6/46 (13%), p=0.423]. In the negative conversion group, the number of patients diagnosed with SLE was significantly higher than the control group [SLE, 3/14 (21%) vs. 1/46 (2%), p=0.036]. However, thrombosis had recurred in one out of three patients with SLE.
Conclusions: The cumulative incidence of thrombotic events was not significantly different between negative conversion group and control group.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5787

SAT0308 CLINICAL, BIOLOGICAL AND IMMUNOLOGICAL FEATURES OF SJÖGREN SYNDROME: A STUDY OF 270 TUNISIAN PATIENTS

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Background: Sjögren syndrome (SS) is a chronic autoimmune disease characterized by a sicca syndrome and a wild spectrum of extra-glandular manifestations.
Objectives: The aim of this study was to describe clinical, biological and immunological characteristics of patients with SS and to compare them in primary and associated SS.
Methods: We conducted a monocentric, retrospective study over a period of 15 years. Patients who fulfilled the American European Consensus Group criteria for Sjögren syndrome were enrolled.
Results: SS was diagnosed in 270 patients. The sex-ratio female/male was 10.73. The mean age at disease onset was 45 years +/- 13 years (range 15–74 years) and at diagnosis was 47 years +/- 13 years (range 15–76) with a mean delay of 3 years (range 0–25 years). Sicca syndrome revealed the disease in most cases; both ocular and buccal dryness (n=48), xerophtalmia (n=21), xerostomia (n=21) or parotid gland swelling (n=17). SS was also revealed by joint involvement (n=39), neurological manifestations (n=26) or interstitial lung disease (n=14). SS was systematically screened in 27 patients with another autoimmune disease and was found in 3 mothers who had a child with congenital atrio-ventricular bloc. Patients complained of xerophtalmia and xerostomia in respectively 95.2% and 95% of cases. Minor salivary biopsy was positive in 92.6% of cases. Parotid gland swelling was noted in 40 cases. Arthralgia and arthritis were respectively noted 77% and 18% of cases whereas myalgia and myositis were found in 11% and 5% of patients. Patients had pulmonary involvements in 27% of cases. Peripheral and central nervous system involvements were confirmed in 22% and 13% of cases and 12 patients presented with psychiatric disorders. Raynaud's phenomenon and purpura were noted in 48 and 17 patients. Biological data showed lymphopenia (n=115), anemia (n=83), thrombocytopenia (n=25) and hypergammaglobulinemia (n=151). Antinuclear antibodies were positive in 210 cases; anti-SSA and anti-SSB were present in respectively 57% and 37% of patients. SS was primary in 155 patients and was associated to another autoimmune disease in 113 patients; systemic lupus erythematosus (n=48), rheumatoid arthritis (n=20), systemic sclerosis (n=19), autoimmune liver disease (n=13) and auto-immune thyroiditis (n=9). Arthralgia (91.2% vs 66.2; $p<0.0001$), arthritis (35.7% vs 5.2%; $p<0.0001$), myalgia (17% vs 7.1%; p=0.012) and Raynaud's phenomenon (33.3% vs 7.7%; $p\leq0.0001$) were significantly less frequent in primary SS. Lymphopenia (61.1% vs 32.9%; $p<0.0001$), anemia (48.6% vs 19.5%; $p<0.0001$), inflammatory syndrome (35.8% vs 17.9; p=0.002) and ANA (92% vs 70.9%; $p<0.0001$) were significantly more frequent in associated SS. Corticosteroids and immunosuppressive therapy were used in respectively 141 and 90 patients because of severe complications. Only 3 case of lymphoma were observed and 3 patients died. The mean duration of follow up was 50 months.
Conclusions: Sicca syndrome is the major symptom of SS but extra-glandular manifestations are less frequent and can be serious causing disability specially neurologic and pulmonary involvements. Some manifestations are significantly more frequent in patients with associated autoimmune diseases like joint involvements, Raynaud's phenomenon, anemia and lymphopenia. These manifestations are mainly related to SLE, rheumatoid arthritis and systemic sclerosis.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3589

SAT0309 CAN WE FORESEE SLE IN ITP PATIENTS? TO DISTINGUISH ITP PATIENTS WITH HIGH RISK OF SLE BY A NATIONWIDE COHORT STUDY-BASED DECISION TREE

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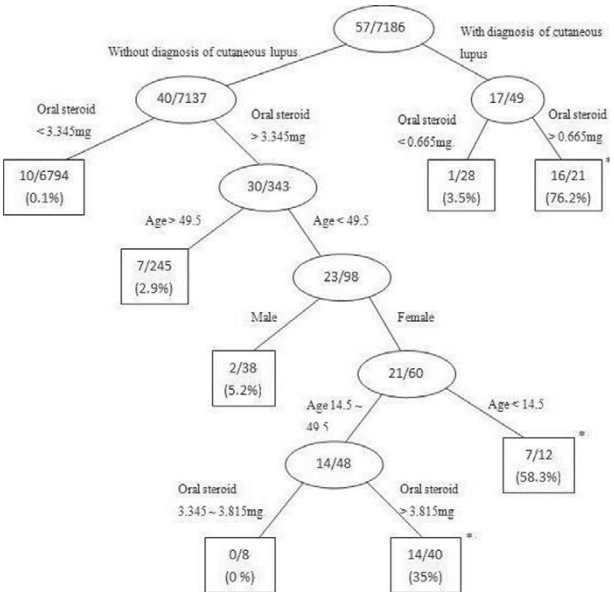
Background: Immune thrombocytopenic purpura (ITP) is an autoimmune-associated thrombocytopenia which is occasionally the initial presentation of systemic lupus erythematosus (SLE), and thus periodical following up has been suggested. Whereas long-term surveillance on all ITP patients would be time and cost-consuming, and thus to distinguish those with high probability of SLE development among ITP patients should be more practical.
Objectives: To distinguish ITP patients with high risk of SLE development by a decision tree model.
Methods: We enrolled ITP patients without previous SLE diagnosis from the National Health Insurance research database between 1997 and 2012 and identified those certificated with catastrophic illness of SLE during follow up, by which the diagnosis was reconfirmed by another rheumatologists. We also analyzed the symptoms and comorbidities as well as the dose of average oral steroid to derive the decision trees, which classified the ITP patients with different probability of development of SLE.
Results: A total of 10,265 ITP patients were enrolled, among whom 80 patients developed SLE while following-up. The whole ITP patients were allocated to training group (7,186 patients including 57 with SLE) and testing group (3,079 patients including 23 with SLE); the former was used for derivation of the decision-tree based model and the latter for validation of the previously mentioned model, and provided high sensitivity (78.2%), specificity (99.2%) and negative prediction value (99.8%, Fig.). To reduce the complexity, we also pruned our decision tree to propose less-complicated models.



Conclusions: We derived classification decision tree suitable for various clinical scenarios of ITP patients, among whom those with high probability of development of SLE would be distinguished.
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Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1359

SAT0310 ULTRASONOGRAPHIC SCORING OF THE MAJOR SALIVARY GLANDS IN SJOGREN'S SYNDROME: A COMPARATIVE STUDY WITH DISEASE ACTIVITY INDEXES

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Background: Sjogren's syndrome (SjS) is characterised by chronic autoimmune inflammation primarily affects the salivary and lacrimal glands. Recently, ultrasonography (USG) of major salivary glands (SG-USG) has been used to evaluate salivary glands in primary and secondary SjS.
Objectives: We aimed to investigate the association between the ultrasonographic scoring of major salivary glands and disease activity indexes in patientswith primary SjS.
Methods: Forty-two primary SjS patients fulfilling ACR-EULAR classification criteria (2002) were included. Disease activity indexes (Sjögren's Syndrome Patients Reported Index (ESSPRI), Visual Analogue Scale (VAS), EULAR Sjögren's Syndrome Disease Activity Index (ESSDAI)] were recorded. Major salivary glands (bilateral parotis and submandibular glands) were scored according to two different scoring system [Hocevar A. (0–48) ve Milic VD. (0–12)].
Results: Demographics, clinical characteristics, disease activity indexes and SG-USG scores were summarised in table 1 and table 2.

Table 1. Demographics and Clinical Characteristics of SjS patients (n=42)

Age (year)	54±11
Gender (F/M)	41/1
Duration of follow-up (month)	55±51
Siccasymptoms	39 (93%)
Arthralgia/arthritis	37 (88%)
Parotitis	9 (21%)
RaynaudPhenomenon	5 (12%)
Leucocytoclasticvasculitis	5 (12%)
Peripheralneuropathy	2 (5%)
Interstitiallungdisease	2 (5%)
Lymphadenopathy	6 (14%)
ANA	34 (81%)
Anti-Ro/La	19 (45%)

Tablo-2: Disease Activity Indexes and SG-USG Scores of SjS Patients

	n=42
ESSPRI-total	15,4±5,4
-dryness	5,7±2,2
-fatigue	5,2±2,6
-pain	5,4±2,6
VAS	55±20
ESSDAI-total	1±1
Hocevar-USG Score	20±10
Milic-USG Score	6±3

Twenty-four (57%) and25 (60%) patients had the cut-offvalues of ≥17 (Hocevar) and ≥6 (Milic USG).The patients with the scores of ≥17 (Hocevar)were found to have higher scores of ESSPRI-total (18±5 vs 14±5, p=0,01). Hocevar and Milic USG scores were shown to be higher in anti-Ro(+) SjS patients (25±10vs14±7and7±3vs4±2, p=0,01).USG scores were not found to be associated with the scores of ESSDAI, VAS and ESSPRI items.

Conclusions: Hocevar scoring system of major salivary glands was found to be related to patient reported activity in SjS. USG scores were associated with anti-Ro positivity. Evaluation of SG-USG might promote the diagnosis and follow-up of the SjS patients.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6196

SAT0311 PROLONGED EXPOSURE TO ANTIPHOSPHOLIPID ANTIBODIES IS ASSOCIATED WITH ENDOTHELIAL DYSFUNCTION IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Antiphospholipid syndrome has been shown to be associated with increased cardiovascular mortality, but the role of antiphospholipid antibodies (aPL) on endothelial dysfunction remains elusive.

Objectives: We investigated the association between endothelial dysfunction and aPL in systemic lupus erythematosus (SLE) patients.

Methods: 188 SLE patients and 62 controls were enrolled. Endothelial function was measured by flow-mediated dilatation (FMD). Cardiovascular risk factors were assessed and quarterly measurement of anti-cardiolipin (aCL) and anti-β_2 glycoprotein I Ab were used to calculate time-integrated values throughout disease duration. Circulating endothelial progenitor cell (EPC), defined by CD34+/KDR+ mononuclear cells, was quantified by flow cytometry.

Results: Median FMD was significantly lower in SLE patient than in controls (6.9 versus 9.3%, $P<0.001$). In univariate analysis, older age, hypertension, thrombocytopenia, and persistent positive lupus anticoagulant (LAC) were associated with decreased FMD in SLE patients ($P=0.021$, $P=0.011$, $P=0.004$, and $P=0.028$). Time-integrated aCL value (TI-aCL), but not a single value, was correlated with decreased FMD ($P=0.001$). Multivariate analysis showed that hypertension and TI-aCL were independent factors for decreased FMD ($P=0.027$, $P=0.008$); addition of positive LAC increased the adjusted probability of decreased FMD ($P=0.023$). FMD was correlated with EPC number ($\gamma=0.342$, $P=0.005$) and TI-aCL was also an independent factor of reduced EPC after multiple adjustment ($P=0.019$). The predicted probability of endothelial dysfunction at median EPC level was higher in group with high TI-aCL than in group with low TI-aCL ($P=0.004$).

Conclusions: Cumulative burden of aPL was closely associated with endothelial dysfunction in SLE patients, which was mediated in part by reduction of EPC.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3063

SATURDAY, 17 JUNE 2017

Scleroderma, myositis and related syndromes - etiology, pathogenesis and animal models

SAT0312 MICRORNA-125B AS A POTENTIAL FIBROTIC AND APOPTOTIC REGULATOR IN SYSTEMIC SCLEROSIS

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Background: MicroRNAs (miRs) are a class of small, noncoding RNAs that regulate many biological processes. Some microRNAs are involved in skin fibrosis.

Objectives: To analyze the differential expression, regulation and the pathophysiological role of miR-125b in systemic sclerosis (SSc).

Methods: For screening a low density array was run on pooled RNA from fibroblasts derived from 3 SSc patients vs. 3 healthy controls (HC). For further validation we performed qPCR on RNA derived from cultured fibroblasts, whole skin biopsies as well as on paraffin fixed dermis and epidermis. Next, fibroblasts were stimulated with pro-inflammatory and/or pro-fibrotic cytokines such as TGFβ, IL-1β, -4, -13, -17A, TNFα and PDGF. In order to identify downstream effects of miR-125b, knockdown with anti-miR-125b (or scrambled controls) in HC fibroblasts was performed. RNA was isolated from healthy fibroblasts (n=4) after knockdown and was proceeded to deep sequencing using Illumina HiSeq2000. Sequencing data were validated using qPCR on HC as well as SSc fibroblasts. Apoptosis was assessed by Caspase-Glo 3/7 assay and immunofluorescence of cleaved caspase 3 on cultured fibroblasts.

Results: Screening identified miR-125b as one of the candidate miRs differentially expressed in SSc. MiR-125b was confirmed by qPCR in primary dermal fibroblasts (SSc =11, HC =8), where it was downregulated by 47% (median expression 53%, $Q_{1,3}$ 33%, 70%; $p<0.01$). MiR-125b expression appeared to be independent from main cytokines operative in SSc. Additionally, the expression of miR-125b was assessed in skin biopsies of both SSc patients (n=4) and HC (n=5). In SSc, miR-125b was downregulated by 35% (median expression 65%, $Q_{1,3}$ 61%, 78%; $p<0.05$). To localize its expression in the skin, we separately analyzed miR-125b expression in dermis and epidermis of paraffin fixed skin. In both cases, expression of miR-125b was downregulated.

RNA sequencing identified >3500 differentially expressed genes with $p<0.05$. More than half of the differently expressed genes with at least 15% change were predicted targets of miR-125b by TargetScan and MiRWalk, indicating successful functional inhibition of miR-125b. Gene ontology revealed extracellular matrix organization and apoptosis regulation as the two main clusters of differentially expressed genes. Among them, BAK1, BMF and BBC3 are participants of the BCL2 apoptosis pathway and predicted targets of miR-125b. Consistent with the sequencing results, qPCR showed that knockdown of miR-125b upregulates these genes 24, 48 and 72 hours after transfection ($p<0.05$ for each). That was confirmed also on protein level by Western blot. Accordingly, miR-125b knockdown resulted in a higher rate of apoptosis (mean±SD: 60% ± 29%, $p<0.01$) compared to scrambled controls, measured by Caspase-Glo 3/7 assay.

Moreover, miR-125b knockdown reduced TGFβ-induced αSMA expression both on RNA and protein levels, suggesting that miR-125b might play an additional role in the cytoskeletal reorganization of fibroblasts during fibrosis.

Conclusions: MiR-125b is differentially expressed in SSc skin and primary dermal fibroblasts. MiR-125b downregulation increases apoptosis, inhibits cytoskeletal reorganization and therefore might become a potential anti-fibrotic therapeutic strategy.

Disclosure of Interest: A. Kozlova: None declared, E. Pachera: None declared, F. Renoux Grant/research support from: Swisslife, M. Rudnik: None declared, B. Maurer Shareholder of: Patent licensed: mir-29 for the treatment of systemic sclerosis, Grant/research support from: AbbVie, Protagen, EMDO, Novartis, Pfizer, Roche, Actelion, A. Jüngel: None declared, J. Distler Shareholder of: 4D Science, Grant/research support from: Anamar, Active Biotech, Array Biopharma, BMS, Bayer Pharma, Boehringer Ingelheim, Celgene, GSK, Novartis, Sanofi-Aventis, UCB, Consultant for: Actelion, Active Biotech, Anamar, Bayer Pharma, Boehringer Ingelheim, Celgene, Galapagos, GSK, Inventiva, JB Therapeutics, Medac, Pfizer, RuiYi, UCB, G. Kania Grant/research support from: Bayer, O. Distler Shareholder of: Patent licensed: mir-29 for the treatment of systemic sclerosis, Grant/research support from: Actelion, Bayer, Boehringer Ingelheim, Pfizer, Sanofi, Consultant for: 4 D Science, Actelion, Active Biotec, Bayer, BiogenIdec, BMS, Boehringer Ingelheim, ChemomAb, EpiPharm, espeRare foundation, Genentech/Roche, GSK, Inventiva, Lilly, medac, Mepha, MedImmune, Mitsubishi Tanabe Pharma, Pharmacyclics, Pfizer, Sanofi, Serodapharm, Sinoxa, Speakers bureau: AbbVie, iQone Healthcare, Mepha

DOI: 10.1136/annrheumdis-2017-eular.3806