OP0189 TUMOR NECROSIS FACTOR INHIBITOR TREATMENT REDUCES SPINAL RADIOGRAPHIC PROGRESSION IN ANKYLOSING SPONDYLITIS BY DECREASING DISEASE ACTIVITY: A LONGITUDINAL ANALYSIS IN A LARGE PROSPECTIVE COHORT

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Background: Whether tumor necrosis factor inhibitors (TNFi) have an influence on radiographic progression in ankylosing spondylitis (AS) remains controversial.
Objectives: To investigate the impact of TNFi use on spinal radiographic progression in AS.
Methods: Patients fulfilling the modified NY Criteria for AS (as assessed by central reading) in the Swiss Clinical Quality Management Cohort with at least 2 years of clinical and radiographic follow-up were included. Spinal X-rays were taken every 2 years and scored independently by 2 blinded readers according to the modified Stoke Ankylosing Spondylitis Spine Score (mSASSS) in chronological time order. Average score of the readers was used. Radiographic progression was defined as an increase by $\geq$2 mSASSS units over 2 years. The relationship between TNFi use before a 2 year X-ray interval and progression within the interval was investigated using binomial generalized estimating equation models with adjustment for potential confounding and multiple imputation of missing covariate data. Ankylosing Spondylitis Disease Activity Score (ASDAS) was regarded as a potential intermediate variable mediating the effect of TNFi on radiographic progression. It was added to the model as a time-varying variable in a sensitivity analysis.
Results: A total of 420 patients with AS contributed to data for 597 x-ray intervals in adjusted analyses (1–5 intervals per patient); BL characteristics: male sex 66%, HLA-B27 81%, mean (SD) age 40.4 (10.9) years, disease duration 13.9 (9.8) years, mSASSS 6.4 (12.4), ASDAS 2.8 (1.1)). 39% of the patients were already on TNFi at first X-ray. Mean mSASSS progression in 2 years was 0.9 (2.7) units. The multivariable model (Table) shows that prior use of TNFi reduced the odds of progression in the next 2 year interval by 49% (odds ratio (OR) 0.51, 95% confidence interval (CI) 0.28–0.92, p=0.03). BL mSASSS and male sex also significantly affected progression. Adding ASDAS as a covariate to the model decreased the estimated effect of TNFi on progression: OR 0.65, 95% CI 0.36–1.17, p=0.15. In this model, a decrease in ASDAS by 1 unit would lower the odds for progression by 0.62 (p=0.001).

Table 1. Longitudinal multivariable analysis of radiographic progression

Variable	OR	95% CI	P value
TNFi use prior to X-ray interval	0.51	0.28–0.92	0.03
NSAID use at start X-ray interval	0.81	0.40–1.63	0.55
mSASSS at start X-ray interval	1.06	1.04–1.07	<0.001
Male gender	3.01	1.56–5.77	0.001
Disease duration	1.01	0.99–1.04	0.38
Current smoking	0.94	0.55–1.61	0.83
HLA-B27	0.99	0.46–2.12	0.98
Nb of exercise sessions per week	0.93	0.80–1.08	0.35
Peripheral arthritis	1.00	0.56–1.79	1.00

Conclusions: TNFi seem to reduce radiographic progression in patients with AS and this effect is mediated, at least in part, by a decrease in disease activity.
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Calcium crystal deposition in rheumatic diseases

OP0190 HISTOLOGICAL CHARACTERIZATION OF ROTATOR CUFF CALCIFIC TENDINOPATHY

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Background: Calcific tendinopathy is one of the most frequent causes of shoulder pain. Calcific deposits lead to chronic discomfort in daily and professional activity. These deposits are composed of carbonated apatite. Although the disease is frequent, its origin stays still largely unknown. Molecular and cellular mechanisms involved in this pathological mineralization process are not clearly identified.
Objectives: The objective of the study was to analyze calcified tendinous samples to understand the organization of the deposits and to characterize the cells potentially involved in their formation.
Methods: Samples were collected from cadaveric subjects. Ultrasound was first used to detect calcified tendons. Then, tendons were collected and fixed in formalin 4% during 48h. They were first analyzed with micro-CT to know the distribution of the calcific deposits. Samples were then decalcified in EDTA, dehydrated and embedded in paraffin. Some samples were not decalcified to allow a better characterization of the calcific deposits. Several histological staining were performed: hematoxylin and eosin (HE), Safranin O/Fast Green (SO/FG) and Von Kossa (no decalcified samples). Immunohistochemistry using anti-Runx2, anti-Sox9, anti-Collagen II and anti-caspase III antibodies has been performed to characterize the cells and tissue around the calcifications.
Results: Six samples were collected (1 normal and 5 calcified). On HE staining, three different histological patterns were observed. Little calcifications disseminated between tendinous fibers (N=2), voluminous ones encapsulated by a fibrous tissue (N=2) and in one sample an intra-tendinous osseous metaplasia. In the fibrous peripheral area of larger calcifications, we observed cells with round nuclei, different from tenocytes. These cells expressed Runx2 and Sox9 suggesting a chondrocyte phenotype. On SO/FG staining, this peripheral area presented a red coloration (proteoglycan specific) as the fibrocartilage at the tendon attachment. However, collagen II clearly present in the fibrocartilage was not present in these areas. As pathological calcification in cartilage can be associated with chondrocytes apoptosis, we sought for anti-Caspase III expression in the cells of the peripheral area. None of the chondrocyte-like cells located around the larger calcifications expressed Caspase III. Finally, one sample had an osseous metaplasia within the tendon with Runx2 positive cells.
Conclusions: Histological analyses of whole calcified tendon tissues showed three different patterns of calcific deposits. We can hypothesize that these patterns correspond to different stages of the disease. Chondrocyte-like cells were observed around larger deposits and could be involved in the mineralization process. Interestingly, they differ from the cells of the fibrocartilage as they did not express collagen II. Further analyses are necessary to characterize their phenotype and understand the steps leading to these deposits within the tendon.
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OP0191 COMPARISON OF ULTRASONOGRAPHY AND RADIOGRAPHY OF THE WRIST FOR DIAGNOSIS OF CALCIUM PYROPHOSPHATE DEPOSITION

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Background: The gold standard for diagnosis of calcium pyrophosphate (CPP) deposition (CPPD) is the identification of CPP crystals in synovial fluid. However, aspiration of synovial fluid can be challenging in small joints such as the wrist, a usual location of arthritis in CPPD. Despite its low sensitivity, the most widely used imaging modality is conventional radiography but ultrasound (US) seems a useful tool for diagnosis of CPPD.
Objectives: We aimed to compare the performance of US and conventional radiography of the wrist for diagnosis of CPPD.
Methods: Patients with joint effusion (knee, hip, shoulder, ankle or wrist) were consecutively included. CPPD was diagnosed by CPP crystals identified in synovial fluid. Patients without CPP crystals in synovial fluid were controls. As recommended, we used the term chondrocalcinosis (CC) to assess imaging features suggesting CPPD. Two blinded operators assessed CC in all patients by US and conventional radiography of the wrist. The presence of CC in triangular fibrocartilage (TFC) and wrist hyaline cartilage in US and TFC and radiocarpal (RC) joint in radiography was noted. A patient was considered to have CC if at least one wrist had imaging features of CC.
Results: We included 58 patients with joint effusion (32 with CPPD). The remaining 26 patients, controls, had rheumatoid arthritis (n=13), spondyloarthritis (n=6), gout (n=6), and osteoarthritis (n=1). The mean age was 67.1±16.3 years. Location of joint effusion was as follows: 34 knees, 15 wrists, 3 shoulders, 2 ankles, 3 hips and 1 elbow. Among CPPD patients, US revealed CC in 30 (93.7%) and radiography in 17 (53.1%) ($p<0.001$). The sensitivity (Se) and specificity (Sp) of US for the diagnosis of CPPD were 94% and 85%, respectively; the positive likelihood ratio was 6.1. When analyzing US features of CC separately, US Se was higher at the TFC than RC joint, 81% and 50% respectively. The Se and Sp of radiography were 53.1% and 100%, respectively. Intraobserver reliabilities for US and radiographic CC were almost perfect: κ coefficient 0.832 [95% confidence interval 0.651–1.0] and 0.880 [0.314–0.880], respectively. In all 58 patients, 113 joints were analyzed (3 patients had radiography of only one wrist). The κ coefficient between US and radiography for CC was moderate: 0.33 [0.171–0.408].
Conclusions: Our study suggests that wrist US should be considered a relevant tool for the diagnosis of CPPD, with higher sensitivity than radiography.
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