Results: Demographics, disease characteristics and nailfold video-capillaroscopic (NVC) pattern details were summarised in table-1. The scores of EUSTAR and EScSG activity indexes were correlated well ($r=0.576$, $p=0.000$) and the agreement between two scores for activity was moderate (cohen kappa:0.407). The percentages of SSc patients described as having active disease or not according to two activity indexes were summarised in table-2. Of the patients, 9.9% had active and 70.9% had inactive disease according to both indexes in this SSc cohort. Twenty-one (for EUSTAR) and 4 patients (for EScSG) were described as active according to one index and not to the other. Revised EUSTAR activity index was found to have 76.5% sensitivity and 81.6% specificity when the activity was defined by EScSG activity index.

Table 1.

Table-1: Demographics, Characteristics and NVC pattern in SSc patients

	All SSc pts n=131
Age (years) $\pm$ SD	50.3 $\pm$ 12.4
Gender F/M	122/10
Duration of Raynaud's (years) $\pm$ SD	9.6 $\pm$ 8.9
Duration of non-Raynaud's (years) $\pm$ SD	6.2 $\pm$ 6.5
Cutaneous involvement	
diffuse	33 (24.4%)
limited	93 (71%)
sclerodermic	6 (4.6%)
ANA	120 (91.6%)
anti-Scl70	38 (29%)
anti-centromer	33 (25.2%)
Clinical findings	
Digital ulcer	60 (45%)
Flex contr	18 (13.7%)
Low DLCO	59 (45%)
Lung disease	51 (38.9%)
pulmHT	19 (14.5%)
NVC	
Normal	7 (5.3%)
Early	29 (22.1%)
Active	23 (17.6%)
Late	69 (52.7%)
Cap number/mm	5.9 $\pm$ 2.1
Mod Rodnan Skin Score	7.3 $\pm$ 6.5
Disease Severity Score (Medsger)	5.3 $\pm$ 3.6
ESR (mm/h)	30.2 $\pm$ 18.3
CRP (mg/dl)	6.2 $\pm$ 10.5
Treatment	
Immunosuppressives	68 (51.9%)
Anti-vasculopathic	34 (26%)

Table 2.

Table-2: The percentage of the patients as having active or inactive disease according to indexes

	EUSTAR activity index	
	active	inactive
EScSG activity index	active 13 (9.9%)	inactive 4 (3%)
	inactive 21 (16%)	inactive 93 (70.9%)

Conclusion: This SSc cohort predominantly had limited cutaneous disease, digital vasculopathy and late scleroderma pattern. Defining active disease was differed in 19% of the patients according to EUSTAR and EScSG activity indexes, former described higher frequency for activity. This difference might be related to validation procedures of these indexes in patients with different predominant stages of SSc disease, content of the index and the features of the cohort.

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AB0224

SYSTEMIC SCLEROSIS SINE SCLERODERMA: CHALLENGES WITH VERIFICATION IN PATIENTS WITH PULMONARY ARTERIAL HYPERTENSION

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Background: Recognizing systemic sclerosis (SSc) in patients without cutaneous involvement is a real challenge due to inapparent clinical picture. 1980 ACR classification criteria for SSc fail to verify the diagnosis in the majority of cases. Therefore, the diagnosis is usually established years and decades after SSc onset at the stage of full-blown visceral disease. Introduction of 2013 ACR/EULAR classification criteria into clinical practice allow early diagnosis of SSc even in cases without skin involvement thanks to the fact, that list of considered criteria includes telangiectasia, pulmonary arterial hypertension (PAH), abnormal nailfold capillaries and SSc-related autoantibodies.

Objectives: To identify specific features in the clinical course of SSc sine scleroderma (ssSSc) in patients with PAH.

Methods: 11 patients with verified SSc diagnosis according to 2013 criteria were included; participants did not have any SSc-specific signs of skin involvement, such as puffy fingers, fingers' skin thickening/induration or skin atrophy. PAH was diagnosed in 11 patients during of right heart catheterization.

Results: Isolated Raynaud's phenomenon (RP) was along-standing diagnosis (more than 5 years) in all patients, except for one woman, in whom the disease manifested with signs of Sjogren's syndrome (SjS) (parotitis). Benign, chronic, and gradually progressing during a long time disease was documented in all patients. In 7 patients out of 11 SSc diagnosis was initially suspected by cardiologists, and later confirmed by detection of antinuclear autoantibodies. The following signs were documented in SSc patients as initial manifesting non-Raynaud symptoms: esophageal dysmotility – in 3 patients, digital ulcers – in 2, telangiectasia – in 2 patients, and dyspnea (PAH symptom) – in 1 patient. None of the patients ever experienced skin thickening typical for SSc. RP was present in all 100%, but digital ischemic alterations – digital tip ulcers, pitting scars were found only in 3 patients. SSc diagnosis was verified based on abnormal nailfold capillaries (in 100% cases), and based on identification of SSc-specific antibodies (anticentromere antibodies – ACA) – in 7 patients. Anti-Ro-antibodies were found in 4 patients, anti-RNP-70 – in 3. SjS was established in 3 out of 4 anti-Ro-antibodies – positive patients and ruled out in one. Myositis was documented in past-medical history in one patient with anti-RNP-70-antibodies positivity. It should be noted, that 3 ACA-negative patients had, nevertheless, a "threshold" score value (9 scores) for SSc diagnosis, exhibiting many clinical features in favor of SSc diagnosis beyond any doubt. Esophageal dysmotility and associated symptoms were found in 10 out of 11 SSc patients. One patient had an SSc-rheumatoid arthritis overlap syndrome (erosive arthritis, joint deformities, positive ACA, rheumatoid factor, anti-CCP).

Conclusion: Introduction of 2013 ACR-EULAR classification criteria for SSc into clinical practice was highly relevant for identification of SSc cases without cutaneous involvement, providing therefore a timely diagnosis in this group of patients, and allowing to prognosticate the clinical course of PAH. 2013 ACR-EULAR classification criteria for SSc is an algorithm for SSc verification in patients with PAH, especially in the absence of typical for SSc cutaneous disease. The earlier PAH-SSc is diagnosed and PAH-specific therapy is initiated, the longer will be patient's lifespan.

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AB0225

CLINICAL SUBTYPE OF PULMONARY ARTERIAL HYPERTENSION ASSOCIATED WITH SYSTEMIC SCLEROSIS

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Background: Despite the similar pathogenesis and clinical picture, pulmonary arterial hypertension in systemic sclerosis (PAH-SSc) in comparison with idiopathic pulmonary arterial hypertension (IPAH) is characterized by a more severe course, an unsatisfactory response to PAH-specific therapy, a poor survival and a

disappointing prognosis. In this connection, before doctors of different specialties, first of all before rheumatologists, cardiologists and pulmonologists, there is a need to highlight the characteristics of the flow of PAH depending on the presence of SSc.

Objectives: To describe specific symptoms of PAH associated with SSc.

Methods: The study included 51 patients with PAH-SSc and 50 patients with IPAH formed the control group. To verify the diagnosis of PAH all patients underwent studies according to the program corresponding to the russian recommendations for the diagnosis and treatment of pulmonary hypertension with mandatory right heart catheterization. The diagnosis of SSc was established in accordance with the classification criteria ACR-EULAR 2013. Univariate logistic regression was used to calculate a probability (odds ratio (OR)) of SSc-associated symptoms.

Results: We identified 29 symptoms that were associated with PAH-SSc. The most significant of them, increasing the risk of detection of SSc in patients with PAH, were age over 45 years (OR 9.7, 95% CI 3.9-24.3, $p < 0.00001$), serum uric acid level $> 387 \mu\text{mol/L}$ (OR 3.8, 95% CI 1.5-9.6, $p = 0.003$), diffusion lung capacity (DLCO) $< 60\%$ (OR 13.8, 95% CI 4.3-44.7, $p < 0.00001$), ratio of forced vital capacity to DLCO < 1.7 (OR 13.0, 95% CI 3.9-42.9, $p < 0.00001$), level of C-reactive protein $> 2 \text{ mg/l}$ (OR 12.9, 95% CI 3.96-41.8, $p < 0.00001$), the presence of pericardial effusion (OR 2.3, 95% CI 1.0-5.1, $p = 0.04$), mean right ventricular pressure $> 15.5 \text{ mm Hg}$. (OR 8.9, 95% CI 3.4-23.1, $p < 0.00001$), diastolic right ventricular pressure $> 4.5 \text{ mm Hg}$. (OR 4.6, 95% CI 1.9-11.2, $p = 0.0003$). Symptoms that reduce the risk of detecting SSc in patients with PAH include mean pulmonary artery pressure $> 55 \text{ mmHg}$. (OR 0.4, 95% CI 0.2-0.9, $p = 0.03$), pulmonary vascular resistance $> 12 \text{ units Wood}$ (OR 0.4, 95% CI 0.2-0.9, $p = 0.02$), hemoglobin level $> 146 \text{ g/l}$ (OR 0.3, 95% CI 0.2-0.8, $p = 0.007$), presense of syncope (OR 0.3, 95% CI 0.1-0.9, $p = 0.02$).

Conclusion: The selection of features of the course of PAH that increase the likelihood of detection of SSc will contribute to the timely diagnosis of SSc, will allow to predict the course of PAH, to approach more carefully the selection and monitoring of the effectiveness of PAH-specific therapy. That will contribute to improving the survival and functional status of patients with PAH-SSc.

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AB0226

NEUTROPHIL EXTRACELLULAR TRAPS ACTIVATE LUNG FIBROBLAST TO INDUCE MYOSITIS-RELATED INTERSTITIAL LUNG DISEASES IN MICE

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Background: Excessive neutrophil extracellular traps (NETs) formation may contribute to myositis-associated interstitial lung diseases (ILD), but the underlying mechanism is not fully revealed.

Objectives: This research aimed to elucidate the mechanism by which NETs contribute to myositis-associated ILD.

Methods: Myositis mice model was established by injected with the rat skeletal muscle homogenate and pertussis toxin. Expressions of ACTA2, CCN2, ADAM12, miR-7 and Smad2 were detected by quantitative real-time polymerase chain reaction (qRT-PCR). Smad2, α -SMA, CCN2 and TLR9 signaling-related proteins were measured by western blot. Soluble collagen I-IV were detected by Sircol collagen assay kit. The proliferation and apoptosis of lung fibroblasts (LFs) were detected by MTT assay or flow cytometry analysis. The interaction between miR-7 and the Smad2 was confirmed by dual-luciferase reporter gene assay.

Results: NET accelerated the progression of ILD and promoted pulmonary fibrosis *in vivo*. miR-7 expression was downregulated in lung tissue of myositis group than control group, and NETs further decreased miR-7 expression. TLR9 and Smad2 were upregulated in lung tissue of myositis group than control group, and NETs further increased TLR9 and Smad2 expressions. *In vitro* experiments showed that PMA-treated NETs accelerated the proliferation of LF and their differentiation into myofibroblast (MF), whereas DNase I decreased the promotion effect of NETs. NETs components myeloperoxidase (MPO) and histone 3 also promoted the proliferation and differentiation of LF. In addition, we demonstrated that TLR9 involved in the regulation of NETs on LF proliferation and

differentiation, and confirmed the interaction between miR-7 and Smad2 in LF. Finally, miR-7-Smad2 pathway was confirmed to be involved in the regulation of TLR9 on LF proliferation and differentiation.

Conclusion: NETs promote myositis-related ILD, and TLR9-miR-7-Smad2 signaling pathway is involved in the proliferation of LFs and their differentiation into MFs.

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Basic science in paediatric rheumatology

AB0227

EXTENSIVE IMMUNOPHENOTYPIC ANALYSIS OF CO-INHIBITORY AND CO-STIMULATORY MOLECULES IN JUVENILE IDIOPATHIC ARTHRITIS (JIA) PERIPHERAL LYMPHOCYTES

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Background: In a previous in-depth phenotypic analysis of PBLs in JIA, we detected differences in cell subpopulations dependent on the age and also some cellular changes that could be often associated with an exhausted phenotype.

Objectives: To analyze the expression of co-inhibitory and co-stimulatory molecules in different cellular subpopulations in Oligoarticular JIA patients stratified by age and treatment.

Methods: Exploratory cross-sectional study. 53 patients fulfilling Oligoarticular JIA (ILAR) criteria and 22 controls were included. All of them were children or young adults (2 to 35 years of age). JIA patients were either not treated (n=14) or treated with MTX (n=14), anti-TNF (n=8), or a combination of both (n=16). JIA disease activity was clinically and biologically assessed. Four flow cytometry panels were designed for the analysis of co-stimulatory/co-inhibitory markers, some typical of "exhausted" cells (PD1, TIM 3, TIGIT, CD226, CD137, HVEM, LIGHT, BTLA), assessed in memory, effector and naive CD4+ and CD8+ T lymphocytes, and also in B lymphocytes and NK cells. Statistical analysis was performed, and FDR correction was applied for p values.

Results: No correlation was found among the different exhaustion/activation markers and age neither in JIA nor in controls. Interestingly, age-related differential trends were observed in the CD8+ compartment in controls, while in JIA patients were detected in the B cell compartment. We didn't observe, after correcting for treatment, any significant difference in lymphocyte subpopulations defined by the above co-inhibitory and co-stimulatory markers in JIA patients in relation to indexes of disease activity. However, there was a tendency towards a higher expression of CD137 in several CD8+ subpopulations of active patients as compared to inactive.

Conclusion: No clear differences were found in PBL subpopulations of oligoarticular-JIA patients regarding co-stimulatory/co-inhibitory molecules. This finding could be explained, at least in part, by the good therapeutic control achieved in this patient population, or by the particular characteristics of this group of patients, in which prevails a more localized expression of the disease. It could be of interest to carry out complementary analysis to further define the differential tendencies observed.

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