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**PILOT IMPLEMENTATION OF ENHANCEMENTS IN SUPERVISED GROUP EXERCISE FOR PEOPLE WITH AXIAL SPONDYLITIS (AXSQA) 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 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 available in the Netherlands [1].

**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 ASPI); 2. High intensity aerobic exercise including intensity monitoring (e.g. by heartrate or Borg-scale); 3. Group education on home exercise app.

**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.

**REFERENCES:**


**Disclosure of Interests:** Artem Popov Speakers bureau: Novartis, Menarini, AstraZeneca, Pfizer, Sewernaya Zvezda, Romepharm, Irina Borodina: None declared. Lubov Sharpina: None declared.

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

**OP0072 SINGLE CELL SEQUENCING REVEALS CLONALLY EXPANDED CYTO TOKIC 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 CMV, EBV, dengue, HIV, SARS-CoV-2. Moreover, expansion of so-called CD8+T cells is reported in the blood of patients with rheumatic diseases such as rheumatoid arthritis (RA), myositis and vasculitis as well as in cardiovascular diseases. Objective: 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 APCA+ RA patients by multi-parameter flow cytometry. We performed single cell sequencing, in combination with 5’ TCRαβ 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 were significantly increased in the SF of ACPA+ RA patients 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_{h})-cell subset11 and associates with the expression of tissue resident memory markers LAG-3, CXC96 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_{h} 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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