FRI0478

SPINAL MOBILITY AND BONE MINERAL DENSITY IN SPONDYLOARTHRITIS

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Background: Osteoporosis is the most frequent comorbidity in axial spondyloarthritis (axSpA). The change in spinal mobility (traditional measures) in patients with axSpA has been associated with low bone mineral density (BMD) although the data are variable (DIM, lateral flexion, BASMI).

Objectives: The aim of our study is to understand the relationship between spinal mobility, BMD and fragility fractures.

Methods: Analytical, observational, longitudinal, and retrospective study of a cohort of patients with axSpA (ASAS criteria). Perimenopausal or menopausal women, diseases and/or osteopenic treatments, biological drugs, immunosuppressive drugs (at least one year before), and treatment with drugs that interfere in the bone metabolism were excluded; bisphosphonates, ranelate of strontium, selective modulators of the estrogen receptor, calcitonin, hormone therapy, denosumab and teriparatide, among others.

Results: 74 patients were studied, 67 were classified as axSpA and 7 as peripheral SpA. Bivariate analysis showed that the group of patients with osteoporosis (14.86%) had a worse DIM ($p = 0.001$), tragus-to-wall distance ($p = 0.001$) and lateral flexion ($p = 0.045$) than patients who did not have osteoporosis. The multiple regression analysis indicated that lumbar spine t/z score was independently associated with BASMI index ($B 0.682$, $p=0.013$), femoral neck t/z score was independently associated with BASFI index ($B 1.575$, $p=0.007$) and with lower levels of 25 OH vitamin D ($B 0.895$, $p=0.028$).

Conclusion: UCOASMI is a validated metrological index with three-dimensional measurements of human spinal mobility that shows higher levels of objectivity and precision than traditional measures. Subsequent studies will compare mobility parameters (UCOASMI) and BMD of patients with axSpA. Clarifying the relationship between spinal mobility, BMD and fragility fractures would help us to better understand the course of the disease in axSpA.

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Disclosure of Interests: Laura Bautista: None declared, Asunción Salmoral: None declared, Inmaculada Gómez Gracia: None declared, Ladehesa Pineda Lourdes: None declared, Pérez Sánchez Laura: None declared, Gómez García Ignacio: None declared, Inmaculada Concepcion Aranda-Valera: None declared, María del Carmen Abalos-Aguilera: None declared, Garrido Castro Juan Luis: None declared, Font Ugalde Pilar: None declared, María del Carmen Castro Villegas Paid instructor for: MSD, Abbvie, Pfizer, Janssen, Lilly, Roche, Alejandro Escudero Contreras: None declared, Eduardo Collantes Estevez: None declared
DOI: 10.1136/annrheumdis-2019-eular.7018

FRI0479

TRENDS IN LOW TRAUMA DISTAL FOREARM FRACTURE INCIDENCE IN WOMEN AND MEN OVER 1995-2015 IN OLMSTED COUNTY, MINNESOTA, USA

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Background: It is unclear how recent practice changes of decreased use of hormone replacement therapy and drug holidays from bisphosphonate therapy have impacted incidence of fragility fractures. Fragility (low trauma) fractures at the distal forearm in women may be more likely to be impacted by these changes as compared with men.

Objectives: We examined the trends in distal forearm fracture incidence over 1995-2015, in both women and men, from Olmsted County, Minnesota, USA.

Methods: Using the Rochester Epidemiology Project, a unique medical records linkage system that allows access to all (inpatient and outpatient) community medical records for Olmsted County residents, we identified all incident distal forearm fractures among residents age ≥ 18 years between 1995-2015. Available medical records were reviewed by trained nurse abstractors to validate distal forearm fractures identified and to determine

their antecedent cause (pathological process [e.g., malignancy], severe trauma [e.g., motor vehicle accidents, sports/other recreational activities] and low trauma [by convention, equivalent to a fall from standing height or less]). Overall incidence rates were summarized separately for women and men, as well as by 5 year strata for different age groups (ages 18-39, 40-59, 60-79 and ≥ 80 yrs). Rates for women and men were each directly age-adjusted to the population distribution of US whites in 2010.

Results: Between 1995-2015, we identified 2727 distal forearm fractures in women (70%, median age 62 yrs; 1915 due to low trauma) and 1193 distal forearm fractures in men (30%, median age 48 yrs; 450 due to low trauma), 92.3% of which were in whites. The overall age-adjusted annual incidence of first distal forearm fracture over 1995-2015 was 233 per 100,000 person-years (p-y) for women and 113 per 100,000 p-y for men. When considering only fractures due to low trauma, the overall age-adjusted annual incidence of first distal forearm fracture over 1995-2015 was 169 per 100,000 p-y for women and 49 per 100,000 p-y for men. Rates of low trauma distal forearm fracture appear to be stable in younger (18-39 yrs) women, but since 2005, seem to be increasing in women age 40-59 yrs (Table). In contrast, rates in older women appear to be decreasing or are stable since 2005. In men, the rates of low trauma distal forearm fracture have been relatively unchanged over the past 20 years, except in men age ≥ 80 yrs where the rates have generally been lower since 2005 (Table).

Distal Forearm Fracture* Incidence per 100,000 p-y by Age Group

Years	18-39 yrs		40-59 yrs		60-79 yrs		≥ 80 yrs	
	Women	Men	Women	Men	Women	Men	Women	Men
1995-99	33	10	131	46	370	81	571	299
2000-04	27	17	102	40	415	72	690	297
2005-09	25	22	126	44	327	89	650	128
2010-15	30	10	145	43	332	75	594	161

*Incidence of fragility (low trauma) fractures at the distal forearm

Conclusion: The trend for increasing low trauma distal forearm fractures in women age 40-59 yrs may reflect the decreased use of hormone replacement therapy, which would likely have particularly impacted this age group. The decrease in fractures in men age ≥ 80 yrs may reflect greater recognition, in recent years, of osteoporosis in older men and initiation of treatment. Whether changes in practice patterns are actually contributing to these observed trends warrants further review.

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None

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2019-eular.7101

FRI0480

CHANGES IN CIRCULATING SCTL4 FOLLOWING ZOLEDRONIC ACID INFUSION

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Background: Acute phase response (APR) is a transient, flu-like reaction to first exposure to intravenous nitrogen-containing bisphosphonate (NBP). APR is characterised by a strong inflammatory response, associated with increases in circulating levels of IL-6 and TNF-, that is thought to be due to activation and increased proliferation of $\gamma\delta$ T cells related to the molecular mechanism of action of NBP.

Cytotoxic T-Lymphocyte Antigen-4 (CTLA-4), in both its soluble (s) and membrane-bound forms, is involved in the downregulation of T cell proliferation, cell cycle progression and cytokine production. High levels of serum sCTLA-4 have been reported in several autoimmune diseases, and its role as both inhibitor and enhancer of the immune response has been proposed.

Objectives: To evaluate the potential relationship between sCTLA-4 and the development of APR in patients treated with zoledronic acid (ZOL).

Methods: Included in the study were patients treated with a single intravenous ZOL infusion 5 mg. Exclusion criteria were previous treatment with ZOL, treatments interfering with CTLA-4, and estimated glomerular filtration rate <35 ml/min. APR was defined as a rise in axillary temperature above 38°C at any time during the first 48 hours and an increase in musculoskeletal pain by more than 10 mm in a visual analogue scale (VAS, from 0 to 100 mm). Clinical and laboratory parameters were assessed at baseline, before ZOL, and at 24, 48 and 72 hours after the infusion.

Results: Ten female patients (mean age 73-10 years) were included (2 had vertebral fractures and the remaining had osteoporosis), 5 of whom experienced APR (APR+) associated with the expected increases in serum CRP and IL-6. Baseline levels of sCTLA-4 did not differ between APR+ and APR- patients and decreased significantly in all from 32.9 ng/ml to 24.9 ng/ml ($p=0.007$) at 24 hr, 16.8 ng/ml ($p=0.004$) at 48 hr and 7.6 ng/ml ($p<0.001$) at 72 hr. Absolute value of sCTLA-4 and mean% change of sCTLA-4 after ZOL were not statistically different between APR+ and APR- patients. At 72 hr, sCTLA-4 decreased by 77% (-23%) in APR+ and by 81% (-20%) in APR- ($p=0.786$). There were no statistically significant correlations between serum sCTLA-4 levels with any clinical or biochemical parameter of APR.

Conclusion: Contrary to our hypothesis, sCTLA-4 was not related to the occurrence of APR after ZOL. The significance of the substantial decrease of circulating levels of sCTLA-4 after ZOL in all studied patients warrants further investigation.

Disclosure of Interests: Gerolamo Bianchi Consultant for: Alfa-Sigma, Amgen, BMS, Celgene, Medac, UCB, Speakers bureau: Abbvie, Abiogen, Alfa-Sigma, Amgen, BMS, Celgene, Daniele Saverino: None declared, Dario Camellino Consultant for: Janssen-Cilag, Novartis, AbbVie, Sanofi, Paid instructor for: Mylan, Andrea Giusti Grant/research support from: Abiogen Pharma, Consultant for: EffRx, Speakers bureau: Abiogen Pharma, Eli Lilly, AMGEN, Erika Iervasi: None declared, Giuseppe Girasole: None declared, Socrates Papapoulos Grant/research support from: No in the last 3 years, Consultant for: Amgen, Axsome, Gador, Radius Health, UCB, Speakers bureau: Amgen, UCB

DOI: 10.1136/annrheumdis-2019-eular.6198

FRI0481 MEDIATORS OF BONE METABOLISM (DKK1, OPG, SCLEROSTIN AND RANKL) IN A COHORT OF PATIENTS WITH ELDERLY-ONSET ARTHRITIS

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Background: Patients with elderly-onset arthritis have greater comorbidity than young patients, with a higher incidence of osteoporosis (OP), probably mediated by increased bone resorption. However, there are few data on bone metabolism mediators in this population.

Objectives: To analyze bone remodeling mediators (DKK1, sclerostin, osteoprotegerin [OPG], and RANKL) in patients with elderly-onset arthritis and its relationship with bone mineral density.

Methods: Longitudinal observational study that included patients with elderly-onset arthritis (> 65 years) without diagnosis of OP or on antiosteoporotic treatment. Phospho-calcium metabolism, quantification of bone remodeling mediators (ELISA, R&D systems) and bone densitometry, were determined in all patients at diagnosis and at 12 months. The results were compared with a control group of the same age and sex ($n=14$). The statistical study was performed using SPSS.

Results: We included 73 patients (37F: 36M), with a mean age of 75±7 years. Most were diagnosed with rheumatoid arthritis (RA) ($n=43$), followed by polymyalgia rheumatica ($n=16$) and others ($n=14$). Fifteen patients were rheumatoid factor (RF) positive and 23 were ACA positive. Five patients had erosions at the diagnosis. 88.64% of patients with RA had an initial DAS28-VSG >5.1. Only 3 patients had previous fragility fractures (2 vertebral and 1 femur fractures).

At diagnosis, patients with elderly-onset arthritis had higher levels of DKK1 and CTX than the control group, with no statistically significant differences in sclerostin, OPG, and RANKL values (table 1). In addition, DKK1 values were negatively correlated with sclerostin ($r=-0.286$, $p=0.016$) and OPG ($r=-0.276$, $p=0.020$). 31.9% had densitometric OP. We found no significant differences in bone remodeling mediators between patients with/without basal OP.

At 12 months, DAS28-VSG was <2.6 in 38.1%. The mean corticosteroid dose was 5.5 mg/day with a cumulative dose of 1630±426 mg. 45.8% received antiosteoporotic treatment (28 patients' bisphosphonates and 5 denosumab). The prevalence of OP at 12 months was 31.3% and 4 patients had new fractures (4 vertebral and 1 femur fractures). We observed a marked decrease in the values of DKK1 (-18.89%, $p<0.001$) and sclerostin (-46.76%, $p<0.001$) and an increase in OPG (11.97%, $p=0.018$).

We didn't found relationship between bone metabolism mediators and cumulative corticosteroid dose. There were not differences in terms of diagnosis (RA or PRM), ACPA positivity, activity scores or treatment with bisphosphonates.

Conclusion: Patients with elderly-onset arthritis have higher Dkk1 values than the control group, and this correlate negatively with sclerostin and OPG. The marked decrease in Dkk-1 and sclerostin at 12 months, and the increase in OPG, suggests a role for these mediators in the bone metabolism of this population. It is important to note the high prevalence of OP in this group of patients.

Table 1. *We excluded patients treated with denosumab. † $p<0.005$ with respect to the control group. ‡ $p<0.05$ with respect to baseline

Variables	Control N=14	Basal patients N=73	12 months patients* N=72
VSG(mm/h)	14±10	55±27†	27±18†‡
PCR(mg/L)	3.6±6.6	38,1±50,6 †	4,9±5,5 †‡
HAQ	-	1,6±0,75	0,51±0,57 ‡
DAS28-VSG(in RA)	-	6,32±1,04	3,10±1,30 ‡
{n=43}			
CTX(ng/mL)	0,33±0,18	0,49±0,19 †	0,26±0,13 ‡
OPG(pg/ml)	3127±948	3319±1134	3647±1466 ‡
DKK-1(pg/ml)	1558±555	2740±1611 †	1516±985 ‡
Sclerostin(pg/ml)	1299±961	1189±626	515±333 †‡
RANKL(pg/ml)	122±184	101±102	-
RANKL indetectable n (%)	9(64.3)	16(22.5)	72(100)

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2019-eular.5305

FRI0482 RISK FACTORS FOR FRAGILITY FRACTURE IN PATIENTS WHO SMOKE: AN OBSERVATIONAL STUDY

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Background: Smoking is a risk factor for osteoporosis and increases the likelihood of a fragility fracture. It is included in the FRAX™ tool, which is used as an aid for bone mineral density (BMD) referral and as a risk stratification for the propensity of developing a fragility fracture. The additive effect of other risk factors including demographics increasing the risk of fracture has not been explored in a large cohort.

Objectives: To investigate the additive predictors of fracture in patients who have smoking as their only risk for fracture, referred for BMD estimation.

Methods: Patients who were referred for bone mineral density (BMD) estimation in a scanner in the North West of England between June 2004 and October 2015 were included in the analysis. Patients with only smoking as a FRAX™ risk factor were then analysed. All patients have their other risk factors for fracture and demographics recorded at time of scan. All patients with other FRAX™ indications for scanning were excluded including Rheumatoid Arthritis, Excess Alcohol, Steroids, family history of fracture and Secondary Osteoporosis. Patients in the smoking group were divided into those that had experienced a fracture and those that had not before comparing with Chi-squared test for categorical variables and T-test for continuous variables. Univariate and multivariate logistic models were then fitted to examine predictors of fracture in this group.

Results: 35,759 patients were referred for scanning during the period. 4096 (11.45%) were referred with smoking as their only indication for scanning. Mean age at scan was 64.43 (SD 12.38) and 3244 (79%) of the cohort were females. 1663(40.60%) had a fracture. Fractures were more prevalent in males with 383 (44.95%) compared to 1280 (39.46%) in females ($p<0.05$).

Univariate predictors shown in the Table 1 below.