Methods: 

Objectives: We aim to examine the presence of GSMD-mediated pyroptosis and its role in activated RASFs.

Results: The expressions of NLRP1, pro-Caspase-1, Caspase-1 p10, GSMDM and its pyroptosis-inducing fragment GSMDM-N were greater in RA synovium than OA synovium. TNF-induced NLRP1, pro-Caspase-1, Caspase-1 p10, GSMDM, and GSMDM-N expression at the transcript and protein level in a time-dependent manner (P < 0.05). Meanwhile, the release of LDH and IL-1 were significantly increased in RASFs after treated with TNF. We also confirmed the presence of pyroptosis in electron microscopy. Furthermore, blocking the JAK pathway with baricitinib significantly reduced TNF-induced pyroptosis at the transcriptional, protein and activity levels (P < 0.05). Finally, blocking the JAK pathway, we observed a reduction of IL-1 bioactivity in RASFs (P < 0.05).

Conclusion: Our results demonstrate an important role of GSMD-mediated pyroptosis and shed lights on a potential pyroptosis-targeted treatment. Meanwhile, JAK inhibition alleviates inflammasome-induced pyroptosis by blocking pyroptosis pathway in RASFs.


Disclosure of Interests: None declared

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SAT0026
HIGHER LEVELS OF NATURAL ANTI-PHOSPHORYLCHOLINE ANTIBODIES ARE ASSOCIATED WITH LOWER RISK OF INCIDENT CARDIOVASCULAR EVENTS IN YOUNGER PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: The increased cardiovascular (CV) risk in rheumatoid arthritis (RA), especially in seropositive RA, is not fully explained by traditional risk factors. Immuno-inflammatory mechanisms and autoantibodies could be involved in the pathogenesis of atherosclerotic disease. Recent studies have suggested that anti-phosphorylcholine antibodies (anti-PC) of IgM subclass counteract the generation of senescent and IL-17+ T-cells, have atheroprotective effects and may play a role in formation and stabilization of atherosclerotic plaque.

Objectives: To investigate the association between IgM anti-PC antibodies with cardiovascular (CV) morbidity in patients with RA in age and sex groups and by serostatus.

Methods: The study population was derived from the BARFOIT early RA cohort, recruited in 1994–1996. The outcome was CV events i.e. AMI, angioplasty, coronary intervention, ischemic stroke and TIA tracked through the Swedish Hospital Discharge and the National Cause of Death Registries. The RA-disease measures and traditional risk factors were assessed according to the protocol. Sera collected at inclusion and the 2-year visit were analyzed with ELISA to determine levels of anti-PC IgM (Athera CVDefine kit, Athera Biotechnologies AB). The Kaplan-Meier estimates and Cox proportional-hazards regression models were applied. Analysis were stratified by median level of IgM anti-PC and performed within strata of age, sex and RA-antibodies.

Results: In all, 654 patients with early RA, 68% women, mean (SD) age 55(14.7) years, DAS28 5.2(1.3), 60% RF-positive and 60% ACPA-positive were included. Logistic regression analysis revealed that, at baseline, a total Krenn score <4.5 [(AUC)95%C.I.: 0.67(0.60-0.74),p<0.001] achieved more likely DAS-remission at 6 months (53.1%) than RA with total Krenn score ≥4.5(28.9%,p<0.001). Interestingly, RA whose ST was biopsied with in 3 months from joint symptoms beginning showed significantly lower ST inflammation as total Krenn score ≥4.5(28.9%,p<0.001). Logistic regression analysis revealed that, at baseline, being VERA, not having DAS-remission at 6 months 

Conclusion: These results suggest that higher levels of IgM anti-PC are associated with a lower risk of incident CV events over 10 years in younger patients. The favourable atheroprotective effect of IgM anti-PC may be a part of explanation of lower risk of atherosclerotic disease in younger patients with seronegative RA.

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SAT0027
DEVELOPMENT AND VALIDATION OF A NOMOGRAM COMBINING CLINICAL AND HISTOPATHOLOGICAL SYNOVIAL FEATURES FOR PREDICTING EARLY TREATMENT RESPONSE IN NAIVE TO TREATMENT RHEUMATOID ARTHRITIS

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Background: Rheumatoid Arthritis (RA) is characterized by synovial tissue (ST) heterogeneity at disease onset in terms of inflammatory degree and microanatomical organization being related to treatment response.

Objectives: To develop a multiparametric tool for baseline treatment response prediction including disease characteristics and histopathologic features of ST biopsies, using a large single center (SYNGemUnit) naive to treatment RA cohort.

Methods: 240 naive to treatment RA who underwent US-guided ST biopsy, at the first clinical evaluation, were enrolled. Clinical and immunological characteristics were recorded for each patient. All ST FFPE sections were stained with H&E and classified by a pathologist, blinded to clinical characteristics, using the Krenn score [1] to assess the degree of ST inflammation. All naive to treatment RA were treated according to the T2T scheme and DAS remission rate at 6-12 months was recorded. On the basis of the regression analysis, a nomogram was constructed that incorporated the significant factors predicting the “achievement of DAS-Remission at 6 months follow-up” in naive RA. The performance of the nomogram was assessed by discrimination and calibration.

Results: Univariate analysis showed that RA who achieved early (6 months) DAS-remission had, at baseline, significantly lower total Krenn score (p<0.001), shorter symptoms duration (p=0.005) and lower disease activity (p<0.001) than RA not achieving this clinical outcome. ROC curve analysis revealed that RA having, at baseline, a total Krenn score ≥4.5 (AUROC:0.70; 95%CI:0.60-0.74,p<0.001) achieved more likely DAS-remission at 6 months (53.1%) than RA with total Krenn score ≤4.5(28.9%,p<0.001). Interestingly, RA whose ST was biopsied within 3 months from joint symptoms beginning showed significantly lower ST inflammation as total Krenn score ≥4.5 (28.9%,p<0.001). Interestingly, RA whose ST was biopsied within 3 months from joint symptoms beginning showed significantly lower ST inflammation as total Krenn score ≥4.5 (28.9%,p<0.001). Interestingly, RA whose ST was biopsied with in 3 months from joint symptoms beginning (44.4%) and RA whose ST was biopsied in 3-12 months (47.6%,p=0.04) or after 12 months (p=0.33) since symptoms beginning.

 Logistic regression analysis revealed that, at baseline, being VERA, not having HDA and having a total Krenn score ≥4.5 were synergistic factors of DAS-remission achievement at 6 months [OR:10.95(95%C.I.:2.28-48.01),p<0.05]. Based on the regression analysis, a nomogram integrating baseline clinical disease activity and duration) and histological (total Krenn score) characteristics was developed in which the value of each of the variables was given a point score. A total score was calculated by adding each single point score and, by projecting the value of the “total points” score to the “probability” line up to 87.5%.

Conclusion: Krenn score is a reliable tool for the semi-quantitative assessment of ST inflammation on US-guided ST biopsies being contingent to baseline disease characteristics and can be integrated within a nomogram to better predict the therapeutic response in naive to treatment RA.


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