VARIABLE	RA n=40	Control n=40	P - VALUE
Age (years), mean (SD)	58,5 (9,4)	58,5 (9,4)	0,998
Sex (female), n (%)	30 (75,0)	30 (75,0)	1,000
Rheumatoid factor, n (%)	32 (80,0)	2 (5,0)	<0,001
Anti-cyclic citrullinated peptide, n (%)	28 (70,0)	0 (0,0)	<0,001
DAS28 average value, mean (SD)	3,6 (0,5)	-	-
Metotrexato (%)	72,5	-	-
biologic disease-modifying antirheumatic drugs (%)	37,5	-	-

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AB0135 LEVELS OF MYOKINES AND RADIOGRAPHIC PROGRESSION IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Myokines, such as irisin and myostatin, are cytokines and growth factors mainly expressed in skeletal muscle, which is also their primary target tissue. They are released into circulation and exert a variety of systemic effects promoting crosstalk among different tissues [1]. Irisin is known to retrieve disuse-induced bone loss by stimulating the osteoblast pathways, while myostatin was demonstrated to be highly expressed in the synovial tissues of rheumatoid arthritis (RA) subjects, with direct role in osteoclastogenesis [2, 3].

Objectives: To investigate whether myokines serum levels can predict one-year radiographic progression in patients with RA.

Methods: Forty female patients with RA, according to ACR/EULAR 2010 classification criteria, were included in the study. Blood samples were collected, and ELISA was used to measure serum levels of irisin and myostatin. Radiographs of hands and feet, taken within three months of the blood collection and a year later, were evaluated using the Sharp-van der Heijde (SvH) score to verify the one-year radiographic progression. The RA activity was assessed by disease activity score based on evaluation of 28 joints (DAS28-ESR). Statistical analysis included Mann-Whitney U test and Spearman correlation. A value of $p < 0.05$ was considered significant.

Results: The mean age of RA patients was 53 years old, mean DAS28-ESR was 4.09, mean disease duration was 11.2 years and mean BMI was 27.33 kg/m². The mean serum levels of irisin and myostatin were respectively 25.61 $\pm$ 8.25 ng/ml and 3011.28 $\pm$ 1271.11 pg/ml. Considering radiographic progression, the mean values of SvH score were 28.3 and 31.3 in the baseline and after one year, respectively, resulting in a mean Δ SvH of 3. Over one year, 89.2% of the patients presented radiographic progression (Δ SvH score > 0), and 10.8% presented rapid progression (Δ SvH score > 5).

SvH score	Irisin (ng/ml)	Myostatin (pg/ml)
Δ SvH = 0	31.66 $\pm$ 10.66	2943.94 $\pm$ 719.96
Δ SvH > 0	26.67 $\pm$ 7.28	2996.90 $\pm$ 1356.66
Δ SvH > 5	31.61 $\pm$ 8.31	3255.81 $\pm$ 975.68

Conclusion: The serum levels of irisin and myostatin were not correlated with one-year radiographic progression. There was a tendency of increased myostatin levels in patients with rapid progression compared to patients with no progression. More studies are needed to investigate whether the myokine levels in the joint environment differ from the circulating concentration.

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AB0136 EVALUATION OF ANALGESIC ACTIVITY OF ALLOPURINOL AND FEBUXOSTAT IN EXPERIMENTAL ANALGESIC MODELS IN MICE

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Background: Allopurinol and febuxostat are xanthine oxidase inhibitor which are used in the treatment of hyperuricemia and gout. Pain is one of the important symptoms in gout patients.

Objectives: The present study is to evaluate the analgesic activity of allopurinol and febuxostat in two analgesic models in mice.

Methods: The analgesic activity of allopurinol (39 mg/kg) and febuxostat (15.6 mg/kg) was evaluated by using central analgesic model of Eddy's hot plate and peripheral analgesic model of acetic acid induced writhing. Both drugs were compared with the positive control, pentazocin for hot plate method & aspirin for the Writhing method. Also both allopurinol and febuxostat were compared with each other.

Results: Both allopurinol and febuxostat showed significant increase in reaction time at various time periods in hot plate method & also showed significant delay in onset of writhing as well as decrease in number of writhes in writhing method. As compared to positive control result allopurinol and febuxostat result were lower. Febuxostat shows better analgesic activity as compared to that of allopurinol.

Conclusion: Allopurinol and febuxostat exhibited analgesic activity in both central and peripheral models of pain.

Disclosure of Interests: None declared

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AB0137 ROLE OF VIMENTIN AS A TARGET OF ANTIBODIES AGAINST CARBAMYLATED PROTEINS IN RHEUMATOID ARTHRITIS PATIENTS

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Background: Patients with Rheumatoid Arthritis (RA) have an increased risk of cardiovascular diseases (CVD). Inflammation and autoantibodies independently promote endothelial dysfunction, which is the earliest, reversible stage of atherosclerosis. *In vitro* studies have demonstrated that antibodies against carbamylated proteins (anti-CarP), recently described in RA patients, can induce the production of proatherosclerotic molecules like Vascular Cell Adhesion Molecule (VCAM-1) and activate Interleukin-1 Receptor-Associated Kinase (IRAK-1), Nuclear Factor κ B (NF- κ B), inducible Nitric Oxide Synthase (iNOS) in endothelial cells (1,2). Moreover, anti-CarP are associated to endothelial dysfunction and subclinical atherosclerosis in RA patients (3).

Objectives: Aims of the present study were: 1) to analyze the role of vimentin as a target of autoantibody response in the serum of patients with RA and 2) investigate the expression of vimentin and carbamylated proteins in endothelial cells.

Methods: Consecutive RA patients were enrolled in this study. Vimentin was carbamylated and used as an antigen for the detection of anti-Vimentin Carbamylated antibodies (CarVim), through immunoenzymatic methods. Cells were incubated with anti-vimentin and carbamylated antibodies. The presence of vimentin and carbamylated proteins was investigated by immunofluorescence on the immortalized endothelial cell line EA.hy 926.

Results: Eighty-eight (88) RA patients were enrolled in this study (F:M = 79:9, mean age = 56 $\pm$ 13 years). Anti-CarVim antibodies were present in 9% of the patients with a mean titre of 442 aU/mL (IQR 303 aU/mL). Vimentin and carbamylated proteins were detected in the endothelial cells by immunofluorescence (Figure 1).

Conclusion: The results of this study confirm that Vimentin is one of the antigenic targets of anti-CarP antibodies present in the serum of RA patients. The presence of carbamylated proteins and vimentin in endothelial cells suggests that anti-Car-Vim could bind the modified protein and determine endothelial activation and subsequent endothelial dysfunction.

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Figure 1. Immunofluorescence on endothelial cell line EA.hy 926 demonstrating the presence of Vimentin (A) and Carbamylated (B) proteins.

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AB0138

INDIVIDUALS WITH ACPA POSITIVE RA PRESENTING INITIALLY WITH PALINDROMIC SYMPTOMS ARE SIGNIFICANTLY LESS LIKELY TO BE RHEUMATOID FACTOR POSITIVE THAN CLASSICAL ACPA POSITIVE RA; COULD THE AETIOPATHOGENESIS DIFFER BETWEEN THESE TWO DISTINCT TYPES OF ACPA POSITIVE RA?

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Background: It remains unclear whether ACPA positive RA presenting initially with palindromic symptoms (PRA) has the same underlying pathophysiology as ACPA positive RA presenting without palindromic symptoms (classical ACPA positive RA). The lung is an initiating site in RA development and rheumatoid factor (RF) is generated within bronchial associated lung tissue (1). RF in combination with ACPA immune complexes can induce TNF α from joint macrophages and potentially induce synovitis (2). Unsurprisingly a positive RF is a risk factor for RA development. Alternatively, palindromic rheumatism in the absence of RA occurs commonly in RF negative individuals (58%) (3). Therefore this form of explosive synovitis often occurs independently of RF, but is commonly associated with ACPA positivity (56%) (3).

Objectives: To identify whether classical ACPA positive RA differs in terms of RF positivity compared to ACPA positive PRA.

Methods: A retrospective case note observational study was undertaken to identify ACPA positive RA patients with or without a palindromic onset. All patients fulfilled the RA 2010 EULAR/ACR classification criteria (4). Patients were stratified for a history of smoking. RF was measured with Tina-quant Rheumatoid Factors II Test System, by Roche Diagnostics Corporation at the time of diagnosis. A value of < 14 IU/ml was considered as negative, weakly positive (14-42 IU/ml) and strongly positive (>42.1 IU/ml) as per EULAR/ACR guidelines (4).

Results: 99 classical ACPA positive RA and 35 ACPA positive PRA were identified. The median RF for PRA was significantly lower than the non-PR onset RA group (25 vs 86 IU/mL, $p = 0.001$). Comparing classical ACPA positive RA with ACPA positive PRA revealed 8/99 (8%) vs. 8/35 (23%) to be RF negative, 23/99 (23%) vs. 11/35 (31%) to be RF weakly positive and 68/99 (69%) vs. 16/35 (46%) to be strongly RF positive. Classical RA patients were significantly less likely to be RF negative, odds ratio 0.25 (95%CI 0.09-0.73), $P=0.01$. RA patients were significantly more likely to be strongly RF positive OR 4.32 (1.88-9.89), $P=0.0005$. Classical ACPA RA patients were more likely to be smokers than ACPA PRA patients 60/99 (61%) vs. 18/35 (51%), however this was not significant OR 1.48 (95 CI 0.68-3.2), $p=0.99$. Classical ACPA RA patients accumulated a greater number of pack years, median of 17 vs 5, however, the difference was not significant $p=0.12$.

Conclusion: The majority of ACPA RA patients presenting with palindromic symptoms have either a negative or weakly positive RF (54%). This contrasts with classical ACPA RA (31%) and suggests that a strongly positive RF is more important in the pathogenesis of classical ACPA RA than ACPA PRA. We suggest that a strongly positive RF and palindromic rheumatism are likely to be independent risk factors for ACPA positive RA.

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AB0140

EFFECT OF THE CO-TREATMENT WITH BACTERICIDAL/PERMEABILITY-INCREASING PROTEIN AND HYALURONIC ACID IN AN IN VIVO MODEL OF ARTHRITIS

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Background: Bactericidal/permeability-increasing protein (BPI) is an antibacterial, anti-inflammatory and antiangiogenic glycoprotein which has been detected in synovial fluid of patients with different arthritis [1].

Objectives: To investigate the effect of BPI alone or in combination with hyaluronic acid (HA) in a mouse model of collagen-induced arthritis (CIA).

Methods: CIA was induced in C57Bl/6 mice ($n=12$ per condition) by immunization with type II collagen/complete Freund's adjuvant emulsion at days 0 and 21 [2]. Development and severity of arthritis were monitored by measuring paw swelling with a caliper and scored (0-5) every 2 days. Arthritic mice (paw score=2) were intraperitoneally injected with 200 μ l of BPI (50 μ g/ml) in PBS in the presence or absence of HA (0.02%). Treatment and arthritis evaluation were carried out twice a week for 2 months. Untreated mice or animals that received HA alone (0.02%) were used as controls. At the experiment endpoints, mice were sacrificed to collect paw and blood samples. Hind paws were processed for histological analysis to assess inflammation, pannus formation, cartilage damage and bone resorption in ankle joints (score 0-5). CXCL1, TNF, IL-6, IL-1 β and VEGF serum levels were determined by ELISA.

Results: All mice reached an arthritis score of 2 after 28-33 days and showed a progressive worsening of clinical signs that peaked at day 49-56, and continued during the entire follow-up period only in control groups. At the end of the experiment, hind paw swelling and scores were lower in BPI-mice (paw thickness=4.76 $\pm$ 0.33 mm; score=4.5 $\pm$ 0.5) than in untreated mice (paw thickness=6.39 $\pm$ 0.95 mm; score=5). Histological analysis revealed leukocyte infiltration (score 3.00 $\pm$ 1.73), synovial proliferation (score 3.50 $\pm$ 0.71), cartilage damage (score 2.50 $\pm$ 0.71) and mild bone resorption (score 1.50 $\pm$ 1.71) in ankle joints of untreated controls. All of these histological changes were decreased (50–80%) in the group that received BPI. CIA induction led to high levels of CXCL1 (834.08 $\pm$ 68.8 pg/ml), TNF (277.72 $\pm$ 15.24 pg/ml), IL-6 (376.04 $\pm$ 46.33 pg/ml), IL-1 β (656.80 $\pm$ 45.6 pg/ml), and VEGF (347.48 $\pm$ 75.58 pg/ml) which were reduced with BPI treatment by 1.9, 14.6, 1.8, 2.9 and 2.7 fold, respectively. Animals injected with HA alone displayed slight improvement of all parameters evaluated but the differences were not significant. The combined use of BPI and HA showed paw swelling (3.65 $\pm$ 0.37 mm), arthritic score (0.67 $\pm$ 0.75) and histological scores for pannus formation (0.4 $\pm$ 0.55), inflammation (0.20 $\pm$ 0.45), cartilage damage (0.0 $\pm$ 0.0) and bone resorption (0.0 $\pm$ 0.0) more remarkably reduced than their separate use. In addition, the lowest levels of CXCL1 (11.44 $\pm$ 1.31 pg/ml), TNF (4.46 $\pm$ 2.23 pg/ml), IL-6 (129.30 $\pm$ 14.25 pg/ml), IL-1 β (81.58 $\pm$ 7.64 pg/ml), and VEGF (107.80 $\pm$ 32.64 pg/ml) were observed in serum of mice co-injected with BPI and HA.

Conclusion: This study shows that BPI attenuates progression of CIA in mice, and this effect is greatly enhanced by co-administration of HA. The combined use of BPI and HA represents an interesting perspective for a new potential intervention in the treatment of arthritis.

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