy people and 60 SLE patients with different clinical manifestations were included in this research. Antibodies to the investigated enzymes were determined in the procedure of an indirect ELISA-test using immobilized form of the corresponding enzyme as antigen array (We have developed this technique). The results of the detection of antibodies to the XO (anti-XO), antibodies to ADA (anti-ADA) and antibodies to the ADC (anti-ADC) were recorded on a spectrophotometer at a wavelength of 450 nm. b_2-glycoprotein-I-dependent (b_2GP-I) to the phospholipid antibodies (aPL) class IgM and IgG were determined by using a commercial test kit “Anti-Phospholipid Screen IgG/IgM” (Orgentec). The levels of IgG aPL/IgM did not exceed 10 GPL/MPL-U/ml in the group of healthy individuals.
Results: According to the survey the number of SLE patients with elevated levels of anti-ADA was 51.6%, the anti-XO - 53.3%. There has been a number of statistically significant correlations between the presence of anti-XO with clinical and laboratory parameters: the level of circulating immune complexes (r=0.297, p=0.024), with a hemoglobin level (r= -0.286, p=0.042), the number of lymphocytes (r= -0.29, p=0.033), and platelets (r= -0,308, p=0.028). In 25 (41.7%) patients with SLE aPL IgG class were detected, in 19 (31.7%) - aPL IgM were detected. As a result of multivariate dispersive analysis leading role of aPL in the development of APS has been established (F=52,5, p<0,001).
In positive for the presence of anti-ADA patients with SLE aPL IgG class (but not aPL class IgM) were detected more frequently and at higher titer than in SLE patients, without this type of antibodies (p=0.029). Joint detection of anti-ADA and aPL in patients with SLE manifestations was associated with cytopenia (p=0.019, Fisher’s exact test). It was also noted that elevated levels of anti-XO were significantly more frequently detected in patients which were also positive for the presence of aPL IgG class (p=0.036) and aPL IgM class (p=0.044). Comparison of the groups of patients with SLE, the positive and negative for the presence of anti-XO, demonstrated a statistically significant increase in the frequency of signs of vasculopathy (chi-square=4.4, p=0.042).
Considering a direct link between the level of anti-XO and the level of the CIC we can assume that the anti-XO in the composition of the CIC have some impact on the transformation of “xanthine oxidase ↔ xanthine dehydrogenase” in the direction of increasing the formation of XO and, as a consequence, a significant increase of generation of superoxide radicals, release of calcium ions into the extracellular space, and, in addition, platelet aggregation and increased blood viscosity.
Conclusions: Antibodies to enzymes PM may be a factor in the development and maintenance of vascular disorders in patients with SLE, and their detection can be used as an additional test in the complex diagnosis of SLE with symptoms of APS.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4728

AB0480 A FUNCTIONAL MAGNETIC RESONANCE IMAGING STUDY ON THE PSYCHOPATHOLOGY OF PATIENTS WITH PRIMARY SJOGREN’S SYNDROME AND ANXIETY DISORDER

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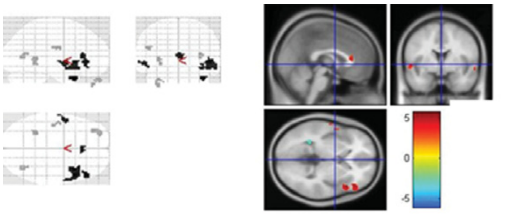
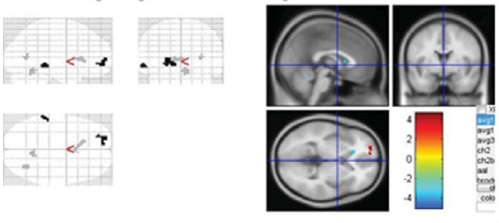
Background: Sjogren syndrome (SS) is a chronic systemic autoimmune disease characterized by exocrine gland inflammation and symptoms of oral and ocular dryness. Anxiety affects as many as 50–70% of persons living with SS. While anxiety is commonly experienced, very little is known concerning the mechanisms of cognitive dysfuction in SS.
Objectives: To reveal the psychopathology of patients with Sjogren’s syndrome and anxiety disorder.
Methods: 12 patients with pSS and anxiety disorder (SAS≥50), 11 patients with pSS, and 10 healthy controls were recruited. (1) Self-rating Anxiety Scale (SAS) were used to assess anxiety level of participations. All the subjects went through functional magnetic resonance imaging (fMRI) while listening actively to neutral words, negative words and negative words alternating with neutral ones.
Results: When subjects listened to neutral words alternating with no words, prefrontal cortex and BA21 were active in patients with pSS and anxiety disorder. When subjects listened to negative words alternating with no words, patients showed increased activity in prefrontal cortex, BA21, anterior cingulate and fusiform. Furthermore, when subjects listen to negative words alternating with neutral words, patients with pSS and anxiety disorder showed more increased



BRODMANN	Pixels	Max t value	P value	coordinates		
32	9	3.80	0.001	43	-21	6
21	34	3.15	0.001	63	-24	-6
47	103	3.11	0.000	31	18	-3
47	41	3.85	0.004	51	38	12

Fig.1 The results of comparison between pSS with anxiety group and pSS group, while listening to negative words alternating with neutral words. （P<0.005）



BRODMANN	Pixals	Max t value	P value	coordinates		
10	40	3.78	0.004	-24	51	-3
	39	3.72	0.004	-9	18	6
47	15	4.39	0.004	-31	27	0

Fig.2 The results of comparison between pSS with anxiety group and health controls, while listening to negative words alternating with neutral words. （P<0.005）