SATURDAY, 17 JUNE 2017

Spondyloarthritis - clinical aspects (other than treatment)

SAT0382 CHANGES IN VOLUMETRIC BONE MINERAL DENSITY AND BONE MICROARCHITECTURE IN PATIENTS WITH ANKYLOSING SPONDYLITIS. A FIVE-YEAR PROSPECTIVE STUDY USING HRPQCT

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Background: Studies have demonstrated increased prevalence of osteoporosis in patients with ankylosing spondylitis (AS) in the hip and lumbar spine assessed by conventional DXA but the peripheral skeleton is less studied. The peripheral skeleton can be studied in detail by high-resolution peripheral quantitative computed tomography (HRpQCT) demonstrating data of the volumetric bone mineral density (vBMD) and bone microarchitecture. We have previously shown that patients with AS from Western Sweden had lower vBMD measured by HRpQCT in radius and tibia compared with healthy controls [1]. No prospective study in this matter has been published in AS.
Objectives: To investigate changes over 5 years in the peripheral vBMD and microarchitecture in patients with AS.
Methods: HRpQCT of ultra-distal radius and tibia was performed in male AS-patients (NY criteria) at baseline and at the five-year follow-up. The patients were also assessed with blood samples and questionnaires.
Results: Of the 69 patients included at baseline 57 (83%) patients were re-examined at the five-year follow-up. Baseline characteristics of the 57 patients [median (IQR)]: age 48 (35 to 61) years, symptom duration 21 (11 to 34) years, ESR 10 (5 to 17) mm/h, CRP 3 (1 to 7), $ASDAS_{CRP}$ 1.8 (1.3 to 2.8) and BASDAI 2.3 (1.2 to 4.2). 23% used TNF-inhibitors, 75% used NSAIDs and 2% bisphosphonates. All measurements at tibia had good quality and matched images had common regions $\geq$80%. The images of radius of 12 patients had to be excluded due to insufficient quality. At tibia, the total, cortical and trabecular vBMD decreased significantly. In the microarchitecture an increase in the trabecular separation was seen (Table). Changes in vBMD were negatively and significantly correlated; Spearman's correlation coefficient between -0.3 and -0.4, to Δ-values (difference between follow-up and baseline) for ESR, CRP (cortical vBMD), $ASDAS_{CRP}$ (total vBMD and cortical vBMD) and BASDAI (total vBMD). At radius, no significant change in vBMD was observed; however, less power for analyses of radius. An increase was seen in the cortical thickness and the trabecular number while the trabecular thickness decreased (Table). Changes in cortical vBMD was negatively and significantly correlated, r $\approx$ -0.3, to Δ-CRP and Δ-$ASDAS_{CRP}$.

Table.

Site		Baseline mean ± SD	Five-year follow-up mean ± SD	Difference mean% ± SD	p-value
Tibia	**Total vBMD, mg/cm³**	297.9 ± 55.5	292.8 ± 55.8	**-1.7 ± 3.9**	**0.002**
	Cortical vBMD, mg/cm³	842.7 ± 54.8	834.1 ± 62.5	**-1.1 ± 1.9**	**0.001**
	Trabecular vBMD, mg/cm³	184.8 ± 34.6	179.5 ±31.9	**-2.6 ± 4.8**	**0.001**
	Cortical thickness, mm	1.22 ± 0.32	1.21 ± 0.32	-1.0 ± 5.2	0.35
	Trabecular thickness, mm	0.08 ± 0.01	0.07 ± 0.01	-1.5 ± 7.3	0.26
	Trabecular number in 1/mm	2.06 ± 0.30	2.04 ± 0.32	-0.7 ± 6.7	0.19
	Trabecular separation, mm	0.42 ± 0.08	0.43 ± 0.08	**1.8 ± 6.9**	**0.027**
Radius	Total vBMD, mg/cm³	319.6 ± 64.9	320.7 ± 69.9	0.1 ±4.7	0.47
	Cortical vBMD, mg/cm³	854.4 ± 54.9	854.1 ± 59.5	-0.1 ±1.9	0.98
	Trabecular vBMD, mg/cm³	177.5 ± 40.5	173.6 ± 41.9	-2.3 ± 6.2	0.082
	Cortical thickness, mm	0.83 ± 0.21	0.85 ± 0.21	**2.5 ± 5.4**	**0.004**
	Trabecular thickness, mm	0.08 ± 0.02	0.07 ± 0.01	**-5.4 ± 10.5**	**0.001**
	Trabecular number in 1/mm	1.96 ± 0.24	2.01 ± 0.24	**4.2 ± 10.8**	**0.041**
	Trabecular separation, mm	0.44 ± 0.07	0.43 ± 0.06	-2.7 ± 10.1	0.080

Conclusions: Over five years, this group of male patients with AS decreased in the vBMD of tibia, both trabecular and cortical. Even though there were alterations in the microarchitecture, no significant change in vBMD of radius was seen. Increases in inflammatory markers and disease activity had a negative impact on the cortical vBMD. The differences in the development of vBMD and microarchitecture in loaded and unloaded skeleton as well as factors associated with the changes needs to be further investigated.
References:
[1] Klingberg, E., et al., Bone microarchitecture in ankylosing spondylitis and the association with bone mineral density, fractures, and syndesmophytes. Arthritis Res Ther, 2013. 15: p. R179.
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SAT0383 BIOMARKERS OF ECM DEGRADATION REFLECT DISEASE ACTIVITY IN RADIOGRAPHIC AND NON-RADIOGRAPHIC SPONDYLARTHRITIS

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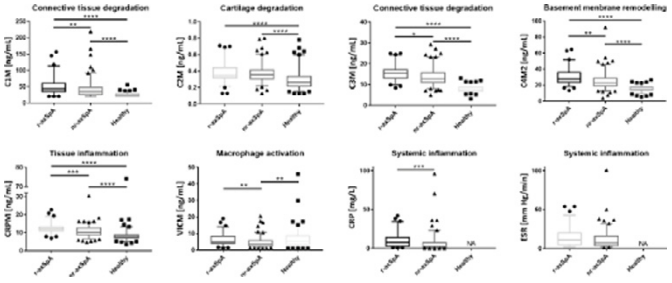
Background: Axial spondyloarthritis (axSpA) comprises two groups - radiographic (r-axSpA) and non-radiographic (nr-axSpA) with varying disease activity, spine involvement and response to biological therapy. An objective biomarker of disease activity may be able to select patients, which will benefit from a given biological treatment.
Objectives: We investigated the association of extracellular matrix (ECM) degradation biomarkers in axSpA patients (r-axSpA and nr-axSpA) with disease activity.
Methods: AxSpA patients (n=193; 72 r-axSpA and 121 nr-axSpA) and 100 healthy controls were included in the study. Biomarkers of type I, II, III and IV degradation (C1M, C2M, C3M, C4M2), MMP-degraded CRP (CRPM) and MMP-degraded and citrullinated vimentin (VICM) were detected by ELISA in serum. Mann-Whitney t-test tested the difference in the biomarker levels between groups and multiple regression analysis investigated the association between biomarkers and clinical manifestations with adjustment for age, gender, BMI, disease duration and CRP. ROC AUC tested the biomarkers capacity to differentiate the patient groups.
Results: Patients with r-axSpA compared to nr-axSpA patients had higher radiographic status and longer disease duration ($p<0.001$), whereas nr-axSpA had more swollen joints (p=0.0093). They were alike in age, BMI and disease activity (ASDAS-CRP, BASDAI and HAQ). All tested biomarkers except VICM were elevated in the axSpA patients compared to healthy subjects (all $p<0.001$). VICM was lower in the axSpA group, particularly in nr-axSpA compared to healthy (p=0.036 and p=0.002 respectively). R-axSpA compared to nr-axSpA patients had higher level of C1M, C3M, C4M2, CRPM and VICM ($p<0.001$, =0.001, <0.001, <0.001 and =0.003), but not C2M (p=0.92). C1M correlated to ASDAS-CRP in both r-axSpA and nr-axSpA (r-partiel: 0.46 and 0.44) with adjustment for age, gender, BMI and disease duration, but the correlation was lost by adjustment for CRP. Also C3M and C4M2 correlated to ASDAS-CRP in both axSpA groups. C2M was in r-axSpA patients moderately correlated to ASDAS-CRP, but minimal after adjustment of CRP (r-partiel: 0.32 unadjusted and 0.18 adjusted). CRPM correlated to ASDAS-CRP with adjustment to CRP in r-axSpA (r-partiel: 0.27 unadjusted, 0.26 adjusted), but not in nr-axSpA (r-partiel: 0.19 unadjusted, 0.03 adjusted).
Especially, C3M and C4M2 could differentiate between healthy and the axSpA patients (AUC 0.95 and 0.89), but also C1M, C2M, CRPM had AUC of $\geq$0.72. VICM was the only biomarker to differ between r-axSpA (AUC 0.92 and nr-axSpA (AUC 0.51).



Conclusions: Biomarkers of ECM turnover, C3M and C4M2 in particular, were associated with r-axSpA and nr-axSpA and could define disease. The biomarkers of ECM degradation, especially C1M, may reflect the pathogenetic background of axSpA.
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SAT0384 RISK OF MYOCARDIAL INFARCTION AND CEREBROVASCULAR ACCIDENT IN ANKYLOSING SPONDYLITIS: A GENERAL POPULATION-BASED STUDY

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Background: There is conflicting data on the risk of myocardial infarction (MI) and cerebrovascular accidents (CVA) in patients with Ankylosing Spondylitis (AS).

Objectives: 1) To assess the future risk of newly recorded MI and CVA events among incident cases of AS compared to non-AS controls from the general population by utilizing physician billing, medication, and hospitalization data that covers the entire province of British Columbia (BC), Canada.
Methods: Our data includes all outpatient visits and hospitalizations (1990–2012) and all dispensed medications (1996–2012) for all BC residents. We conducted a retrospective matched cohort study of all patients >18 years of age satisfying the following criteria: 1) two ICD-9 or 10 codes (720.0 or M45) for AS at least two months apart and within a 2-year period by any physician or hospitalization; 2) all AS cases had at least a 7-year run-in period before the 1st ICD code for AS in order to consider the case as incident. Each AS patient was matched with up to 10 controls by birth year, sex, and entry cohort time. The outcomes were a newly recorded MI (ICD-9-CM: 410 or ICD-10-CM: I21) or CVA (ICD-9 codes: 433–434, ICD-10 codes: I63-I66) event from hospital or death certificates. We estimated relative risks (RRs), adjusting for age, sex, and entry cohort time as well as multivariable models adjusting for confounders including glucocorticoids and non-steroidal anti-inflammatory drugs using a Cox proportional hazard model.
Results: 7,190 individuals with newly diagnosed AS were identified (48.7% female, mean age of 45.8 yrs). 7,148 and 7,107 were free of previous CVA/MI, respectively. 80 developed CVA (incidence rate=1.8 per 1000 patient years) and 115 had MI (incidence rate=2.6 per 1,000 patient years) (Table 1). The age-, sex-, and entry-time-matched RR for CVA was 1.60 (95% CI, 1.25–2.03) and MI was 1.52 (95% CI, 1.24–1.85). When adjusted for cardiovascular risk factors (obesity, angina, COPD, hospitalizations in year before index date, Charlson's comorbidity index, oral glucocorticoids, cardiovascular drugs, anti-diabetic medication, HRT, contraceptives, fibrates, statins, NSAIDs, and Cox-2 inhibitors), the estimated RR was 1.34 (1.04–1.73) for CVA and 1.21 (0.98–1.49) for MI.

Table 1. Relative risk of incident CVA and MI according to AS status

	AS (N=7,148)	Non-AS (N=71,489)
CVA events, n	80	492
Incidence Rate of CVA/1000 Person-Years	1.81	1.13
Incidence Rate Ratio of CVA (95% CI)	1.60 (1.25–2.03)	1.0
Multivariable RR of CVA (95% CI)	**1.34 (1.04–1.73)**	1.0
	AS (N=7,107)	Non-AS (N=71,033)
MI events, n	115	748
Incidence Rate of MI/1000 Person-Years	2.62	1.73
Incidence Rate Ratio of MI (95% CI)	1.52 (1.24–1.85)	1.0
Multivariable RR of MI (95% CI)	**1.21 (0.98–1.49)**	1.0

Conclusions: This large population-based study demonstrates an increased risk of CVA, but not for MI. These findings support that increased monitoring for this potentially fatal outcome and its modifiable risk factors is warranted for AS patients.
Disclosure of Interest: None declared
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SAT0385 SIMILARITIES AND DIFFERENCES BETWEEN PATIENTS FULFILLING NON-RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS AND UNDIFFERENTIATED SPONDYLOARTHRITIS CRITERIA: RESULTS FROM THE ESPERANZA COHORT

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Background: Patients with spondyloarthritis (SpA) were classified in five subgroups: ankylosing spondylitis (AS), psoriatic arthritis, arthritis associated with inflammatory bowel disease, reactive arthritis and undifferentiated SpA (uSpA). ASAS criteria classify patients in peripheral SpA and axial SpA (axSpA), being the latest classified in two groups: classical AS and non-radiographic axSpA (nr-axSpa). Whether or not patients with nr-axSpA represent the same group of patients that used to be classified as uSpA remains unclear.
Objectives: To evaluate the similarities and differences between patients with predominant axial disease classified currently as nr-axSpA versus those traditionally classified as uSpA.
Methods: Baseline data from the ESPeranza program (a multicenter national initiative to early diagnose SpA between 2008 and 2011) was used. Inclusion criteria for this program were: age <45 years and inflammatory back pain plus ≥1 SpA features with symptoms duration between 3 and 24 months. Demographic, clinic, laboratory and image results were compared between two groups: 182 patients with nr-axSpA and 166 patients classified as uSpA. In order to get a deeper knowledge of the differences between nr-axSpA and uSpA, we also compared: i) 88 patients only classified as nr-axSpA, ii) 72 patients only classified as uSpA; iii) 94 patients fulfilling both criteria. Student-t test for continuous variables and Pearson Chi-square test for categorical variables were used.
Results: Compared to patients classified as uSpA patients with nr-axSpA were younger, had HLA-B27 positive more frequently and higher values of CRP. On the other hand, they had history of SpA less frequently and lower values for BASDAI, BASFI and ASQoL (table). No differences were observed for gender, work incapacity, dactilitis, enthesitis, Pt's and Phy's VAS, BASMI and BASRI.

Table 1. Results are presented in mean ± standard deviation for continuous variables and n (%) for categorical variables

	Both, nr-axSpA & undifferentiated SpA N (%) = 94	Only nr-axSpA N (%) = 88	Only undifferentiated SpA N (%) = 72	p value*
Age (years)	30.9±7.3	32.2±6.9	35.2±6.9	**<0.01**
Male	61 (64.9)	50 (56.8)	34 (47.2)	0.2
Family history	48 (51.1)	21 (23.9)	30 (41.7)	**<0.05**
HLA-B27	81 (86.2)	65 (73.9)	6 (8.3)	**<0.001**
Enthesitis	29 (30.9)	18 (20.5)	22 (30.6)	0.1
BASDAI	3.7±2.3	3.8±2.1	4.7±2.3	**<0.01**
BASFI	2.2±2.2	2.1±2.1	2.9±2.5	**<0.05**
ASQoL	5.9±4.7	5.2±4.5	7.4±5.2	**0.01**
CRP (mg/L)	10.7±14.3	9.8±16.5	5.1±9.1	**<0.05**

*p value for differences between nr-axSpA and undifferentiated SpA (Student-t test for continuous variables and Pearson Chi-square test for categorical variables).

Conclusions: Compared with patients traditionally classified as uSpA, patients who are currently classified as nr-axSpA are diagnosed earlier, are more frequently HLA-B27 carriers and have higher disease activity according to objective parameters. On the other hand, they report lower values for patient reported outcomes.
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SAT0386 EXTREME PATIENT REPORTED OUTCOME (PRO) IN EARLY SPONDYLOARTHRITIS: A SURROGATE FOR FIBROMYALGIA? ITS IMPACT ON TNF-ALPHA BLOCKERS TREATMENT EFFECT?

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Background: In case of a concomitant fibromyalgia (FM) with axial spondyloarthritis (axSpA), there is a risk of misclassifying a patient as active (e.g. BASDAI >4), and to falsely consider him as refractory to NSAIDs/ biologics, since FM patients often report higher level of pain and fatigue[1]. We hypothesized that not only are extreme patient reported outcome (PRO) potentially surrogate marker of FM in axSpA, but also that this extreme PRO may have an impact on the TNF-α blockers (TNFb) treatment effect
Objectives: A) To describe the prevalence of extreme PRO in an early axSpA cohort. B) To compare the phenotype of axSpA patients with and without extreme PRO. C) To assess the impact of extreme PRO on the TNFb efficacy.
Methods: This analysis was performed on the DESIR cohort which included 708 adult patients (>18 and <50 years) with inflammatory back pain suggestive of axSpA (according to the rheumatologist's conviction of ≥5/10) for >3 months but <3 years duration. All patients were biologic naïve at inclusion and were followed up every 6 months for the first 2 years. At baseline, data pertaining to demographics, BASDAI, history of depression, type of medications (antidepressants or muscle relaxants) used and concomitant diseases were collected. It is worth noting that no systematic assessment of the fulfilment of the ACR criteria for FM was performed in this study; thus, we created a "FM gold standard" according to the available data (i.e., presence of either Muscle relaxants/ Depression/ Anti-depressant drug treatment/ Fibromyalgia comorbidity reported in the CRF). BASDAI was the selected PRO for this study due to its widespread use in clinical practice. BASDAI was tested against this "FM gold standard": we plotted ROC curves to define the best cut-off to define an "extreme PRO" for BASDAI. Phenotype of patient's with/without extreme PRO scores was compared. Impact of extreme PRO score on TNFb efficacy was assessed by comparing the retention rate of the first TNFb by Cox analysis.
Results: ROC curves to define an "extreme PRO" determined a different cut-off for each BASDAI question (i.e. >6, >5, >1, >4, >5 and >3 for question 1 to 6, respectively), and the need of at least 4 out of these 6 cut-offs to fulfil the "extreme PRO" condition; giving us a prevalence of 42.9% (304 patients) of extreme PRO in DESIR. Phenotypically, this group with extreme PRO, consisted of older patients (34.6 (8.3) vs 33.1 (8.8)), had more females (184 (60.5%) vs 195 (48.8%)), reported less sacroiliitis [radiographic and MRI, (36 (12%) vs 76 (19.4%)) and (82 (27.6%) vs 148 (37.8%)), respectively], showed less HLA B27 positivity (160 (52.6%) vs 248 (62.2%)), had higher CRP values (102 (34.3%) vs 102 (26.5%)), and more arthritis/ enthesitis history (212 (69.7%) vs 190 (47.5%)/ 182 (59.9%) vs 166 (41.5%)). A lower retention rate was observed in the group of patients with "extreme PRO" (Figure 1)
Conclusions: Coexistence of extreme PRO might be considered as a surrogate marker for FM in axSpA patients. Moreover, it appears to have a negative impact on TNF-α blockers retention rate.
References:
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