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Outcome in juvenile idiopathic arthritis

OP0338 FREQUENCY OF COMORBIDITIES IN JIA PATIENTS – RESULTS OF AN OBSERVATIONAL COHORT STUDY

K. Minden¹, N. Betenstehl², J. Klotsche¹, E. Seipelt³, S. Tatsis⁴, I. Foeldvari⁵, G. Ganser⁶, G. Horneff⁷. ¹Epidemiology Unit, German Rheumatism Research Centre, Berlin; ²Oberhavelkliniken, Hennigsdorf; ³Immanuel Krankenhaus Berlin-Buch, Berlin; ⁴Kath. Marienkrankenhaus; ⁵Zentrum für Kinder- und Jugendrheumatologie, Hamburg; ⁶St. Josef-Stift, Sendenhorst; ⁷Asklepios Kinderklinik, Sankt Augustin, Germany

Background: Juvenile idiopathic arthritis (JIA) is a chronic inflammatory disease that often persists into adulthood. In addition to disability and poorer quality of life, JIA is associated with increased long-term morbidity and mortality. The long-term risk of comorbidities in JIA patients is uncertain and guidance on risk assessment is not currently available.

Objectives: To determine the frequency of comorbid conditions in adult JIA patients.

Methods: Patients with JIA transferred from the biologic registry BIKER to the follow-up (FU) registry JuMBO were included in this analysis. All comorbidities, except for serious infections, prospectively recorded by physicians to BiKeR or JuMBO were considered. Comorbidity rates among the various JIA categories were assessed. The Medical Dictionary for Regulatory Activities (MedDRA) was used for disorder coding. Differences in the occurrence of comorbidities between JIA categories were analyzed by multinomial logistic regression.

Results: A total of 1,022 young adults (67% female) with JIA and a mean FU of 7.8 (SD=3.5) years (ys) were included in this analysis. The patients' mean age was 22.5 ys (SD=3.7), and disease duration was 12.9 ys (SD=5.9) at the last FU. The majority were classified as polyarticular JIA (36.4%) at BiKeR enrollment. Patients had received a mean of 2.9 (SD=1.3) DMARDs, 77% were ever treated with biologics.

Comorbidities were reported for more than half of the patients (54%), 24.5% of the conditions were stated for the first time in adult age. Eye disorders were the most common comorbid condition group (15.1%), followed by skin and subcutaneous tissue disorders (9.3%), and psychiatric disorders (5.5%). The most frequently reported single diseases were uveitis in 14.4%, chronic secondary pain syndrome in 4.4%, hypertension in 3.6%, and psoriasis in 3.3%. In addition, inflammatory bowel diseases were reported in 2.5% of cases, other immune-mediated disorders, namely autoimmune thyroiditis in 2.5%, type1 diabetes in 0.7% and celiac disease in 0.3%, depression in 2.3%, anxiety in 0.3%, osteoporosis in 1.6%, and amyloidosis in 0.4%. Among the reported comorbidities, there was one case with a cerebrovascular accident, but none with ischemic heart disease, heart failure or diverticulitis. The rate of comorbid condition accrued in the various JIA categories (table 1) differed significantly, with the highest rate in patients with extended oligoarthritis.

Table 1: Frequency of major comorbidities (in %) in the various JIA categories in young adult age

Comorbid condition	Sys JIA N= 48	OA persist. N=97	OA ext. N=169	PA RF- N=278	PA RF+ N=94	ERA N=205	PsA N=97	P value
Any comorbid condition	58.3	47.2	64.1	45.7	47.9	51.7	62.9	0.007
Uveitis	4.2	14.4	34.9	7.9	0	16.6	10.3	<0.001
Psoriasis	2.1	1.0	0.6	1.1	0	3.4	19.6	<0.001
IBD	4.2	0	3.6	1.4	1.1	3.4	5.2	0.233
Hypertension	10.4	2.1	4.1	2.5	2.1	3.4	3.1	0.032
Osteoporosis	10.4	0	1.8	1.8	1.1	0	1.0	<0.001
Amyloidosis	4.2	0	0	0.4	0	0	0	0.001
Chronic secondary pain syndrome	2.1	5.2	4.7	6.1	3.2	4.9	1.0	0.394
Depression	4.2	1.0	2.4	2.2	1.1	2.4	3.1	0.927
Autoimmune thyroiditis	2.1	1.0	1.8	2.2	5.3	1.5	6.2	0.156
Type 1 diabetes	0	0	0	1.1	2.1	1.0	0	0.445
Celiac disease	0	0	0.6	0	1.1	0	0	0.202

Sys JIA - Systemic JIA; OA persist. - Oligoarthritis persistent; OA ext. - Oligoarthritis extended; PA - Polyarthritits; RF- - Rheumatoid factor negative; RF+ - Rheumatoid factor positive; ERA - Entesitis-related arthritis; PsA - Psoriatic arthritis; IBD - inflammatory bowel disease

Conclusions: Young adults with JIA have a high rate of comorbidity overall, with extraarticular JIA manifestations being the most frequently reported comorbid conditions. Comorbidity rates vary among the various JIA categories. Patients with systemic JIA have the highest rate of cardiovascular risk factors and osteoporosis, while patients with extended OA have the highest rate of uveitis. An underreporting or unawareness of comorbidities by rheumatologists is possible, guidance on risk assessment in adults with JIA is needed.

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None declared, G. Horneff Speakers bureau: Abbvie, Pfizer, Roche, Novartis, MSD

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Systemic sclerosis

OP0339 IDENTIFICATION OF A TRANSCRIPTOMIC SIGNATURE CORRELATED WITH MODIFIED RODNAN SKIN SCORE (MRSS) IN PATIENTS WITH DIFFUSE CUTANEOUS SYSTEMIC SCLEROSIS

I. Ageusop¹, S. Illiano², C. Rocher², E. Boitier³, J. Murphy⁴, Y. Allanore⁵, C.P. Denton⁶, O. Distler⁷, D. Khanna⁸, F. Benderitter². ¹Sanofi-Aventis Deutschland GmbH, Frankfurt am Main, Germany; ²Sanofi R&D, Chilly-Mazarin; ³Sanofi R&D, Alfortville, France; ⁴sanofi, Bridgewater, United States; ⁵Paris Descartes University, Paris, France; ⁶Centre for Rheumatology, Royal Free Hospital, London, United Kingdom; ⁷Department of Rheumatology, University Hospital Zurich, Zurich, Switzerland; ⁸Scleroderma program, University of Michigan, Ann Arbor, United States

Background: To support internal compound development in systemic sclerosis, a study was performed to identify an mRSS signature in a longitudinal approach by analyzing skin biopsies.

Objectives: Identification of a gene signature that could be used as a quantitative surrogate marker for the mRSS independent of any treatment.

Methods: 77 forearm skin biopsies from 32 patients at baseline, and from the same patients after 8 weeks of treatment with SAR100842 (a LPA1 antagonist) or placebo (N=30) and after an additional 16 weeks of treatment with SAR100842 (N=15) in a phase 2 trial, were collected. Total RNA was extracted with the RNeasy® Fibrous Tissue Mini kit according to the manufacturer's instructions. Total RNA was quantified by spectrofluorometry and qualified by capillary electrophoresis using Agilent Bioanalyzer 2100. Whole transcriptome analysis was performed using Affymetrix chips. Genes highly correlated (Pearson's correlation) with the mRSS were identified at each treatment visit. A signature was identified as a set of genes whose expression levels correlated consistently either positively or negatively with the mRSS at all study visits regardless of treatment group. The correlation value between the genes and the mRSS at baseline had to be >0.5 or <-0.5. The association between mRSS and the single composite marker obtained was investigated. A multivariate analysis of the correlation between the identified genes was performed using the median polish algorithm and PCA. The gene signature underwent pathway analysis using QIAGEN's Ingenuity Pathway Analysis (IPA).

Results: This methodology led to the identification of 64 genes considered for the signature and viewed as a single composite marker that was highly correlated to the mRSS. A principal component analysis was computed and the first component explaining the maximum variance in the signature was highly correlated to the mRSS at baseline and week 8. This correlation was confirmed with the median polish algorithm (Pearson's correlation coefficient of -0.75 and -0.73 respectively). The most significant disease and disorder biological functions associated with the mRSS signature genes were related to immunological diseases. A significant enrichment was also detected for genes associated with inflammatory response and connective tissue disorders with p-values from 2.98E-05 to 2.47E-02.

Conclusions: An mRSS signature was identified using skin biopsies in SSC patients. Some of these genes (i.e. IRF7, THBS1, COMP or BANK1) have been published using similar approaches in other sets of SSC patients (1), which supports our results. The functional categories of this signature are characteristic

for scleroderma pathology reflecting autoimmunity, vasculopathy, inflammation and fibrosis. This mRSS signature needs to be validated in a larger set of SSC patients including assessment of change over time.

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[1] Mahoney et al. PLOS Computational Biology 2015; Vol 11; 1–20.
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How diet influences musculoskeletal diseases

OP0340 WEIGHT LOSS FOR OVERWEIGHT AND OBESE INDIVIDUALS WITH GOUT: A SYSTEMATIC REVIEW OF LONGITUDINAL OBSERVATIONAL STUDIES

S.M. Nielsen¹, E.M. Bartels¹, M. Henriksen^{1,2}, H. Gudbergesen¹, H. Bliddal¹, A. Astrup³, F.K. Knop^{4,5,6}, L. Carmona⁷, W. Taylor⁸, J.A. Singh⁹, F. Perez-Ruiz¹⁰, L.E. Kristensen¹, R. Christensen¹. ¹The Parker Institute, Bispebjerg and Frederiksberg Hospital; ²Department of physical and occupational therapy, Bispebjerg and Frederiksberg Hospital; ³Department of Nutrition, Exercise and Sports, Faculty of Science, University of Copenhagen; ⁴NUTF Center for Basic Metabolic Research; ⁵Department of Clinical Medicine, Faculty of Health and Medical Sciences, University of Copenhagen, Copenhagen; ⁶Center for Diabetes Research, Gentofte Hospital, University of Copenhagen, Hellerup, Denmark; ⁷Instituto de Salud Musculoesquelética, Madrid, Spain; ⁸Department of Medicine, University of Otago, Wellington, New Zealand; ⁹Department of Medicine, University of Alabama at Birmingham, Birmingham, Alabama, United States; ¹⁰Rheumatology Division, Hospital de Cruces, Baracaldo, Vizcaya, Spain

Background: Weight loss is a commonly recommended treatment for gout, but the magnitude of effect to expect has to our knowledge not previously been evaluated in a systematic review.
Objectives: The aim of this systematic review was to determine the benefits and harms associated with weight loss in overweight patients with gout.
Methods: Based on a pre-defined protocol (CRD42016037937), we searched six databases for longitudinal studies, quantitatively reporting the effect of weight loss in overweight gout patients. Risk of bias was assessed using the ROBINS-I tool. The quality of the evidence was assessed using GRADE.
Results: From 3,991 potentially eligible studies, 10 were included (incl. one RCT). Interventions included diet with/without physical activity, bariatric surgery, diuretics, metformin, or no intervention. Due to clinical heterogeneity of the included studies, data are presented for each study and synthesised separately. The effect on serum uric acid (sUA) ranged from -168 to 30 µmol/L, and 0% to 60% patients achieved sUA normalisation (i.e. sUA <360 µmol/L). Six out of eight studies (75%) showed beneficial effects on gout attacks. A dose-response relationship was indicated in two studies for sUA, sUA normalisation and gout attacks. At short term (<3 months) after bariatric surgery, one study showed temporary increase in sUA, and another showed temporary increased number of gout attacks. Other possible harmful effects, measured by proxies such as withdrawals due to adverse events and serious adverse events, were poorly reported.
Conclusions: The available evidence is in favour of weight loss for overweight

Abstract OP0341 – Table 1

Abnormality	Joints % (n)			Median score (IQR)		Difference* (90% CI)
	HC (n=10)	OA no pain (n=11)	OA pain (n=15)	OA no pain (n=11)	OA pain (n=15)	
Fluid	30 (3)	73 (8)	67 (10)	2 (0, 4)	1 (0, 2)	0 (-2, 1)
Capsulitis/synovitis	– (0)	36 (4)	60 (9)	1 (0, 1)	0 (0, 2)	0 (0, 2)
Extracapsular oedema	– (0)	45 (5)	73 (11)	0 (0, 2)	2 (0, 3)	1 (0, 2)
CL thickening	50 (5)	100 (11)	100 (15)	2 (2, 4)	2 (2, 4)	1 (-1, 2)
CL oedema	40 (4)	91 (10)	87 (13)	2 (1, 3)	3 (2, 4)	1 (0, 3)
CL degeneration	40 (4)	91 (10)	100 (15)	3 (1, 5)	4 (2, 6)	1 (-1, 3)
Proximal joint bone oedema	– (0)	9 (1)	20 (3)	0 (0, 0)	0 (0, 0)	0 (0, 0)
Distal joint bone oedema	– (0)	27 (3)	20 (3)	0 (0, 1)	0 (0, 0)	0 (0, 0)
Proximal joint bone cyst	– (0)	27 (3)	47 (7)	0 (0, 2)	0 (0, 2)	0 (0, 1)
Distal joint bone cyst	10 (1)	27 (3)	7 (1)	0 (0, 1)	0 (0, 0)	0 (0, 0)

*Accounting for clustering of joints within patients. CI = confidence interval; HC = healthy controls; IQR = inter-quartile range; CL = collateral ligaments.

Figure 1: PRISMA flow diagram
ACR, American College of Rheumatology; CENTRAL, Cochrane Central Register of Controlled Trials; EULAR, The European League Against Rheumatism; ICTRP, the World Health Organization International Clinical Trial Registry Platform portal; pts, patients.

gout patients, with low, moderate and low quality of evidence for an effect on sUA, sUA normalisation, and gout attacks, respectively. At short term, temporary increased sUA and gout attacks may occur after bariatric surgery. There is an urgent need to initiate rigorous prospective studies (preferably RCTs) to provide more trustworthy estimates of benefits and harms of weight loss in overweight gout patients.

References:

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Can targeting disease activity in hand osteoarthritis improve our treatment in the 21st century

OP0341 CAN PAIN IN HAND OSTEOARTHRITIS BE ASSOCIATED WITH MRI COLLATERAL LIGAMENT ABNORMALITIES?

A.L. Tan^{1,2}, M.-A. D'Agostino^{1,3}, E. Hensor^{1,2}, A. Grainger², P. Emery^{1,2}, D. McGonagle^{1,2}. ¹Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds; ²NIHR Leeds Musculoskeletal Biomedical Research Centre, Chapel Allerton Hospital, Leeds, United Kingdom; ³Rheumatology Department, Hôpital Ambroise Paré, Paris, France

Background: Many patients with hand osteoarthritis (OA) have little symptoms. Bone oedema and synovitis have been associated to pain in OA, but inflammation involving ligaments has not been studied, likely limited by inadequate MRI resolution. We have previously found significant ligament pathology in early and established hand OA (HOA) [1].
Objectives: We hypothesise that the well innervated ligaments are key to a better understanding of the relationship between joint structure and pain in HOA. This