outcome of PM/DM-ILD. High levels of serum IL-6, IL-8, IL-10, IL-18, CCL2, CXCL10, TNF- α , and IFN- α were detected in PM/DM-ILD cases, suggesting the pathological involvement of activated macrophages, type 1 T helper (Th1) cells, and neutrophils (ref 1, 2). However, investigation of the pathomechanism using serum cytokines remains insufficient in PM/DM-ILD. We hypothesised that multiple inflammatory cytokine pathways related to the above inflammatory cells would be involved in the pathomechanism of PM/DM-ILD.

Objectives: We measured serum cytokine levels before and during treatment of patients with PM/DM-ILD and examined the associated pathomechanism.

Methods: Serum cytokines were collected from 40 PM/DM-ILD patients. Principal components analysis (PCA) and cluster analysis were used to classify patients into subgroups. We compared cytokine profile of the survivors and dead patients as well as anti-MDA5 antibody-associated ILD and anti-ARS antibody-associated ILD. We also examined the association of various cytokines with disease activity indicators and prognosis of ILD.

Results: PCA revealed that the diversity of cytokines was driven by three groups: (1) neutrophilic and M1-macrophage-driven cytokines, (2) Th1 cell-driven and M2-macrophage-induced cytokines, and (3) M2-macrophage-driven cytokine. Based on cluster analysis, patients were classified into two subgroups according to the cytokine levels of all groups (Figure A). Ninety percent of patients who died of ILD were included in clusters with high cytokine levels (Figure B). Serum cytokine levels of all groups were significantly higher in the anti-MDA5 antibody-positive patients than in the anti-ARS antibody-positive patients. Factors of poor prognosis in PM/DM-ILD correlated significantly with serum cytokine levels of groups 1 and 2. Among the 3 groups, serum cytokine levels of group 1 were significantly higher initially and at 2 and 4 weeks in the death group.

Conclusion: These findings suggest that the activation of monocytes, macrophages, and Th1 cells, and neutrophils plays a role in the pathomechanism. Group 1 cytokines could be efficient biomarkers for predicting prognosis of PM/DM-ILD.

REFERENCES

- [1] Gono T, et al. *Rheumatology (Oxford)* 2014;53:2196–203
- [2] Oda K, et al. *Sci Rep* 2017;7:1635.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2019-eular.6614

SAT0288

A SYSTEMATIC REVIEW OF SYSTEMIC SCLEROSIS CLINICAL TRIALS SINCE 2005. LACK OF EARLY DISEASE TARGETING, CONFUSION RELATED TO DISEASE DURATION DEFINITION AND LOW LEVEL OF INCORPORATION OF THE NEW CLASSIFICATION CRITERIA

Konstantinos Melissaropoulos¹, Dimitrios Daoussis², Ioannis Antonopoulos¹, Alexandra Filippopoulou¹, Stamatis-Nick Liossis². ¹Patras University Hospital, Rheumatology, Patras, Greece; ²Patras University Hospital, University of Patras Medical School, Rheumatology, Patras, Greece

Background: It is still unknown whether treatment in very early systemic sclerosis (SSc) can affect long term outcomes.

Objectives: To systematically review clinical trials in SSc during the last 14 years aiming at answering the following questions: 1) how many clinical trials in SSc have targeted early disease and whether treatment of patients with early disease leads to better clinical outcomes, 2) how is disease duration defined in SSc clinical trials and whether data on duration since Raynaud's onset are provided and 3) whether the new 2013 ACR/EULAR SSc criteria have been incorporated in clinical trials throughout the last 5 years.

Methods: A search in published studies indexed in MEDLINE was performed from Jan-2005 to Dec-2018. The *Clinical Trial* filter was activated and the terms "systemic sclerosis treatment" used. Studies were included

if they evaluated adult patients with systemic sclerosis, concerned systemic treatments, presented data for clinical endpoints assessing fibrosis and were prospective in design.

Results: Seventy-three studies with a total number of 3078 patients met the inclusion criteria and were subjected to data extraction. The total weighted mean disease duration (adjusted to the number of patients in each study) was 38.55 months which is more than 3 years, the usual threshold for defining early disease. Baseline total weighted mean MRSS was 21.54 indicating that most patients had full blown fibrotic disease. Only 24 studies (32.9%) recruited early (<36 months disease duration) cohorts, with only 4 studies among them concerning very early disease (<18 months disease duration). We next focused on studies that did not specifically target early disease (n=49) and explored whether disease duration associated with clinical outcomes. We identified such an analysis only in 13 studies. In 8/13 studies there was no difference regarding outcomes according to disease duration. Nevertheless, in 4/13 studies investigators reported better outcomes in patients with shorter disease duration with only one study showing the opposite. Significant heterogeneity was found regarding disease duration definition. Four separate definitions were identified: 1) "From first non-Raynaud's symptom" (49.3%), 2) "From disease diagnosis" (11%), 3) "From skin thickening onset" (5.5%), 4) "From first symptom" (11%). The remaining studies (23.3%) presented no clear definition in their manuscript for disease duration in their cohorts. The stratification of the studies according to year of publication showed a tendency for greater consistency regarding the definition used in recent years since most studies published from 2015 and onwards use the definition "From first non-Raynaud's symptom". Data regarding the duration since Raynaud's onset were available only in 9 studies (12.3%). A separate analysis of all articles published from 2014 until 2018 was performed to explore the incorporation of the new 2013 ACR/EULAR criteria. Only 6 studies (25%) incorporating the new criteria were identified.

Conclusion: 1) The majority of patients recruited in clinical trials throughout the last 14 years do not have early disease, 2) Only one third of the studies were specifically designed to target early disease, 3) The question of whether early implementation of therapy may lead to better clinical outcomes cannot be definitely answered based on existing data, 4) there is confusion related to disease duration definition across SSc clinical trials but an obvious trend towards improvement was evident throughout the last few years and 5) there is still a very low level of incorporation of the new classification criteria in SSc trials.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2019-eular.3777

SAT0289

THE ROLE OF CAPILLAROSCOPY IN THE EARLY DIAGNOSIS OF SYSTEMIC SCLEROSIS

Atusa movasat Hajhkan, Henry Moruno, Ana Isabel Turrión, Cristina Bohórquez, Ana Pérez Gómez, Fernando Albarrán, Eduardo Cuende, Ana Sánchez Atrio, Lucía Ruiz, Paula Pretel, Laura Barrio, Valentina Emperiale, Adrián Abbasi, Melchor Álvarez de Mon. *Príncipe de Asturias University Hospital, Alcalá de Henares, Madrid, Spain*

Background: Systemic Sclerosis is a multisystem autoimmune disease characterized by fibrosis of the skin and internal organs and vascular damage. The diagnosis is usually made in the late stages, when irreversible damage has already occurred. Recently, we have established new criteria to detect early cases of the disease. Performing capillaroscopy and its findings are crucial in the diagnosis of early systemic Sclerosis or "prescleroderma" and there may be changes seen in capillaries of patients without skin manifestations.

Objectives: To analyze the nailfold capillaroscopy findings in patients with anti-centromere or anti-topoisomerase antibodies and evaluate their usefulness for the diagnosis of systemic sclerosis.

Methods: Of a total of 255 capillaroscopy performed in our Rheumatology department, those patients with positive anti-centromere or anti-topoisomerase were selected. In all cases, capillaroscopy was performed in eight fingers, always by the same observer. The following findings were considered pathological or scleroderma pattern: Local or global capillary loss (> 20%), hemorrhages: two or more in at least two fingers and enlarged capillaries: two or more capillary with double or more caliber in at least two different fingers.

Statistical analysis was performed with SPSS 19.0 program.

Results: The study included 69 patients: 5 (7.2%) males and 64 (92.8%) women, 14 (20.3%) smokers, 47 (68.1%) non-smokers and 8 (11.6%) quitters. The characteristics of the patients included in the study were as follows: 20 patients (30%) were previously diagnosed of systemic sclerosis (19 limited and one diffuse), of which 4 patients had concomitant primary biliary cirrhosis Syndrome (Reynolds), 1 patient with

primary biliary cirrhosis and positive anti-centromere without the presence of Raynaud, one patient diagnosed with Sjögren's syndrome with positive anti-centromere without presence of Raynaud, 26 patients with suspected early systemic sclerosis and 21 patients with disease-specific autoantibodies in the absence of Raynaud. Nailfold capillaroscopy was normal in 32 patients (46.4%) and pathological (scleroderma pattern) in 37 patients (53.6%); we detected limited enlarged capillaries in 26.2%, generalized enlarged capillaries also in 26.2%, giant capillaries in 37.7%, local loss of capillaries in 27.9%, global loss of capillaries in 8.2%, hemorrhages in small claims in 29.5% and abundant hemorrhages in 9.8%. All patients previously diagnosed of systemic sclerosis had a pathological capillaroscopy except one. However, no changes were observed in capillaroscopy in patients who had only disease-specific autoantibodies in the absence of Raynaud's phenomenon. While, the 26 patients who were referred for suspected systemic sclerosis (at least with the presence of Raynaud and autoantibodies) in 18 (69.9%) of these scleroderma pattern was observed with subsequent diagnosis of early systemic sclerosis or "prescleroderma".

Conclusion: Nailfold capillaroscopy is a useful and inexpensive tool for the diagnosis of systemic sclerosis. The scleroderma pattern is very specific of this disease and we can make an early diagnosis even in patients who only have autoantibodies and Raynaud's phenomenon, without the presence of other severe manifestations. We have also observed that the absence of Raynaud's phenomenon is associated with a normal result on capillaroscopy.

REFERENCE

- [1] Nailfold digital capillaroscopic findings in patients with diffuse and limited cutaneous systemic sclerosis. Saeedeh Shenavandeh, Mahyar Yousefpour Haghighi, Mohammad Ali Nazarinia. *Reumatologia* 2017; 55, 1: 15–23

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2019-eular.5612

SAT0290

TRADITIONAL AND DISEASE-RELATED RISK FACTORS FOR ARTERIAL AND VENOUS THROMBOTIC EVENTS (TE) IN IDIOPATHIC INFLAMMATORY MYOPATHIES (IIM)

Antonella Notarnicola¹, Simone Barsotti², Linnea Näsman³, Quan Tang³, Marie Holmqvist¹, Ingrid E. Lundberg¹, Aleksandra Antovic¹. ¹Karolinska Institutet and Karolinska University Hospital, Rheumatology Unit, Department of Medicine, Stockholm, Sweden; ²University of Pisa, Rheumatology Unit – department of clinical and experimental medicine, Pisa, Italy; ³Karolinska Institutet, Rheumatology Unit, Department of Medicine, Stockholm, Sweden

Background: Thromboembolic cardiovascular diseases (CVD), affecting both arterial and venous sides, are one of the leading causes of death in patients with Idiopathic Inflammatory Myopathies (IIM), with highest peak of mortality within the first year after diagnosis (1).

Objectives: To assess the prevalence of traditional and disease-related risk factors for arterial and venous thrombotic events (TE) in patients with IIM by comparing those reporting TE (cases) with those without history of TE (comparators). To compare clinical characteristics, autoantibody profile inclusive antiphospholipid antibodies (aPL) and serum levels of adhesion molecules (VCAM, ICAM and e-selectin) between cases and comparators as well as between cases reporting arterial vs venous TE.

Methods: Using national and international registries, and medical charts, we identified 58 cases and 195 comparators with IIM followed at Karolinska University Hospital between 1993 and 2014. Information on gender, age at the time of diagnosis, IIM subgroup, presence of interstitial lung disease (ILD), myositis specific antibodies (MSAs), was retrospectively collected. Information on traditional risk factors for arterial and venous TE (essential hypertension, diabetes, dyslipidemia, smoking, malignancy) was retrieved for both groups. Serum levels of aPL and adhesion molecules were analyzed in stored sera from the time of diagnosis in both groups, before TE in cases and in 40 age and gender matched healthy controls (HC).

Results: One out of 5 IIM patients (22.92%) had suffered from at least one TE, which was observed especially during the first 5 years after diagnosis. Myocardial infarction was the most frequent TE, followed by pulmonary embolism and deep venous thrombosis. In the multivariate analysis, male gender and older age were independent risk factors for TE. Essential hypertension had statistically significant higher prevalence in cases than comparators. Arterial TE was more common in polymyositis, while venous TE occurred more frequently in patients with

dermatomyositis, history of malignancy and in those with MSAs. At time of IIM diagnosis, the prevalence of aPL was 6% with no difference between cases and comparators. Significantly higher levels of VCAM and ICAM were obtained in IIM patients compared to HC (Fig.1 and Fig.2). ICAM levels were found significantly higher in comparators than cases (Fig.2). Lower levels of e-selectin were associated with higher odds of developing TE, especially in males and older patients, with no difference between arterial and venous TE (Fig.3).

Conclusion: A high risk of arterial and venous TE should be taken into account in patients with IIM, particularly close to time of diagnosis, with extra attention in male patients and older individuals. Preventive measures should be considered especially in patients with concomitant essential hypertension and malignancy. Lower serum levels of e-selectin might predict TE in IIM patients but the mechanism for this risk factor is not known.

REFERENCE

- [1] Doblog GC, Svensson J, Lundberg IE, Holmqvist M. Mortality in idiopathic inflammatory myopathy: results from a Swedish nationwide population-based cohort study. *Ann Rheum Dis*. 2018;77(1):40-7.

Figure 1

Figure 2

Figure 3

Disclosure of Interests: Antonella Notarnicola: None declared, Simone Barsotti: None declared, Linnea Näsman: None declared, Quan Tang: None declared, Marie Holmqvist: None declared, Ingrid E. Lundberg Grant/research support from: Dr. Lundberg has received honoraria from Bristol Myers Squibb and MedImmune and is currently receiving a research grant from Bristol Myers Squibb and from Astra Zeneca., Consultant for: She is a scientific advisor for Bristol Myers Squibb, and aTyr, Aleksandra Antovic: None declared

DOI: 10.1136/annrheumdis-2019-eular.5615