and depression. During the follow-up period, there was a significant deterioration or stagnation of the achieved positive results in the IG. However, improved functional ability during the intervention period persisted in the IG in the follow-up period as well. Only numerical improvements in the IG during the intervention compared to the numerical deterioration in CG, that did not reach statistical significance, were observed in some subjectively assessed domains of QoL (SF-36) and fatigue (FIS – in physical dimension).

Conclusions Our specialized ADL training led to a significant improvement in the observed parameters that was clinically significant in a substantial proportion of patients, and prevention of the expected worsening of muscle weakness and quality of life.

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Disclosure of Interest None declared.

P045

EFFECT OF SPECIALIZED 6-MONTH PHYSICAL-OCCUPATIONAL INTERVENTION WITH SUBSEQUENT 6-MONTH FOLLOW-UP PERIOD IN PATIENTS WITH SCLERODERMA – PRELIMINARY DATA

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Career situation of first and presenting author Student for a master or a PhD.

Introduction Systemic sclerosis (SSc) is accompanied by stiffness and contraction of tissue, predominantly of the skin, caused by fibrosis and resulting in reduced quality of life. The aim of our study was to determine the effect of specialized physical-occupational intervention (POI) on hand/face function and strength, and quality of life of SSc patients.

Objectives The study included a total of 55 patients who fulfilled the EULAR/ACR criteria for SSc (2013) and had skin involvement leading to hand-function impairment and mouth handicap. 25 patients were recruited into the intervention group (IG) and 30 patients into the control group (CG). Both groups received educational material for home exercise, but only the IG underwent a 6 month intervention with a subsequent 6 month follow-up period.

Methods Patients were assessed by a physician and a physiotherapist blinded to intervention at months 0, 3, 6, and 12, and parameters evaluating hand/face and quality of life were recorded. Patients also filled out PRO (patient reported outcomes) questionnaires and provided blood for routine laboratory analysis and bio-banking. Data analysis was done between groups and within the group.

Results Compared to the observed statistically significant deterioration in the CG, we found a statistically significant improvement in the IG in objectively assessed function and strength of hand, distance between incisors and lips and functional ability (SHAQ). Only numerical improvements in the IG during the intervention compared to numerical deterioration in CG that did not reach statistical significance were observed

in subjectively assessed hand function and mouth handicap, functional ability (HAQ) and in some domains of QoL (SF-36) and fatigue (FIS—in cognitive function). During the follow-up period, there was a significant deterioration or stagnation of the achieved positive results in the IG.

Conclusions Our specialized POI intervention led to a significant improvement in the observed parameters that was clinically significant in a substantial proportion of patients, and prevention of the expected worsening of hand/face function and strength and quality of life.

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P046

NECROSTATIN-1 AMELIORATES NEUTROPHILIC ASTHMA BY INHIBITING NEUTROPHIL RELEASE NETS

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Career situation of first and presenting author Student for a master or a PhD.

Introduction Neutrophilic asthma is Corticosteroid-resistant and increases the burden of global health care. Multiple studies have indicated that there are a large amount of neutrophil extracellular traps (NETs) in the airways of neutrophil asthmatics.¹ Although NETs are able to entrap and kill pathogens, extensive accumulation of NETs which aggravate the condition of asthmatics and promote the progression of the disease.² However to our knowledge, the mechanisms by which NETs influence the progression of asthma have not been clearly elucidated and neutrophilic asthma requires novel effective therapeutic strategies.

Objectives We sought to explore the underlying mechanisms of NETs aggravate the severity of asthma, and to investigate a new strategy of effective treatment against corticosteroid-insensitive neutrophilic asthma.

Methods Mouse models of neutrophil-dominated asthma and phorbol ester (PMA) aggravated neutrophil asthma were used in this study to clarify the role of NETs in the pathogenesis of neutrophil asthma. Neutrophil release NETs was detected in bronchoalveolar lavage fluid (BALF) of neutrophil-dominated asthma. Finally a small molecule Necrostatin-1 (Nec-1) which has been shown to inhibit neutrophil release NETs was tested for its therapeutic effects against neutrophilic airway inflammation.

Results NETs could induce human epithelium human bronchial epithelial cell death and detachment *in vitro* study. NETs significantly increased in neutrophil asthma model and PMA aggravated neutrophil asthma. *In vivo* studies, Nec-1 could relieve airway hyperresponse, also reduced total protein, myeloperoxidase activity and inflammatory cytokines. Histological examination of the lungs also showed that Nec-1 markedly reduced the inflammation. We further explored that Nec-1 could induce human neutrophils and mice BALF neutrophils apoptosis. BALF and lung tissue immunofluorescence showed neutrophils increased expression of cleaved-caspase.³

Conclusions NETs could damage airway epithelium and trigger inflammatory responses. Nec-1 inhibit neutrophil release NETs ameliorates neutrophil airway inflammation. May be

the inherent mechanism of Nec-1 inhibit neutrophil release NETs is related to it specifically promotes neutrophil apoptosis.

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P047

THE PLASMA CELL BONE MARROW NICHE IN ACPA+ RA PATIENTS CONTAIN CITRULLINE SPECIFIC CELLS

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Career situation of first and presenting author Post-doctoral fellow

Introduction Anti-citrullinated antibodies (ACPA) in RA have been postulated to contribute to disease pathogenesis. This has been supported by studies of monoclonal APCA generated by cloning from single cell sorting of different B cell subsets from peripheral blood and synovial fluid. It has been debated if the bone marrow (BM) compartment of RA patients hosts long lived plasma cells producing ACPA or if ACPA are primarily coming from plasmablasts at the sites of inflammation, e.g. the synovium.

Objectives The main objectives were to study primary lymphoid tissue from RA patients, the BM plasma cell IgG repertoire and further characterize recombinantly expressed antibodies from selected sequences to explore if ACPA producing long lived plasma cells reside in this niche.

Methods For this study we collected bone marrow from proximal or distal femur of RA patients undergoing hip replacement surgery due to secondary osteoarthritis. BM samples were processed from four ACPA+RF+ and one ACPA-RF+ RA patients. Mononuclear cells were obtained by Ficoll separation and CD138+ plasma cells were single cell sorted by flow cytometry. Paired heavy and light chains were PCR amplified, sequenced and analyzed by V-Quest and IgBLAST towards the IMGT database to annotate variable gene usage. Selected sequences were cloned and expressed as IgG in Expi293 cells.

Results Overall 465 paired IgG BM plasma cell sequences were obtained, 97 from the ACPA- patient and 368 (range 20–194) from ACPA+ patients. We observed statistically significant changes in heavy chain variable gene usage with lower VH-1 and higher VH-3 frequency in the ACPA+ sequences compared to ACPA- sequences. We also found statistically significant increase in VH N-glycosylation in ACPA+ sequences (22.6% ACPA+ vs 12.4% ACPA-; $p=0.03$). There was however no difference in mutation numbers. From these, 34 clones were selected, based on mutation numbers and presence of Fab N-glycosylation sites, for subsequent mAb-expression. Among the 34 clones we found two CCP2+ and cit-peptide

positive clones and one malondialdehyde-acetaldehyde (MAA) adduct reactive clone, originating from different APCA+ patients.

Conclusions We could identify BM plasma cells producing autoantibodies to malondialdehyde-modified proteins and citrullinated peptides, isolated from RA patients. Hence, we show for the first time, that not just at the site of inflammation but also long-lived plasma cells in bone marrow do produce RA specific autoantibodies.

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P048

PREDICTIVE VALUE OF THE DIFFERENT CAPILLAROSCOPIC PATTERNS IN EARLY RAYNAUD PHENOMENON

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Introduction The Raynaud phenomenon (RP) affects 3%–5% of the population. Most RPs are primary. The risk of the onset of autoimmune disease associated with RP (ADRP) is around 12%, and the diagnosis is usually made within 2 years of its onset. Capillaroscopy is a innocuous and inexpensive technique that is very useful in the study of RP.

Objectives The primary goal was to evaluate the capillaroscopic findings and their different patterns in patients with RF as the only symptom and establish their relationship between the subsequent development of ADRF. We have evaluated the relationship between the presence of the antinuclear antibodies (ANA) and the association with ADRF.

Methods We conducted an observational, descriptive, cross-sectional study of 98 patients with RP as the main manifestation. Periungual capillaroscopy was performed from the 3rd to the 5th finger of both hands. Sociodemographic variables, and results of ANA were described. To assess the validity of capillaroscopy as a diagnostic test, we determined the sensitivity, specificity, and positive and negative predictive value (PPV, NPV).

Results 73.5% were women. The median time of evolution of the RP was 2.5 years. 76% were ANA negative.

The evaluation of the predictive capacity of capillaroscopy for the development of EARP yields the following Results.

sensitivity: 83,3% (62,6–95,2), specificity: 78% (66,8–86,9), PPV 34,1% (24,5–45,3), PNV 97,1% (93,3–98,8).

The capillaroscopic findings were: 62% no alterations, 21.4% no specific capillaroscopy changes, 14.3% 'scleroderma' type capillaroscopic pattern, and 2% characteristic pattern of mixed connective tissue disease (MCDT). None of the patients who did not present alterations developed autoimmune disease. Of the 21 patients who presented nonspecific changes, 5 developed limited systemic sclerosis (SSc), 3 MCTD, and 1 diffuse SSc. Of the 14 patients who presented 'scleroderma' type capillaroscopic pattern, 5 develop limited SSc, 3 diffuse SSc, 2 MCTD and 1 did not present autoimmune disease. Of the two patients with characteristic alterations of MCDT, 1 developed this disease. When analyzing the relationship between the presence of ANA and the association