high-resolution visualization and effective treatment options are available, quite a large number of TA patients remain undiagnosed and untreated for years [2].

Objectives: To assess the influence of timely TA diagnosis and treatment initiation on the survival rate and cardiovascular events risk.

Methods: A retrospective cohort study included 183 patients (139 females, 44 males), enrolled during the period from 1979 to 2018 after TA diagnosis verification according to ACR1990 criteria [3]. All subjects have been followed up at the Sverdlovsk Regional Clinical Hospital 1. Cox regression model was used to compare survival rate.

Results: By enrollment, females median age was 35 [25%-75%: 24 - 44] and in males median age was 34 [26 - 42]. Median time duration from the first symptoms onset to the diagnosis verification was 3 [1-7] years in females and [1.5 - 8] years in males. The most common affected arteries were subclavian (55%), carotid (53%), and renal (42%). 5-year survival rate was 92%; 10-year survival rate was 90%; 15-year survival rate was 80%. The median term of survival was 34 [20 - 41] years. 31 deaths (18 males and 13 females) occurred during the follow-up period. Median age of death was 36 [32-44] in females, and 50 [40-57] in males. The average disease course duration at the time of death was 9.25 years, median term being 6.5 [3-16] in females and 5 [3-10] in males. Also a total of 72 cardiovascular events were recorded during the follow-up period: 27 in men and 45 in women. The median duration of AT course by the development of the first ever event was 10 (5 - 20). There were 24 cases of ischemic stroke, 3 transient ischemic attacks, 4 cases of hemorrhagic stroke. Median age of the first ever event was 38 (30 - 49.5). Time duration 4 years or more from AT symptoms onset to diagnosis was associated with significantly more frequent cardiovascular events (OR 1.8; 95% CI 1.07 - 3.34); and premature deaths (see table) by the 5th year of follow up (OR 2.9; 1.27- 6.55).

Conclusion: In a retrospective cohort, time duration 4 years or more from TA symptoms onset to diagnosis verification was associated with higher risk of cardiovascular events and lower survival rate.

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Disclosure of Interests: Artem Popov Speakers bureau: Novartis, Menarini, AstraZeneca, Pfizer, Severnaya Zvezda, Romepharm, Irina Borodina: None declared, Lubov Shardina: None declared

DOI: 10.1136/annrheumdis-2021-eular.3964

Like a gearwheel: HPR's research, education, and practice

OP0071-HPR

PILOT IMPLEMENTATION OF ENHANCEMENTS IN SUPERVISED GROUP EXERCISE FOR PEOPLE WITH AXIAL SPONDYLOARTHRITIS (AXSPA) IN THE NETHERLANDS

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Background: Supervised group exercise (SGE) for people with axSpA is widely available in the Netherlands [1]. Its contents have barely changed over the past 30 years, despite new evidence-based insights to improve the quality of SGE [1,2].

Objectives: To evaluate the process and effect of the implementation of enhancements in SGE for people with axSpA in the Netherlands.

Methods: This implementation study was executed in four regions, organising nine axSpA-specific SGE classes. The implemented enhancements included: 1. Exercise personalisation based on periodic assessments, including the 6-Minute Walk Test (6MWT) and the Ankylosing Spondylitis Performance Index (ASPI; improved/not improved); 2. High intensity aerobic exercise including intensity monitoring (e.g. by heartrate or BORG-scale); 3. Group education on home exercise and physical activity (e.g. promotion of an app). The implementation strategy was executed over a period of one year and consisted of a one-day training for the supervisors and bimonthly telephone support.

To evaluate the implementation effect, a survey was sent to 95 SGE participants, including two questions evaluating changes in the programme and in own functioning, as well as the 'ASAS Health Index' (ASAS HI) and the 'Short Questionnaire to Assess Health-enhancing physical activity' (SQUASH), which were also administered at baseline. In addition, the data from the periodic assessments (6MWT and ASPI) were used. Changes were analysed with the Wilcoxon Signed-Rank Test.

To evaluate the implementation process, apart from specific questions in the patient survey, semi-structured interviews with supervisors from each region were conducted.

Results: The survey was returned by 60/95 (63%) SGE participants (72% male, median age 60 years).

Effects: As shown in Table 1, 33% experienced improved functioning, 37% improved performance on ASPI and the improvements on 6MWT were statistically significant, $p < .05$, whereas there were no significant changes in ASAS HI and SQUASH.

Table 1.

SGE Participants (n=60)	
Effect evaluation	
Self-reported improvements in functioning, n (%)	20/60 (33)
Change in 6MWT score, median (IQR)	10 (-20;62)*
Improved on ASPI, n (%)	20/54 (37)
Change in ASAS HI score, median (IQR)	0 (-1;1.9)
Change in number of days with exercise (SQUASH), median (IQR)	0 (-1;2)
Evaluation of enhancements	
Satisfied with overall programme changes, n (%)	35/60 (58)
Satisfied with amount of exercise personalisation, n (%)	51/58 (88)
Assessment is applied, n (%)	50/58 (86)
Assessment is favourable, n (%)	47/50 (94)
Satisfied with amount of aerobic exercise, n (%)	39/56 (70)
Satisfied with exercise intensity, n (%)	44/57 (77)
Heartrate monitoring is applied, n (%)	29/59 (49)
Heartrate monitoring is favourable, n (%)	27/29 (93)
Familiar with axSpA-specific home exercise app, n (%)	12/56 (21)
Exercises at home using the app, n (%)	1/56 (2)

* $p < .05$

Process: The semi-structured interviews with the SGE supervisors (n=4, 25% male, aged 28-56 years, SGE experience 8-30 years) showed that: 1. exercise personalisation was difficult and periodic assessments were only maintained in two regions; 2. all regions increased focus on high intensity aerobic exercise and three monitored intensity; 3. none provided structural group education on home exercise. Table 1 shows that the majority of participants was satisfied with the overall programme changes, the personalisation, the assessments and the high intensity aerobic exercise and that heartrate monitoring and education on a home exercise app were applied in less than half of the participants.

Conclusion: After a training for SGE supervisors and telephone support, a set of enhancements was only partially implemented. However, the majority of participants was satisfied with applied changes and about a third improved functioning. For a nationwide implementation, a more extensive strategy addressing specific barriers is warranted.

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Acknowledgements: The authors thank The Dutch Arthritis Society and all participants, coordinators, boards, and guiding therapists from the four included SGE regions.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.739

New toys in rheumatology: single cell RNA and epigenetic sequencing, the holy grail?

OP0072

SINGLE CELL SEQUENCING REVEALS CLONALLY EXPANDED CYTOTOXIC CD4+ T CELLS IN THE JOINTS OF ACPA+ RA PATIENTS

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Background: CD4+ T cells with cytotoxic functions (CD4+ CTL) have gained attention in recent years. Accumulating evidence supports their importance in defense against human viral infections such as CMV¹, EBV², dengue³, HIV^{4,5} and SARS-CoV-2⁶. Moreover, expansion of so called CD28null cytotoxic CD4+ T cells have been reported in the blood of patients with rheumatic diseases such as rheumatoid arthritis (RA)⁷, myositis⁸ and vasculitis⁹ as well as in cardiovascular diseases¹⁰.

Objectives: Here, we aimed to investigate the presence and clonal expansion of CD4+ CTL in the peripheral blood (PB) and synovial fluid (SF) of RA patients using single cell technologies.

Methods: We assessed the expression of cytotoxic effector molecules and transcription factors in CD4⁺ T cells in synovial fluid (n=21) and paired peripheral blood (n=16) from ACPA- and ACPA+ RA patients by multi-parameter flow cytometry. We performed single cell sequencing, in combination with 5' TCRab sequencing, on purified CD4⁺ T cells from the peripheral blood (PB) and synovial fluid (SF) of ACPA+ RA patients (n=7).

Results: Flow cytometry experiments show that Granzyme-B+ Perforin-1+ CD4⁺ CTL are significantly increased in the SF of ACPA+ RA patients as compared to ACPA- RA patients (p=0.0072). The presence of CD4⁺ CTL could be confirmed by single cell sequencing in SF of each ACPA+ RA patient tested (n=7). Moreover, we found that the adhesion G-protein coupled receptor GPR56 is selectively expressed on the recently described peripheral helper (T_{PH}) T-cell subset¹¹ and associates with the expression of tissue resident memory markers LAG-3, CXCR6 and CD69. In blood, we confirmed a previous report¹² showing that GPR56 delineates cytotoxic CD4⁺ T cells. Finally, expanded TCR clones expressing cytotoxic effector molecules were identified in synovial fluid of ACPA+ RA patients and, for some patients, in their corresponding peripheral blood.

Conclusion: We identified GPR56 as a marker of T_{PH} cells in SF of ACPA+ RA patients that associates with tissue residency receptors. The combination of single cell sequencing and multi-parameter flow cytometry highlights the importance of CD4⁺ CTL in ACPA+ RA and suggests a potential therapeutic target (Figure 1).

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Acknowledgements: We thank the patients who donated samples and the medical staff at the Rheumatology Clinic of Karolinska University Hospital. Julia Boström, Gloria Rostvall, and Susana Hernandez Machado are acknowledged for organizing the sampling, storage, and administration of biomaterial. This study is supported by grants from Dr. Margaretha Nilssons, the Nanna Svartz, the Ulla and Gustaf af Ugglas foundations and the Swedish association against rheumatism.

Figure 1. Cytotoxic CD4⁺ T cells and GPR56+ peripheral helper CD4⁺ T cells are two T-cell subsets identified in SF of ACPA+ RA patients.

Disclosure of Interests: Alexandra Argyriou: None declared, Marc H Wadsworth II Employee of: Pfizer, Inc, Cambridge, MA 02139, United States, Adrian Lendvai: None declared, Stephen Christensen Employee of: Pfizer, Inc, Cambridge, MA 02139, United States, Aase Hensvold: None declared, Christina Gerstner: None declared, Kellie Kravarik Employee of: Pfizer, Inc, Cambridge, MA 02139, United States, Aaron Winkler Employee of: Pfizer, Inc, Cambridge, MA 02139, United States, Vivianne Malmström: None declared, Karine Chemin: None declared
DOI: 10.1136/annrheumdis-2021-eular.1403

OP0073

SINGLE-CELL TRANSCRIPTOMICS UNCOVERS DEFECTIVE BONE MARROW EARLY B CELL DEVELOPMENT IN A SUBSET OF LUPUS PATIENTS ASSOCIATED WITH AGGRAVATED INFLAMMATION

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Background: Systemic lupus erythematosus (SLE) is a systemic autoimmune disease that occurs when the body's immune system attacks own tissues and organs. B cells play a central role in SLE pathogenesis by producing autoantibodies as well as antibody-independent functions. Peripheral B cell abnormality is well known in lupus patients such as expansions of plasmablasts and atypical memory B cells, which are associated with active diseases. However, little is known about the B cell development in the bone marrow of lupus patients.

Objectives: We conduct this survey to explore the disorder of the B cell development in the bone marrow of lupus patients.

Methods: In this study, we have performed the scRNASeq to profile the bone marrow B cell compartment in lupus patients and healthy donors.

Results: We identified that in a subset of lupus patients, the early B cells (proB and preB cells) were strongly decreased, which were confirmed by flow cytometry in an expanded cohort. Furthermore, bone marrow B cells from these patients showed a strong proinflammatory signature revealed by pathway analysis. Interestingly, BCR repertoire analysis showed that the IGHV-4-34 was highly enriched in these patients, indicating an enhanced B cell tolerance defect. Finally, a panel of proinflammatory cytokines (TNF-α, IL-1α, IL-12p70, IFN-γ, et al.) were strongly increased in the bone marrow plasma of these patients compared with early B normal patients and healthy donors, confirming a localized proinflammatory microenvironment.

Conclusion: Altogether, the current study has revealed that a defective early B cell development in lupus patients is associated with a more severe B cell tolerance defect and aggravated inflammation, which may shed new light on developing novel therapies by targeting relevant pathways.

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Acknowledgements: This work was funded by Special project of clinical medicine of Nantong University (Grant/Award number: 2019LQ001), National Natural Science Foundation of China (Grant/Award number: 81671616, 81871278 and 82071838).

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3061

Education

OP0074

A FRAMEWORK OF POTENTIAL INTERVENTIONS TO ACCELERATE GENDER-EQUITABLE CAREER ADVANCEMENT IN ACADEMIC RHEUMATOLOGY

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