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Abstracts

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the effects of HLA-B27/hβ dependent on the presence of gut microbiota. This has led to the hypothesis that T cells and has been linked to aberrant features of HLA-B27, but it is also de-
690 the precise mechanism(s) remain incompletely understood. In HLA-B27/hβ
HLA-B27 plays a key role in the pathogenesis of spondyloarthritis (SpA), yet
the National Institute of Arthritis and Musculoskeletal and Skin Diseases, National
GENIC RATS: WHAT IS THE RELATIONSHIP?
MICROBIOTA AND GUT INFLAMMATION IN HLA-B27 TRANS-
Hyaluronan (HA) is well known to be a major component of the extracellular matrix (ECM) of synovial tissue in SpA patients. We have recently reported that HA can upregulate c-Met expression in synoviocytes and fibroblasts, which is associated with the development of fibrotic lesions. In the present study, we aimed to further investigate the role of HA in the pathogenesis of SpA.

Methods: We performed in vitro and in vivo experiments. In vitro, we used synoviocytes and fibroblasts from healthy volunteers and SpA patients. We measured the expression of c-Met and its downstream target proteins, including Akt and ERK1/2, in response to HA. In vivo, we used a rat model of SpA, which was induced by intraperitoneal injection of Tina-Ac. We measured the expression of c-Met and its downstream target proteins, including Akt and ERK1/2, in synoviocytes and fibroblasts isolated from the pannus.

Results: In vitro, we observed a significant upregulation of c-Met expression in synoviocytes and fibroblasts from SpA patients compared to healthy volunteers, which was further enhanced by HA stimulation. HA also significantly upregulated the expression of Akt and ERK1/2 in synoviocytes and fibroblasts from SpA patients. In vivo, we observed a significant upregulation of c-Met expression in synoviocytes and fibroblasts isolated from the pannus of SpA rats, which was further enhanced by HA stimulation. HA also significantly upregulated the expression of Akt and ERK1/2 in synoviocytes and fibroblasts isolated from the pannus of SpA rats.

Conclusion: Our results suggest that HA plays a key role in the pathogenesis of SpA by upregulating c-Met expression in synoviocytes and fibroblasts. This finding has important implications for the development of novel therapeutic strategies targeting c-Met in SpA.

INV2
INNATE LYMPHOID CELLS AT THE BARRIER AND INFLAMMA-
TION: HALT OR GO?
Cupedo T.
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erlands
The intestinal epithelium is of vital importance, as it is both a barrier to protect
us from intestinal microorganisms, and is responsible for uptake of nutrients and
water. Damage to the intestinal barrier occurs during chronic intestinal inflam-
amation, as well as during chemotherapies and radiotherapy used to treat cancer. Enhanc-
ing intestinal epithelial repair would reduce disease recurrence in inflammatory
bowel disease patients and improve the efficiency of anti-cancer treatments. Re-
cently we discovered that intestinalrepair is not epithelial cell-intrinsic, but is
controlled by group 3 innate lymphoid cells (ILC3).

INV3
MICROBIOTA IN IBD, FROM INVENTORY TO THERAPEUTIC
INTERVENTION
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The pathogenesis of the inflammatory bowel disease (IBD) is linked to an ac-
tivation of the gastro-intestinal immune system toward the gut microbiota in
genetically susceptible hosts and under the influence of environment. The mi-
crobial community in the human gastrointestinal tract is fundamental to the
health and is under the influence of both environmental and genetic factors.
Loss of the fragile equilibrium within this complex ecosystem, termed dysbi-
osis, is involved in numerous pathologies, including IBD. Patients with IBD exhibit
an altered gut microbiota composition with notably a decreased abun-
dance of anti-inflammatory bacteria such as Faecalibacterium prausnitzii. We
also observed alteration in the fungal microbiota composition in these patients.
The association of several polymorphisms of innate immunity genes involved
in microbial sensing with IBD is another argument for the involvement of the
gut microbiota in the IBD pathogenesis. Some genetic factors involved in IBD
might indeed act through a microbiota effect. We notably demonstrated that this
is the case for the IBD susceptibility gene CARD9. Gut microbiota alterations
are thus not only a consequence of intestinal inflammation but a key actor in
the disease pathogenesis. Fecal microbiota transplantation studies, by showing
some efficacy in IBD confirm that the gut microbiota can now be considered as
a potential therapeutic target.

INV4
MICROBIOTA AND GUT INFLAMMATION IN HLA-B27 TRANS-
GENIC RATS: WHAT IS THE RELATIONSHIP?
Colbert R.A., Gill T.
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HLA-B27 plays a key role in the pathogenesis of spondyloarthritides (SpA), yet
the precise mechanism(s) remain incompletely understood. In HLA-B27/hβ
transgenic (HLA-B27 Tg) rats that develop SpA-like disease there is striking
activation of the IL-23/IL-17 axis with expansion of CD8+ Th17 and Th1 cells,
as well as Th17 cells that express IFNγ. Disease occurs independently of CD8+
T cells and has been linked to aberrant features of HLA-B27, but it is also de-
pendent on the presence of gut microbiota. This has led to the hypothesis that
this allele may promote SpA by altering gut microbiota. We recently examined
the effects of HLA-B27/hβ expression on gut microbial dysbiosis in different
rat strains, and found that changes in microbiota are strongly dependent on the
genetic background and/or environment of the host.

In contrast, dysregulated cytokines and immune pathways are strikingly similar
in different rat strains, with increases in TNF, IFNγ and Th17 cytokines such as
IL-23 and IL-17 implicated in inflammation. Despite differences in the taxonom-
ic classification of dysbiotic microbes, determination of their functional profile
using PICRUSt software predicted highly similar metabolic functions. We
then employed a novel ‘inter-omic’ analysis to explore the relationship be-
between diverse microbes and common host immune dysregulation. To do this
we correlated the relative frequency of microbes (16S rRNA sequencing) with
host gene expression levels (RNASeq) in the cecum to colon of HLA-B27
Tg and wild type (WT) rats on Dark Agouti (DA), Lewis (LEW) and Fischer
backgrounds. This revealed several organisms whose relative frequency was
strongly associated with dysregulated cytokines driving Th17 and Th1 pathways
of inflammation in both the cecum and colon. While some microbes were dif-
ferentially abundant in HLA-B27 Tg vs. WT comparisons on both Lewis and
Fischer backgrounds (e.g. Clostridium), most were unique to either LEW (e.g.
Prevotella) or Fischer (e.g. Akkermansia). Interestingly, many microbes that cor-
related strongly with immune dysregulation were not identified by analyzing ef-
fects of HLA-B27 alone in DA, LEW or Fischer strains (e.g. Lachnospiraceae).
PICRUSt revealed common perturbed metabolic pathways during inflammation
(e.g. glycogen biosynthesis, steroid biosynthesis) despite dramatic differences in
dysbiotic microbes.

The impact of HLA-B27 on gut microbiota in experimental SpA is best explained
by an ecological model of dysbiosis rather than alteration of a single or a few
organisms that then impact disease. Inter-omic analysis reveals the complexity
of HLA-B27-associated dysbiosis, where perturbation of common metabolic
pathways by different gut microbiota during inflammation implicates functional
effects that may be key to evoking and perpetuating similar host immune dys-
regulation. This work underscores the importance of microbial communities and
their functions in experimental SpA pathogenesis.

INV5
EXPLORING GENDER DIFFERENCES IN THE CLINICAL PHE-
NOTYPE AND RESPONSE TO TREATMENT IN AXIAL SPON-
DOARTHRITIS
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tology, San Francisco, USA
Until the inclusion of patients with non-radiographic disease, Ankylosing Spon-
dylitis (AS) was thought to affect men slightly more commonly than women. Ex-
pansion to axial spondyloarthritides (axSpA) suggests an equigender distribution.
Women tend to have a lower burden of serologic inflammation, damage and
progression, but similar reported disease activity and yet relatively greater functional
impairment. Response to biologic treatment may be different across men and
women. The aim of this presentation is to examine the gender differences in the
clinical phenotype and response to treatment in axSpA by reviewing the observa-
tional and clinical trial literature and existing cohorts to address these questions.

INV6
DO WOMEN COME FROM VENUS AND MEN FROM MARS?
MYTHS AND TRUTHS ABOUT GENDER DIFFERENCES IN AX-
IAL SpA - SO THERE MAY BE SOME TRUTH AFTER ALL: WHAT IS THE UNDERLYING BIOLOGY?
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Sex matters, especially in axial spondyloarthritides (axSpA). Gender differences
have long been observed in patients with AS, yet little is known about the under-
lying biology of the sex/gender gap. This talk aims to close the conceptual gap
so that researchers and clinicians may address the physical gap between men and
women with axSpA.

In discussing the underlying biology of axSpA in males and females, it is impor-
tant to distinguish gender from sex. Gender encompasses social and behavioural
aspects associated with being male or female, whereas sex is specific for the
biological effects of being XX or XY. This talk will focus on sex differences in
axSpA, and more generally in the immune system.

By the end of the talk, SpA Congress attendees will have a basic knowledge of
normal autosomal (non X/Y) gene expression differences and immunologi-

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cal variation between the sexes. How the immune system controls nociception (pain sensing) in males and females will be introduced. Recent studies detailing differences in the immune profiles of males and females with axSpA, and how such differences may explain variation in disease manifestation and response to therapy will be speculated.

It is hoped that the importance of considering sex as a variable in future SpA research will be considered, and that the impact of sex in clinical trials will be examined. Indeed, sex is perhaps the easiest variable to consider on the path to personalized medicine.

INV7
PAINFUL RISK TO BE FEMALE? WHAT WE KNOW, AND WHY IT IS NOT SO TRIVIAL!

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For many painful diseases females exhibit a substantially higher proportion of patients than males. These phenomenon cuts across many pain diseases of most diverse etiologies, e.g. low back pain, postsurgical pain, neuropathic pain, complex regional pain syndrome, restless legs syndrome a.o. (e.g. Butler et al, 2013, Choineire et al). This is, however, not simply trivially explained by social behavioral traits/social role, e.g. the known higher rate of females seeking medical counseling although this may further inflate disproportionate patient figures. To get insight into the potential mechanisms involved in higher likelihood of females to precipitate pain disease we first have to look into gender differences in somatosensory processing. Large scale studies (e.g. by the German Research Network on Neuropathic Pain DFNs; have established reference data bases in healthy adults that cover all age ranges (18 – 85 years, Rolke et al, 2006, Magerl et al, 2010, Pfau et al, 2014). The main finding derived from these data bases is higher pain sensitivity in females in general (Magerl et al, 2010). Notably, this is not seen in other (non-nociceptive) somatosensory modalities (e.g. cold, warmth tactile detection). By contrast, this gender difference is largely absent in children (aged 6 – 16 years) suggesting the segregation of female vs. male pain sensitivity with the onset of puberty (Blankenburg et al, 2010). The latter predicts covariation in male vs. female even more so with the menstural cycle. However, although this has been studied over decades the design of most studies is poor providing little conclusive evidence for a role of gender-specific impact of gonadal hormones. It is now common sense that psychological comorbidities contribute substantially to the magnitude of pain perception, either experimental or clinical (c.f. the extensive U.S. phenotype-genotype association study on pain perception OPPERA; Ostrom et al, 2017). Notably, scores in most of these comorbidities are significantly higher in female than male subjects/patients. In a recent survey that we conducted in 22nd year medical students (n=170) female students exhibited signifi cantly stronger expression of personality traits that are linked to emotional dysregulation and lesser control, namely they rated higher scores of neuroticism (i.e. they feel easily activated, they described themselves as significantly more anxious, more depressed, more behaviorally inhibited, more vulnerable, more stressed, and more pain-catastrophizing (more specifically as more help less and more ruminating towards experimental pain; Mannheim Study on Pain Perception and Risk). Many of these traits were significantly positively correlated to the magnitude of perceived pain, although correlation coefficients were low. In an ongoing study on pain perception in patients with major depressive disorder, a disease that also has a higher preponderance in females, we could show that exaggerated pain perception is largely explained by patients level of depression, pain catastrophizing and acute perceived stress. Recent epidemiological data show a strong overlapping of polygenetic risk for chronic pain and major depressive disorder (McIntosh et al, 2016). Another factor boosting pain sensitivity is shortage and fragmentation of sleep (Lavigne et al, 2010, Schiwer et al, 2013, Sanders et al, 2016). Again, sleep disturbances are substantially more frequent and more severe in females (Lavigne et al, 2010, Penzel et al, 2015). In aggregate, there is no single physiological predictor explaining the higher pain sensitivity of females. However, there is a multiplicity of risk factors that occur more frequently and/or that are more severe in females, which in aggregate may lead to the higher pain sensitivity of females and most likely also to the higher proportion of female patients in male predominant diseases.

References

INV8
FROM BUGS TO BENCH AND THE BEDSIDE AND BACK

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Epidemiological and clinical data has provided ample evidence in the past that exposure to bacteria, on the background of a mostly genetically determined immunological background, plays a crucial role in the pathogenesis of axial spondyloarthritides (axSpA). Main candidate bacteria are enteritis-causing bacteria, bacteria of the normal gut flora and Chlamydia trachomatis. Furthermore, MRI-investigations of the axial skeleton have confirmed – in addition to earlier histological data - that the disease starts with inflammation at the cartilage/bone interface and that it starts normally in the sacroiliac joint. Subsequently, many attempts have been undertaken to identify immune responses to bacterial antigens and – on the assumption that hiding and persisting of bacterial antigens in the bone is unlikely – attempts have been made to identify immunodominant cartil age antigens which might crossreact with bacterial antigens, however until now without convincing success.

Advances in osteoimmunoology have helped to better understand the interaction between bony inflammation and new bone formation and have provided new bone biomarkers which have been used in clinical trials as markers of new bone formation, as predictors of new bone formation and as predictors of treatment responses. Such biomarkers are of great clinical relevance because new bone formation is a slow process and the currently available imaging methods for scor ing new bone formation have a low sensitivity. Applying the MRI method to the axial skeleton allowed also to detect bone inflammation earlier and has lead to earlier diagnosis in a disease which had a large gap between the occurrence of first symptoms and making a diagnosis in the past. Although until now the immunological pathway(ies) leading to inflammation (and subsequently new bone formation) has not yet been identified investigation of peripheral blood, synovial fluid and – most importantly – of spine tissue tak en from patients with axSpA gave evidence that TNF-IL-17 and IL-23 might play a role in the pathogenesis and might be therapeutic targets. Indeed, TNF-inhibition had been proven highly effective – maybe even more effective in comparison to other chronic inflammatory diseases – as a treatment of axSpA. Subsequently, a similar level of response has been found in clinical trials with
IL-17 inhibitors. But other targeted therapies which have been proven to be effective in other diseases such as rheumatoid arthritis have failed. Most surprisingly, also inhibition of IL-23 failed as a treatment of ankylosing spondylitis, despite its known link with IL-17 and despite many preclinical data hinting at a potentially important role of IL-23 in the pathogenesis of axSpA. Thus, although we have witnessed quite advances in a better understanding of the different aspect of the axSpA disease most advances over the last 15-20 years, with benefit for the patient, has come from clinical research leading to earlier diagnosis and the introduction of new and effective therapies.

INV1

**IMMUNE EFFECTOR CELLS IN SpA: WHAT ARE THE PATHWAYS?**


Despite much investigation, the pathogenesis of Ankylosing Spondylitis (AS) and related Spondyloarthritides (SpA) remains mysterious. However pro-inflammatory leukocytes undoubtedly play a key role and several cytokine pathways have been implicated in their generation and effects.

An important role for the TNF alpha pathway has been confirmed by immunological, genetic and therapeutic data. Biologic therapies are well established and small molecule inhibitors in development.

Both GWAS and experimental data strongly support roles for the IL-23/IL-17 axis in driving inflammation in SpA/AS. In recent years several groups have contributed to a body of work showing that “type 17” immune responses, involving the key pro-inflammatory cytokines IL-17A and IL-23, play important roles. Clinical trials treating patients with secukinumab, a blocking antibody against IL-17A, have shown clear efficacy. It is now appreciated that a number of epigenetic pathways impact on Th17 responses and could be targets for therapeutic intervention. We have used Th17 differentiation/expansion assays using CD4+ T cells from patients with SpA/AS to screen epigenetic inhibitors. We have identified roles for CBP30 (1) and BRPF family members (Chen unpublished) in driving Th17 responses, in addition to the key transcription factor ROR-γt (2).

It is now clear that both Th17 CD4 T cells and other type 17 immune cells (which can also include CD8+ and gamma delta T cells and innate lymphoid cells including NK cells) produce multiple cytokines in addition to IL-17A that themselves constitute important target pathways. Thus IL-17F, IL-21, IL-22, IL-26, TNF-α, CCL20 and Granulocyte macrophage colony stimulating factor (GM-CSF) are all potentially pro-inflammatory cytokines produced by “Th17 family leukocytes”. CSF2 (the gene for GM-CSF expression) has recently been associated with “pathogenic” human Th17 cells. GM-CSF is an important hematopoetic growth factor and immune modulator, and is produced by T cells, innate lymphoid cells, macrophages and stromal cells. GM-CSF plays a key role in neutrophil and monocyte recruitment, dendritic cell and osteoclast differentiation, making it a potent pro-inflammatory cytokine. A major role for GM-CSF has been shown in murine arthritis models. Our study of SpA patients (3) has shown increased frequencies of GM-CSF-expressing CD4+ and other T cells in AS/SpA peripheral blood. This is even more dramatic in synovial fluid, and is not confined to CD4 T lymphocytes. GM-CSF-producing cells have a specific transcriptional signature. These preclinical data would support clinical trials of GM-CSF neutralization in SpA.

In summary a number of different immune effector cells and pathways contribute to SpA pathogenesis, many of which constitute potential therapeutic targets.

**References**


INV1V

**AUTO-IMMUNITY VERSUS AUTO-INFLAMMATION IN EYE DISEASE IN SpA**

Forrester J.V, 3

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Uveitis is a frequent extra-articular manifestation of disease in SpA. Uveitis however has many causes. More than half of cases of uveitis are caused by infection while the remaining cases are considered non-infectious or “undifferentiated”. Uveitis in SpA is considered non-infectious and, until recently, was presumed to be autoimmune in nature. Uveitis in SpA is almost exclusively anterior (acute / recurrent) but evidence for autoimmunity in anterior uveitis is essentially lacking both in terms of specific antigenic triggers and in development of representative experimental models. Uveitis, particularly anterior uveitis, is in reality a systemic disease manifested in the eye and is a feature of a number of systemic diseases, particularly autoinflammatory diseases. Autoinflammatory diseases are classically described in relation to specific genetic defects but more recently a number of chronic inflammatory polygenic diseases are being viewed as having an autoinflammatory basis. This applies particularly to the case of SpA. Autoinflammatory processes in uveitis are well recognised with regard to activation of innate immune cells, through activation of pathogen recognition receptors such as Mincle and decin-1 and signalling through pathways such Card-9/Syk, with generation of cytokines such as IL-1. Moreover, autoinflammatory diseases are exacerbated if not initiated by infection and infections, particularly latent infections, are increasingly recognised as the underlying cause of “non-infectious” or “undifferentiated” uveitis. This presentation examines the role of autoimmunity, autoinflammation and infection in uveitis in the context of SpA. In particular the role of the microbiome in determining the outcome of intraocular inflammatory disease (aka uveitis) will be discussed.

**INV16**

**HOW PEPTIDE-LOADING COMPLEX AFFECTS MHC CLASS I BIOLOGY**

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Identifying and eliminating infected or malignantly transformed cells are fundamental tasks of the adaptive immune system. For immune surveillance, the cell’s metastable proteome is displayed as short peptides on major histocompatibility complex class I (MHC I) molecules to cytotoxic T-lymphocytes.

Our knowledge about the track from the proteome to the presentation of peptides has greatly expanded, leading to a quite comprehensive understanding of the antigen processing pathway. I will report on the mechanisms of antigen translocation, chaperoning, editing, and final quality control. Based on an integrative approach, the contribution of individual proteins as well as the architecture of the MHC I peptide-loading complex (PLC) and other MHC I editing complexes, also in the context of viral immune evasion, are addressed. The work provides the framework for understanding the quality control of antigen selection and identifies the molecular details underlying the onset of an adaptive immune response.

**Reference**


Clinical and Experimental Rheumatology 2018
The association of HLA-B27 with spondyloarthritis (SpA) has been known for decades. Its primary role in SpA pathogenesis has been definitively demonstrated using the HLA-B27 transgenic rat model. Numerous studies have provided invaluable information on the molecular and cellular alterations determined by HLA-B27. Yet the detailed mechanisms through which HLA-B27 alters the cell functions to determine the inflammatory process leading to disease have remained elusive. To address this gap, we have undertaken a detailed analysis of the gene expression programme of dendritic cells in patients compared with controls. These cells are thought to play a key role in SpA pathogenesis, as shown by the rat model study. More specifically, we derived dendritic cells from blood monocytes in culture and stimulated them with LPS to mimic an exposure to an inflammatory stimulus. We then analyzed their transcriptome by RNA-seq. In addition, we informed these data with the genomic sequence of the HLA-B locus and its flanking region, as there is strong evidence of linkage disequilibrium surrounding the HLA-B27 allele. Finally, we integrated these two genomic layers with the microbiota that shows substantial variation in SpA patients. Importantly, to overcome the major path to understanding the path a large fraction of patients are B27+ while most controls are B27-negative, making it difficult to discriminate the effects of HLA-B27 and those of the disease process, we analyzed three groups of subjects, including B27+ patients, B27+ healthy subjects and B27-negative healthy controls. Altogether, our multi-omic approach will hopefully provide an integrated view how the HLA-B27 allele influences the behavior of dendritic cells in relation to health and disease.

INV17
HLA-B27 AND MULTI-OMICS: WHERE DOES IT BRING US?
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The association of HLA-B27 with spondyloarthritis (SpA) is a group of chronic inflammatory disorders of the joint affecting primarily the axial skeleton but also peripheral limbs. Extra-articular manifestations are also considered a hallmark of SpA disorders of the joint affecting primarily the axial skeleton but also peripheral limbs. For instance, the failure to demonstrate the validity of such hypothesis, particularly in the model organism and it is an invaluable system to understand complex molecular mechanisms. Indeed, most basic biological and physiological properties as well as signaling pathways are conserved between mammals and Drosophila, allowing to model genetic aspects of numerous human pathologies. It is being increasingly used to gain insight into the molecular and genetic aspects of inflammation. To further test the hypothesis that expression of HLA-B27 molecule, in association with β2m, triggers cellular disturbance, we produced transgenic Drosophila expressing SPA-associated HLA-B27 subtypes in combination with human β2m, speculating that this simplified animal model could facilitate deciphering of the non-canonical cellular and molecular effects of HLA-B27. Using the UAS-Gal4 inducible system, we tested the effect of different patterns of expression of these transgenes and highlighted genetic interaction with essential signaling pathways. We then tested whether our results could be extended to HLA-B27 transgenic rat model.
Results. Drosophila that are transgenic for SPA-associated B*2705 or B*2704 alleles, in combination with β2m, display striking phenotypes, including a wing crossveinless phenotype and a reduced eye size when the HLA-B27/β2m transgenes are co-expressed in these tissues. In contrast, neither Drosophila single transgenic for HLA-B27 alone, nor transgenic for the SPA-non-associated allele HLA-B*0702 with or without β2m2, developed such phenotypes. Importantly, the wing phenotype appears to result from a genetic interaction with the BMP pathway and is associated with misregulation of dpp. A recent report linking the HLA-B27 transgenic rat model, as compared with controls, with its misregulation of the BMP pathway observed in our Drosophila model tends to confirm the result of a human Mendelian disorder closely reminiscent to SpA, i.e. Fibrodysplasia Ossificans Progressiva.

INV18
IS FRUIT FLY RELEVANT TO SpA?
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Introduction/Aim. Spondyloarthritis (SPA) is a group of chronic inflammatory disorders of the joint affecting primarily the axial skeleton but also peripheral limbs. Extra-articular manifestations are also considered a hallmark of SPA (e.g. inflammatory bowel diseases). SPA is highly inheritable, even though the environment plays an important role in the development of the disease. The most important part of heritability comes from the HLA-B27 allele of the Major Histocompatibility Complex (MHC), that is present in 70-90% of patients, as compared with 6-8% of the Caucasian population. The classical class I MHC molecule in most instances, in association with the β2microglobulin (β2m) invariant light chain, by presenting antigenic peptides to stimulate information on the molecular and cellular alterations determined by HLA-B27. As the molecular mechanisms underpinning the genetic associations at specific loci are being determined it is also becoming apparent that different variants at the same locus have marked differences in underlying biological effects. Given that these variants are often differentially associated with the related diseases as the molecular mechanisms underpinning the genetic associations at specific loci are being determined it is also becoming apparent that different variants at the same locus have marked differences in underlying biological effects. Given that these variants are often differentially associated with the related diseases as the molecular mechanisms underpinning the genetic associations at specific loci are being determined it is also becoming apparent that different variants at the same locus have marked differences in underlying biological effects. The findings from these genetic studies have provided major insights as to the causation of the disease and have contributed to major therapeutic developments, for example providing the first evidence that the IL-23 pathway was involved in the disease and contributing to the trial of compounds targeting that pathway which are now in widespread clinical usage. The genes of the discovered represent novel potential therapeutic targets, against which drug development is underway. As the molecular mechanisms underpinning the genetic associations at specific loci are being determined it is also becoming apparent that different variants at the same locus have marked differences in underlying biological effects. Given that these variants are often differentially associated with the related diseases as the molecular mechanisms underpinning the genetic associations at specific loci are being determined it is also becoming apparent that different variants at the same locus have marked differences in underlying biological effects. As the molecular mechanisms underpinning the genetic associations at specific loci are being determined it is also becoming apparent that different variants at the same locus have marked differences in underlying biological effects. As the molecular mechanisms underpinning the genetic associations at specific loci are being determined it is also becoming apparent that different variants at the same locus have marked differences in underlying biological effects.

INV19
GENETIC STUDIES IN ANKYLOSING SPONDYLITIS: PROGRESS AND TRANSLATION
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Twin and family studies have shown that both the risk of developing AS is largely genetic, and that its clinical manifestations are also under major genetic control. The heritability of AS in the UK Biobank and also shown in unbiased population level studies to be high (common variant heritability 69.1%, compared with 99.9% for Crohn’s disease, 15.9% for ulcerative colitis, and 16.3% for rheumatoid arthritis). By early 2018 115 non-MHC loci had been identified as being defnitely associated with AS (either at genome-wide levels of significance (p<5x10^-8) in an AS-specific analysis or in a set-based meta-analysis, with demonstration of an association of an AS independently at that locus). The MHC associations of AS are also complex, with multiple alleles of HLA-B, and of other HLA-ALPs, being associated with increased risk of or protection from the disease. In total roughly 30% of the genetic risk of the disease has now been explained by genetic studies. An ongoing genome-wide association study involving >26,000 cases and ~600,000 healthy controls is nearing completion and is likely to substantially add to the number of genetic associations known, as well as defining more precisely the variants involved.

Recent discoveries in AS genetics will be discussed with a particular emphasis on the significance of these findings to clinical practice in diagnosis and management of AS.
INV20
LESSONS FROM EPIGENETICS FOR SpA
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Rapid advances in our ability to interrogate the regulation of gene expression through epigenetic mechanisms offer new opportunities to understand mechanisms underlying disease pathogenesis, in particular by shedding light on how genetic differences associated with disease risk may be acting. Currently there is a major challenge to link possession of specific disease-associated genetic markers with functional mechanism, notably noncoding variants modulating gene expression. Identifying the specific genes and pathways modulated by these genetic variants is essential for taking forward such findings to understand disease processes and potential therapeutic targets. In my talk I will show how epigenetic evidence can be used to inform and interpret genome-wide association studies in the setting of SpA with a particular focus on drug target prioritisation. I will outline how understanding chromatin interactions and mapping expression quantitative traits in different immune cell types and conditions of innate immune activation can be leveraged. I will describe approaches to define the epigenetic landscape of ankylosing spondylitis in patients, with application to major immune cell populations in peripheral blood.

INV21
OPERATION TRANSFORMATION: THE IMPACT OF GENES AND LIFE STYLE IN JOINT DISEASE
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Obesity is one of the major public health challenges of our day. It kills 1000 people per million of the population per year – yet appears on almost no death certificates. The environment is a major driver of obesity – work, home, school and societal. We now know how the body mounts a robust metabolic and behavioural defence against weight loss. We know that obesity impacts on every disease and makes every disease worse. We know that obesity upregulates proinflammatory genes that impact negatively on the course of disease. In this lecture the drivers of obesity will be reviewed. The nature of the defence against weight loss by the immune system will be explored. The use of RNA sequencing for exploring the negative effects of obesity on inflammation and resolution of inflammation will be reviewed.

INV22
ROLE OF ECTOPTIC BMP SIGNALING IN PATHOGENIC OSSIIFICATION AND ANGIGENESIS
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Introduction. Ectopic formation and accumulation of extraskelatal bone characterize rare pediatric musculoskeletal disorders including Multiple Osteochondromas (MO) and Fibrodysplasia Ossificans Progressiva. MO, also known as Hereditary Multiple Exostoses (HME) and the subject of the present study, is characterized by benign tumors –called osteochondromas or exostoses- that form normally essential to maintain a balance amongst these contrasting mechanisms. One major mechanism of regulation relies on the ability of HS chains to interact with and restrict the distribution and activities of key signaling proteins including bone morphogenetic protein (BMP), hedgehog and fibroblast growth factor (FGF) family members. However, it was known (i) whether the HS deficiency during MO would lead to aberrant distribution and ectopic action of signaling proteins in tissues neighboring the growth plates and most importantly the perichondrium and (ii) whether these changes were responsible for skeletal deformities, growth retardation, chronic pain and other cell types. Studies conducted over the last few years, we set out to test these possibilities in animal disease models and in turn, provide a rational for clinical trials on osteochondroma prevention.

Conditional postnatal mouse models of MO consisted of floxed Ext1 mice mated with transgenic Cre and CreER lines targeting different cell populations within and around the growth plate, including Gdf5Cre and Aggrecan-CreER. Osteochondroma onset and outgrowth were analyzed and quantified in a variety of approaches including micro-computed tomography (microCT), histology, histochemistry and in situ hybridization. Cartilaginous portions of each osteochondroma were evaluated in serial sections after staining with alcian blue or safranin O, followed by 3D reconstruction. Distribution and activity of signaling proteins including BMP members and their downstream effectors, -phosphorylated SMAD1/5/8 proteins were determined by immunohistochemical procedures using commercial antibodies. Similar procedures were used to analyze recruitment of angiogenic and cancer cells.

Results. Because osteochondromas start out as cartilaginous outgrowths flanking the growth plates, we initially asked whether their formation was preceded by expression of ectopic chondrogenic signals within perichondrium, possibly acting as osteochondroma-inducing agents. We focused on BMP signaling because of its well established and recognized roles in promoting chondrogenesis. We found that conditional ablation of Ext1 alleles did in fact lead to strong ectopic activation of canonical BMP signaling in perichondrial cells flanking the growth plates in long bones, ribs and cranial base. In controls, the perichondrium had a stereotypic histological organization and structure, with the inner portion consisting of skeletal progenitors with a cuboidal shape and an outer portion with osteofibroblastic cells intermixed with blood vessel and other cell types. In mutants, ectopic BMP signaling was accompanied by a violation of these arrangements and boundaries, a change in cell morphology particularly within the inner portion, and eventually neo-differentiation of cartilage cells. With time, the latter became organized in a growth plate-like structure oriented at 90° angle with respect to the main skeletal axis, continued to grow outwardly, and eventually underwent ossification propelled by osteogenic and angiogenic cells recruited from the surroundings. Interestingly, ectopic chondrogenesis and osteochondroma-like formation developed also along the growth plate of control wild type, long bone explants in which the perichondrium had been locally implanted with a bead containing the small molecule HS agonist Surfen. Biochemical and surface plasmon resonance assays showed that Surfen had displayed endogenous BMPs bound to HS chains, making them available for biological action. Pros imity ligation assays showed that treatment with Surfen or heparinase led to a rapid rearrangement of cell surface BMP receptors, formation of tetrameric complexes, and activation of signaling via pSMADs. Given the potency of ectopic BMP signaling in inducing osteochondroma formation, we asked whether it may represent a therapeutic target. Juvenile floxed Ext1:Aggrecan-CreER mice injected with tamoxifen once were treated with the BMP signaling antagonist LDN-193189 (or vehicle) by oral gavage for 6 to 8 weeks. MicroCT and other analytical data showed that while numerous osteochondromas had developed in control vehicle-receiving mice, osteochondroma formation had been reduced by over 90% by drug treatment.

Conclusions. The results of our studies provide strong and novel evidence that osteochondromas derive from progenitor cells located within perichondrium and that canonical BMP signaling is a major disease- inducing mechanism. Perichondrium has long been known to contain endogenous BMPs and other chondrogenic factors and to concurrently express anti-chondrogenic mechanisms, including Noggin and fibroblast growth factor (FGF) and Wnt pathways. Thus, HS is normally essential to maintain a balance amongst these contrasting mechanisms and allow perichondrium to maintain its phenotype. The HS deficiency during MO would alter and tilt these fine-tuning mechanisms toward ectopic chondrogenesis. It remains unclear the manner in which the HS deficiency elicits subsequent ossification and angiogenic processes that contribute to pathogenesis. Because HS interacts with a very large number of growth and signaling factors, its deficiency in MO may directly or indirectly elicit those processes as well. Despite these lingering and interesting questions, however, our data do provide the first evidence that osteochondromas are amenable, and responsive, to drug treatment. The future challenges thus lie in the design and implementation of a clinical trial to test a drug treatment for the prevention or inhibition of osteochondroma formation in patients with MO.
INV26

IS LOW RADIATION CT OF THE SPINE SUITABLE TO ASSESS STRUCTURAL PROGRESSION IN SpA?

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New bone formation is the hallmark of axial SpondyloArthritis (axSpA). Calcification of ligaments leads to syndesmophyte formation, ultimately bridging the entire spine. Two-dimensional conventional radiography is the standard method for assessment of structural damage in the spine in patients with axSpA. However, only the cervical and lumbar spine can be assessed reliably. And even only the anterior corners of the vertebrae. Consequently, only limited information can be derived from conventional radiographs.

The modified Stoke Ankylosing Spondylitis Spinal Score (mSASSS) is the most reliable and sensitive scoring method. However, it takes two years to show progression in a sufficient number of patients to use it as an outcome in a clinical trial. Three-dimensional imaging has a clear advantage for assessment of the spine: overprojection of other structures do not hamper the assessment. MRI has proven a very valuable method for the assessment of inflammation in the spine. Structural lesions such as fatty lesions and erosions can also be assessed. But new bone formation is hard to assess on MRI. In contrast, CT scanning is the most appropriate method to assess bone. The drawback of CT is the high radiation dose.

However, with the development of new hardware (multislicer scanners) and software, the radiation dose could be reduced substantially. With a maximum dose of 4mSv a good quality image of the entire spine can be made (background radiation of 2mSv). It is expected that this dose can be reduced in the future. The low dose CT (ldCT) provides slices in three planes of the entire spine. Especially, the addition of the thoracic spine is promising: this doubles the number of vertebrae that can be assessed, while it is known that a lot of the inflammation can be seen in this part of the spine and early syndesmophytes are frequently observed in the thoracic-lumbar junction. Moreover, the entire vertebral rim can be assessed, not only the (collapsed) anterior corners on a lateral view. This opens the options for a more sensitive method but has also the risk of reduced reliability and specificity. Therefore, in order to test the possibility of the use of ldCT, before it can be introduced as an outcome measure to replace conventional imaging. Recently, a new scoring method was developed and validated: the CT Syndesmophyte Score (CTSS) (1). The method is evaluating a vertebral unit (known from MRI scoring): the lower half of a vertebra, the intervertebral disc space and the upper half of the next vertebra. Only syndesmophytes are assessed and the scores are based on the bridging of the intervertebral disc height (IVDH): 1 = <50% of the IVDH, 2 = ≥50% of the IVDH but no bridging, 3 = Ankylosis/bridging syndesmophyte. This is assessed in each quadrant in multiple planes and the highest score per quadrant is used for the score. The range of the scoring method is 0 tot 552 (23 VUs, 8 quadrants per VU, max score of 3 per quadrant). It was shown that the score showed good interreader reliability both for status scores and for change scores over two years. Most syndesmophytes were indeed observed in the thoracic spine and also most change happened in this part of the spine. Increase in scores was based both on the formation of new syndesmophytes and the growth of existing syndesmophytes. When comparing the mSASSS with the CTSS in 50 patients with a follow-up of two years the CTSS was more sensitive than the mSASSS. For example, an increase in score of at least 3 could be found in 6% of the patients with the mSASSS and in 30% of the patients with the CTSS (2).

These are the first promising results of using ldCT as an outcome measure. This needs further evaluation in a true treatment trial to test the discrimination. Also, reducing the interval may become an option, which would make trials with a structural outcome much more viable.

References

INV27

DO WE NEED TO BOTHER MEASURING BONE PROLIFERA- TION IN AXIAL SpA? INSIGHTS FROM CLINICAL TRIALS

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The introduction of tumour necrosis factor inhibitors (TNF) about 20 years ago has led to the hope of disease modification of ankylosing spondylitis, since biologics showed for the first time a decrease of inflammatory activity on MRI, with the latter being theoretically also directly linked to new bone formation. However, the first open-label extensions of randomized-controlled trials with a treat- ment duration of 2 years failed to show any positive effect on the radiographic progression in AS patients when compared to historical cohorts that had not been exposed to biologics. Nevertheless, later data indicated that this lack of influence on radiographic progression might have been due to many different reasons that were not taken into account in these first analyses, such as the radiographic status at baseline, CRP levels or insufficient duration of follow-up. Furthermore, most recent data from MRI studies also indicated that the most important link to influence radiographic progression with biologics might not be the sup- pression of inflammation but the protection of bone to show tissue metaplasia to post-inflammatory findings, while early suppression of inflammation might be the key to even completely inhibit radiographic progression in AS patients. Indeed, most recent cohort data have been able to demonstrate an association between TNF-blocker treatment and reduced risk of spinal structural progression (e.g. formation of syndesmophytes).

Furthermore, early escalation of treatment from NSAIDs to biologics and long-term treatment with biologics have also independently been able to show posi- tive effects on radiographic progression in patients with AS. Finally, also newer biologics such as IL-17A inhibitors have also provided promising results in terms of overall low radiographic progression rates as measured by validated scoring systems.

Currently, first head-to-head trials of different biologics are underway to examine any possible differences between the available compounds with a primary out- come of their effect on spinal radiographic progression. It remains to be shown whether and how these results will also become clinically relevant in terms of decrease or even inhibition of spinal mobility restrictions, in order to be able to postulate a ‘real’ disease modifying effect of biologic treat- ment in axial spondyloarthritis.
Oral Presentations

O1

GUT DYSBIOSIS IN ANKYLOSING SPONDYLITIS IS ASSOCIATED WITH INCREASED FECAL CALPROTECTIN

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Introduction/Aims. Intestinal dysbiosis may be involved in the pathogenesis of ankylosing spondylitis (AS). We aimed to define differences in the gut microbiota composition between patients with AS, ulcerative colitis (UC) and healthy controls (HC) and determine the relations between gut microbiota, fecal calprotectin (FCal) and disease related variables in AS.

Methods. Fecal microbiota was analyzed in patients with AS (N=150), UC (N=18) and HC (N=17) using 16S rRNA sequence technique in a targeted approach. Fecal bacterial abundance and profile was also compared with a healthy reference group creating a Dysbiosis Index score (DI 1-5). The AS patients were assessed with questionnaires, back-mobility tests, FCal, ESR and CRP.

Results. Principal component analysis showed highly separate clustering of the microbiota in stool samples from patients with AS, UC and HC. We found an expansion of Proteobacteria and a contraction of Bacteroidetes and Lachnospiraceae in AS. Dysbiosis (defined as DI≥3) was found in 88% of AS and an elevated DI correlated with increased FCal (r=0.303; p<0.001). Samples from AS patients with FCal<50 (n=57) and >200 mg/kg (n=36) clustered separately in AS patients and HLA-B27 transgenic rats. Inflammasome activation was evaluated. The role of IL-1β-dependent mechanisms and modulation of NLRP3, NLRC4 and AIM2 was confirmed in AS isolated peripheral monocytes, directly correlated with the ASDAS-CRP, and paralleled by increased serum levels of IL-1β.

Conclusions. The fecal microbiota signature differed greatly between patients with AS, UC and HC. An increased FCal, suggestive of intestinal inflammation, was associated with aberrations in the microbiota composition and increased dysbiosis.

O2

INFLAMMASOMES ACTIVATION OCCURS IN THE INFAMED TISSUES OF AS PATIENTS AND DRIVES IL-23 EXPRESSION AND ILC3 EXPANSION

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Background. A growing body of evidences indicate that the aberrant activation of innate immune systems, occurring in genetically predisposed patients, drives inflammatory processes in Ankylosing Spondylitis (AS) (1).

Objectives. Aim of this study was to evaluate the activation and the functional relevance of inflammasome pathways in patients with AS. Methods. Intestinal, synovial and bone marrow expression of inflammasome pathways, pyroptosis and IL-1β and IL-18 was evaluated in AS patients. Analysis of organic acid extraction was performed as previously described (2). The expression of the metabolite-sensing receptors GPR43 and GPR109A involved in the regulation of the intestinal inflammasome was also assessed. The role of intestinal dysbiosis in modulating inflammasome activation was also studied in AS patients and HLA-B27 transgenic rats. Inflammasome activation was evaluated in isolated peripheral AS monocytes. The role of LPS, PGE2 and nicotine in inducing monocyte inflammasome activation and the role of inflammasome in modulating IL-23 production and ILC3 expansion was also evaluated.

Results. Activation of inflammasomes was observed in the inflamed gut, synovial and bone marrow samples of AS patients and associated with an increased expression of caspase-1, IL-1β and IL-18. AIM2 expression was observed in the context of tuft cells and of adherent ileal bacteria. Inflammasome activation in AS gut, was associated with the occurrence of dysbiosis and isolated bacteria from the gut of AS patients induced inflammasome activation on isolated PBMC from healthy controls. Increased pyroptosis was also observed in the gut as demonstrated by the membrane localization of Gadermin D. Isolated intestinal bacteria from AS samples, significantly modulated inflammasome activation in isolated monocytes. Reduced Short-chain fatty acids concentrations and increased expression of GPR43 and GPR109 were demonstrated in the ileal samples. Inflammasome activation was also observed in the inflamed gut of HLA-B27 TG rats and suppressed by antibiotics treatment. Increased expression of NLRP3, NLRC4 and AIM2 was confirmed in AS isolated peripheral monocytes, directly correlated with the ASDAS-CRP, and paralleled by increased serum levels of IL-1β.

In in vitro studies, LPS and nicotine strongly activated NLRP3, NLRC4 and AIM2 pathways in AS monocytes. The CC genotype of PTGER4 SNP rs896969 was associated with a significantly increased activation of inflammasome in AS. Inflammasome activation in AS monocytes was required for the induction of IL-23p19 expression in an IL-1β-dependent way. Finally, inflammasome inhibition blocked IL-23-induced ILC3 expansion.

Conclusions. Inflammasome activation occurs in AS patients and is modulated by a plethora of different tissue-specific and circulating stimuli. Inflammasome drives IL-23p19 production in a IL-1β-dependent mechanism and modulate ILC3 expansion in AS patients possibly representing a future area of therapeutic interventions in AS.

References

O3

TRANSMEMBRANE TNF SIGNALING THROUGH TNF-RI INDUCES SPA-LIKE INFLAMMATION, WHEREAS SIGNALING THROUGH TNF-RII IS CRUCIAL FOR NEW BONE FORMATION

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Introduction and Aim. TNF can drive strictly distinct inflammatory pathways depending on its expression form. We have shown that transmembrane (tm)TNF rather than soluble TNF contributes to key pathological features of spondyloarthritids (SpA), including the key hallmark pathological new bone formation. The aim is to delineate the cellular and molecular mechanisms by which selective tmTNF overexpression leads to SpA-like pathology.

Methods. tmTNFtg mice (TgA86) were crossed with TNF-R1 or TNF-R2 knockout mice and followed clinically for SpA development. Calvarial fibroblasts were cultured and differentiated towards osteoblasts.

Results. SpA was observed in all tmTNF−/− and tmTNF−/−xTNF-R1−/− mice but not in tmTNF−/−xTNF-R2−/− mice and confirmed by histology. Whereas this indicates that TNF-R1 is required for tmTNF−/− induced inflammation, it was striking that 50% of the tmTNF−/− versus none of the tmTNF−/−xTNF-R1−/− mice depicted clear histological signs of endochondral new bone formation. To test whether TNF-R2 is involved in new bone, calvarial fibroblasts from tmTNF−/−, tmTNF−/−xTNF-R1−/−, tmTNF−/−xTNF-R2−/− and wild type mice were differentiated with osteogenic medium with or without IL-17A. tmTNF overexpression fibroblasts enhanced osteogenic differentiation as observed by alkaline phosphatase and alizarin red staining and increased mRNA levels of Collagen type I and ALP compared to wild type fibroblasts. This enhancement in osteogenesis was maintained in tmTNF−/−xTNF-R1−/− fibroblasts but abolished in tmTNF−/−xTNF-R2−/− derived fibroblasts.

Conclusion. The SpA-like phenotype in tmTNFtg mice is crucially dependent on TNF-R1 to drive inflammation, but TNF-R2 signaling is required for new bone formation under inflammatory conditions.
PROGNOSTIC MARKERS IN AXIAL SPONDYLOARTHRITIS (PROMISE) – ALPHA 1 ANTI TRypsIN AND BETA 2 MICROGLOBULIN MAY DIFFERENTIATE ANKYLOSING SPONDYLITIS FROM NON RADIOGRAPHIC axSpA, MECHANICAL BACK PAIN AND HEALTHY CONTROLS

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Introduction. Over recent years, a clear need for additional biomarkers in axSpA has been identified, for diagnosis, prognostication and treatment response. Multiple biomarkers have been explored, but there remains uncertainty as to their utility in clinical practice and their inter-relationship.

Aim. In this cross-sectional study we evaluated a broad panel of serum biomarkers, from a large mixed cohort of patients with Ankylosing Spondylitis (AS), non-radiographic axial spondyloarthritis (nr-axSpA), mechanical back pain (MBP) and healthy controls (HC). We aimed to evaluate these biomarkers to describe diagnostic subgroups.

Methods. A panel of 46 serum biomarkers were analysed by Myriad RBM using multiplexed immunoassays (Fig. 1.) in a cohort of patients from a tertiary referral centre, consented as part of the Bath Spondyloarthritis Biobank. AS patients met mNY criteria, and nr-axSpA patients satisfied ASAS classification. Validated patient reported outcomes (including BASDAI, BASFI) and BASMI were completed. 50 HC blood samples were collected at University College London for biomarker analysis.

Results. 331 patients were included (59.5% AS, 8.2% nr-axSpA, 15.7% MBP, 15.1% HC). 64.7% were male, mean age 44.2 years (SD 16.6), mean disease duration in the AS group of 22.4 years (SD 13.6) with 84% HLA B27 positive.

Logistic regression identified an increased odds of AS versus control for alpha 1 antitrypsin (AAT) (OR 44.8 [95%CI 15.9 to 126.3]) and beta 2 microglobulin (B2M) (OR 19.8 [95% CI 8.4 to 46.4]). ROC curves for AS patients versus controls for AAT and B2M demonstrated AUC of 0.94 and 0.93 respectively (Figs. 2 & 3).

Discussion. AAT and B2M have been identified as potential biomarkers differentiating distinct diagnostic groups in this preliminary analysis. Further sub group analysis is planned, along with evaluation of biomarkers with radiographic imaging.

IMPACT OF GUT INVOLVEMENT IN EARLY SPONDYLOARTHRITIS – THE DESIR COHORT

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Inflammatory bowel disease (IBD) is a well-known extra articular feature of spondyloarthritides (SpA), with a pathophysiological relationship.

Aims. To evaluate in the DESIR cohort the prevalence and incidence of IBD over the first 5 years of follow-up, and factors associated.

Methods. DESIR is a prospective observational cohort of patients with recent onset (<3 years) inflammatory back pain, suggestive of axial SpA. All available factors in the database were compared between patients with and without past or present IBD (with medical confirmation) at baseline and at M60, and incident cases of IBD over the 5 years of follow-up, by univar and multivarate analysis.

Results. At baseline, 706 patients were analyzed, 35 had a past history or a concurrent IBD: prevalence 4.94% [CI 95%: 3.3-6.5]. IBD was significantly associated in multivariate analysis with history of uveitis; OR 3.62 [1.95-6.74], levels of DKK-1: OR 1.03 [1.02-1.05] and TNF serum level: OR 1.17 [1.08-1.26]. IBD was not associated with phenotypic presentation (peripheral arthritis, enthesitis, dactylitis, uveitis) or baseline serum levels of other cytokines (IL-6, IL-17, IL-23).

At M60, 480 patients were analyzed, 58 with IBD: prevalence 12.1% [9.17-14.99]. In multivariate analysis, IBD was associated with fulfillment of modified New York criteria: OR 4.85 [2.23-10.57], sick leave: OR 1.01 [1.005-1.014], BASDAI: OR 1.10 [1.05-1.16], and with smoking: OR 2.79 [1.53-5.07]. No association with MRI scores, enthesis, psoriasis, BMD.

After a 5-year follow-up period, 23 incident cases of IBD were recorded, giving an estimated occurrence rate of 0.95/100 [0.57-1.35] patient-years in this population. Incidence of IBD was independently associated (multivariate) with: HLA B27: OR 0.36 [0.22-0.59], fulfillment of modified New York criteria at M0: OR 3.35 [1.85-6.08], family history of IBD: OR 3.31 [1.62-6.77].

Conclusion. In early SpA, IBD occurs with an incidence of around 1/100 patient-years, and is associated with poor outcome at 5 years, family history of IBD, absence of HLA-B27, fulfillment of modified New York criteria.
O6

GENDER DIFFERENCES IN TNFI TREATMENT ADHERENCE AND RESPONSE IN AS PATIENTS: A PROSPECTIVE LONGITUDINAL COHORT STUDY

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Introduction/Aim. Despite several observations of gender differences in TNF inhibitor (TNFI) treatment response and adherence in ankylosing spondylitis (AS) patients, limited studies were conducted. Our aim is to assess gender differences in TNFI treatment adherence and response in a longitudinal cohort study over a 10-year follow-up period in AS patients.

Methods. AS patients (fulfilling the modified New York Criteria) treated consecutively with TNFI were included in a prospective, observational cohort. Data were collected at baseline, screening, 3 and 6 months and thereafter every 6 months on demographics, lifestyle factors, inflammatory markers (C-reactive protein [CRP]) and disease specific parameters (Bath Ankylosing Spondylitis Disease Activity Score (BASDAI), Ankylosing Spondylitis Disease Activity Score (ASDAS), Bath Ankylosing Spondylitis Metrology Index (BASMI)). TNF response was defined by BASDAI50% response criteria (50% of the initial score or improvement of ≥2 points) and ASDAS response criteria (improvement of >1.1 points). Kaplan-Meier Survival curves and Generalized Estimating Equations (GEE)-analyses were performed.

Results. In total 359 AS patients (33.4% females) were included with a mean follow-up of 5.1 years. Women showed a significantly lower follow-up duration than men, 4.5 vs. 5.4 years. Patients who were lost to follow-up, were mostly female (35%) vs. male (26%). Women showed a significant lower follow-up duration over the entire follow-up period. According to both the BASDAI and the ASDAS response criteria, females had an overall significantly lower percentage of response.

Conclusion. A clinically relevant lower BASMI (higher mobility) than males (0.23 points).

O7

FATTY LESIONS DETECTED ON MRI SCANS IN PATIENTS WITH ANKYLOSING SPONDYLITIS ARE BASED ON THE DEPOSITION OF FAT IN THE VERTEBRAL BONE MARROW

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Background. Fatty lesions (FL), similar to bone marrow edema (BME) and sclerosis (SCL), are characteristic findings in MRI examinations of patients with ankylosing spondylitis (AS) and degenerative disc disease (DDD). It has recently been shown that FL are associated with syndesmophyte formation in AS. The anatomic correlate of FL has not been studied to date. Current assumptions are solely based on non-invasive data.

Objective. To examine the cellular composition of FL in the edges of vertebral bodies of patients with AS or DDD by histology.

Methods. Patients with AS or DDD undergoing planned kyphosis correction surgery by spinal osteotomy (in AS) or surgery to correct spinal stenosis (in DDD) were included into this biopsy study. The spinal surgeon (HB) took all biopsies mainly in the area close to the vertebral edge in many of which FL had been seen by MRI (Fig. 1a for AS and 1b for DDD). Biopsies were decalcified, embedded in paraffin, cut and stained by hematoxylin and eosin. The marrow composition was analyzed and the cellularity graded (% surface area) by two different investigators blinded to patients’ diagnosis. Four different marrow compositions could be differentiated: (i) fat, (ii) fibrosis, (iii) inflammation and (iv) hematopoiesis (normal).

Results. A total of 60 biopsies mostly obtained from the lower thoracic spine and the lumbar spine of 21 AS patients (mean age 51.7 years, mean disease duration 24.6 years) and of the lumbar spine in 18 DDD patients (mean age 60.1 years) were available. On the patient level, the histological appearance of MRI-FL was different between the groups: fat marrow was present in biopsies of 19 AS (90%) but in only 5 DDD (28%) patients. Inflammatory marrow changes, resembling monocellular infiltrates, were found in 8 AS (38.1%) and 14 DDD (77.8%) patients at areas with concomitant FL and BME on MRI, while marrow fibrosis was seen in 6 AS (28.6%) and 4 DDD (22.2%) patients at areas with concomitant FL and SCL on MRI.

In the semiquantitative histopathological analysis, the mean distribution (standard deviation) of the various bone marrow tissue types in the biopsies differed between the AS vs. D in a similar way, with 43% (±26.3%) vs. 16% (±30.3%) for fatty marrow, 11% (±15.5%) vs. 55% (±42%) for inflammatory marrow and 9% (±16.1%) vs. 13% (±27.8%) for fibrotic marrow, respectively.

Conclusion. The presence of FL on MRI corresponds to fat deposition in the bone marrow of patients with advanced AS. These data show that the MRI change termed “fatty lesion” is indeed based on the deposition of fat in the vertebral bone marrow in AS. Since vertebral bone marrow is physiologically harboring hematopoiesis, AS seems to lead to a change in the bone marrow microenvironment with local disruption of hematopoiesis and replacement by fat. The link between fat and new bone formation should be studied in earlier disease stages.

O8

PREVALENCE OF INFLAMMATORY AND CHRONIC CHANGES SUGGESTIVE OF AXIAL SPONDYLOARTHRITIS IN MAGNETIC RESONANCE IMAGES OF THE AXIAL SKELETON IN INDIVIDUALS <45 YEARS IN THE GENERAL POPULATION AS PART OF A LARGE COMMUNITY STUDY (SHIP)

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Background. Magnetic resonance imaging (MRI) is crucial for classification and diagnosis of axial spondyloarthritis (axSpA). Characteristic MRI lesions of axSpA are bone marrow edema (BME) or structural fatty lesions (FL) of the sacroiliac joints (SIJ) and spine. However, the specificity of these lesions has been questioned, since patients with chronic back pain but no axSpA may also have a positive MRI, as shown in recent cohort studies.

Objective. To investigate the prevalence of BME and FL on MRI of the spine and the SIJ in the general population.

Methods. Volunteers <45 years of the population based Study of Health in Pomerania (SHIP)12 underwent MRI examinations of the spine (sagittal orientation, T1 and T2 MRI sequences) and the SIJ (coronal orientation, STIR sequences), independently of clinical symptoms. Two trained readers blinded for age and gender examined the MRI of the lumbar spine and SIJ and FL (spine) suggestive of axSpA using the ASAS definitions: a lesion in the SIJ was considered positive if located periarticularly and in the middle part of the joint and A lesion in the spine was considered positive if detected at the edge of the vertebral body. Clearly degenerative lesions involving the vertebral endplate or being accompanied by abnormalities of the intervertebral disc (protrusion or prolapse) were not counted.

Results. A total of 802 complete MRI sets (spine and SIJ) of 394 male (49.1%) and 408 female volunteers (50.9%) was evaluated. The mean age of all patients was 37.5±6.2 years. BME in the SIJ suggestive of axSpA were found in 144
Individuals (18%), with an equal distribution between males (n=74, 18.8%) and females (n=70, 17.2%). A similar pattern of BME was found in the spine, again with no differences between males and females. However, the location of the lesions was different: 9.5% had ≥1 lesion in the cervical, 18.6% in the thoracic and 7.4% in the lumbar spine. Overall, 88.6% male and 84.6% female volunteers were found to have ≥1 and 54.6% male and 46.1% female volunteers were found to have ≥3 positive spinal lesions in any spinal region. In comparison, the prevalence of FL was higher (36.7% volunteers in the cervical, 72.4% in the thoracic and 52.7% in the lumbar spine). Overall, 86.5% volunteers were found to have ≥1 and 90.2% volunteers were found to have ≥3 positive spinal lesions in any spinal segment.

Logistic regression analysis showed that age was the only demographic characteristic that independently contributed to the occurrence of both BME (RR=1.22, 95%CI 1.03-1.46, p=0.025) or FL (RR=1.12, 95%CI 1.07-1.19, p=0.001).

Conclusions. This large population-based study with healthy volunteers a relatively high prevalence of inflammatory and structural MRI lesions was found. Whether these lesions are to be explained by mechanical stress needs to be further studied. The high prevalence of BME and FL in the axial skeleton in the general population indicates a limited diagnostic value of these MRI findings. Thus, those should be interpreted with caution in relation to diagnosis, classification and assessment of disease activity.

References
1. Bundesgesundheitsbl 2012

O9 VALIDATION OF ASAS MRI LESION DEFINITIONS IN AXIAL SPONDYLOARTHRITIS: DATA FROM THE ECHOGRAPHY IN SPONDYLOARTHRITIS COHORT (ECHOSPA)

Maksymowych W.P.1,2, Loeser E.3,4,5, Wichter V.3,6,7, Gomma R.6,7, Ribot O.1,2,8,9, Breban M.1, D’Agostino M.A.1, Lambert R.G.2
1University of Alberta; 2CARE Arthritis; 3Ambroise Pare Hospital, Boulogne-Billancourt; 4CHRU Vandoeuvre les Nancy, France

Introduction/Aims. The ASAS MRI group has generated updated consensus MRI lesion definitions in the SIJ and spine (ASAS_MRI_def). We aimed to assess the distribution, reliability of detection, and construct validity of active and structural lesions per these definitions in an early axSpA cohort.

Methods. Consecutive outpatients with age <50 years and symptoms >3 months suggestive of SpA were enrolled. MRI scans from 412 of 470 cases were evaluated by 2 readers and an adjudicator. ASAS_MRI_def were recorded in an ASAS-consensus derived eCRF according to global assessment (lesion present/absent) and detailed scoring of individual lesions (SPARCC SIJ inflammation, SPARCC SIJ structural). Reliability of detection was analyzed using kappa and detailed scoring by ICC. For construct validity we calculated optimal cut-offs for bone marrow edema (BME) and erosion that defined active and structural lesion typical of axSpA, respectively.

Results. Active and structural lesions typical of axSpA were present in 9.7% and 10.8%, respectively, and ASAS positive MRI in 9.3%. Subchondral BME (13.6%) and erosion (9.4%) were the most frequent. Active but not structural lesions were present in 3.0% while the converse was evident in 4.0%. AxSpA was clinically diagnosed at baseline in 88.1% and all categories of active and structural lesions were higher in those with axSpA. Substantial k values (95%CI) were evident for detection of these lesions with comparable reliability for active and structural lesions: active lesion (0.76 [0.65-0.88]), ASAS positive MRI (0.78 [0.66-0.89]), structural lesion (0.76 [0.65-0.87]). Detailed scoring per SIJ quadrant that reflect expert opinion as to what constitutes an active or structural lesion typical of axSpA are provided in the Table.

Table.

<table>
<thead>
<tr>
<th>Number of SIJ Quadrants</th>
<th>Active Lesion Typical of AxSpA</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Sensitivity</td>
</tr>
<tr>
<td>BME Score ≥2</td>
<td>100%</td>
</tr>
<tr>
<td>BME Score ≥3</td>
<td>100%</td>
</tr>
<tr>
<td>BME Score ≥4</td>
<td>97.5%</td>
</tr>
<tr>
<td>Structural Lesion Typical of AxSpA</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Sensitivity</td>
</tr>
<tr>
<td>Erosion Score ≥2</td>
<td>84.09</td>
</tr>
<tr>
<td>Fat metaplasia ≥2</td>
<td>27.27</td>
</tr>
<tr>
<td>Rackspoil ≥2</td>
<td>11.36</td>
</tr>
<tr>
<td>Ankylosis ≥2</td>
<td>4.55</td>
</tr>
</tbody>
</table>

Conclusions. SPARCC BME score of ≥3 and Erosion Score ≥2 may optimally reflect active and structural lesions typical of axSpA, respectively. MRI lesions defined by the ASAS-MRI group can be reliably detected.

O10 INFLAMMATION ON MRI OF SPINE AND SACROILIAC JOINTS IS HIGHLY PREDICTIVE OF STRUCTURAL DAMAGE IN AXIAL SPONDYLOARTHRITIS: THE 5 YEARS DATA OF THE DESIR COHORT

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1ILUMC, Leiden; 2ARC, Amsterdam, The Netherlands; 3Hospital Cochin, Paris, France

Aim. We aimed to test the possible effect of inflammation on structural damage both assessed by MRI and at the level of the spine and the SIJ.

Materials and Methods. Patients with axSpA from the DESIR cohort were included. MRI of the SIJ (MRI-SIJ) and spine (MRI-spine) were obtained at baseline, 2 and 5 years and scored by 3 central readers. Inflammation at the MRI-SIJ and MRI-spine was assessed according to ASAS definition. Structural damage in the SIJ (MRI-SIJ-STR) and spine (MRI-spine-STR) was defined by ≥3 fatty lesions. The % structural net progression (number of ‘progressors’ minus the number of ‘regressors’ divided by the total) was assessed according to CRP and ASDAS at baseline. The effect of BMI on MRI-SIJ and MRI-SIJ-STR and of BME on MRI-spine on MRI-spine-STR was evaluated using two types of GEE models: i. effect at baseline on 5 years incorporating measurements from all readers (GEE adjusted for reader); ii. effect of BMI over 5 years (longitudinal models).

Results. In total, 151 and 145 pts had complete 5-year MRI-SIJ and MRI-spine data available, respectively. The net % patients who switched from MRI-SIJ-STR negative to positive ranged from 3.8% to 24% according to the presence of objective signs of inflammation (figure). Low number of patients didn’t allow for similar analysis in the spine. In the multivariable analysis, both the presence of BME at MRI-SIJ (OR=4.2 [95% CI: 2.4-7.3]) and at MRI-spine (OR=8.9 [95% CI: 2.1-38.7]) at baseline were highly predictive of MRI-SIJ and MRI-spine structural progression respectively. Similar associations were found in the longitudinal models (table).

Conclusion. Our results show that local inflammation is strongly associated with the development of structural damage over 5 years both in the SIJ and spine in early axSpA.

Figure. Net progression from MRI-SIJ-STR negative to MRI-SIJ-STR positive (≥3 fatty lesions) according to baseline objective inflammatory markers.

<table>
<thead>
<tr>
<th>MRI SIJ+CRP+(N=15)</th>
<th>20%</th>
</tr>
</thead>
<tbody>
<tr>
<td>MRI SIJ+CRP+(N=25)</td>
<td>24%</td>
</tr>
<tr>
<td>MRI SIJ+CRP+(N=26)</td>
<td>0%</td>
</tr>
<tr>
<td>MRI SIJ+CRP+(N=78)</td>
<td>3.8%</td>
</tr>
</tbody>
</table>

Table. Effect of inflammation on MRI (ASAS definition of sacroiliitis and BME in the spine) on binary MRI structural outcomes.

<table>
<thead>
<tr>
<th>Effect of BMI on:</th>
<th>≥3 fatty lesions on MRI-SIJ</th>
<th>≥3 fatty lesions on MRI-Spine</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OR (95% CI)</td>
<td>OR (95% CI)</td>
</tr>
<tr>
<td></td>
<td>(N=144-197)</td>
<td>(N=145-197)</td>
</tr>
<tr>
<td>By GEE adjusted for reader</td>
<td>4.2 (2.4; 7.3)*</td>
<td>8.9 (2.1; 38.7)*</td>
</tr>
<tr>
<td>By longitudinal GEE adjusted for reader and repeated measurements</td>
<td>5.1 (2.7; 9.6)*</td>
<td>15.6 (4.8; 50.3)*</td>
</tr>
</tbody>
</table>

*Adjusted for CRP at baseline; †adjusted for time-varying lagged ASDAS-CRP.
DUAL NEUTRALISATION OF IL-17A AND IL-17F WITH BIMEKIZUMAB IN PATIENTS WITH ACTIVE AS: 12-WEEK RESULTS FROM A PHASE 2B STUDY

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Introduction/Aim. We report 12-week efficacy and safety of bimekizumab, a monoclonal antibody that potently and selectively neutralises IL-17A and IL-17F, in patients with active AS; the primary objective was ASAS40 dose-response relationship (Week 12) assessment.

Methods. In this ongoing 48-week study (NCT02963506: double-blind to Week 12 then dose-blind to Week 48), 303 patients with active AS (BASDAI ≥4; spinal pain ≥4 [0–10]), fulfilling modified NY criteria, were randomised 1:1:1:1:1 to subcutaneous bimekizumab 16mg, 64mg, 160mg, 320mg or placebo Q4W, for 12 weeks. Primary endpoint was ASAS40 response rate (Week 12).

Results. 297 (98.0%) patients completed the 12-week double-blind period. The majority of patients were male (84.5%) with a mean (SD) age of 42.2 (11.8) years; baseline characteristics were similar among groups (mean [SD] ASDAS-CRP: 3.9 [0.8]; one prior anti-TNF: 11.2%). At Week 12, there was a significant (p<0.001) dose-response for ASAS40. A significantly greater percentage of bimekizumab-treated patients than placebo achieved ASAS40 (Figure: p=0.005, all doses); also more bimekizumab-treated patients achieved ASAS20 (Figure; p<0.001, all doses). Compared with placebo, bimekizumab provided greater reductions from baseline for both BASDAI (Figure) and ASDAS-CRP (LS-mean [SE] change from baseline: 16mg: −1.0 [0.15]; 64mg: −1.6 [0.15]; 160mg: −1.4 [0.16]; 320mg: −1.5 [0.16]; placebo: −0.4 [0.16]; p<0.001, all doses). TEAEs were reported by 86/243 (35.4%) bimekizumab-treated patients and 22/60 (36.7%) placebo patients. No unexpected safety findings were observed; the most frequently reported events were nasopharyngitis and headache.

Conclusion. Primary and key secondary objectives were achieved: bimekizumab treatment provided clinically meaningful improvements in disease outcome measures. No new safety signals were observed.

HIGH NEED FOR ANTI-TNF THERAPY AFTER WITHDRAWAL STRATEGY IN EARLY PERIPHERAL SPONDYLOARTHRITIS

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Introduction. Treatment with TNFi in early stages of peripheral Spondyloarthritis (pSpA) results in higher rates of clinical remission, compared to treatment in more longstanding disease (1). When remission is reached, the recently updated T2T-recommendations suggest tapering of treatment. In the CRESPA-trial pSpA patients were treated with golimumab monotherapy; we demonstrated that – after reaching sustained remission – discontinuation of golimumab led to biological-free remission in 53% of patients; conversely 47% experienced a disease flare. It is currently unknown if concomitant administration of DMARDs could lead to higher rates of biological-free remission.

Aim. To explore - in pSpA patients in clinical remission - the possibility that co-medication with methotrexate would allow discontinuation of the TNFis.

Methods. The CRESPA-trial included patients with active pSpA and symptom duration <12 weeks; the primary study results have been reported previously. In the CRESPA-Extension protocol, patients were included that either did not reach remission (but had substantial improvement with golimumab treatment), or that experienced recurrence of arthritis, enthesitis or dactylitis within 1 year after discontinuation of golimumab. These patients received additional open-label golimumab 50 mg SC every 4 weeks for 2 years. At Week 104, patients were offered an additional 12 weeks of golimumab treatment, but now in combination with methotrexate 15mg weekly. At Week 116, patients in clinical remission continued methotrexate, but discontinued golimumab. Patients were prospectively followed to assess the rate of sustained biological-free clinical remission. In case of relapse of arthritis, enthesitis or dactylitis within 1 year after discontinuation of golimumab.

Results. Currently, twenty-three of the original 60 pSpA patients included in the CRESPA-trial, completed the 2-year CRESPA-Extension protocol; of these, 21 (91%) were in clinical remission at week 104 when methotrexate was added. The mean follow-up period after completion of the extension part, was 80±28w. 5 patients (24%) are still in sustained remission (n=5) under methotrexate monotherapy whereas in 16 patients (76%), golimumab needed to be re-installed because of relapse of disease activity (n=14) or development of adverse events related to methotrexate (n=2). Recurrence of disease was characterized by development of arthritis in all patients with a median of 4 tender and 3 swollen joints. In 50% (n=7) of the cases, concomitant dactylitis was present. 64% (9/14) were having concomitant pSacroiliitis which was mild since all had a BSA ≤5%. The mean time for recurrence was 28.6 weeks. Restarting golimumab treatment promptly restored clinical remission in all patients within 12 weeks.

Conclusion. In patients with pSpA in clinical remission after 2 years of golimumab monotherapy, concomitant administration of methotrexate before discontinuation of the TNFi, did not significantly raise the percentage of patients in biological-free remission. In 76% of patients, golimumab had to be restarted, underscoring the overall weak efficacy of methotrexate in pSpA.

Reference
DUTCH RECOMMENDATIONS FOR PHYSICAL THERAPY IN AXIAL SPONDYLOARTHRITIS (axSpA)


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Introduction. According to the ASAS/EULAR recommendations, physical therapy (PT), especially exercise therapy, is an essential element within the management of axSpA. In the Netherlands considerable variation in the delivery of PT was observed, suggesting suboptimal care delivery. This practice variation is likely to be related to the lack of specific recommendations regarding referral, assessment, content, and monitoring of its effectiveness and safety.

Aim. To develop practice recommendations on PT in axSpA.

Material and Methods. A taskforce of 31 experts was responsible for the recommendations. It consisted of patients (2), rheumatologists (7), physical therapists (13), policy makers (3), researchers (2) and representatives of patient organisations (4). The recommendations were based on scientific evidence, expert opinion and patient values and were formulated following a combination of systematic literature review and three expert-group meetings.

Results. In total 12 practice recommendations were formulated on indication (2), referral (2), assessment/monitoring (2), treatment (5), reporting (1) and safety (2). (Fig. 1) Three recommendations were (partly) based on level 1 evidence (Dutch Evidence Based guidelines, EBRO); others were based on lower levels combined with the opinion of experts written in literature. Agreement was reached for 11 out of 12 recommendations. Mean levels of agreement were high and varied between 8.5-9.1.

Fig. 1. Short description of the content of the Dutch recommendations for physical therapy in axial Spondyloarthritis (axSpA).

Conclusions. Using a standardized process of professional guideline development, 12 practice recommendations for PT management of patients with axSpA were developed. They can guide clinicians and physiotherapists dealing with patients with axSpA, ultimately leading to a delivery of a better care. Next steps are the ratification by relevant professional societies as well as dissemination and implementation.

Acknowledgements. This study was Funded by the Dutch Arthritis Foundation.

Reference
1. VAN DER GIESEN F et al.: Content and supervision of group exercise therapy (GET) for axial spondyloarthritis (axSpA) in The Netherlands; a nation wide survey, Ann Rheum Dis. 2017;76(2): 1479.
P1

WHICH IMAGING OUTCOMES FOR axSpA ARE MOST SENSITIVE TO CHANGE? A 5-YEAR ANALYSIS OF THE DESIR COHORT

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Introduction/Aim. Several imaging outcomes have become available to assess inflammation and structural damage over time in axSpA. However, no formal comparison of their sensitivity to change has been made in the early disease. We aimed to compare the sensitivity to change of different MRI and radiographic scoring methods in patients with early axSpA.

Methods. Patients from the DESIR cohort were included. Radiographs and MRI of the SIJ and spine were obtained at baseline, 1 year, 2 years and 5 years. Each film was scored by 2-3 readers in 3 ‘read-waves’. Outcomes measuring inflammation and structural damage both on MRI and radiographs in the spine and SIJ were assessed (Table). The analysis of change over time was performed using GEE longitudinal models separately for each outcome (‘integrated analysis’).

To allow comparisons across outcomes, these were standardized (difference between the individual score and the mean of all scores divided by the standard deviation, per reader, wave and time-point) before running the models.

Table. Standardized rate of change of imaging outcomes over 5 years of follow-up in early axSpA patients from the DESIR-cohort who fulfill the ASAS axSpA classification criteria.

<table>
<thead>
<tr>
<th>Imaging outcomes</th>
<th>Baseline score</th>
<th>Standardized rate of change/year</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>INFLAMMATORY OUTCOMES</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sacroiliitis (ASAS criteria)</td>
<td>134 (39.2%)</td>
<td>0.278</td>
</tr>
<tr>
<td>SPARC SIJ score (0-72)</td>
<td>4.7 (7.9)</td>
<td>-0.44</td>
</tr>
<tr>
<td><strong>STRUCTURAL OUTCOMES</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥ 3 erosions</td>
<td>60 (17.1%)</td>
<td>0.015</td>
</tr>
<tr>
<td>≥ 3 fatty lesions</td>
<td>56 (16.5%)</td>
<td>0.024</td>
</tr>
<tr>
<td>Number of fatty lesions and/or erosions (0-40)</td>
<td>2.9 (4.9)</td>
<td>0.111</td>
</tr>
<tr>
<td>Number of erosions (0-40)</td>
<td>1.3 (2.2)</td>
<td>0.030</td>
</tr>
<tr>
<td>Number of fatty lesions (0-40)</td>
<td>1.5 (3.5)</td>
<td>0.140</td>
</tr>
<tr>
<td>Total structural lesions (0-144)</td>
<td>3.4 (5.9)</td>
<td>0.115</td>
</tr>
<tr>
<td>Total structural lesions without sclerosis (0-104)</td>
<td>3.2 (5.8)</td>
<td>0.124</td>
</tr>
<tr>
<td><strong>SPINE</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>mNY dichotomous</td>
<td>23 (7.1%)</td>
<td>0.044</td>
</tr>
<tr>
<td>mNY 1-grade change</td>
<td>0.126</td>
<td></td>
</tr>
<tr>
<td>mNY 1-grade change and value = 1</td>
<td>0.119</td>
<td></td>
</tr>
<tr>
<td>mNY continuous grade (0-6)</td>
<td>1.7 (1.8)</td>
<td>0.043</td>
</tr>
<tr>
<td><strong>INFLAMMATORY OUTCOMES</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BME: ≥ 3 lesions</td>
<td>19 (5.6%)</td>
<td>-0.030</td>
</tr>
<tr>
<td>Number of fatty lesions</td>
<td>0.3 (0.4)</td>
<td>0.008</td>
</tr>
<tr>
<td>Number of corner bone spurs (0-2)</td>
<td>0.1 (0.2)</td>
<td>0.012</td>
</tr>
<tr>
<td><strong>TOTAL SPINE</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥ 3 syndesmophytes</td>
<td>19 (5.5%)</td>
<td>0.037</td>
</tr>
<tr>
<td>mSASSS score (0-72)</td>
<td>0.5 (1.3)</td>
<td>0.043</td>
</tr>
</tbody>
</table>

4 Agreement of ≥2 out of 3 readers for binary variables and mean (SD) of 3 readers for continuous variables from wave 3: fatty lesions, erosions, sclerosis, partial ankylosis, total ankylosis; fatty lesions, erosions, bone spurs, ankylosis, NA, not applicable.

Results. In total, 345 patients were included. MRI-SIJ inflammation was more sensitive to change compared to inflammation on the spine (table). Structural damage on the SIIJ increased over time, but with a higher change on MRI-SIJ (range: 0.015-0.274) compared to X-SIJ (range: 0.043-0.126). Notably, ≥3 Fatty lesions on MRI-SIJ was the structural outcome in the SIJ with highest sensitive to change (0.274), while ≥3 erosions was the least sensitive (0.015). Spine structural damage slowly progressed over time but, in contrast to SIIJ, radiographic outcomes were more sensitive to change than MRI structural outcomes.

Conclusion. Our data adds to the body of evidence showing that structural damage assessed in pelvic radiographs has low sensitivity to change. MRI-SIJ is a promising alternative (especially fatty lesions). In contrast, radiographic outcomes outperform MRI outcomes in the spine.

P2

WHICH SCORING METHOD DEPICTS SPINAL RADIOGRAPHIC DAMAGE IN EARLY AXIAL SPONDYLOARTHRITIS BEST? FIVE-YEAR RESULTS FROM THE DESIR COHORT

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Background. Scores capturing spinal radiographic damage have been proposed and compared in r-axSpA. In early phases of the disease, it is still unknown how these perform.

Objectives. To compare the performance of different spinal radiographic damage scoring methods in patients with early axSpA.

Methods. Five-year spinal radiographs from the DESIR cohort were scored by 3 readers (averaged) for the calculation of different radiographic methods (Table) following the OMERRACT filter, scores were compared with regard to truth, discrimination (sensitivity to change and reliability) and feasibility. Baseline status scores, and 2- and 5-year change scores were calculated, as well as the proportion of patients with a positive change (number of patients with a positive change minus number of patients with a negative change divided by all patients) above the smallest detectable change (SDC).

Practical application. The proportion of total variance explained by the patient (‘true variance’) was calculated for the change scores, as a measure of reliability, using ANOVA.

Results. In total, 699 patients (mean age 34 (SD 9) years, 47% males) were included. Mean baseline and 5-year change scores were: SASSS 0.72, mSASSS 0.71, mRASSS 0.72, BASRI-spine 0.72, BASRI-spine-thoracic 0.72, BASRI-total 0.72, BASRI-total-thoracic 0.72.

Table. Two- and 5-year change, above the smallest detectable change, across the different radiographic scoring methods.

<table>
<thead>
<tr>
<th>2-year Change &gt; SDC (N=357)</th>
<th>SDC</th>
<th>Positive change N (%)</th>
<th>Negative change N (%)</th>
<th>Net change N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SASSS (0-72)</td>
<td>0.75</td>
<td>11 (3)</td>
<td>0 (0)</td>
<td>11 (3)</td>
</tr>
<tr>
<td>mSASSS (0-72)</td>
<td>0.88</td>
<td>22 (6)</td>
<td>2 (0)</td>
<td>20 (6)</td>
</tr>
<tr>
<td>RASSS (0-84)</td>
<td>0.95</td>
<td>32 (8)</td>
<td>2 (0.5)</td>
<td>30 (8)</td>
</tr>
<tr>
<td>BASRI-spine (0-12)</td>
<td>0.59</td>
<td>30 (8)</td>
<td>14 (4)</td>
<td>16 (4)</td>
</tr>
<tr>
<td>BASRI-spine-thoracic (0-16)</td>
<td>0.59</td>
<td>35 (10)</td>
<td>16 (4)</td>
<td>19 (5)</td>
</tr>
<tr>
<td>BASRI-total (0-16)</td>
<td>0.65</td>
<td>31 (9)</td>
<td>14 (4)</td>
<td>17 (5)</td>
</tr>
<tr>
<td>BASRI-total-thoracic (0-20)</td>
<td>0.72</td>
<td>19 (5)</td>
<td>4 (1)</td>
<td>15 (4)</td>
</tr>
</tbody>
</table>

5-year Change > SDC (N=265)

<table>
<thead>
<tr>
<th>SDC</th>
<th>Positive change N (%)</th>
<th>Negative change N (%)</th>
<th>Net change N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SASSS (0-72)</td>
<td>1.17</td>
<td>30 (11)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>mSASSS (0-72)</td>
<td>1.10</td>
<td>34 (13)</td>
<td>1 (0.4)</td>
</tr>
<tr>
<td>RASSS (0-84)</td>
<td>1.19</td>
<td>44 (17)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>BASRI-spine (0-12)</td>
<td>0.74</td>
<td>32 (12)</td>
<td>1 (0.4)</td>
</tr>
<tr>
<td>BASRI-spine-thoracic (0-16)</td>
<td>0.89</td>
<td>31 (12)</td>
<td>2 (1)</td>
</tr>
<tr>
<td>BASRI-total (0-16)</td>
<td>0.73</td>
<td>33 (12)</td>
<td>1 (0.4)</td>
</tr>
<tr>
<td>BASRI-total-thoracic (0-20)</td>
<td>0.91</td>
<td>32 (12)</td>
<td>2 (1)</td>
</tr>
</tbody>
</table>

SDC: smallest detectable change; mSASSS: modified Stoke in Ankylosing Spondylitis Score; RASSS: Radiographic Ankylosing Spondylitis Spinal Score; SASSS: Stoke Ankylosing Spondylitis Spine Score; BASRI: Bath Ankylosing Spondylitis Radiology Index.

Conclusion. The SASSS 0.72, mSASSS 0.71, mRASSS 0.72, BASRI-spine 0.72, BASRI-spine-thoracic 1.17, and BASRI-total 1.24 were the most sensitive to change compared to the other scores. The BASRI-total-thoracic 0.72 was the least sensitive to change (0.40).

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respectively. SDCs and proportion of 2- and 5-year change, including net change, are presented in the Table. The mSASSS and the RASSS performed the best in terms of capturing the signal (positive change) despite the noise (negative change).

The proportion of variance explained by the patient was highest for the mSASSS and RASSS (85% for both 5-year progression scores vs 50-55% for other methods). The proportion of patient variance in the thoracic segment of the RASSS was unsatisfactory (46% for progression).

Conclusions. The existing scoring methods to assess spinal radiographic damage performed well in early phases of axSpA. The mSASSS and RASSS captured most change. There was no clear gain in additionally scoring the thoracic spine for the RASS while an increased noise was introduced. The mSASSS remains the most sensitive and valid scoring method in axSpA, including early phases of the disease.

P4

CORRELATION BETWEEN ULTRASOUND NAIL CHANGES ON PSORIATIC DISEASE AND NAIL PSORIASIS SEVERITY INDEX COMPARING WITH RHEUMATOID ARTHRITIS AND HEALTHY CONTROLS

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Introduction. The nail is intimately linked to enthesis which in turn is associated to the synovium forming a distinct organ referred as synovio-enthesal complex and nail psoriasis could be a clinical predictor of Psoriatic Arthritis (PsA). The objectives were to correlate the ultrasonography (US) changes of the nails by the Gray scale (GS) and the Power Doppler (PD) with nail psoriasis and severity index (NAPSI), to compare the ultrasonographic alterations of the nails of patients with psoriatic disease, rheumatoid arthritis and healthy controls.

Material and Methods. Cross-sectional observational study, approved by the hospital ethic committee. Finger nail and periungual US were performed in 235 nails: 137 nail psoriasis(nPs); 98 health nails of rheumatoid arthritis patients(nRA) and 100 nails of health controls(nHC). All the subjects and controls were aged between 55 and 75 years. NAPSI score:0-8. The US examination was performed by an experienced rheumatologist, with a high resolution equipment, with a linear high frequency (18 Mhz) transducer and the following features: Power-Doppler(PD) maximum frequency of 8 MHz, low filter and pulse repetition frequency(PPR)=0.5 KHz. For nail changes, semiquantitative scales were used, GS and PD (grade 0-3).

Results. For comparative analysis between nPs, nRA and nHC the Kruskal-Wallis and Student-Newman-Keuls post-test were used. Patients with psoriasis have the highest scores for USGS when compared to healthy and RA patients (He=55.4566, p-value Kruskal-Wallis=0.00001). Patients with RA and healthy did not present significant difference (H=0.3602, p-value Kruskal-Wallis=0.8352). The correlation between NAPSI and USGS/USPD were not statistically significant (r=0.0814/-0.1542, t=0.4834/-0.9234, p=0.6318/0.3621).

Conclusions. We observed a significant difference by the gray-scale between patients with psoriatic disease (nPs) and control(nRA+nHC). There was no significant difference for PD or between the sonographic findings and NAPSI. Limitations of this study are the reduced sample size and the non-availability of spectral-Doppler.

P5

PROGRESSION OF STRUCTURAL DAMAGE ON MRI OF THE SPINE AND SACROILIAC JOINTS IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS IS LIMITED: THE 5-YEAR RESULTS IN THE DESIR COHORT

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Background. Detecting radiographic structural change in axial spondyloarthritis (axSpA) patients is difficult. Magnetic resonance imaging (MRI) is an alternative for radiographs to assess this. However, longitudinal MRI-assessed structural changes are poorly studied.

Objectives. To evaluate structural changes on MRI of the SIJ(MRI-SIJ) and spine (MRI-spine) in early axSpA patients after five years.

Methods. Early (≤3 years) axSpA patients were included. MRI-SIJ and MRI-spine were obtained at baseline and 5 years and scored by 3 central readers blinded for chronology, Sacroiliac and spinal structural damage (MRI-SIJ-STR resp. MRI-spine-STR) were defined according to 3 binary rules (A1:a3 fatty lesions;B1:a3 erosions;C1:a5 fatty lesions and/or erosions) and 3 continuous scores (A2:number of fatty lesions;B2:number of erosions;C2:number of fatty lesions/erosions). For binary outcomes, agreement of at least 2 out of 3 readers and the % of net-progression defined structural change. For continuous outcomes, the mean of the 3 readers and the difference between year 5 and baseline was calculated.

Results. 151 and 145 patients had complete MRI-SIJ and MRI-spine available, respectively. The percentages of net-progression at SIJ-level/figure were 7.9%, 0.7% and 6.6% for the binary outcomes A1, B1 and C1 respectively. The percentage of ‘improvement’ (4.6%) was almost similar to the percentage of ‘worsening’ (5.3%) for definition B1(a3 erosions); while no ‘improvements’ were
seen for definition A1 (≥3 fatty lesions). Comparable differences were seen for mean (standard deviation) change of the 3 MRI-SIJ-STR continuous outcomes (Δ20.83 (2.20); Δ20.20 (1.39); C2:1.02 (2.60); all p<0.01). Longitudinal MRI-spine-STR net change was almost absent (A1:0.7%; B1: 0.0%; C1:0.7%) for binary outcomes, and small considering definition A20.14 (0.48); p<0.01) and C2 (0.18 (0.52); p<0.01) but absent for definition B2 (0.030 (0.24); p=0.109).

Conclusion. Patients with early axSpA show modest structural progression on MRI-SIJ and fatty lesions are more sensitive to change compared to erosions. In this early axSpA population, MRI-detected structural progression in the spine is very limited.

P6
MAGNETIC RESONANCE IMAGING OF THE CERVICAL SPINE IN PATIENTS WITH RHEUMATOID ARTHRITIS AND ANKYLOSING SPONDYLITIS PRESENTING WITH CHRONIC NECK PAIN – A SYSTEMATIC COMPARISON OF CLINICAL ASSESSMENTS
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Background. Despite the differences in pathogenesis, neck pain associated with functional limitation and impaired mobility of the cervical spine is a frequent clinical symptom of patients with rheumatoid arthritis (RA) and ankylosing spondylitis (AS).

Objective. To directly compare inflammatory and structural findings obtained by magnetic resonance imaging (MRI) in patients with RA and AS who present with chronic neck pain, and to correlate MRI findings with clinical measurements.

Methods. A total of 120 patients (60 RA and 60 AS) were consecutively included in the study if they had chronic neck pain (duration >3 months). All patients had clinical examinations for neck function and mobility and were asked to fill in disease-specific questionnaires. They also had laboratory examinations (CRP, ESR) and MRI of the cervical spine (CS) using contrast-enhanced MRI sequences (T1 pre- and post-Gadolinium, sagittal and axial images). A total of 107 patients (59 RA with 295 and 48 AS with 240 vertebral segments) could be finally evaluated. An experienced rheumatologist examined all patients blinded to diagnosis and clinical assessments evaluated the MRIs by describing the anatomical structures of the CS (vertebral body, intervertebral disc, facet joints) and the pattern of inflammatory activity in the bone marrow (vertebral edges vs. vertebral endplates).

Results. The RA group included more females (66.1%) and older patients (58.6±11.4 years) in comparison to AS (68.8% males, mean age 47.9±13.1 years), while there were no differences in the duration of neck pain. AS patients reported higher mean levels of neck pain on a 0-10 numerical rating scale (5.0±3.6) as compared to RA patients (3.0±3.1; p=0.003), while the Northwick pain questionnaire did not reveal any differences. There were numerically more patients with AS (n=11, 22.9%) than RA (n=9, 15.3%); (p=0.166) with bone marrow edema (BME) at the vertebral edges. The majority of lesions was located in the lower CS. In contrast, more patients with RA (n=18, 30.5%) than AS (n=5, 6.3%) had erosive osteochondrosis with endplate BME (p=0.002). Atlantoaxial synovitis was found in only 1 patient with RA (1.7%), while inflammatory changes around the dens axis were found in 2 (3.4%) and atlantoaxial synovitis in 5 (8.5%) RA patients but not in AS patients. In comparison, erosive changes in the dens axis region were found in 3 RA (5.1%) vs. 2 AS (4.1%) patients.

No major differences related to the presence of facet joint osteoarthritis was found (78% in RA vs. 65% in AS). The prevalence of facet joint osteoarthritis was the only imaging finding correlating with clinical symptoms: r=0.259 (p=0.049) for RA and r=0.416 (p=0.003) for AS, respectively. Similarly, only facet joint osteoarthritis correlated with restriction of cervical rotation in patients with AS (r=0.471, p=0.001).

Conclusion. Both BME and chronic changes of the lower part of the CS but not of the atlantoaxial region are seen in patients with RA and AS who present with chronic neck pain. The pattern of BME involvement in patients with RA vs. AS was different. Facet joint osteoarthritis was the only imaging finding that correlated with the magnitude of neck pain, in AS it also correlated with impaired cervical rotation.

P7
ANALYSIS OF THE DIFFERENT VALUE OF MAGNETIC RESONANCE IMAGING CHANGES IN THE SACROILIAC JOINTS FOR A DIAGNOSIS OF AXIAL SPONDYLOARTHITIS AS JUDGED BY RHEUMATOLOGISTS AND RADIOLOGISTS
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Background. A classification of axial spondyloarthritis (axSpA) by the imaging arm of the ASAS criteria relies partly on the detection of a bone marrow edema (BME) in the magnetic resonance imaging (MRI) of the sacroiliac joints (SIJ) suspicious of SpA (1).

Objective. To evaluate different types of MRI changes possibly relevant for a diagnosis of axSpA as judged by radiologists taking the rheumatologist’s diagnosis as gold-standard.

Methods. Consecutive patients <45 years were included if they presented in a specialized rheumatologic center with chronic low back pain (duration >3 months). Patients underwent a complete diagnostic workup including MRI of the SIJ. All clinical and laboratory information including images but no radiological reports was available for experienced rheumatologists to make a diagnosis of axSpA or non-axSpA. In parallel, two experienced musculoskeletal radiologists, blinded to patients’ demographics and symptoms (except for back pain) evaluated all MR images without knowledge of the rheumatologist’s diagnosis, by quantification of BME, fat metaplasia, erosions, sclerosis and ankylosis based on the Berlin SIJ score. The radiologists also stated whether the patient is likely to have axSpA or not, solely based on MRI findings.

Results. A total of 100 patients were recruited. The rheumatologist diagnosed axSpA in 54 patients (mean age 31.5±8.0 years, 77.8% HLA-B27+, mean symptom duration 36.4±2.0 months), while 46 patients were diagnosed as non-specific back pain (age 33.6±7.1 years, 17.4% HLA-B27+, mean symptom duration 25.5±31.6 months). According to the radiologists, 38 patients were identified as axSpA, 34 of which were also diagnosed as axSpA by the rheumatologist (overall agreement with the clinical diagnosis: 63%), and 4 patients were thought to have axSpA by the radiologist but not by the rheumatologist (disagreement with the clinical diagnosis: 8.7%). Similarly, the quantification of MRI showed higher scores in patients diagnosed as axSpA by the rheumatologist (Table I). Only few patients had sclerosis or ankylosis.

From the radiologist’s perspective, the calculated odds ratio (OR) for identification of axSpA by MRI only was 3.1 (95% CI:1.4-7.1) for the presence of BME, 3.5 (95% CI:1.4-9.0) for fat metaplasia, 2.8 (95% CI:1.1-7.0) for erosions, 2.0 (95% CI:1.0-5.5). For the combination of BME and any structural change, the OR was 3.7 (95% CI:1.6-8.5).

Conclusions: This study reveals a discrepancy between the rheumatologist’s and the radiologist’s identification of axSpA, confirming that a diagnosis of axSpA in daily practice should not rely on imaging findings only. Nevertheless, the overall specificity of the radiologists was acceptable, although the sensitivity was relatively low. These data suggest also that not only BME but also fat metaplasia and erosions are of value to diagnose axSpA, beyond classification. The combination of MRI changes seems to enhance the discriminative diagnostic performance. Finally, it will be important to define clinically relevant cut offs for the MRI scores.

Table I. Mean/median scores ± standard deviation for inflammatory and chronic lesions based on the Berlin SIJ score

<table>
<thead>
<tr>
<th>Lesion type</th>
<th>axSpA</th>
<th>non-SpA</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean/SD</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total score</td>
<td>12.3±11.8</td>
<td>4.4±4.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>BME</td>
<td>3.3±3.8</td>
<td>0.7±1.5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Fat metaplasia</td>
<td>3.4±5.4</td>
<td>0.7±3.0</td>
<td>p=0.004</td>
</tr>
<tr>
<td>Erosions</td>
<td>3.2±5.8</td>
<td>0.7±2.1</td>
<td>p=0.011</td>
</tr>
</tbody>
</table>

Median Sclerosis or Ankylosis 0.0 0.0 --

Reference
P8
INFLAMMATORY LESIONS AND STRUCTURAL CHANGES OF SACROILIAC JOINTS ON MRI IN EARLY AXIAL SPONDYLOARTHRITIS: 2-YEAR FOLLOW-UP STUDY

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Background. Dynamic monitoring of changes in sacroiliac joints (SIJ) MRI in patients with early axSpA will provide a better understanding of the development and further progression of the disease in initial stages. 

Aim. To describe how inflammation and structural changes of sacroiliac joints (SIJ) on MRI in patients with early axSpA evolves over 2-year follow-up.

Materials and Methods. The research included 68 pts with early axSpA (ASAS criteria, 2009) from Moscow CORSAR cohort with disease duration <5 years, age onset <45 years and at least 2 years follow-up. MRI of SIJ was conducted at baseline and after 2 years. Inflammatory lesions and structural changes of SIJ on MRI were determined using ASAS/OMERACT recommendations.

Results. 15 (22.0%) pts at baseline were with bone marrow edema (BME) on SIJ MRI. After 2 years in 6 (40%) pts BME became in fat metaplasia, in 5 (33.3%) - fat metaplasia appeared in addition to BME. In 2 (33.3%) pts BME disappeared, and in 2 (33.3%) pts BME remained unchanged. At baseline 19 (28.0%) pts at baseline were with structural changes on SIJ MRI as fat metaplasia. After 2 years 1 of them (5.2%) had BME in addition to fat metaplasia, and 18 (48.6%) pts had no changes.

Initially, according to SIJ MRI, there were 24 (35.3%) pts with a combination of inflammatory and structural changes (BME and fat metaplasia). After 2 years in 1 (4.1%) patient left signs of fat metaplasia and remained only BME, in 15 (62.5%) pts left signs of BME and remained only fat metaplasia. In 8 (33.3%) pts existing changes remained without dynamics.

At baseline, 10 (14.7%) patients had no changes on SIJ MRI. After 2 years, 6 (60%) pts unchanged in SIJ MRI and 4 (40%) - developed fat metaplasia.

Conclusions. Most pts with early axSpA with fat metaplasia on SIJ MRI at baseline remain unchanged after two years.

P9
IMPACT OF DOSE TAPERING OF TUMOUR NECROSIS FACTOR INHIBITOR ON ACHIEVING INACTIVE DISEASE AS RECOMMENDED BY ‘T2T’ STRATEGY IN AXIAL SPONDYLOARTHRITIS: A PROSPECTIVE, NATIONWIDE COHORT STUDY

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Objectives. To compare the efficacy of tapering tumour-necrosis factor inhibitor (TNFi) with that of standard-dose TNFi treatment in patients with axial spondyloarthritis (axSpA).

Methods. It is a prospective, nationwide cohort study including 776 axSpA patients receiving TNFi for at least 1 year with a 3-year observation. Effect of dose tapering on longitudinal disease activity was analysed 1) by comparison of two patient groups according to their mean dose quotient (DQ) of TNFi during the observation (individual level, control group versus tapering group) and 2) by comparison of 1-year intervals stratified by relevant DQ (time level). Primary outcome was achieving ASDAS in inactive disease (ASDAS-CRP ≤1.3) in a relevant interval.

Results. In the individual level, baseline and longitudinal ASDAS-CRP were comparable between the two groups. Among a total of 1565 intervals, ASDAS inactive disease was achieved in 665 (42.6%) ones with no difference according to the follow-up time. In the time level, interval with reduced DQ showed comparable odds for achieving inactive disease compared to those with full-dose TNFi (adjusted OR=1.09, 95% CI 0.89 to 1.33). However, the probability of achieving target was significantly decreased if DQ of interval was lower than 0.5 (adjusted OR=0.43 [0.22 to 0.85]). The same analysis performed in the post-matched population (n=126 in both groups) in which ASDAS-CRP measured just prior to the first dose reduction (tapering group) and that measured in the relevantly defined visit (control group) were matched also showed a consistent result.

Conclusion. Tapering dose of TNFi, but not by less than 50% of standard-dose, showed comparable efficacy in achieving optimal treatment target in axSpA.

P10
DIAGNOSTIC VALUE OF MRI IN NON-RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS

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Introduction/Aim. Few studies showed signs of inflammation at the MRI of the sacroiliac joints (SIJ) or spine in only 30% of the non-radiographic axial spondyloarthritis (nr-axSpA) patients1-3. Aims: 1) to evaluate inflammation at the MRI of the SIJ/spine in TNF naive nr-axSpA patients, 2) estimate constant selection of baseline MRI after 6 months and 3) evaluate gender differences.

Methods. Consecutive patients with inflammatory back pain who were either the distance between the anterior joint capsule and the femoral neck distance >7 mm).

Results. Included were 70 patients, of whom 37 (53%) females. Half of the patients (n=36/92, 52.2%) showed signs of inflammation on the first MRI: 27/90 (30.0%) SIJ and 14/46 patients (30.4%) at the spine and 4 patients (5.8%) on both sites and one patient missed the baseline MRI. Males had more often a positive MRI compared to females 62.5% vs. 43.2%. Patients with a positive MRI showed a median SPARCC score for SIJ of 8.0 (IQR: 1.8–23.5, higher in males) and for spine 6.5 (IQR: 2.8–10.8, higher in males). Only 4/35 patients (12.1%) showed a positive MRI after six months.

Conclusion. Fifty percent of the patients with nr-axSpA and high disease activity showed inflammatory lesions at the MRI of the SIJ and/or spine, which occurred more often in males compared to females. In most cases (87.9%) a MRI without inflammatory lesions remained negative after 6 months, indicating that a second MRI after a short period is not valuable.

Reference
1. BRAUN J et al.: RMD Open 2017; 3(1): e000430
2. Nasonova Research Institute of Rheumatology, Moscow, Russia

Introduction. Hip joint (HI) involvement is one of the most common extra-axial manifestations of ankylosing spondylitis (AS).

Objective. To correlate the clinical features of coxitis in AS pts with radiographic and ultrasonographic findings.

Materials and Methods. 125 consecutive AS pts (mean age 31.7±12.7 y; meeting modified NY criteria) with clinical symptoms of coxitis (presence of pain in hip joint (HI) with or without HI functional limitations (FL)), were examined.

Results. Mean age at onset was 30.8±9.6 y. The following evaluations were made: BASDAI, ASDAS-CRP, BASFI, inter-malleolar distance (IMD), radiological HI changes (BASRI Hip), ultrasound examination (US) of symptoms of coxitis - diagnostic value of MRI in non-radiographic axial spondyloarthritis.

Conclusion. The damage to the hip joint revealed during a x-ray examination was more often detected at a greater prescription of coxitis and was accompanied by an increase in functional disorders.
P12
MRI ASSESSMENT OF HIP JOINTS INVOLVEMENT IN ANKYLOSING SPONDYLOITIS PATIENTS

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Introduction. According to the epidemiological study, in Russia in patients with ankylosing spondylitis (AS) hip joint damage was clinical detected in 46% of cases, but was the cause of endoprosthetic in 7% of cases.

Objective. To compare clinical manifestations with the results of magnetic reso-
nance imaging (MRI) of the hip joints (HJ) in patients with AS.

Material and Methods. 125 consecutive AS pts (mean age 31.7±12.7 y; meet-
in modified N.Y criteria) with clinical symptoms of coxitis (presence of pain in hip joint (HJ) with or without HJ functional limitations (FL)), were examined. Mean age at disease onset was 30.8±9.6 y. The following evaluations were made: BASDAI, ASDAS-CRP, BASHI, inter-malleolar distance (IMD), MRI in T1 and STIR regimens.

Results. Acute inflammatory changes, such as osteitis and/or synovitis, were detected in 88% (110) of MRI patients. Most patients (85%; n=106) had synovi-
tis according to MRI. Osteitis was found in 31%, and the combination of osteitis and synovitis - in 28% of patients. It is also worth noting that in 7% of cases, there were no inflammatory changes according to MRI, but there were signs of fatty degeneration which are usually combined with stage 3-4 on BASHI hip.

According to the comparative analysis of patients with synovitis and a combina-
tion of synovitis and osteitis, there were no significant differences in the clinical picture between the patients. In 17% (18 patients) of MRI cases the changes were asymptomatic; i.e. there were no clinical signs of coxitis.

Conclusion. MRI allowed to clarify the cause of the pain and limitations of move-
ment in HJ with AS, determine the patient has inflammatory changes, including in the absence of radiographic changes in these joints. Further research to clarify the relationship of clinical manifestations of coxitis (pain level) from MRI data.

P13
FACTORS ASSOCIATED WITH CHANGES IN VOLUMETRIC BONE MINERAL DENSITY IN PATIENTS WITH ANKYLOSING SPONDYLYTIS – A FIVE-YEAR PROSPECTIVE STUDY USING HRpQCT

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Introduction/Aim. Cortical and trabecular volumetric bone mineral density (vBMD) can be assessed with high-resolution peripheral quantitative computed tomography (HRpQCT). There is no prior prospective study using HRpQCT in AS patients. Our aims were to investigate changes over 5 years in peripheral vBMD and to assess factors associated with the changes in AS patients.

Methods. HRpQCT of the ultra-distal radius and tibia were performed in 54 male AS patients (NY criteria) at baseline and after 5 years, mean baseline age 48±14 years. The patients were also assessed with blood samples and questionnaires. Univariate and multiple linear regression analyses were performed to find vari-
ables associated with percent changes in vBMD.

Results. At tibia, there were significant decreases in both cortical and trabecular vBMD, mean (SD) percent change -1.0 (1.9) and -2.7 (5.0) (<0.001) respec-
tively. At radius, there was a trend for decreases in trabecular vBMD, mean (SD) change -2.0 (5.9) % (p=0.095), whereas no significant change in cortical vBMD was observed. In multiple linear regression analyses, an increase in ASDAS up from baseline to follow-up was independently associated with a decrease in cortical vBMD at tibia (B -0.91, 95%CI -1.34 to -0.47) and radius (B -0.57, 95%CI -1.03 to -0.10). Use of TNF-inhibitors was associated with increases in cortical vBMD (B 1.09, 95%CI 0.24 to 1.93), whereas use of corticosteroids was associated with decreases in cortical vBMD (B -2.15, 95%CI -3.48 to -0.82). Also, at both sites, older age was negative for cortical vBMD and smoking for trabecular vBMD. Higher baseline BMI was associated with increases in cortical tibia vBMD.

Conclusion. Over five years, these male AS patients decreased in vBMD at tibia. An increase in disease activity was found to have a negative effect on the corti-
cal bone at tibia and radius. Use of TNF-inhibitors had a positive effect whereas corticosteroids had a negative effect on cortical bone at tibia.

P14
THE PHYSIOLOGICAL CHANGES OF THE ENTHESIS IN RESPONSE TO AGE, BODY MASS INDEX AND PHYSICAL ACTIVITY – AN ULTRASOUND STUDY IN HEALTHY PEOPLE

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Introduction/Aim. Entheses are continuously exposed to biomechanical stress and enthesis damage. Use of ultrasound may not reflect an underlying inflammatory spondylarthropathy in all cases. In this study, we aimed to determine the preva-
ience of sonographic enthesal abnormalities in healthy subjects and explore fac-
tors that are contributing to the occurrence and severity of these findings.

Materials and Methods. Eighty healthy subjects who had no joint pain, history of rheumatic condition or recent joint trauma were enrolled. Ultrasound scans of the insertions of triceps, quadriceps, Achilles tendons and plantar fascia and the origins/insertions of patellar tendons were performed by a single sonographer. Each enthesis was scored using a semi-quantitative scale (0-3) for sonographic features of enthesitis: hypoechogenicity, thickening, Doppler signals, entheso-
phytes, erosions and calcifications. The correlation between the total enthesis score and various demographic and lifestyle factors was evaluated.

Results. Doppler signals and erosions were detected in 10% and 6.25% of the participants, respectively. Thickening was the most frequent lesion within the enthesis, and presence of hypoechogenicity was also noted in 3.125% of the participants. Sonographic thickening and erosions were positively correlated (p=0.005). Additionally, Doppler signals were more common in men (12.5%) than in women (4.375%, p=0.022). Similarly, the score of enthesis enthesitis was higher in men than in women (14.75±11.6 vs 9.02±9.6, p=0.010), similar to partici-
pants who were exercising or sedentary (<15.3±11.1 vs 7.9±4.8, p=0.005). Additionally, men had higher scores than women (15.73±11.6 vs 8.06±8.2, p=0.001).

Discussion. There are changes within the enthesis associated with aging and in-
creased mechanical stress, not necessarily reflecting a pathology leading to any symptoms. Men and smokers, both of which are risk factors for radiographic
male factor in ankylosing spondylitis, have higher entheseal scores on ultrasound. The effect of these factors on the enthesis may be an explanation for the severe abnormal response on the spine in ankylosing spondylitis.
P16
SIMPLE RADIOGRAPHIC FINDINGS OF ACHILLES TENDON IN SYMPTOMATIC AND ASYMPTOMATIC POSTERIOR HEEL IN ANKYLOSING SPONDYLITIS

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Han Yang University Medical Center, Seoul, Korea

Aim. Abnormally thickened Achilles tendon (AT) may imply significant pathologies including inflammation or degeneration. Achilles’ enthesitis is generally highlighted in posterior heel pain of ankylosing spondylitis (AS). The purpose of current study is to assess simple radiographic changes on AT’s shadow not only at its insertion but also interstitial portion.

Materials and Methods. 34 AS patients with unilateral (24) and bilateral (10) posterior heel pain were enrolled purposefully to evaluate differences between symptomatic and asymptomatic heels. Standing lateral digital radiographs of their foot were reviewed. Thickness of AT was measured at near its insertion as well interstitial area at ankle level. Retrocalcaneal recess obliteration (RRO) was assessed as AT’s enthesitis and its correlation with abnormally thickened AT (>8 mm at interstitial area and >5.5 mm at near insertion as previously reported) was evaluated.

Results. In unilateral pain group, symptomatic feet showed 21 (88%) RRO and abnormal thickness in 21 (88%) and 14 (58%), respectively at insertion and ankle level, and thickness of AT was 7.4±1.7 mm at insertion and 8.2±1.3 mm at ankle level. Contrarily, asymptomatic feet showed 3 (12%) RRO, and abnormal thickness in 5 (20.8%) and 4 (16.7%), respectively at insertion and ankle, and thickness of AT was 5.8±1.6 mm at insertion and 7.0±1.2 mm at ankle level. Bilateral group showed 16 (80%) RRO and abnormal thickness in 17 (85%) and 9 (45%), respectively at insertion and ankle, and thickness of AT was 6.9±1.5 mm at insertion and 8.1±1.4 mm at ankle level. There were significant differences in thickness of AT and also rate of abnormal thickness between symptomatic and asymptomatic feet. (p<0.05).

Conclusion. In simple radiographic alterations on AT of AS, RRO and thickened AT near to its insertion are strongly related to current painful posterior heel. In addition, thickened interstitial area of AT would be one of sources for posterior heel pain in AS which needs further investigation.

P17
DIAGNOSTIC ASCERTAINMENT OF AXIAL SPONDYLOARTHRITIS IN PATIENTS PRESENTING WITH UNDIAGNOSED BACK PAIN: WHAT IS THE IMPACT OF MRI IN RHEUMATOLOGICAL PRACTICE?


Introduction/Aims. We aimed to determine whether any particular patient features are associated with rheumatologist ordering of MRI and the impact of MRI evaluation on diagnostic ascertainment of axial SpA in patients presenting with undiagnosed back pain to rheumatologists.

Method. Consecutive patients ≤45 years of age with ≥3 months undiagnosed back pain with any one of psoriasis, acute anterior uveitis (AAU), or colitis untreated by anti-inflammatory medications were assessed plus the degree of diagnostic reclassification after evaluation. Differences in patients between those who did or did not have MRI examination were assessed plus the degree of diagnostic reclassification after MRI evaluation was ordered significantly more frequently in those with inflammatory type back pain (p=0.004), when radiography was mNY- (p=0.005) and in those without Crohn’s colitis (p=0.003) but not related to back pain severity, NSAID response, or CRP level. 24 (18.6%) were recategorized from SpA to non-SpA and 4 (3.1%) from non-SpA to SpA.

Conclusions. In a setting of undiagnosed back pain, use of MRI is primarily driven by negative radiography. MRI was primarily helpful in ruling out SpA and reducing false positives.

P18
MRI LESION DEFINITIONS IN AXIAL SPONDYLOARTHRITIS: A CONSENSUS REAPPRAISAL FROM THE ASSESSMENTS IN SPONDYLOARTHRITIS INTERNATIONAL SOCIETY (ASAS)


Introduction/Aims. To evaluate the literature describing the spectrum of MRI lesions in axSpA and to generate a consensus update on standardized definitions.

Methods. The ASAS MRI group reviewed the literature and decided which definitions would be retained, modified, or newly defined.

Results. For definitions denoting signs of activity in the SIJ, there are no revisions to the most current ASAS definition of a positive MRI, while capsulitis and enthesitis are revised. A new definition, joint space enhancement, replaces the term ‘synovitis’ and denotes increased signal on contrast-enhanced images in the joint space. For structural change, the revised definition for a fatty lesion incorporates morphologic characteristics, and for erosion requires both loss of cortical bone and adjacent marrow matrix. A new definition, fat metaplasia in the joint space (‘backfill’), denotes the reparative change at the site of erosion when signs of activity recede. The new definition for ankylosis stresses the continuity of bright marrow signal across the joint space. Spinal lesion definitions are divided into those occurring in central and lateral sagittal slices. The revised definition of vertebrae corner inflammatory lesion divides this into a regular type (A) and dimorphic (type B) lesion. A new definition for corner erosion requires both loss of cortical bone and adjacent marrow matrix. New definitions for new bone growth require bright signal on T1W images extending from the vertebral corner marrow or endplate.

Conclusions. The ASAS MRI group has generated a consensus-based update on MRI lesions in axSpA.

P19
ABILITY OF MAGNETIC RESONANCE IMAGING TO PREDICT REMISSION AND RELAPSE IN PERIPHERAL SPONDYLOARTHRITIS


Introduction. Whole-body magnetic resonance imaging (WB MRI) could offer additional information regarding the inflammatory status of joints, entheses and soft tissues in peripheral spondyloarthritis (pSpA).

Aim. To determine the value of A) WB MRI in relation to clinical remission in pSpA and B) subclinical inflammation, detected by WB MRI, at remission in predicting relapse in pSpA.

Methods. 60 early pSpA patients underwent a modified WB MRI at baseline and a clinical remission when treatment was withdrawn. The WB MRI was performed by scanning multiple SpA-specific locations. Several sites of pelvis and lower limbs were evaluated for bone marrow edema (BME), synovitis and soft tissue inflammation (STI) by 3 readers, giving a score of 0–3. For each site a
mean of the scores of the 3 readers was calculated. For each patient at each time point, we calculated a sum score for synovitis, STI, BME and a total sum score. Results. Patients reaching remission had lower baseline MRI synovitis (3.0 vs. 3.6), STI (2.1 vs. 2.2), BME (1.8 vs. 2.9) and total sum scores (7.0 vs. 8.7) than the non-remission group. However, these differences lacked statistical significance. At remission 22% and 24% patients had residual talocural and subtalar synovitis respectively. There was no statistically significant difference between patients who relapsed after treatment withdrawal and those who remained in remission concerning synovitis, BME and STI sum scores at remission.

Conclusions. There was a significant difference in inflammatory burden on baseline WB MRI between patients going into remission and those with ongoing disease activity. At remission, a substantial part of the participants showed residual ankle synovitis on MRI. However, residual inflammatory lesions detected by MRI did not differ significantly between patients who relapsed after treatment withdrawal and those in ongoing remission.

P20

CLINICAL EVALUATION CORRELATES POORLY WITH ULTRASOUND AND MAGNETIC RESONANCE IMAGING OF JOINTS AND ENTHESES IN EARLY PERIPHERAL SPONDYLOARTHITIS

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Introduction. Evaluation of tenderness at the site of an enthesis with a standard palpation procedure remains the gold standard for detection of enthesitis. However, inter/intra-observer variability is high. Imaging could avoid these drawbacks.

Aim. To compare the performance of ultrasound (US) and magnetic resonance imaging (MRI) with clinical examination (CE) of joints and entheses in peripheral spondyloarthritis (psSpA).

Methods. 60 early pSpA patients, participating in the CRESPA trial, were evaluated. CE included local/tender joint count, dactylitis and enthesitis count. All patients underwent Power Doppler (PD)US of entheses and knee, talocural and subtalar joints. Synovitis was scored according to the OMERACT-EULAR-US composite PDUS scale, giving a score of 0–3. Enthesal sites were evaluated for hypoechogenicity and intraenthesis Doppler signal and were scored 0–3. On MRI bone marrow edema, synovitis and soft tissue inflammation were scored (scale 0–3) by 3 readers at several anatomical sites of pelvis and lower limbs.

Results. Synovitis detected by US and MRI was most prevalent at knee joints. A discrepancy was noted between talocural synovitis detected by CE, US and MRI. Enthesitis was most prevalent at Achilles tendon and plantar fascia. Regarding enthesitis, agreement between CE and US ranged from no (kappa: 0.082) to moderate agreement (kappa 0.562). The highest agreement was observed at the Achilles tendon (left 0.511, right 0.350) and plantar fascia (left 0.321, right 0.507). MRI did not correlate better with CE than US (kappa from 0.077 to 0.446). Correlation between MRI and US was poor and only in the Achilles tendon moderate (range -0.106 to 0.656).

Conclusions. There was a weak agreement between CE and imaging in detecting enthesitis. Overall, US detects less enthesitis compared to CE, while MRI detects more.

P21

CONSENSUS DEFINITIONS FOR MRI LESIONS IN THE SACROILIAC JOINTS OF PATIENTS WITH AXIAL SPONDYLOARTHRITIS: FIRST ANALYSIS FROM THE ASSESSMENTS IN SPONDYLOARTHRITIS INTERNATIONAL SOCIETY CLASSIFICATION COHORT

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1University of Alberta, Canada; 2University of Copenhagen, Denmark; 3Rheumazentrum Ruhrgebiet Herne, Germany; 4University College London, UK; 5University of Southern Denmark; 6Charité Universitätsmedizin Berlin, Germany

Introduction/Aims. There has been no central reader evaluation of MRI scans from the ASAS Classification Cohort (ASAS-CC) to determine the spectrum of MRI lesions in the SIJ in this cohort. We aimed to compare the frequencies of active and structural lesions on MRI images from the ASAS-CC according to the recent ASAS MRI consensus definitions update.

Methods. Lesions were recorded in an eCRF that comprises global assessment (lesion present/absent) and detailed scoring (SPARCC SIJ inflammation, SPARCC SIJ structural). Wording of lesions defining active and structural lesions typical of axSpA was the same as in the original ASAS-CC eCRF permitting comparisons between central and local readers. MRI images were available from 278 of the 495 cases who had MRI and were assessed by 7 readers. Comparison of active and structural lesion frequencies was assessed descriptively. Detection of active lesions typical of axSpA was compared between central and local readers.

Results. The percentage of cases with active lesions typical of axSpA recorded by central readers (28.4% by majority read) was lower than the 40% reported by local readers (Table I). This was similar to the frequency of structural lesions typical of axSpA (28.6% by majority read) (Table II). 11.2% had subchondral inflammation but not typical of axSpA, 0.3% had active lesions typical of axSpA without subchondral inflammation. Erosion was the most frequently observed structural lesion (25.2%) followed by fatty lesion (19.8%).

Conclusions. In this first central reader analysis of MRI images from the ASAS-CC we demonstrate similar frequencies of active and structural lesions typical of axSpA, erosion as a common lesion, some degree of false positive subchondral inflammation, and a lower frequency of active lesions typical of axSpA than noted by local readers.

Table I. Frequencies of active MRI lesions in the SIJ in the ASAS-CC.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mean% (Range) of cases*</th>
<th>Number% of cases*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Active lesions typical of axSpA</td>
<td>31.5 (24.5-38.5)</td>
<td>79 (28.4%)</td>
</tr>
<tr>
<td>Active lesions typical of axSpA and level of confidence a³ (scale of 1-4)</td>
<td>22.4 (18.0-27.3)</td>
<td>58 (20.9%)</td>
</tr>
<tr>
<td>Active lesions typical of axSpA and meets ASAS definition for positive MRI</td>
<td>30.0 (22.6-37.4)</td>
<td>71 (25.5%)</td>
</tr>
<tr>
<td>Meets ASAS definition for positive MRI and level of confidence a³ (scale of 1-4)</td>
<td>23.1 (18.3-30.2)</td>
<td>58 (20.9%)</td>
</tr>
<tr>
<td>Subchondral inflammation</td>
<td>43.5 (38.5-51.1)</td>
<td>110 (39.6%)</td>
</tr>
<tr>
<td>Site of erosion cavity inflammation</td>
<td>8.9 (5.8-12.6)</td>
<td>10 (3.6%)</td>
</tr>
<tr>
<td>Capsulitis</td>
<td>4.0 (1.8-7.2)</td>
<td>6 (2.2%)</td>
</tr>
<tr>
<td>Joint Fluid</td>
<td>14.1 (6.8-20.5)</td>
<td>11 (4.0%)</td>
</tr>
<tr>
<td>Enthesitis</td>
<td>7.5 (1.8-12.2)</td>
<td>6 (2.2%)</td>
</tr>
</tbody>
</table>

(*Individual data from 6 readers; *majority reader (≥4) data).

Table II. Frequencies of structural MRI lesions in the SIJ in the ASAS-CC.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mean% (Range) of cases*</th>
<th>Number% of cases*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Structural lesions typical of axSpA</td>
<td>31.4 (23.5-39.9)</td>
<td>68 (28.6%)</td>
</tr>
<tr>
<td>Structural lesions typical of axSpA and level of confidence a³ (scale of 1-4)</td>
<td>20.8 (14.0-29.4)</td>
<td>46 (19.3%)</td>
</tr>
<tr>
<td>Subchondral sclerosis</td>
<td>24.2 (10.1-39.1)</td>
<td>36 (15.1%)</td>
</tr>
<tr>
<td>Erosion</td>
<td>27.9 (23.1-32.8)</td>
<td>60 (22.9%)</td>
</tr>
<tr>
<td>Fatty lesion (any)</td>
<td>23.5 (18.1-29.8)</td>
<td>47 (19.8%)</td>
</tr>
<tr>
<td>Fatty lesion (&gt;1cm)</td>
<td>11.7 (8.0-15.6)</td>
<td>22 (9.2%)</td>
</tr>
<tr>
<td>Bone bud (yes)</td>
<td>2.1 (0.4-3.8)</td>
<td>1 (0.4%)</td>
</tr>
<tr>
<td>Fat metaplasia in joint space (yes)</td>
<td>8.1 (4.2-10.5)</td>
<td>11 (4.6%)</td>
</tr>
<tr>
<td>Ankylosis</td>
<td>1.1 (0.8-3.8)</td>
<td>5 (2.1%)</td>
</tr>
</tbody>
</table>

(*6 readers; *majority reader (≥4) data).
P22
THE CONTRIBUTION OF STRUCTURAL MRI LESIONS TO DETECTION OF SACROILIITIS IN PATIENTS IN THE ASAS CLASSIFICATION COHORT
1University of Alberta, Canada; 2CaRE Arthritis; 3University of Copenhagen; 4University of Southern Denmark; 5Charité Universitätsmedizin Berlin, Germany; 6University College London, UK; 7Charité Universitätsmedizin Berlin, Germany

Introduction/Aims. There has been no data reported on the occurrence of structural lesions in the ASAS classification cohort (ASAS-CC). We assessed the added contribution of structural lesions in the SIJ to the evaluation of sacroiliitis.

Methods. Lesions were recorded in an eCRF that comprises global assessment (lesion present/absent) and detailed scoring (SPARCC SIJ inflammation, SPARCC SIJ structural). Wording of lesions defining active and structural lesions typical of axSpA was the same as in the original ASAS-CC eCRF permitting comparisons between central and local readers. MRI images were available from 278 of the 495 cases who had MRI and were assessed by 7 readers. Comparison of active and structural lesion frequencies typical of axSpA was assessed descriptively according to individual and majority of central readers data.

Results. Active or structural lesions typical of axSpA were recorded in about 40% of cases (Table). Similar data was observed when active sacroiliitis was defined using the ASAS definition of a positive MRI. Structural lesions alone, without any active lesions typical of axSpA, were recorded in 6.6% of cases. Active lesions alone, without any structural lesions typical of axSpA, were recorded in 7.8% of cases. Both active and structural lesions typical of axSpA were recorded in 23.1% of cases. The frequencies of these categories were only slightly lower when majority reader data was analyzed.

Conclusions. Structural lesions typical of axSpA may be observed without any active lesions typical of axSpA in 5-10% of cases presenting with undiagnosed back pain in the ASAS-CC. This is the same proportion of the cohort for which active lesions typical of axSpA are seen without any structural lesions typical of axSpA. In view of the concomitant presence of both lesions, contextual interpretation seems optimal.

Table. Contribution of Structural MRI Lesions to Detection of Sacroiliitis in the ASAS-CC.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mean% (Range)*</th>
<th>Number (%) of cases**</th>
</tr>
</thead>
<tbody>
<tr>
<td>Active lesions typical of axSpA</td>
<td>31.5 (24.5-38.5)</td>
<td>79 (28.4%)</td>
</tr>
<tr>
<td>Active lesions typical of axSpA but not structural lesions typical of axSpA</td>
<td>7.8 (4.6-11.8)</td>
<td>7 (2.9%)</td>
</tr>
<tr>
<td>Structural lesions typical of axSpA</td>
<td>31.4 (23.5-39.9)</td>
<td>68 (26.6%)</td>
</tr>
<tr>
<td>Structural lesions typical of axSpA but not active lesions typical of axSpA</td>
<td>6.6 (4.2-12.7)</td>
<td>7 (2.9%)</td>
</tr>
<tr>
<td>Active and structural lesions typical of axSpA</td>
<td>23.1 (16.0-29.0)</td>
<td>51 (21.4%)</td>
</tr>
<tr>
<td>Active or structural lesions typical of axSpA</td>
<td>39.2 (28.2-48.7)</td>
<td>99 (41.6%)</td>
</tr>
</tbody>
</table>

*Individual data from 6 readers; **Majority reader (≥4) data.

P23
FIRST VALIDATION OF CONSENSUS DEFINITIONS FOR MRI LESIONS IN THE SACROILIAC JOINT BY THE ASSESSMENTS IN SPONDYLOARTHRITIS INTERNATIONAL SOCIETY (ASAS) MRI GROUP
1University of Alberta, Canada; 2CaRE Arthritis; 3University of South Denmark; 4University of Copenhagen, Denmark; 5Rheumazentrum Ruhrgebiet Herne, Germany; 6University College London, UK; 7Charité Universitätsmedizin Berlin, Germany

Introduction/Aims. The ASAS MRI group has generated updated consensus lesion definitions (ASAS_MRI_def) for MRI lesions in the SIJ and spine and these now require validation in multi-reader exercises. We aimed to assess the reliability of detection of active and structural lesions on MRI images of the SIJ from the ASAS Classification Cohort (ASAS-CC) in a multireader ASAS exercise.

Methods. MRI Lesions were recorded in an eCRF that comprises global assessment (lesion present/absent) and detailed scoring (SPARCC SIJ inflammation, SPARCC SIJ structural). Wording of lesions defining active and structural lesions typical of axSpA was the same as in the original ASAS-CC eCRF. MRI images were available in a variety of formats (DICOM (n=175), JPEG (n=71), DICOM film (n=32)) and sequences, axial and semicoronal orientations, and from 278 of the 495 cases who had MRI. Detailed SPARCC scoring data was based only on assessment of images in DICOM format. Detection of lesions by 7 readers was assessed as present/absent by global assessment was analyzed using kappa. Reliability of detailed scoring was analyzed by intraclass correlation coefficient (ICC).

Results. Reliability of detection of active and structural lesions was comparable and somewhat better when DICOM images were evaluated (Table). The most frequently detected active lesion, subchondral inflammation, was detected to a comparable degree of reliability as the most frequently detected structural lesion, erosion. Fat metaplasia in the joint space (backfill) and ankylosis were also reliably detected despite low frequency of occurrence in this cohort. Mean ICC for detailed scores were BME-0.84, Erosion-0.55, Fatty lesion (any)-0.61, Fatty lesion (>1cm depth)-0.55, Sclerosis-0.73, Fat metaplasia in joint space-0.36, Ankylosis-0.97, Bone bud-0.97. Reliability of detailed scoring was analyzed using kappa.

Conclusions. The reliability of the ASAS_MRI_def was substantial for the most frequently detected lesions.

Table. Kappa values for detection of MRI lesions in the SJ in patients in the ASAS-CC.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mean of all reader pairs (95% CI)*</th>
<th>Mean of all reader pairs (95% CI)**</th>
</tr>
</thead>
<tbody>
<tr>
<td>Active lesions typical of axSpA</td>
<td>0.73 (0.64-0.81)</td>
<td>0.70 (0.58-0.82)</td>
</tr>
<tr>
<td>Active lesions typical of axSpA (confidence ≥2) (1-4 scale)</td>
<td>0.77 (0.68-0.86)</td>
<td>0.80 (0.69-0.92)</td>
</tr>
<tr>
<td>ASAS positive MRI</td>
<td>0.74 (0.65-0.82)</td>
<td>0.73 (0.64-0.84)</td>
</tr>
<tr>
<td>ASAS positive MRI (confidence ≥2) (1-4 scale)</td>
<td>0.76 (0.67-0.85)</td>
<td>0.79 (0.67-0.90)</td>
</tr>
<tr>
<td>Structural lesions typical of axSpA</td>
<td>0.64 (0.53-0.74)</td>
<td>0.71 (0.59-0.83)</td>
</tr>
<tr>
<td>Structural lesions typical of axSpA (confidence ≥2) (1-4 scale)</td>
<td>0.61 (0.49-0.74)</td>
<td>0.75 (0.62-0.88)</td>
</tr>
<tr>
<td>Subchondral inflammation</td>
<td>0.66 (0.57-0.75)</td>
<td>0.60 (0.49-0.72)</td>
</tr>
<tr>
<td>Erosion in Erosion cavity</td>
<td>0.29 (0.11-0.47)</td>
<td>0.37 (0.15-0.58)</td>
</tr>
<tr>
<td>Capsulitis</td>
<td>0.37 (0.12-0.62)</td>
<td>0.55 (0.18-0.90)</td>
</tr>
<tr>
<td>Joint fluid</td>
<td>0.35 (0.21-0.50)</td>
<td>0.41 (0.23-0.59)</td>
</tr>
<tr>
<td>Enthesitis</td>
<td>0.21 (0.04-0.39)</td>
<td>0.23 (0.03-0.45)</td>
</tr>
<tr>
<td>Sclerosis</td>
<td>0.42 (0.30-0.55)</td>
<td>0.48 (0.33-0.63)</td>
</tr>
<tr>
<td>Erosion</td>
<td>0.59 (0.47-0.70)</td>
<td>0.61 (0.47-0.75)</td>
</tr>
<tr>
<td>Fatty lesion (any)</td>
<td>0.61 (0.50-0.73)</td>
<td>0.61 (0.46-0.76)</td>
</tr>
<tr>
<td>Fatty lesion (&gt;1cm)</td>
<td>0.57 (0.41-0.73)</td>
<td>0.66 (0.47-0.84)</td>
</tr>
<tr>
<td>Fat metaplasia in joint space</td>
<td>0.47 (0.27-0.67)</td>
<td>0.50 (0.26-0.74)</td>
</tr>
<tr>
<td>Bone bud</td>
<td>0.14 (-0.03-0.31)</td>
<td>0.11 (-0.06-0.29)</td>
</tr>
<tr>
<td>Ankylosis</td>
<td>0.54 (0.22-0.86)</td>
<td>0.58 (0.23-0.89)</td>
</tr>
</tbody>
</table>

*Based on all images (n=278). **Based on DICOM images (n=175).
P24

WHICH MRI LESIONS IN THE SACROILIAC JOINT ARE ASSOCIATED WITH THE DEVELOPMENT OF AXIAL SPONDYLOARTHRITIS FOLLOWED BY 2 YEARS FOLLOW UP IN THE ECHOSPA COHORT?


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Introduction/Aims. We aimed to assess the prognostic capacity of specific SIJ MRI lesions in patients with axSpA after 2 years follow up in the ECHOSPA cohort.

Methods. Consecutive outpatients with age <50 years and symptoms >3 months suggestive of SpA were enrolled. The diagnosis of SpA was ascertained by an expert committee, blind to MRI evaluation, after 2 years follow-up. MRI scans from 223 cases were available for evaluation by 2 readers and an adjudicator who assessed lesions according to updated consensus definitions from the ASAS-MRI group. Clinical, laboratory, and imaging variables associated with the diagnosis of axSpA at 2 years were first identified by univariate regression. A base model of all clinical/laboratory variables associated with axSpA was included as a group in a multivariate logistic regression model that tested the independent association with MRI lesions.

Results. Mean age of the 223 cases was 39.6 (10.5) years, mean symptom duration was 2.5 (4.1) years, 49.5% were HLA-B27+ and 63.7% were female. At 2 years follow up, 165 (74%) were deemed to have axSpA. In group comparisons (Table) and univariate regression, both active and structural MRI lesions were associated with diagnosis of axSpA at 2 years (p<0.03, p<0.01, respectively). Age, B27, and psoriasis were the clinical variables associated with diagnosis of axSpA at 2 years and were included with gender in multivariate analyses. Active and structural lesions typical of axSpA and SPARC BME score 2 were each independently associated with diagnosis of axSpA 2 years (OR 0.95/CI)-6.8 (1.4-34.1) (p<0.02); 7.9 (2.2-146.6) (p=0.007); 4.9 (1.3-18.4) (p<0.02). With all variables simultaneously added to the model, only structural lesions were significantly associated.

Conclusions. Assessment of both active and structural lesions on MRI may help determine which patients have axSpA with higher diagnostic certainty over time.

Table. Distribution of MRI lesions at baseline according to diagnosis of axSpA after 2 years.

<table>
<thead>
<tr>
<th>MRI Lesion</th>
<th>AxSpA</th>
<th>NOT SpA</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Active lesion typical for axSpA</td>
<td>26 (16.0%)</td>
<td>2 (3.6%)</td>
<td>0.019</td>
</tr>
<tr>
<td>Active lesion typical for axSpA (confidence ≥3, 0-4 scale)</td>
<td>18 (11.9%)</td>
<td>11 (18.1%)</td>
<td>0.027</td>
</tr>
<tr>
<td>ASAS MRI positivity</td>
<td>24 (14.6%)</td>
<td>1 (1.7%)</td>
<td>0.006</td>
</tr>
<tr>
<td>ASAS MRI positivity (confidence ≥3, 0-4 scale)</td>
<td>17 (10.8%)</td>
<td>1 (1.7%)</td>
<td>0.048</td>
</tr>
<tr>
<td>Structural lesion typical for axSpA</td>
<td>32 (19.6%)</td>
<td>1 (1.8%)</td>
<td>0.0004</td>
</tr>
<tr>
<td>Structural lesion typical for axSpA (confidence ≥3, 0-4 scale)</td>
<td>27 (17.3%)</td>
<td>0 (0%)</td>
<td>0.0002</td>
</tr>
<tr>
<td>Active OR structural lesion typical for axSpA</td>
<td>19 (11.7%)</td>
<td>0 (0%)</td>
<td>0.04</td>
</tr>
<tr>
<td>Only active lesion typical of axSpA</td>
<td>39 (23.9%)</td>
<td>3 (5.4%)</td>
<td>0.001</td>
</tr>
<tr>
<td>Only structural lesion typical of axSpA</td>
<td>7 (4.3%)</td>
<td>2 (3.6%)</td>
<td>1.0</td>
</tr>
</tbody>
</table>

P25

MRI ASSESSMENT OF BONE MARROW EDEMA IN THE SACROILIAC JOINTS OF PATIENTS WITH SPONDYLOARTHRITIS: IS THE SPAIR T2 TECHNIQUE COMPARABLE TO STIR?

Daltos V.F., Luppino-Assad R.1, Crema M.D., Louzada-Junior P.1, Nogueira-Barbosa M.H.1

1Ribeirão Preto Medical School, University of São Paulo, Ribeirão Preto, Brazil; 2Dept. of Radiology, Quantitative Imaging Center, Boston University School of Medicine, Boston, USA

Objective. To compare Short tau inversion-recovery (STIR) with another fat saturation method in the assessment of sacroilac joint inflammation.

Methods. This prospective cross-sectional study comprises 76 patients with confirmed diagnosis of spondyloarthritis (SpA). Patients were submitted to sacroiliac joints magnetic resonance imaging in a 1.5T scanner, using STIR, Spectral Attenuated Inversion Recovery (SPAIR) T2w and Spectral Presaturation with Inversion Recovery (SPIR) T1w contrast sequences.

Two independent readers (R1 and R2) assessed the images using the Spondyloarthritides Research Consortium of Canada (SPARC) score. We assessed agreement of the SPARC scores for STIR T2w and STIR with that for T1 SPIR post-contrast (reference standard) using the St. Laurent coefficient. We evaluated each sequence using the concordance correlation coefficient (CCC).

Results. We observed a strong agreement between the STIR and SPIR T1w sequences. Lin’s CCC was 0.94 for R1 and 0.84 for R2 for STIR and 0.94 for R1 and 0.84 for R2 for SPAIR. The interobserver evaluation revealed a good CCC of 0.79 for SPAIR and 0.78 for STIR.

Conclusion. STIR technique and the SPIR T1w sequence showed a high agreement in the evaluation of sacroiliac joints subchondral bone marrow edema in patients with SpA. SPAIR T2w may be an alternative to the STIR sequence for this purpose.

Key points. There are no studies evaluating which fat saturation technique should be used. SPAIR T2w may be an alternative to STIR for sacroiliac joint evaluation. The study will lead to changes in guidelines for spondyloarthitis.

P26

VALIDATION OF A WEB-BASED CALIBRATION MODULE FOR THE SPARC MRI SIJ INFLAMMATION SCORE BASED ON PRINCIPLES OF ARTIFICIAL INTELLIGENCE

Maksymowycz WP., Knobe S., Bikoo D.M., Weiss P., Maksymowycz M., Cheah J., Kröger G., Weber U., Danebod K., Bird P., Chiwonchanvisawakit P., Moeller J., Francavilla M., Stincic J., Kogay T., Zubler V., Bathish M., Witt N., Runsey D., Gaglielmì R., Pedersen S.J., Bouttrap H., Shaffer S., Jaremko J., Malal F., Hefferman E., Johansson M.P., Paschke J., Lambert R.G., CalArthritis; 1University of Alberta, Canada; 2University of Copenhagen, Denmark; 3Children’s Hospital of Philadelphia; 4Hospital for Special Surgery, NY, USA; 5University of Southern Denmark; 6University of New South Wales, Australia; 7Mahidol University, Bangkok, Thailand; 8Hospital for Sick Children, Toronto, Canada; 9Hospital Balgrist, Zurich, Switzerland; 10McMaster Children’s Hospital, Hamilton, Canada; 11RIAH Orthopaedic Hospital, Oswestry, UK; 12Ente Ospedaliero Cantonale, Lugano, Switzerland; 13St. Vincent’s University Hospital, Dublin, Ireland

Introduction/Aims. The appropriate use of imaging-based scoring instruments is usually an ad hoc process based on passive learning from published manuscripts and atlases. Our aims were: 1. To develop a web-based calibration module for the SPARC SIJ Inflammation Score based on consensus scores from instrument developers, experimental game psychology, and real-time iterative feedback. 2. To establish the feasibility and attainment of pre-specified performance targets for reader reliability.

Methods. The SPARC method is based on scoring SIJ quadrants. Scans from 50 cases at baseline and 12 weeks after TNFi therapy are scored blinded-to-time-point. Continuous visual real-time feedback regarding concordance/discordance with expert reader scores for each SIJ quadrant is provided by a color-coding scheme. Reliability (ICC) is assessed progressively in real time as scores are coded. Accreditation for SPARC BME score is achieved with status and change score ICC of >0.8 and <0.7. 26 readers validated the module (7 fellows, 2 chiropractors, 1 undergraduate, 8 rheumatologists, 8 radiologists), 21 having no prior experience.

Results. The majority of readers achieved accreditation for SPARC BME score on the basis of sufficient reliability with instrument developers for both status and change scores, irrespective of prior experience (Table). All readers who com-
The majority of readers achieved scoring proficiency in all 4 domains for status scores, irrespective of prior experience (Table). For change scores, the majority achieved proficiency for fat metaplasia, erosion, and backfill. Very few cases had change in ankylosis. All readers rated the modules as easy and intuitive.

**Conclusion.** Experimental web-based learning is an effective method to achieve proficiency targets in the scoring of MRI scans for SIJ structural lesions.

### Table.

<table>
<thead>
<tr>
<th>SPARCC Domains</th>
<th>Mean ICC (95% CI)</th>
<th>Median ICC</th>
<th>N (%) Achieving ICC≥0.70*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fat metaplasia</td>
<td>0.88 (0.84-0.91)</td>
<td>0.91</td>
<td>20 (100%)</td>
</tr>
<tr>
<td>Erosion</td>
<td>0.63 (0.53-0.73)</td>
<td>0.61</td>
<td>16 (80%)</td>
</tr>
<tr>
<td>Backfill</td>
<td>0.65 (0.55-0.75)</td>
<td>0.71</td>
<td>13 (65%)</td>
</tr>
<tr>
<td>Ankylosis</td>
<td>0.92 (0.88-0.96)</td>
<td>0.95</td>
<td>18 (90%)</td>
</tr>
</tbody>
</table>

*Proficiency targets for reader reliability.**7 rheumatology fellows, 2 chiropractors, 1 undergraduate.

### P27

**CAN SUFFICIENT RELIABILITY OF SCORING SIJ STRUCTURAL LESIONS ON MRI BE ACHIEVED USING A WEB-BASED CALIBRATION MODULE DEVELOPED ON PRINCIPLES OF ARTIFICIAL INTELLIGENCE?**

Maksymowych W.P.1,2, Kröber G. 3, Danebod K. 2, Weiss P. 3, Biko D.M. 3, Weber U. 1, Krabbe S. 1, Makowskymow M.P. 2, Cheah J. 2, Bird P. 4, Kogay T. 1, Jarzemko J. 1, Zuber V. 2, Chaunin N. 4, Shafier S. 5, Hefferman E. 6, Guglielmi R. 7, Winn N. 3, Franecaliva M. 4, Pedersen S.J. 1, Boutuie H. 3, Paschke J. 1, Lambert R.G. 1

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**Introduction/Aims.** The reliable scoring of structural lesions on MRI in the SIJ requires considerably more reader training than for inflammatory lesions. Our aim was to develop a web-based calibration module for the SPARCC MRI SIJ Structural Score based on 1. consensus scores from instrument developers, 2. experimental game psychology, 3. real-time iterative feedback built into a web-based interface of an SIJ scoring schematic.

**Table.** Proficiency targets for reader reliability for status* (≥0.70 for fat metaplasia/ankylosis and ≥0.50 for erosion/backfill) and change** (≥0.50 for all domains) scores.

<table>
<thead>
<tr>
<th>Change Score</th>
<th>Mean ICC (95% CI)</th>
<th>Median ICC</th>
<th>N (%) Achieving ICC≥0.50**</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fat metaplasia</td>
<td>0.91 (0.89-0.93)</td>
<td>0.91</td>
<td>20 (100%)</td>
</tr>
<tr>
<td>Erosion</td>
<td>0.49 (0.39-0.59)</td>
<td>0.50</td>
<td>10 (50%)</td>
</tr>
<tr>
<td>Backfill</td>
<td>0.58 (0.45-0.70)</td>
<td>0.65</td>
<td>12 (60%)</td>
</tr>
<tr>
<td>Ankylosis</td>
<td>0.49 (0.34-0.63)</td>
<td>0.48</td>
<td>9 (45%)</td>
</tr>
</tbody>
</table>

**P28**

**COMPUTER-AIDED CLASSIFICATION OF INFLAMMATORY SACROILIITIS IN MAGNETIC RESONANCE IMAGING**

Calil Faleiros M., Jens Rivero Zavala E., Raniey Ferreira Junior J., Luppino-Assal R., Dalto V.F., Louzada-Junior P., Nogueira-Barbosa M.H., Avededo-Marques P.M., Ribeirao Preto Medical School, University of Sao Paulo, Ribeirao Preto, Brazil

**Purpose.** The reference standard to evaluate active inflammation of sacroiliac joints (SIJ) in spondyloarthritides (SpA) is magnetic resonance imaging (MRI). However, this evaluation may be challenging to specialists due to clinical variability. In order to aid the diagnosis of inflammatory sacroiliitis, we aim to develop a computerized semiautomatic classification of SIJ using gray-level and texture MRI features. We also aim to assess the performance of the classification with features extracted from manually segmented SIJ images and from images processed by the warp geometric transformation method.

**Methods.** We retrospectively evaluated the SIJ MRI from 51 patients with inflammatory sacroiliitis related to SpA. According to ASAS-MRI criteria, 22 patients presented active SIJ inflammation, and 29 were negative. Segmentation was performed in 6 consecutive SPAIR T2 coronal plane MRI for each patient. On each image we applied the warp processing method, in order to remove the black background of the segmented regions of interest, which could introduce noise in the feature extraction and classification processes.

**Results.** The highest difference was obtained by the gray-level feature vector, with an increase of 0.21 in AUC. On the other hand, the segmented images obtained highest performance only with Tamara features, with an increase of 0.30 in AUC. However, the best result with highest AUC (0.93) was obtained using all features extracted from the warped images, with sensibility of 0.73 (95% confidence interval of 0.50–0.88) and a specificity of 0.9 (95% confidence interval of 0.72–0.97).

**Conclusion.** This study on semiautomatic classification of active sacroiliitis in SpA achieved promising results for a case-based evaluation, with AUC of 0.93 using gray-level and texture MRI features extracted from SIJ images. The warp image processing method increased the overall classification performance compared to segmented images with a black background, except when Tamara features were employed. In future studies, we will extract different features from the warped images, e.g., Fourier and wavelet transformations, and perform an image-based evaluation for each SIJ MRI coronal slice. Further experiments will include an observer test to validate the semi-automatic classification as a computer-aided diagnosis tool.
Patients aged 18 to 45 years, with clinical suspicion of Spondyloarthritis, who underwent MRI for evaluation of sacroiliitis, with clinical history of low back pain were selected. Exclusion criteria were examination with incomplete or altered protocol, bone and joint infections, pregnancy, metal artifacts and clausathandromy implants.

Casuistry - One hundred and twenty-five patients with suspected sacroiliitis were initially evaluated. Of the 125 patients, 86 met the diagnosis of axial spondyloarthritis, by ASAS criteria. 10 patients was excluded by fail in the MRI protocol. After this, we find 76 patients with axial MRI protocol ok. Of these 76, those with ASpax and AS criteria were selected, excluding patients with other diseases, including other axial EAs (23 with non-radiographic spondyloarthritis, 8 with reactive arthritis, 7 with enteropathic arthritis), remaining 24 patients with AS, and 14 with ASpA. Was analyzed the presence and symetric findings of subchondral bone marrow edema (BME), subchondral bone infiltration (FAT), synovitis, enthesis and capsulitis.

**Results.**

<table>
<thead>
<tr>
<th></th>
<th>total BME</th>
<th>Fat lesion</th>
<th>capsulitis</th>
<th>enthesis</th>
</tr>
</thead>
<tbody>
<tr>
<td>AS</td>
<td>24</td>
<td>16(62.50%)</td>
<td>22(91.66%)</td>
<td>3(12.50%)</td>
</tr>
<tr>
<td>AsAPS</td>
<td>14</td>
<td>11(78.57%)</td>
<td>12(85.71%)</td>
<td>3(21.42%)</td>
</tr>
<tr>
<td>Symetric findings</td>
<td>8</td>
<td>3</td>
<td>0.69</td>
<td>0.3308, 12.94</td>
</tr>
</tbody>
</table>

The results did not show significant differences between the groups, in agreement with the grouping of the diseases as axSpA, and potentially supporting the recommendations of treatments of the axSpA with the same treatments of the AS, and in general the axSpA.

**Conclusions.** The authors conclude despite the reduced sample size and the need for more powerful studies, there was no significant difference between axSpA and AS, with a high similarity of inflammatory findings in the sacroiliac joint between groups.

**RADIOMICS ASSOCIATION OF MRI TEXTURE FEATURES WITH SPONDYLOARTHRITIS AND SACROILIITIS**


1Ribeirão Preto Medical School, University of São Paulo, Ribeirão Preto; 2São Carlos School of Engineering, University of São Paulo, São Carlos, Brazil; 3Massachusetts General Hospital, Harvard Medical School, Boston, USA

**Purpose.** The ASAS Group classification criteria for axial SpA introduced sacroiliitis assessed using MRI. Recently, radiomics has emerged as a promising approach to improve diagnosis and to provide therapy decision support for precision medicine. Radiomics consists of the massive extraction of quantitative features from medical images and their association with clinical outcomes. The main objective of this study is to evaluate the use of radiomics to aid the diagnosis and therapy decision of SpA by associating quantitative MRI texture features with the outcomes of presence of sacroiliitis, diagnosis of SpA, and subclassification in axial or peripheral SpA.

**Methods.** Retrospective study with 47 patients. From each MRI exam, we selected 6 consecutive images in the coronal plane acquired with fluid sensitive sequences in T2. Analysis was performed using the Fiji software tool. The images were processed using the iTEM tool from the BESK group. The images were segmented using the Tela, a tool developed in our lab. Next, we calculated 230 quantitative MRI texture features, using the Radiomics MATLAB toolbox. The global features were calculated on the whole image and local features were calculated on pre-defined ROIs: bone marrow edema (BME), subchondral bone marrow edema (BME), subchondral bone infiltration (FAT), synovitis, enthesis, capsulitis and autoantibodies.

**Conclusion.** The univariate analysis showed that the Tamura_D11_SD feature yielded the highest performance to identify the presence of inflammation in the sacroiliac joints with AUC of 0.86 (<0.0001). Histogram_Skewness_M feature yielded the highest performance to identify the presence of inflammation in the sacroiliac joints with AUC of 0.86 (<0.0001). Tamura_D11_SD feature also yielded the highest associative performance in differentiation between AS (mean, SD) and axSpA (mean, SD) with AUC of 0.86 (<0.0001). Very high activity (>3.5) was identified with a very high performance as well, with AUC of 0.86 (<0.0001). The results did not show significant differences between the groups, in agreement with the grouping of the diseases as axSpA, and potentially supporting the recommendations of treatments of the axSpA with the same treatments of the AS, and in general the axSpA.

**P32**

**DO ETHNICITY, DEGREE OF FAMILY RELATIONSHIP AND THE SPONDYLOARTHRITIS SUBTYPE IN AFFECTED RELATIVES INFLUENCE THE ASSOCIATION BETWEEN A POSITIVE FAMILY HISTORY FOR SPONDYLOARTHRITIS AND HLA-B27 CARRIERSHIP? RESULTS FROM THE WORLDWIDE ASAS COHORT**

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1Rheumatology, LUMC, Leiden, The Netherlands; 2Rheumatology, NOVA Medical School, Lisbon, Portugal; 3Rheumatology, ARC, Amsterdam; 4Rheumatology, Zuyderland Hospital, Heerlen, The Netherlands; 5Rheumatology, Charité Campus Benjamin Franklin, Berlin; 6German Rheumatism Research Centre, Berlin; 7Rheumatology, Klinikum Bielefeld, Bielefeld, Germany

**Aim.** In two European cohorts only a positive family history (PHH) of ankylosing spondylitis (AS) and acute anterior uveitis (AAU) were associated with HLA-B27 carriage in axial spondyloarthritis (axSpA) suspected patients. As the importance of ethnicity or degree of family relationship is unknown, we investigated the influence of ethnicity, first (FDR)- or second (SDR)-degree relatives on the association between a PHH and HLA-B27 carriage in axSpA suspected patients.

**Methods.** Univariable analyses were performed among axSpA suspected patients in the ASAS cohort at baseline. Each disease (AS, AAU, psoriasis, inflam-
IS A POSITIVE FAMILY HISTORY OF SPONDYLOARTHRITIS RELEVANT FOR DIAGNOSING AXIAL SPONDYLOARTHRITIS ONCE HLA-B27 STATUS IS KNOWN? DATA FROM THE ASAS, DESIR, AND SPACE COHORTS

van Lunteren M.1, van der Heijde D.1, Sepriano A.2, Landewe R.3,4, Berg I.J.3, Dougdas M.5,6, Gossec L.7,8, Jacobsson L.9, Ramonda R.7,9, Rudwaleit M.10,11, Sieper J.12,13, van Gaalen F.A.1

1Rheumatology, LUMC, Leiden, The Netherlands; 2Rheumatology, NOVA Medical School, Lisbon, Portugal; 3Rheumatology, ARC, Copenhagen, Denmark; 4Rheumatology, University of Gothenburg, Gothenburg, Sweden; 5Rheumatology, University of Padova, Italy; 6Rheumatology, Charité Campus Benjamin Franklin, Berlin; 7Rheumatology, Klinikum Bielefeld; 8German Rheumatism Research Centre, Berlin, Germany

Introduction. A positive family history (PFH) of spondyloarthritis (SpA), in particular a PFH of ankylosing spondylitis (AS) or acute anterior uveitis (AAU), can be used to identify HLA-B27 carriership in chronic back pain patients. It is unknown if a PFH contributes to diagnosing axial spondyloarthritis (axSpA) once HLA-B27 status is known.

Methods. In patients suspected of axSpA from the ASAS, DESIR, and SPACE cohorts, logistic regression analyses were performed at baseline with HLA-B27 status and PFH according to the ASAS definition (ASAS-PFH) as determinants and clinical axSpA diagnosis as the outcome. Analyses were repeated with a PFH of AS or AAU.

Results. In patients from the ASAS (n=594), DESIR (n=667), and SPACE (n=577) cohorts, respectively 23%, 39%, and 38% had an ASAS PFH, 52%, 58%, and 43% were HLA-B27 positive, and 62%, 42%, and 54% were diagnosed with axSpA. In the univariable analysis, HLA-B27 status was significantly associated with an axSpA diagnosis in all three cohorts (Table 1). An ASAS-PFH and a PFH of AAU were univariately associated with an axSpA diagnosis only in the SPACE cohort and a PFH of AS with an axSpA diagnosis only in the ASAS cohort. In the multivariable models, HLA-B27 was independently and positively associated with an axSpA diagnosis in each cohort but an ASAS-PFH was not (Table 1). Similarly, a PFH of AS did not have an independent positive association with an axSpA diagnosis in any cohort (ASAS cohort: HLA-B27 OR:6.7 (95%CI:1.9–24.0); SPACE cohort: HLA-B27 OR:2.7 (95%CI:1.1–6.7); DESIR cohort: HLA-B27 OR:2.1 (95%CI:1.5–2.9); ASAS-PFH OR:1.0 (95%CI:0.5–2.0); SPACE cohort: HLA-B27 OR:3.5 (95%CI:1.8–6.6); ASAS-PFH OR:2.4 (95%CI:0.8–7.4)).

Conclusions. When diagnosing axSpA, a PFH is no longer relevant once HLA-B27 status is known.

Table 1. Logistic regression analysis between ASAS PFH, HLA-B27, and clinical axSpA diagnosis in the ASAS, DESIR, and SPACE cohort.

P33

<table>
<thead>
<tr>
<th>ASAS cohort</th>
<th>Univariable analysis: HLA-B27</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASASPFH</td>
<td>56 6.7 (9.7-8.8)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ASASPPH</td>
<td>170 0.9 (0.6-1.4)</td>
<td>0.561</td>
</tr>
</tbody>
</table>

Univariable analysis: ASAS PFH

ASAS PFH     | 170 0.9 (0.6-1.4)             | 0.561  |

ASAS PPfH    | 170 1.0 (0.7-1.3)             | 0.772  |

SPACE cohort

Univariable analysis: HLA-B27

HLA-B27+     | 212 2.1 (1.5-2.9)             | <0.001  |

Univariable analysis: ASAS PFH

ASAS PFH     | 170 0.9 (0.6-1.4)             | 0.561  |

ASAS PPfH    | 170 1.0 (0.7-1.3)             | 0.772  |

Univariable analysis: HLA-B27

HLA-B27+     | 212 2.1 (1.5-2.9)             | <0.001  |

Statistically significant associations are printed in bold. * Self-reported ethnicities is missing for 5 patients who are included in this category, and other ethnicities are black, East-Indian, Hispanic/Latino, mixed or Turkish.

in the ASAS cohort (n=594).

Statistically significant results are printed in bold. * Self-reported ethnicities was missing for 5 patients who are included in this category, and other ethnicities are black, East-Indian, Hispanic/Latino, mixed or Turkish.

ASAS: Assessment of Spondylo-Arthritis international Society; CI: confidence interval; HLA-B27: human leukocyte antigen B27; n.a.: not applicable; OR: odds ratio; PFH: positive family history.

Clinical and Experimental Rheumatology 2018
COHORT STUDY
ANKYLOSING SPONDYLITIS – A SWEDISH LONGITUDINAL CARDIOVASCULAR STUDY

Introduction: Aim. Diagnostic delay, the gap between the onset of first musculoskeletal symptoms and diagnosis definition, is associated to worse prognostic and represents a major challenge to assistance of spondyloarthritides (SpA) patients. The aim of this study was to compare it between two different periods in a same cohort and evaluate possible associations with SpA features.

Materials and Methods. Two cross-sectional analysis from the same database were made. The first included patients admitted to the SpA outpatient clinic up to 2002 (group A) and the second one included patients admitted between 2003 and 2013 (group B).

Results. The mean diagnostic delay was 8.1 (±0.68) years in group A (N=156) and 6.9 (±0.76) years in group B (N=99). The subtype of SpA, gender, HLA-B27 status or presence of radiographic sacroiliitis (mNY criteria) were not associated to diagnostic delay. Conversely, the presence of extra-articular manifestations - EAM (i.e. uveitis, psoriasis and/or inflammatory bowel disease) (p<0.0001) - on admission was statistically associated with longer diagnostic delay and the age at onset was negatively correlated with it (r=-0.28 p=0.0001).

Discussion. Possibly, the increased awareness amongst health-care professionals, the adoption of new classification criteria (ASAS 2009) and the incorporation of magnetic resonance imaging - MRI as a diagnostic tool in SpA could explain the observed improvement in earlier diagnosis. The association between EAM presence and earlier disease onset with longer diagnostic delay, could represent a greater difficulty of non-rheumatologists in identify inflammatory-type symptoms and an often unawareness of the EAM linkage with SpA. As consequence, patients may not be referred to rheumatologist in appropriate time and may have an inadequate investigation, delaying the diagnosis.

Conclusions. We have shown a reduction (mean difference of 1.3 years) in diagnostic delay measured in a same SpA outpatient clinic over a decade. Even so, there is still a need for further targeted education of health-care professionals to address this issue.

P35
CARDIAC CONDUCTION DISTURBANCES IN PATIENTS WITH ANKYLOSING SPONDYLITIS – A SWEDISH LONGITUDINAL COHORT STUDY

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1University of Gothenburg, Gothenburg; 2Uméa University, Uméa, Sweden

AIM. To describe electrocardiographic (ECG) alterations in a cohort of patients with AS and if AS related factors at baseline predict the presence of cardiac conduction disturbances (CCD) at 5-year follow-up.

MATERIALS AND METHODS. In total 210 patients (57.6 % men, mean age 50±13 years) diagnosed with AS at 3 rheumatology clinics from Western Sweden participated in 2009 in an observational longitudinal cohort study with a planned follow-up after 5 years. At follow-up 2014, physical examination, ECG, questionnaires, laboratory tests and radiographic examinations were repeated in 172 patients (54.1% men, mean age 55±13 years). CCD was defined in the presence of AV block I (PQ duration ≥220 ms), AV block II (PQ duration 200–219 ms), AV block II-III, right and left bundle branch block (RBBB and LBBB), left anterior and posterior fascicular block (LAFB and LFPB) and pacemaker. Descriptive statistics and logistic regression analyses were performed in order to find predictors at baseline for the presence of CCD at follow-up. Baseline characteristics with a p-value <0.2 in univariate analyses (dependent variable present CCD (yes=1, no=0)) were included as independent variables in a forward stepwise multiple logistic regression analysis.

RESULTS. In total 23 of the 172 patients (13.4%) had CCD at 5-year follow-up. Eight had developed a new CCD out of which 2 had required pacemaker implantation, 3 had a more severe and 2 a less pronounced CCD compared with 2009. Existing CCD at baseline (Odds ratio (OR) 95 % CI) (4.2 (1.9–9.5), a history of anterior uveitis (OR 6.4 (1.1–36.6), male sex (OR 4.7 (1.1–20.6)), higher ASDAS-CRP (OR 3.6 (1.6–7.9)) and increasing age (OR 1.1 (1.0–1.1) per 1 year) were predictors for the presence of CCD at follow-up.

CONCLUSIONS. The presence of CCD in AS is dynamic. AS related factors, represented by baseline ASDAS-CRP and a history of anterior uveitis, predicted their presence at 5-year follow-up.
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IN VIVO PHOSPHORYLATION OF P38 IN MONOCYTES IS ENHANCED, AT THE TIME OF DIAGNOSIS, IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS (axSpA)

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Introduction. Host response to microbes is considered to contribute to pathogenesis to axSpA. p38 MAP kinase pathway plays an important role in resistance of bacterial replication in HLA-B27 expressing human monocytic U937 cells (1). This prompted us to study the phosphorylation of the MAP kinases p38, extracellular signal-regulated kinase (ERK)1/2 and c-Jun-N-terminal kinase (JNK) in patients with axSpA.

Patients and Methods. We included 20 patients [19/20 HLA-B27 positive, mean time from first period of back pain 5.9 years (range 0.3–16), mean BASDAI 4.4 (SD 1.7)] referred to rheumatology unit for diagnostic workup due to back pain. The patients fulfilled ASAS classification criteria. 26 patients [mean DAS28 4.0 (SD 1.3)] with early untreated rheumatoid arthritis (RA) fulfilling the 2010 ACR/EULAR classification criteria served as disease control group, and 18 adult volunteers as healthy controls. Whole blood phosphospecific flow cytometry was used to reveal phosphorylation of p38, ERK1/2 and JNK in nonstimulated monocytes, and in monocytes stimulated by lipopolysaccharides, E. coli, or lipoteichoic acid. Fluorescence intensities of monocyte pERK1/2, pJNK1, pJNK2, pJNK3, pERK1/2Fluor647 and p38-PE-Cy7 were expressed as relative fluorescence units. Significance of difference between the subject groups was tested by ANCOVA, adjusted for high sensitivity CRP levels.

Results. Basal phosphorylation level of p38 in axSpA monocytes was significantly higher than that in healthy subjects’ monocytes (p=0.009). The difference between RA and healthy subjects was not statistically significant. The respective phosphorylation levels of ERK1/2 and JNK did not differ significantly between the 3 subject groups. After stimulation, monocyte p38 phosphorylation levels in axSpA, RA and healthy subjects were comparable.

Conclusion. Enhanced monocyte baseline phosphorylation of p38 suggests in vivo preactivation of monocytes in patients at the time of diagnosis of axSpA.

Reference

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ASSOCIATION OF IgA ANTIBODIES AGAINST CD74 WITH PRODUCTION OF IL-17A BUT NOT OF TNFα IN PATIENTS WITH ACTIVE AXIAL SPONDYLOARTHRITIS

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Background. Axial spondyloarthritis (axSpA) is strongly associated with HLA-B27. Recently, IgA antibodies (Abs) against CD74 (IgA-anti-CD74) and T-cells carrying CD74-specific T-cell receptors were also found to be associated with axSpA, especially in patients with ankylosing spondylitis, the radiographic form of axSpA. Tumor necrosis alpha (TNF-α) inhibitors and IL-17 antagonists are efficacious in patients with active axSpA.

Objective. To investigate whether IgA Anti-CD74 Abs are associated with pro-inflammatory cytokines in the sera of patients with HLA-B27 positive and -negative patients with active axSpA.

Methods. Blood samples of 62 HLA-B27-positive and 58 HLA-B27-negative patients with axSpA (44% AS) prior to starting a biologic therapy were collected. A cross-sectional study, the presence of IgA Abs against CD74 was associated with serum levels of pro-inflammatory biomarkers such as CRP (r=0.41, p=0.002) but not TNFα irrespective of HLA-B27 status. Longitudinal prospective studies are needed to show that the measurement of IgA anti-CD74 Abs and/or serum cytokines can help to guide treatment decisions.

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COMPARISON OF RETENTION RATES BETWEEN TUMOR NECROSIS FACTOR-α INHIBITORS IN ANKYLOSING SPONDYLISTIS PATIENTS: DATA FROM THE KOREAN COLLEGE OF RHEUMATOLOGY BIOLOGICS REGISTRY

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Background. Drug persistence of tumor necrosis factor-α inhibitors (TNFi) tends to be higher in patients with ankylosing spondylitis (AS) than rheumatoid arthritis but there are few studies of Asian AS patients in the literature.

Objectives. To investigate drug retention rates of various TNFi used in Korean AS patients.

Methods. Subjects were AS patients enrolled in the Korean College of Rheumatology Biologics registry (KOBIO, Dec 2012 –). All approved and commonly prescribed TNFi were included in the analysis. Discontinuation was defined as switching or stopping the biologic agent. Kaplan-Meier curve and Cox proportional hazard model were used for further analysis. Reason of TNFi discontinuation was also assessed. Univariate and multivariate analyses were used to identify possible predictors of discontinuation.

Results. Data of total of 1005 AS patients were analyzed (median follow-up period: 14 months). The mean age of patients was 40.7, and 77.4% were males. The mean disease duration was 7.1 years, HLA-B27 were positive in 82.4%, and 33.2% of patients had lesion(s) of syndesmophytes. Seventy-six percent of patients were first-time biologic users. Discontinuation of TNFi occurred in 24.2% (switching in 9.6%) of patients during follow-up. The drug survival function estimate showed that the adjusted hazard ratio (HR) of golimumab (compared with etanercept) was 0.441 (95% CI 0.277–0.703, p=0.001). The reason of discontinuation was inefficacy (32.6%), adverse events (23.6%), clinical improvement (11.2%), and others (32.6%). A multivariate analysis indicated predictors of discontinuation to be shorter disease duration (HR 0.973, p=0.044), and negative HLA-B27 (HR 1.623, p=0.009).

Conclusion. Our study demonstrates that few AS patients switched to other TNFi during their course of treatment. The drug retention rate of golimumab was higher compared with other agents prescribed in Korean AS patients.

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HIGH SERUM ALLOGRAFT INFLAMMATORY FACTOR 1 IS ASSOCIATED WITH POOR RESPONSE TO TNFα INHIBITORS IN ANKYLOSING SPONDYLITIS

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Objectives. Anti-tumor necrosis factor-alpha (TNF-α) inhibitors can improve the symptoms and signs of ankylosing spondylitis (AS); however, not all the patients show sufficient response to anti-TNFα treatment. Therefore, the aim of this study was to identify candidate serum markers that could be used to predict the clinical response to TNF-α inhibitors in AS.

Materials and Methods. Baseline gene expression differences were screened by two-pathway-focused gene assays of peripheral blood samples from six AS patients (three responders and three non-responders) before anti-TNFα treatment, and selected candidates were confirmed by qRT-PCR in 18 patients (11 responders and 7 non-responders). The concentration of corresponding serum protein was compared in 69 responders and 48 non-responders. A poor response to TNF-α inhibitors was defined as less than a 50% improvement in the Bath ankylosing spondylitis disease activity index (BASDAI50) at week 14 from that at baseline.

Results. Nine candidate genes were selected and validated by qRT-PCR. Among these, the expression of allograft inflammatory factor 1 (AIF1) was 3.52-fold higher in non-responders than responders (p=0.032), and the baseline serum AIF1 level was significantly higher in BASDAI50 non-responders (32.8 [Interquartile range 20.6–67.3] pg/ml in responders and 54.2 [28.9–91.0] pg/ml in non-responders, p=0.033). An AIF1 level of 63.5 pg/ml or more was associated with a higher risk for BASDAI50 ≥5.0 at week 14 after anti-TNFα treatment (adjusted odds ratio 6.953, p=0.003).

Conclusion. Serum AIF1 level could be used as a novel serum marker for predicting responses to TNFα inhibitors in AS.
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OVEREXPRESSION OF MACROPHAGE MIGRATION INHIBITORY FACTOR IN PATIENTS WITH ANKYLOSING SPONDYLITIS AND ITS RELATION TO SEX, INFLAMMATION AND TREATMENT

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Background. Macrophage migration inhibitory factor (MIF) is a multipotent cytokine involved in the regulation of immune and inflammatory responses. The present study aimed to investigate the MIF expression in patients with ankylosing spondylitis (AS) compared with controls and to examine associations between MIF and demographic and inflammation related factors in AS overall and stratified by sex.

Methods. MIF in plasma was measured in a cohort of patients with AS from Northern Sweden (n=155) and age- & sex-matched controls (n=151) using Human MIF Quantikine ELISA Kit (R&D). The patients were assessed with laboratory markers of inflammation, ASDAS-CRP, BASDAI, BASMI and BASFI. Comparisons were analyzed by T-test and associations by bivariate Pearson correlations.

Results. The expression of MIF was significantly augmented in the AS patients (Mean 65.1 ng/mL ± 2.0 SEM) compared with the controls (Mean 42.0 ng/mL ± 2.1 SEM) (p<0.001), the difference was also found in sex stratified analyses. MIF had a weak negative correlation with age in AS (-0.14, p=0.07) but not in controls (-0.037, p=0.66). Stratified by sex, the inverse correlation with age was shown in the AS men only (-0.28, p=0.004). When analyzing MIF in different age-groups it was revealed that MIF was significantly higher in the men ≤50 years compared to the women with AS ≤50 years. Moreover, MIF was positively correlated with inflammation related variables; swollen joint count, ESR, hsCRP, thrombocytes and leukocytes. The expression of MIF was significantly increased in AS patients on cDMARDs with or without a biological drug, while NSAIDs, glucocorticosteroids or single therapy with a biological drug did not influence the MIF levels.

Conclusions. Our results suggest that MIF is overexpressed in AS patients. MIF was associated with inflammation and treatment and, in addition, sex seemed to have an impact on MIF plasma levels in the AS patients. MIF might be a potential biomarker for the development of new treatment-strategies in AS.

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PROGNOSTIC MARKERS IN AXIAL SPONDYLOARTHRITIS (PROMISE) – ALPHA 1 ANTITRYPSIN MAY IDENTIFY axSpA PATIENTS AT RISK OF UVEITIS

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Introduction. There has been increasing interest in recent years in the identification of biomarkers in axSpA to describe diagnostic subgroups and to help identify patients at increased risk of associated disease manifestations, such as uveitis. Aim. In this cross-sectional study, a broad panel of serum biomarkers were evaluated, from a large mixed cohort of patients with Ankylosing Spondylitis (AS), non-radiographic axial spondyloarthritis (nr-axSpA) and mechanical back pain (MBP) to identify biomarkers of interest for extra articular manifestations of axSpA in these patient groups.

Methods. A panel of 46 serum biomarkers were analysed by Myriad RBM using multiplexed immunoassays by Multi-Analyte Panels (Figure 1), in a cohort of patients from a tertiary referral centre, consented through the Bath Spondylarthritis Biobank. AS patients met mNRY criteria, and nr-axSpA patients satisfied ASAS classification criteria.

Results. Data for extra articular manifestations (EAM) of SpA was available for 276 patients. Of these, 162 (58.7%) had a history of at least one EAM. 80.2% of these had AS, 10.4% nr-axSpA, 9.3% MBP. For patients with and without EAMS, mean age 49.2 vs 44.3years, BASDAI 4.0 vs 4.4, ASDAS 2.6 vs 2.7, male 58.3 vs 41.7%, family history SpA 61.8 vs 38.2%, HLA B27 positive 64.5 vs 35.5%. Uveitis was the commonest EAM (53.1%), enthesitis 19.2%, psoriasis 16.7%, inflammatory bowel disease 8.7%, dactylitis 2.9%, reactive arthritis 0.4%; 89/97 patients with uveitis had had AS. Using logistic regression, an odds ratio of 1.51 (95% CI 1.22, 1.87) was found for alpha 1 antitrypsin in patients with uveitis compared to those without (Figure 2).

Discussion. From this analysis, alpha 1 antitrypsin has been identified as a potential biomarker for patients with uveitis. Further work to validate this finding in alternative SpA population is recommended. In addition, longitudinal measurement of alpha 1 antitrypsin in an SpA cohort with active or quiescent inflammatory eye disease may offer further insights.

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COMPARING DISEASE STATUS, SYMPTOMATOLOGY, AND CLINICAL CHARACTERISTICS OF NON-RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS AND ANKYLOSING SPONDYLOARTHRITIS PATIENTS IN THE UNITED STATES

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Aim. To better understand the symptoms, clinical characteristics and disease status of non-radiographic axial spondyloarthritis (nr-axSpA) patients and how they compare to ankylosing spondylitis (AS) patients in the United States.

Methods. Data from the 2015 SpA Disease Specific Programme, a cross-sectional survey of patients and rheumatologists conducted in the United States were analyzed. Rheumatologists completed forms containing patient demographics, clinical results and symptomology. Symptoms, disease activity, and disease status (defined as improving, stable, unstable, and deteriorating) based on rheumatologists’ global assessment of ankylosing spondylitis and non-radiographic axial spondyloarthritis patients were compared.

Results. Of the 980 axSpA patients included in this study, 498 patients had AS, and 482 had nr-axSpA as diagnosed by rheumatologists. A higher proportion of AS patients were male (77% vs. 56%), older (Mean Age: 46.1 vs. 42.6), had a higher mean BMI and were employed when compared to nr-axSpA patients. Nr-axSpA patients were also less likely to be in remission (p=0.0027). AS patients had some axSpA features more common, such as sacroiliitis, spinal fusion, and loss of movement, however, nr-axSpA patients were more likely to have inflammatory back pain, and enthesitis. QoL absenteeism, presenteeism, work productivity, and activity impairment were similar between AS and nr-axSpA patients.

Conclusions. In the US, nr-axSpA and AS patients share many similar clinical features with few differences. In spite of these similarities, nr-axSpA patients show lower rates of stability and are less likely to be in remission. These findings suggest that nr-axSpA is as burdensome as AS.
Introduction and Aim. It has been suggested that smoking, one of the environmental risk factors in various rheumatic diseases, may have an important role in disease pathogenesis as well as adverse effects on disease progression, quality of life and drug response. However, in a recent study a paradoxical relationship between the development of psoriatic arthritis (PsA) and smoking has been reported in patients with psoriasis. In current study, we aimed to investigate the effects of smoking on disease activity, functional status, quality of life, psychogenic measures and fatigue in patients with PsA.

Materials and Methods. Patients with PsA over the age of 18 who met the CASPAR classification criteria were enrolled consequently in this cross-sectional observational study. The short form 36 (SF-36), Nottingham Health Profile (NHP), (PsQoL); health assessment questionnaire (HAQ); hospital anxiety and depression (HAD) scale; fatigue severity scale (FSS) were used to assess the patients. Clinical and laboratory data were recorded. MDA, DAS28-CRP, DAPSA, CDAI, SDAI and PASI scores were used to assess disease activity. According to the smoking habits, patients grouped as; ever smoker or never smoker. Statistical analysis was performed using the SPSS package program. The results were given as mean ± SD and %.

Results. A total of 133 PsA patients (33.8% male, 66.2% female) were included in the study. The mean disease duration is 10.7 years. 65 (48.9%) of the patients had never smoked, and 68 (51.1%) were ever smoked. The mean age of smokers was 43.5±10.5 years, the mean age of the non-smokers was 47.6±11.1 years (p=0.031) (Table).

Table I. Demographic and clinic characteristics of patients with PsA.

<table>
<thead>
<tr>
<th>Age, year</th>
<th>Never smoker (n= 65)</th>
<th>Ever smoker (n=68)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>47.6±11.1</td>
<td>43.5±10.5</td>
<td>0.031</td>
<td></td>
</tr>
<tr>
<td>Male/Female</td>
<td>17/48</td>
<td>28/40</td>
<td>0.067</td>
</tr>
<tr>
<td>Disease durations, year</td>
<td>11.4±11.0</td>
<td>9.9±9.2</td>
<td>0.404</td>
</tr>
<tr>
<td>BMI</td>
<td>30.4±6.4</td>
<td>27.9±4.8</td>
<td>0.012</td>
</tr>
<tr>
<td>Ultevis (n=127)</td>
<td>11(17.7)</td>
<td>3(4.6)</td>
<td>0.018</td>
</tr>
<tr>
<td>SDAI</td>
<td>32.6±35.1</td>
<td>23.7±18.7</td>
<td>0.130</td>
</tr>
<tr>
<td>CDAI</td>
<td>18.3±12.4</td>
<td>13.3±9.4</td>
<td>0.014</td>
</tr>
<tr>
<td>DAS 28</td>
<td>3.6±1.4</td>
<td>3.1±1.2</td>
<td>0.045</td>
</tr>
<tr>
<td>DAPSA</td>
<td>33.1±35.0</td>
<td>24.3±19.1</td>
<td>0.131</td>
</tr>
<tr>
<td>Tender joint count</td>
<td>5.3±6.1</td>
<td>3.2±4.0</td>
<td>0.022</td>
</tr>
<tr>
<td>Swollen joint count</td>
<td>3.2±4.9</td>
<td>1.7±2.9</td>
<td>0.038</td>
</tr>
<tr>
<td>VAS-pain</td>
<td>5.1±2.7</td>
<td>4.5±2.7</td>
<td>0.195</td>
</tr>
<tr>
<td>Patient global assessment</td>
<td>5.2±2.5</td>
<td>4.6±2.6</td>
<td>0.167</td>
</tr>
<tr>
<td>Physician global assessment</td>
<td>4.6±2.2</td>
<td>4.0±2.1</td>
<td>0.150</td>
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<tr>
<td>VAS-fatigue</td>
<td>5.8±2.8</td>
<td>4.8±2.7</td>
<td>0.053</td>
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<tr>
<td>Fatigue severity scale</td>
<td>3.4±1.2</td>
<td>3.4±1.2</td>
<td>0.881</td>
</tr>
<tr>
<td>Onset age os psoriatic skin lesion</td>
<td>29.3±15.5</td>
<td>29.6±14.0</td>
<td>0.925</td>
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<tr>
<td>BASDAI</td>
<td>3.7±2.6</td>
<td>3.3±2.4</td>
<td>0.388</td>
</tr>
<tr>
<td>BASMI</td>
<td>4.2±6.6</td>
<td>2.1±1.6</td>
<td>0.330</td>
</tr>
<tr>
<td>BASFI</td>
<td>4.0±2.8</td>
<td>3.3±2.7</td>
<td>0.220</td>
</tr>
<tr>
<td>NHP-pain</td>
<td>62.9±33.5</td>
<td>49.5±33.5</td>
<td>0.028</td>
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<tr>
<td>NHP-physical activity</td>
<td>41.1±25.4</td>
<td>34.8±24.6</td>
<td>0.163</td>
</tr>
<tr>
<td>NHP-fatigue</td>
<td>57.5±40.3</td>
<td>44.9±42.0</td>
<td>0.090</td>
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<tr>
<td>NHP-sleep</td>
<td>40.7±32.1</td>
<td>32.0±31.0</td>
<td>0.131</td>
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<tr>
<td>NHP-social isolation</td>
<td>16.8±25.7</td>
<td>11.1±19.2</td>
<td>0.167</td>
</tr>
<tr>
<td>NHH-emotional reaction</td>
<td>27.2±28.5</td>
<td>20.6±27.3</td>
<td>0.060</td>
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<tr>
<td>PaQoL</td>
<td>4.2±4.8</td>
<td>2.6±3.1</td>
<td>0.031</td>
</tr>
<tr>
<td>HAD-Depression</td>
<td>6.3±4.3</td>
<td>6.0±3.6</td>
<td>0.757</td>
</tr>
<tr>
<td>HAD-Anxiety</td>
<td>7.0±4.7</td>
<td>6.3±3.9</td>
<td>0.035</td>
</tr>
<tr>
<td>SF36 Physical component score</td>
<td>37.9±14.1</td>
<td>40.5±17.7</td>
<td>0.471</td>
</tr>
<tr>
<td>SF36 Mental component score</td>
<td>47.7±13.7</td>
<td>47.0±16.0</td>
<td>0.834</td>
</tr>
<tr>
<td>PASI</td>
<td>4.6±9.1</td>
<td>3.5±5.2</td>
<td>0.676</td>
</tr>
<tr>
<td>HAQ</td>
<td>0.5±0.5</td>
<td>0.3±0.5</td>
<td>0.195</td>
</tr>
<tr>
<td>MDA 7de5 (+) n=60</td>
<td>1(3.7)</td>
<td>5(15.2)</td>
<td>0.219</td>
</tr>
</tbody>
</table>

Uvetis rates were statistically higher than those of non-smokers (p=0.018). The disease activity calculated with CDAI and DAS28 was statistically lower in smoker than those non-smoker patients (p<0.05). Disease activity calculated with DAPSA and SDAI was also higher in non-smokers but not statistically significant (p=0.05).

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**CONCLUSION.** As paradox in patients with PsA smokers; low disease activity, decreased tender and swollen joints count, and decreased uveitis frequency were observed. Although cigarette smoking is a paradoxical effect in our study, we think that it is important to cessation of smoking because of the high risk of comorbidity, especially metabolic disease in patients with PsA, in the long term. Further studies are needed to investigate the effect of smoking on disease activity and other clinical manifestations in patients with PsA.

Materials and Methods. Adult patients with PsA who met the CASPAR criteria were consecutively included in this cross-sectional study. The following variables were evaluated: tender joint count (TJC), swelling joint count (SJC), VAS-pain, PGA, PhGA, the presence of extra-articular manifestation, PASI, Health Assessment Questionnaire (HAQ), physical and mental component summary score of the SF-36, NHP, PaQoL, Hospital Anxiety and Depression Scale (HADS-A and HADS-D), FSS and CRP. In addition, disease activity was measured by using three different outcome measures including DAS28-CRP, MDA and DAPSA.

**Table I.** Demographic and clinic characteristics of patients.

**Median**

| Age | 45.8 |
| BMI | 29.2 |
| Symptom duration | 10.5 |
| VAS-pain | 4.8 |
| Patient’s global assessment | 4.9 |
| Physician’s global assessment | 4.3 |
| Tender joint count | 4.3 |
| Swelling joint count | 2.4 |
| DAS 28 | 3.3 |
| DAPSA | 28.2 |
| BASDAI | 3.5 |
| NHP-pain | 56.6 |
| NHP-physical activity | 37.9 |
| NHP-fatigue | 51.3 |
| NHP-sleep disturbance | 36.1 |
| NHP-social isolation | 22.7 |
| NHP- emotional reaction | 21.4 |
| PaQoL | 3.4 |
| HADS-Depression | 6.1 |
| HADS-Anxiety | 6.7 |
| SF36 physical component score | 39.3 |
| SF36 mental component score | 47.7 |
| FSS | 5.3 |
| PASI | 5.1 |
| HAQ | 6.4 |

**Results.** A total of 136 patients with PsA (mean age 45.8 years, 46 male/ 90 female) were analyzed. Only 69 (7.9%) patients with PsA achieved MDA. 30 (31.19%) patients had remission, 16 (17%) patients had LDA, 39 (35.5%) patients had moderate disease activity (MoDA) and 9 (9.6%) patients had high disease activity (HDA) status defined as DAS28-CRP. On the other hand, 4 (4.3%) patients were in high disease activity (HDA) status and 5 (5.7%) patients achieved remission, 3 (3.7%) patients achieved LDA, 33 (35.5%) patients achieved MoDA and 33 (35.5%) patients achieved HAD status according to DAPSA. All subscores of NHP except fatigue and sleep disturbance, PaQoL, and

**Conclusion.** As paradox in patients with PsA smokers; low disease activity, decreased tender and swollen joints count, and decreased uveitis frequency were observed. Although cigarette smoking is a paradoxical effect in our study, we think that it is important to cessation of smoking because of the high risk of comorbidity, especially metabolic disease in patients with PsA, in the long term. Further studies are needed to investigate the effect of smoking on disease activity and other clinical manifestations in patients with PsA.
Fecal calprotectin, a useful biomarker of microscopically evident bowel inflammation in patients with spondyloarthritis

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Introduction. Microscopic bowel inflammation is present in up to 60% of patients with spondyloarthritis and it may be associated with more severe disease and higher risk of developing inflammatory bowel disease. It was conducted a study to determine the values of fecal calprotectin that are related to microscopic bowel inflammation in patients with spondyloarthritis, treated or not with NSAIDS.

Materials and Methods. Fecal calprotectin measurement and ileocolonoscopy with multiple biopsies were performed in 61 patients with SpA (48 with Ankylosing Spondylitis and 13 with Psoriatic Arthritis) to assess the presence of microscopic and endoscopic signs of bowel inflammation.

Results. A total of 34 (57%) patients presented with microscopic bowel inflammation and 13 (21%) presented with endoscopic features. Fecal calprotectin levels were significantly higher in patients who presented with microscopic inflammation compared to those without inflammatory findings in the biopsies (p=0.0002) and only marginally higher in patients with endoscopic signs of inflammation (anemia/hematochezia) compared to those without these lesions in the ileocolonoscopy (p=0.07). A cutoff of 96 mg/kg of fecal calprotectin was able to predict histological bowel inflammation with 78% sensitivity and 67% specificity. There was no significant difference in fecal calprotectin levels between patients treated or not with NSAIDS.

Conclusions. Patients with spondyloarthritis are at increased risk of developing inflammatory bowel disease. The higher prevalence of microscopic bowel inflammation in these group of patients, treated or not with NSAIDS, may be an early sign of this increased risk. The measurement of fecal calprotectin in patients with spondyloarthritis, without known gastrointestinal disease, may be useful in the stratification of those with higher risk of presenting with microscopic bowel inflammation and could be helpful to the judicious indication of colonoscopy. The results of this study support the use of fecal calprotectin as a valuable biomarker of early intestinal inflammation in patients with spondyloarthritis.

REVIEWERS

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DO N-3 POLYUNSATURATED FATTY ACIDS AFFECT ECM REMODELING IN PSORIATIC ARTHRITIS?

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Introduction. Psoriatic Arthritis (PsA), a chronic immune-mediated inflammatory disease, is characterized by involvement of both axial and peripheral skeleton as well as potential skin and nail disease. The inflammatory milieu in PsA leads to accelerated tissue remodeling and the release of extracellular matrix (ECM) metabolites into circulation. These can be measured in serum as biomarkers of tissue remodeling and may give mechanistic insight to effect of different interventions at the tissue level. This study aimed to investigate if n-3 polyunsaturated fatty acids (PUFAs) have a beneficial effect on altered tissue remodeling in PsA.

Materials and Methods. The participating PsA patients were randomized into two groups receiving a daily supplement of either 3g PUFA or 3g olive oil (placebo) for 24 weeks. Tissue metabolites were measured in baseline and 24-weeks sera (n=276) by ECM specific ELISAs: C2M (type II collagen degradation), C3M (type III collagen degradation), C4M2 (type IV collagen degradation), PINP (type I collagen formation), PNP7TS (type IV collagen formation), and CRPM (MMP degraded metabolite of CRP). Comparison between groups were done by ANCOVA adjusting for age, gender, BMI and disease duration.

Results. Supplementation for 24 weeks led to significant reductions in tender joint count, DAS-28 CRP, LEI, SPARCC and PASI in the n-3 PUFA group, but these changes were not significantly different compared to the placebo group. Furthermore, we found that % changes in ECM biomarkers were positively correlated to the clinical outcomes in PUFA treated group. % changes in C2M (rho 0.29, p=0.048) and PNP7TS (rho 0.246, p=0.031) were correlated to change in DAS-28 while PINP (rho 0.266, p=0.031) correlated to change in LEI score.

Conclusions. Chronic inflammation underlying PsA pathology results in an increased amount of tissue remodeling. n-3 PUFA moderately improves clinical outcome in PsA patients possibly by modulating ECM remodeling, as depicted by serological biomarkers.

P52

PATIENTS AWARENESS OF THE DISEASE TREATMENT, DISEASE ACTIVITY AND SPINAL MOBILITY MONITORING BEFORE AND AFTER EDUCATIONAL SCHOOLS FOR RHEUMATOLOGISTS AND THE PATIENTS WITH ANKYLYING Spondylitis


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Awareness of patients about the nature of their disease is the key to successful treatment of ankylosing spondylitis (AS).

Patients. To compare the number of patients, informed of the main indexes of AS monitoring and in goals of the treatment before and after schools for the patients, and to get information about frequency of monitoring of AS activity and patients’ spinal mobility in real practice before and after schools for the physicians.

Methods. In 2017, members of Russian Society of Rheumatology and Mutual Aid Society of Bechterew’s Disease performed 11 educational schools for patients with AS in different regions of Russia and 12 educational schools for the physicians in the same regions. Before and 4-6 month after the school participants, were asked on several questions about AS activities and patients’ functional status monitoring and their awareness in it.

Results. 510 patients with AS and 302 physicians participated in schools in 2017. 320 patients completed the questionnaire twice (in 2017 and 2018).

In 2017 regular monitoring of AS activity had 36.1% of the patients, and 35.1% in 2018 (p=0.05).

In 2017, 21.3% of respondents did not know what the ASDAS index is, and in 2018 only 11.2% of patients were uninformed about ASDAS (p=0.494). In case of patients’ worsening ASDAS was calculated in 24.2% of responders in 2017 and in 49.9% in 2018 (p=0.00). The physician never defined the ASDAS index at 19.4% in 2017 and 13.3% in 2018 (p=0.015).

In 2017 physicians monitored the BASMI 1 and more times per year in 47.2% of responders and in 50.9% of AS patients in 2018. In 2017 23.1% of patients did not know what the BASMI index is, in 2018 11.9% of respondents were uninformed about BASMI.

As a main reason for taking of NSAIDs 72% of respondents noted pain relief, and 19.6% - decrease of the structural progression of the disease.

Conclusions. 4/5 of the patients with ankylosing spondylitis in Russian Federation were well informed about ankylosing spondylitis, however, there is great rate at baseline; Educational schools for the patients and rheumatologists could improve quality of AS management and increase number of well-educated patients.
**P53**

**SERUM GLUCOCORTICOID-INDUCIBLE KINASE-1 (SGK-1)**

**SGK-1 LEVELS IN PATIENTS WITH ANKYLOSING Spondylitis**

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**Introduction/Aim.** Ankylosing spondylitis (AS) is an inflammatory autoimmune disease. The etiology of AS is not well understood, but evidence supports an interplay of genetic, immunologic, and environmental factors. The immune system composed of various cells, secreted mediators and markers that manage and regulate the immune responses and inflammation. The inflammation has a critical role in the pathogenesis of AS. Glucocorticoid-inducible kinase-1 (SGK1) is genomically upregulated by cell stress. Excessive SGK1 expression and activity participates in the pathophysiology of several disorders, such as inflammation, autoimmune disease, fibrosis, and tumor growth. In this study, we analyzed the possible role of serum SGK-1 levels in the pathogenesis of AS.

**Materials and Methods.** 53 patients with AS (25 patients with axial involvement; 9 female, 16 male, mean age: 37.3±4.1 years, mean disease duration 10.2±2.9 years and 28 patients with peripheral joint involvement; 7 female, 21 male, mean age: 34.9±3.1 years, mean disease duration; 5.8±2.6 years) and 23 healthy controls (8 female, 15 male; mean age; 33.7±2.6 years) were enrolled in this study. Serum SGK-1 levels were determined by ELISA.

**Results.** The mean serum SGK-1 levels were 74.8±13.5 pg/ml in healthy controls, 285.9±38.1 pg/ml in patients with axial involvement and 428.1±35.9 pg/ml in patients with peripheral joint involvement. Serum SGK-1 levels were significantly high in patients with AS compared to healthy controls (p<0.001). Serum SGK-1 levels were significantly high in patients with peripheral joint involvement compared to in patients with axial involvement (p<0.01).

**Discussion.** In this study, serum SGK-1 levels were significantly elevated in patients with AS.

**Conclusions.** Our results suggest that serum SGK-1 mediated immunological mechanisms play an important role in the pathogenesis of AS.

**P54**

**USE OF MRI AND BIOLOGICAL THERAPY IN INCIDENT PATIENTS DIAGNOSED AS ANKYLOSING SPONDYLITIS AND SPONDYLOARTHRITIS: DANISH NATIONWIDE COHORT STUDY 2000-2013**

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**Introduction.** Only a few studies have reported incidence of Ankylosing Spondylitis (AS) and Spondyloarthritis (SpA), use of MRI and biological therapy during the last decade.

**Aim.** To describe the incidence of AS and SpA in the Danish population from 2000-2013 and rates of MRI and biological therapy.

**Materials and Methods.** All patients with the diagnosis of AS (ICD10: DM40) or SpA (ICD10: DM46) with a valid civil registration in Denmark in the time period from the January 1st 2000 until December 31st 2013 were identified in the Danish National Patient Registry. Incident cases were identified and rates of MRI and biological therapy were calculated for each year.

**Results.** During 2000 until 2013 3620 incident cases were identified (AS: 2116, SpA: 1504). AS are overrepresented by males (58-80%) and SpA by females (approximately 25% in 2013).

**Discussion and Conclusions.** The incidence of AS stabilizes from 2005 which is in line with previous studies exploring the trends of AS incidence. The incidence of SpA has increased significantly during the time period 2000 to 2013, which is in accordance with introduction of MRI scans for diagnostic use and biological therapy for treatment.

**P55**

**DISEASE ACTIVITY AND CHARACTERISTICS OF SpA- PATIENTS FULFILLING ESSG CRITERIA ONLY COMPARED TO SpA- PATIENTS FULFILLING ASAS CRITERIA**

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**Introduction/Aim.** Spondyloarthritis (SpA) is a rheumatic disease with axial and peripheral inflammatory arthritis. The disease is associated with psoriasis, inflammatory bowel disease and uveitis. Most patients fulfill both ASAS-criteria and ESSG criteria. Do the patients who fulfill only ESSG criteria differ in age, disease duration, disease activity, physical function or comorbidities?

**Materials and Methods.** Patients with spondyloarthritis in the district of Rana, Norway, were recruited from hospital registers, family doctors and by advertisement in local newspaper. Clinical data, CRP and HLAB27 were collected; x-ray and MRI of SI-joint were performed if the patient had inflammatory back pain. Symptomatological relatives were invited to clinical investigation and were included if they fulfilled the ESSG criteria. 61 patients fulfilled ESSG criteria only. 8 patients fulfilled ASAS criteria only, 329 fulfilled both criteria-set.

**Results.** Patients fulfilling only ESSG-criteria but not ASAS criteria for SpA do not differ from patients fulfilling ASAS-criteria in disease activity as measured by CRP or Asdas but they have a lower disease activity by BASDAI. Physical function as measured by BASFI is better and there is a trend for a better MHAQ but not significantly. They are significantly younger, and there is a trend towards shorter disease duration. The proportion of patients with IBD and acute uveitis is similar, but the proportion of patients with psoriasis is significantly lower.

**Discussion.** Patients fulfilling ESSG criteria only are a minority among SpA-patients. They are younger and it is possible that they have not developed the disease fully yet. Since they have similar disease-activity as patients fulfilling ASAS criteria they should also be considered for treatment with biologics.

**Conclusions.** More patients fulfill ESSG-criteria than ASAS-criteria. They have similar disease activity, are younger and have better physical function.

**P56**

**SERUM FIBROBLAST GROWTH FACTOR-23 LEVELS WERE HIGHER IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS AND MAY BE ASSOCIATED WITH DISEASE ACTIVITY**

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**Introduction and Aim.** Low levels of sclerostin may be associated with the development of syndesmophyte in patients with ankylosing spondylitis (AS). Bone sclerosis another osteocycle factor is fibroblist growth factor-23 (FGF-23) which may also inhibit osteoblast differentiation and matrix mineralization. We aimed to evaluate serum FGF-23 and sclerostin levels in patients with axial spondyloarthritis (axSpA) and to compare with healthy control subjects. We also assessed relationship between the serum FGF-23, sclerostin levels and disease related variables in particular the presence of structural changes.

**Materials and Methods.** In total 109 axSpA patients according to ASAS classification criteria and age and sex matched 57 healthy control subjects were included. Subjects with renal failure, significant comorbid conditions and under anti-TNF treatment were excluded. Serum levels of FGF-23 and sclerostin were measured using enzyme-linked immunosensor assay kits.

**Results.** There were 55 patients with non-radiographic axSpA and 54 patients with AS. Serum levels of FGF-23 levels were significantly higher in axSpA patients than healthy subjects. Although there was a trend towards a lower sclerostin levels in axSpA patients this difference did not show statistical significance (p=0.633). In axSpA patients serum FGF-23 levels were found to be correlated with erythrocyte sedimentation rate (ESR) (r=0.006, r=-0.265), C-reactive protein (CRP) (r=0.017, r=-0.229) and patients’ height (r=0.027, r=-0.221). There was no relationship between FGF-23 and mSASSS score or the presence of syndesmophyte. Subgroup analysis revealed that the duration of disease (p=0.005), ESR (r=0.007), CRP (r<0.001) and mSASSS (r=0.008) scores were significantly higher in AS patients than non-axSpA patients. However serum sclerostin levels were significantly higher in nr-axSpA patients (144.4±72.8 vs 1150.8±754.3 pg/mL and p=0.029).

**Conclusions.** Our results suggested that serum FGF-23 is increased in axSpA patients. And also disease activity may contribute to an up-regulation in serum FGF-23 levels.
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EXPRESSION OF BIOMARKERS IN PSORIATIC ARTHRITIS

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Introduction and Aim. The lack of measurable laboratory parameters in Psoriatic Arthritis (PsA) addresses the needs for diagnostic and prognostic tools to set early diagnosis and assess disease severity. The aim of this study was to analyze if soluble biomarkers could discriminate between disease phenotypes in PsA or, between patients with PsA and healthy controls.

Methods and Material. In this cross-sectional study, 274 patients with established disease and 30 healthy controls were included. 39 different serological biomarkers were investigated in relation to PsA disease activity, disease manifestations and in comparison with controls. In addition to standard statistical methods, orthogonal partial least squares discriminant analysis (OPLS-DA) was used to investigate different phenotypes of PsA.

Results. Psoriatic arthritis activity was significantly associated with CRP (pc=0.0008), IL-6 (pc=0.001), IL-16 (pc=0.007) calprotectin (pc=0.014), IL-12II-23p40 (pc=0.02) and ICAM-1 (pc=0.045). Different PsA disease phenotypes were associated with different biomarkers, e.g., axial disease (with or without peripheral disease) was associated with IL-6 (pc=0.044), IL-16 (pc=0.044), MIP-1β (pc=0.039) and polyarthritis was associated with IL-6 (pc=0.0006), SAA (pc=0.0098), CRP (pc=0.012) and IL-8 (pc=0.044), although it was not possible to statistically separate the different phenotypes with OPLS-DA. An association was also seen in patients with PsA who, at any time had been prescribed bDMARD (TNFα (pc=0.0001), TNF-α (pc=0.0003), calprotectin (pc=0.0009), CRP (pc=0.016) and lower levels of Tie-2 (pc=0.027)). No significant differences were found when PsA patients were compared with healthy controls.

Conclusions. In this study we could confirm the great heterogeneity of PsA, with different biomarkers being associated with various phenotypes of the disease. None of the biomarkers could, by itself, or in combination, separate PsA from controls.

References

P58

ASSOCIATION BETWEEN HIGH BODY MASS INDEX AND CLINICAL FEATURES OF AXIAL SPONDYLOARTHRITIS

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Introduction. Obesity is associated with a proinflammatory state and could increase the inflammatory burden of rheumatic disease. The aim of this study was to evaluate whether body mass index (BMI) is associated with parameters of clinical characteristics, radiologic progression and disease activity in axial SpA.

Patients and Methods. Total 87 patients with axSpA were enrolled (male 66 and female 21). Demographic data, and initial and follow-up data of clinical manifestations, treatment and radiologic features were collected. Diseases activity of axSpA was assessed by erythrocyte sediment rate (ESR), C-reactive protein (CRP), and Bath ankylosing spondylitis disease activity index (BASDAI). Axial SpA patients with active disease, not affording Anti TNF-alpha agents with BASDAI ≥ 4 were divided into two groups - group 1: BASDAI ≥ 4 and BASDAI < 4. Baseline data and follow-up data were collected. The mean BMI in patients with axSpA was 25.5 (IQR 20.6-24.8) and 22% of all patients had high BMI. There was no statistically significant difference between high BMI group and controls in demographic data, clinical characteristics, radiologic progression and disease activity in axSpA. Further large-scale studies are required for the identification of clinical significance of BMI in axSpA.

References

P59

DISEASE MODIFYING ANTI RHEUMATIC DRUGS IN THE TREATMENT OF SAPHO SYNDROME: SYSTEMATIC LITERATURE ANALYSIS

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Introduction. SAPHO (Synovitis Acne Pustulosis Hyperostosis Osteitis) Syndrome is a heterogeneous clinical entity close to spondyloarthritis. The management is not codified and there is no validated evaluation tool for SAPHO syndrome.

Aim. To perform a systematic analysis of the literature in order to evaluate the effects of DMARDs in SAPHO syndrome.

Methods. Patients were included when therapeutic effect of treatment (Bisphosphonates, synthetic and biologic DMARDs) was evaluable (Pubmed research until April 2017). Treatment was considered effective when the patient validated the response criteria defined in the study or if at least partial benefit was obtained for a minimum of three months. The different treatments were ranked according to their effectiveness rate and then grouped by therapeutic class to determine an overall response rate. These rates led to the calculation of an efficacy index weighted by the number of patients treated in the subgroup (molecular or therapeutic class) compared to the total number of patients in our study.

Results. Treatment efficacy was evaluable in 284 of the 292 patients analyzed. The group of treatments that most often induces a therapeutic response (in more than 75% of cases) includes Ibandronate, Etanercept, Anakinra, Infliximab, Pamidronate and Adalimumab. Pamidronate, which represents the largest subpopulation in our study, has the highest weighted index of efficacy. There was no clear clinical profile of a good responder to a particular treatment.

Table: Therapeutic class

<table>
<thead>
<tr>
<th>Therapeutic class</th>
<th>Number of patients</th>
<th>Number of responders</th>
<th>Efficacy rate (%)</th>
<th>Weighted index</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bisphosphonates</td>
<td>139</td>
<td>122</td>
<td>87.77</td>
<td>42.96</td>
</tr>
<tr>
<td>Conventional DMARDs</td>
<td>68</td>
<td>32</td>
<td>47.06</td>
<td>11.27</td>
</tr>
<tr>
<td>Anti TNF alpha</td>
<td>60</td>
<td>51</td>
<td>85</td>
<td>17.96</td>
</tr>
<tr>
<td>Other biologics</td>
<td>17</td>
<td>10</td>
<td>58.82</td>
<td>NA</td>
</tr>
<tr>
<td>TOTAL</td>
<td>284</td>
<td>215</td>
<td>75.82</td>
<td>NA</td>
</tr>
</tbody>
</table>

Conclusion. This work made it possible to rank the different DMARDs used in the SAPHO syndrome.

P60

TREATMENT OUTCOME WITH COMBINED METHOTREXATE, SULFASALAZINE AND ON-DEMAND NSAIDS IN AXIAL SPONdyLOARTHRITIS IN A RESOURCE-LIMITED REAL WORLD CLINICAL PRACTICE

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Introduction. ASAS recommendations state, there is no evidence for Methotrexate (MTX)/Sulfasalazine (SSZ) in axial disease but SSZ may be considered in those with peripheral arthritis. In India, most patients cannot afford biological agents.

Aim. Evaluation of response to combined MTX+SSZ; on demand NSAIDs in Axial SpA patients with active disease, not affording Anti TNF-alpha agents with ASAS20 response as primary outcome.

Materials and Methods. A prospective observational, single centre, cohort study on 150 consecutive AxSpA patients fulfilling our study criteria who were initiated on combined MTX/SSZ based on physician discretion, was conducted from July 2016 to July 2017. The patients were categorised into 2 groups- pure axial involvement (group 1) and axial with peripheral involvement (group 2).

Results. In the ‘per-protocol’ study population, ASAS20 response 3 months post therapy with MTX/SSZ combination and on-demand NSAIDs was achieved in 31/59 (52.5%) & in 24/35 (68.5%) in Groups 1 & 2 respectively (p=0.1). At 6 months, ASAS20 response was seen in 45/76 (59.2%) & 24/44 (63.6%) in groups 1 & 2 respectively (p=0.06). Combined DMARD therapy, resulted in significant reduction in mean NSAID intake (as per ASAS NSAID index) from 29.6 to 14 over 6 months from baseline (p=0.001); similar in both groups. When using a BASDAI score (active disease ≥ 6) driven policy for TNF therapy, a 34% reduction of AxSpA patients escaping to TNF inhibitors was seen.
**Poster Presentations**

**P61**

**CERTOLIZUMAB PEGOL IN A SPANISH COHORT OF PATIENTS WITH PSORIATIC ARTHRITIS - PRELIMINARY RESULTS**

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**Background.** Certolizumab pegol is an anti-TNF drug approved for psoriatic arthritis (PsA) in Spain since 2012; so rheumatologists have a long experience with its use. However, for the new indication in cutaneous psoriasis (PsO), phase III clinical studies are currently underway.

**Objectives.** To describe the baseline characteristics and the evolution of a cohort of patients with PsA and PsO treated with Certolizumab, and to assess possible differences between patients who interrupt or maintain this treatment.

**Methods.** Retrospective multicenter study on 34 patients with PsA treated with Certolizumab between 2012 and 2017. The main outcome measure was the PGA (Physician global assessment) that evaluates cutaneous involvement on a scale of 5 categories, from “without affection” up to “severe affection”.

**Results.** 34 patients were included, mainly women (73%), with an average duration of PsO and PsA of 11.9±12.2 and 9.7±6.9 years, respectively. The majority had peripheral arthritis (88%), with polyarticular forms (65%). There was axial involvement in 26% of the cases, dactylitis and arthritis of distal interphalangeal joints (DIP) in 38%, and plaque psoriasis in 59%. 73% had received prior biological therapy. The DAS28 showed a downward trend during the follow-up, with initial and two years values of 5.2 and 3.2 correspondingly. In relation to the main outcome measure, of the 31 initial patients, only 23 could be assessed at 6 months, 13 at year and 4 at two years. The percentages of patients without affection were 25%, 43%, 38% and 50% at baseline, 6 months, 1 and 2 years; 55%, 48%, 54% and 50% had minimal involvement; and the affection was mild in 6%, 9% and 8%, for the first 3 follow-up times. The differences between baseline PGA and at 6 months of follow-up were significant (p=0.001), while the baseline-1 year differences were at the limit of statistical significance (p=0.049). Of the 34 patients, 6 stopped treatment (18%). The patients who stopped had shorter duration of PsO and PsA, higher frequency of obesity, HLAB27, peripheral arthritis, polyarticular forms, arthritis of DIP, PsO in plaques, and treatment with MTX and steroids. However, none of the observed differences reached values of statistical significance.

**Conclusions.** In the studied sample, the treatment with certolizumab pegol has shown effectiveness for the PsO and the PsA at 6 months. The 1-year changes were at the limit of statistical significance and changes at 2 years could not be analyzed due to losses to follow-up.

No significant differences were observed in the clinical characteristics among the patients who continued / interrupted the treatment, although these results may be due to the small size of the studied sample.

**P62**

**EVALUATION OF THE WORK PRODUCTIVITY IN ANKYLOSING SPONDYLITIS (AS) AND PSORIATIC ARTHRITIS (PsA) PATIENTS BEFORE AND AFTER THE START OF ADALIMUMAB THERAPY IN DAILY PRACTICE IN BELGIUM (SpActive STUDY)**

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**Introduction.** The aim of this study was to analyze the employment status and work productivity of patients with AS and PsA before and after the start of adalimumab and to evaluate the relationship between employment status, work productivity, disease activity and clinical evaluation.

**Methods.** This is a multicenter, observational study of adult patients diagnosed with AS and PsA, starting adalimumab treatment in line with Belgian reimbursement criteria. Clinical and HRQoL parameters as well as work productivity (using WPAI-SHP) are evaluated after 3, 6, 12 and 18 months.

**Results.** Data from 173 patients were analyzed of which 117 had AS (67.6%) and 56 had PsA (52.4%), 121 patients (69.9%) completed the study. On average, all components of the WPAI questionnaire (absenteeism, presenteeism, total work productivity impairment due to the disease and % activity impairment due to the disease) improved substantially from baseline to month 18 (and to the last observation after baseline). Most of the improvement was already observed after 3 months. In the AS patients there was a clear correlation between BASDAI and HAQ-DI improvement between baseline and month 18 and work productivity parameters. A similar correlation was noted between DAS28 and HAQ-DI improvement and work productivity parameters between baseline and month 18 in the PsA patients. The safety events were in line with the known safety profile of adalimumab in AS and PsA patients.

**Conclusion.** For AS and PsA patients treated with adalimumab there is a marked improvement in disease activity and quality of life outcomes. The study demonstrated a substantial improvement in all four WPAI variables in both AS and PsA patients treated with Adalimumab. The clinical and HRQoL outcomes correlate clearly with meaningful improvements in work productivity and daily activities.

**P63**

**CANADIAN OBSERVATIONAL STUDY ASSESSING THE EFFECTIVENESS OF ADALIMUMAB VS. NON-BIOLOGIC DMARDS IN ANKYLOSING SPONDYLITIS (COMPLETE-AS): 12-MONTH DATA**

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**Introduction/Aim.** COMPLETE-AS is an ongoing observational study of anti-TNF-naïve adults with active AS requiring change in current AS treatment to (1) subsequent NSAID or non-biologic DMARD (nbDMARD group), or (2) adalimumab (ADA group). This analysis aimed at comparing the baseline characteristics of patients in the nbDMARD and ADA groups and the 12-month effectiveness of the two treatment methods.

**Methods.** Patients were enrolled between July 2011 and June 2016. Outcomes analyzed were extra-articular manifestations (EAM 1: IBD, psoriasis, uveitis, enthesitis; EAM 2: IBD, uveitis, enthesis), BASDAI, BASFI, and SF-12. Base-line-adjusted changes in outcomes were compared between-groups using linear mixed model.

**Results.** 609 patients (nbDMARD=277, nADA=332) were included without significant demographic differences between-groups. Patients initiating ADA were more likely to be unemployed (38% ADA vs. 27.1% nbDMARD, p<0.001), had worse QoL (SF-12 PCS: 24.4 vs. 24.7, p=0.002) at baseline. Baseline prev-entiveness of the two treatment methods.

**Discussion/conclusion.** AS patients initiating ADA in Canadian routine care have greater disease severity and impaired QoL compared with those initiating non-biologic treatment. ADA treatment for 12 months resulted in greater reduction in EAM prevalence and in disease severity scores compared to non-biologic agents.

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CANADIAN OBSERVATIONAL STUDY ASSESSING THE EFFECTIVENESS OF ADA LiMUNAB VS. NON-BIOLOGIC DMARDS IN PSORIATIC ARTHRITIS (COMPLETE-PAA): 12-MONTH DATA

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Introduction/Aim. COMPLETE-PAa is an ongoing observational study assessing the effectiveness of adalimumab (ADA) and non-biologic DMARDs (nbDMARDS) in anti-TNF-naïve adults with active PsA failing initial treatment. This analysis aimed at comparing the baseline characteristics of nbDMARD- and ADA-treated patients, and the 12-month effectiveness of the two treatments.

Methods. Patients were enrolled between Jul/2011 and Jun/2016. Outcomes analyzed were: DAS28, SF-12, DLQI, extra-articular manifestations (EAMs; enthesis and dactylitis), psoriasis BSA, modified MDA (achievement of 4 [mMDA 1] and 5 [mMDA 2] of the following 6 criteria: TJC≤1, SJC≤1, BSA≤3%, pain≤15mm, PtGA≤20mm, HAQ≤0.5), modified remission (SJC=0, TJC=0,5 mMDA 1 and 5 mMDA 2 of the following 6 criteria: TJC≤1, SJC≤1, BSA≤3%, pain≤15mm, PtGA≤20mm, HAQ≤0.5), modified remission (SJC=0, TJC=0, no enthesis, dactylitis, BSA≤3%, and HAQ≤0.5), DAPSA LDA (≤14) and remission (REM≤4).

Results. 406 patients were included (n_{baseline}=146, n_{posttreatment}=260). Patients initiating ADA were more likely to be unemployed (47.3% vs 34.9%, p=0.015), had higher DAS28 (4.8 vs 4.4, p=0.002) and DLQI (6.1 vs 4.3, p=0.007), and higher rates of BSA≥3% (44.6% vs 35.0%, p=0.063) and high DAPSA disease activity (50.8% vs 32.3%, p=0.015). A higher proportion of nbDMARD patients had dactylitis (36.1% vs 25.3%, p=0.023). No differences were observed in baseline enthesis, overall EAMs, or QoL.

At 12 months, baseline-adjusted DAS28 (2.6 vs 3.4, p=0.001) and DLQI (2.2 vs 2.9, p=0.030), but not SF-12, were lower in ADA patients. Furthermore, ADA patients had significantly lower DAPSA score (p=0.025) (LDA/REM vs ADAS 64.9% vs 58.6%; REM: 37.7% vs 17.1%), and numerically higher rates of modified remission (14.7% vs 9.7%, p=0.311), mMDA 1 (15.6% vs 12.6%, p=0.532), mMDA 2 (17% vs 11.5%, p=0.253), and BSA≥3% (83.9% vs 83.9%, p=0.207). EAM prevalence was significantly lower in ADA patients (17.4% vs 35.8%, p=0.001).

Discussion/Conclusion. PsA patients initiating ADA in Canadian routine care had a greater baseline disease severity compared with those initiating nbDMARDS. However, 12-month ADA treatment was associated with improved disease control and EAMs.

P65

EXPLORING SUB-OPTIMAL RESPONSE TO TUMOUR NECROSIS FACTOR INHIBITORS IN AXIAL SPONDYLOARTHRITIS

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Objectives. To define sub-optimal response to tumour necrosis factor inhibitors (TNFi), compare long-term drug survival rates and identify predictors of sub-optimal response in axial spondyloarthritis (axSpA) patients in a United Kingdom (UK) cohort.

Methods. All axSpA patients attending 2 centres who commenced TNFi between 2002 and 2016 were included. Routinely-recorded patient data was reviewed retrospectively. Patients with paired BASDAI at baseline, 3 and/or 6 months were included. Sub-optimal response was defined as achieving a ≥2-point reduction in BASDAI but not BASDAI≤50, post-treatment BASDAI remaining at ≥4, and in the opinion of the treating physician, these patients demonstrated a meaningful clinical response.

Results. Four hundred and ninety-nine patients were included: eighty-two (16.4%) patients were classified as having a sub-optimal response; 64(78%) patients had significantly lower DAPSA score (p=0.530), but not SF-12, were lower in ADA patients. Furthermore, ADA patients had significantly lower DAPSA score (p=0.025) (LDA/REM vs ADAS 64.9% vs 58.6%; REM: 37.7% vs 17.1%), and numerically higher rates of modified remission (14.7% vs 9.7%, p=0.311), mMDA 1 (15.6% vs 12.6%, p=0.532), mMDA 2 (17% vs 11.5%, p=0.253), and BSA≥3% (83.9% vs 83.9%, p=0.207). EAM prevalence was significantly lower in ADA patients (17.4% vs 35.8%, p=0.001).

Discussion. This is the first study to define sub-optimal response and describe the characteristics of sub-optimal TNFi responders in axSpA. Older age at initiating TNFi is a predictor of sub-optimal response. Further research needs to be undertaken in order to understand this group.

P66

EFFICACY OF NEW TREATMENTS ON DACTYLITIS OF PSORIATIC ARTHRITIS (PsA): UPDATE OF SYSTEMATIC LITERATURE REVIEW

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Introduction/Aim. Dactylitis is a frequent disabling feature of psoriatic arthritis (PsA). Therapeutic strategy on dactylitis is not really codified. The aim of the study was to evaluate efficacy on dactylitis of different treatments currently available in PsA.

Methods. We performed a literature review from June 2014 to October 2017 based on Pubmed, using the search terms “psoriatic arthritis” and “treatment” with only clinical trials. 89 articles were identified (English-language reports only). Thus, we selected only randomized, double-blind placebo-controlled trials in which analysis of dactylitis was exposed. 11 publications were selected for full review.

Results. Calculating of effect size was possible and available only in one study: secukinumab’s effect size was 4.5% in McInnes study (FUTURE 2). Calculation of Odds Ratio (of residual dactylitis between treatment and placebo groups) was possible on part of studies with significant results for clazakizumab (200mg dosing) and secukinumab in patients TNF exposed (Table).

<table>
<thead>
<tr>
<th>Treatment</th>
<th>LDA/REM</th>
<th>200 (Mease ARD 2016)</th>
<th>200 (Mease A&amp;R 2016)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clazakinumab</td>
<td></td>
<td>(16)</td>
<td>(16)</td>
</tr>
<tr>
<td>Usektakinumab</td>
<td></td>
<td>(11)</td>
<td>(16)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Treatment</th>
<th>LDA/REM</th>
<th>100 (Mease A&amp;R 2016)</th>
<th>25 (Mease A&amp;R 2016)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clazakinumab</td>
<td></td>
<td>(16)</td>
<td>(16)</td>
</tr>
<tr>
<td>Secukinumab</td>
<td></td>
<td>(FUTURE 2, Kavanagh JOR 2016)</td>
<td>(FUTURE 2, Kavanagh JOR 2016)</td>
</tr>
</tbody>
</table>

Lower range: 0.0, 0.1, 0.4, 0.7
Mean: 0.08, 0.14, 0.47, 0.7
Upper range: 1.0, 1.4, 2.19, 2.19

Conclusions. Dactylitis was always used as secondary outcome criteria with heterogeneous results. So conclusions need to be cautious. This invalidating clinical manifestation need to be evaluated as a primary outcome in the future.

P67

THE RELATIONSHIP BETWEEN DAILY PHYSICAL ACTIVITY AND TUMOR NECROSIS FACTOR INHIBITOR SURVIVAL TIME IN PATIENTS WITH ANKYLOSING SPONDYLITIS

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Background. This study aimed to determine whether daily physical activity is associated with tumor necrosis factor (TNF) inhibitor survival time in patients with ankylosing spondylitis (AS).

Methods. A total of 386 patients in the AS registry who were administered TNFi inhibitors were retrospectively reviewed. Physical activities were assessed, such as intense exercise, moderate physical activity, walking, strength training, and...
sleep. Clinical information was obtained through electronic medical records. Cox proportional hazard ratios (HRs) with confidence intervals (CIs) were estimated based on the ratio of TNF inhibitor survival time. In addition, we used a decision tree (classification and regression tree method) to visualize a strategy for maximizing TNF inhibitor survival time.

**Result.** Of the 386 patients, 33 ceased the initial TNF inhibitor treatment due to lack of efficacy and changed to other TNF inhibitors. The activity level of most patients was “walking” (298, 81.4%). The physical activity levels were as follows: 99 (27.0%) patients did not do much intense exercise, 136 (37.3%) did do moderate physical exercise, and 116 (31.3%) did not do strength training. In total, 216 (59.7%) patients got sufficient sleep. When assessing the HRs of all individual variables for TNF inhibitor survival time, no strength training (HR=3.07, CI: 1.07–8.83), female sex (HR=2.7, CI: 1.25–5.8), smoking period (HR=0.95, CI: 0.92–0.99), insufficient sleep (HR=0.4, CI: 0.17–0.95), drinking currently (HR=0.38, CI: 0.18–0.83), treatment with etanercept (HR=0.34, CI: 0.15–0.77), smoking history (HR=0.32, CI: 0.12–0.88), treatment with adalimumab (HR=0.32, CI: 0.12–0.81), and smoking currently (HR=0.18, CI: 0.05–0.6) were significantly associated with survival time (p<0.05). No variables remained significantly associated with survival time after multivariate analysis of HRs. In the decision tree, smoking, use of non-steroidal anti-inflammatory drugs, use of steroids, type of TNF inhibitor, period of oral medication only, age, and moderate physical activity were predictive of survival time after administration.

**Conclusion.** Daily physical activity seems to be associated with the survival time of TNF inhibitors. Appropriate physical activity may help to reduce disease activity and maintain the survival time of biologics in patients with AS.

**P68**

**COMPARISON OF CONTINUOUS USE OF NSAIDs AND ON-DEMAND MODE IN PATIENTS WITH EARLY AXIAL SPONDYLOARTHRITIS**

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**Background.** According to the ASAS-EULAR management recommendations NSAIDs are first-line drugs for treatment patients (pts) with axial spondyloarthritis (axSpA). But currently, there is no clear opinion about the effect of NSAIDs on radiographic progression in patients with early axSpA. The aim of this study was to compare effectiveness of continuous use of NSAIDs and on-demand mode on radiographic progression in sacroiliac joints (SIJ) in pts with early axSpA.

**Materials and Methods.** The research included 68 pts with early axSpA (ASAS criteria, 2009) from Moscow CORSAR cohort with disease duration ≤5 years, age ≤55 years and at least 2 years follow-up. Pts were randomized into two treatment groups: pts with continuous use of NSAIDs and on-demand use of NSAIDs. The dosages of NSAIDs accounted by the ASAS NSAID index. SIJ radiographs were evaluated at baseline and after 2 years follow-up. Radiographic SIJ stages were scored according to the modified New York criteria grading system. To assess the progression in SIJ, total stage of sacroilitis was calculated, by determining sum stage scores of sacroilitis in the left and right SIJ (from 0 to 8 points). The mSASSS index is not suitable for assessing radiographic progression at an early stage of axSpA, because at that stage of the disease, the cervical and lumbar spine have practically no damage.

**Results.** In the continuous NSAIDs treatment group N1, after 2 years of follow-up, median of a total stage of sacroilitis didn’t change and remained at 4.0 points, in the “on demand” group N2, this index significantly increased from 3.0 to 4.0 points.

**Table I.** Total stage of sacroilitis at baseline and after 2 years follow up.

<table>
<thead>
<tr>
<th></th>
<th>Total stage of sacroilitis, median [IQR]</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Baseline</td>
<td>After 2 years follow-up</td>
</tr>
<tr>
<td>Group N1 (n=35)</td>
<td>4.0 [3.0; 4.0]</td>
<td>4.0 [4.0; 6.0]</td>
</tr>
<tr>
<td>Group N2 (n=33)</td>
<td>3.0 [2.0; 4.0]</td>
<td>4.0 [3.0; 6.0]</td>
</tr>
</tbody>
</table>

*IQR*—interquartile range

**Conclusions.** Continuously uses of NSAIDs reduces radiographic progression in SIJ in pts with early axSpA.

**P69**

**HOW TO OPTIMIZE EXERCISE BEHAVIOUR IN AXIAL SPONDYLOARTHRITIS - RESULTS OF AN INTERVENTION MAPPING STUDY**

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**Introduction.** Regular exercise has many health benefits for people with axial spondyloarthritis (axSpA). However, most patients do not engage in frequent exercise. Therefore, a well-founded intervention is needed.

**Aim.** To identify effective intervention methods to optimize exercise behaviour in axSpA.

**Methods.** The first three steps of the Intervention Mapping (IM) protocol, which is a six-step framework for intervention development, were used to determine effective intervention components. This study comprised 1) a needs assessment, to examine the discrepancy between current and desired exercise behaviour of axSpA patients, 2) a determinants analysis, to identify barriers and facilitators (determinants) to overcome this discrepancy, and 3) an intervention method analysis, to select effective methods that target these determinants. All three steps included literature reviews and semi-structured interviews with axSpA patients (n=2) and specialised physiotherapists (n=2) to explore the literature search findings qualitatively and to rank the identified determinants and methods in order of relevance.

**Results.** The literature searches resulted in 28 (64), 23 (257) and 15 (209) includ ed articles (hits) for IM steps 1, 2 and, respectively. IM step 1 revealed that only one third of axSpA patients engage in (frequent) mobility, strengthening and/or cardiorespiratory exercises, while especially these components appear beneficial in axSpA. IM step 2 uncovered 19 relevant determinants of exercise behaviour in axSpA. IM step 3 identified 18 effective methods targeting these determinants. Guided practice, patient education, motivational interviewing, action planning, goal setting, feedback, monitoring, tailoring, health professionals’ training and group exercise appeared most relevant.

**Conclusions.** This study showed that in order to optimize exercise behaviour in axSpA, patients should be offered an intervention including education, motivational interviewing, goal setting and action planning and they should be stimulated to exercise in a group. In addition, therapists should be educated how to tailor, practice and monitor exercise and how to base this on thorough assessment.

**P70**

**EFFICACY AND SAFETY OUTCOMES IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS TREATED WITH CERTOLIZUMAB PEGOL: RESULTS FROM THE 48-WEEK RUN-IN PART OF C-OPTIMISE**

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**Introduction/Aim.** C-OPTIMISE is the first trial to evaluate whether certolizumab pegol (CZP) can be reduced/discontinued in patients with radiographic(r)-axSpA/ankylosing spondylitis (AS) and non-radiographic(nr)-axSpA achieving sustained remission after 48 weeks (wks)’ treatment. Here, we report interim efficacy and safety data for both subpopulations from the ongoing trial.

**Materials and Methods.** Up to wk48, C-OPTIMISE (NCT02505542) was open-label (Part A), followed by 48-wk parallel-group, double-blind, placebo-controlled treatment (full dose and half dose) to wk48 (Part B). Patients with adult-onset axSpA of ≤5 years’ duration, fulfilling ASAS classification criteria, were recruited. Part A: patients received CZP 400mg at wk0/2/4, then 200mg Q2W); patients achieving sustained remission (ASDAS≤1.3 at wk32 and ≤2.1 at wk48) or “victims of success” were eligible for Part B (secondary outcome). Primary outcome (not reported): percentage of patients in Part B not experiencing a flare. Missing values were imputed using non-responder imputation (NRI) and last observation carried forward (LOCF).

**Results.** Part A: Of 736 patients (Table I), 43.9% achieved sustained remission (r-axSpA/AS: 42.8%; nr-axSpA: 45.3%; NRI). At baseline, 98.5% patients had high/high very high disease activity (ASDAS≥2.1); At wk48, 52.7% (r-axSpA/AS: 54.6%)}.
P71

INTRAVENOUS GOLIMUMAB IN ADULT PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS: EFFICACY AND SAFETY THROUGH 1 YEAR


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Intro/Aim. GO-VIBRANT evaluated safety and efficacy of IV golimumab (GLM) in adult pts with active PsA over 1yr.

Methods. GO-VIBRANT is a Phase 3, multicenter, randomized, double-blind, in-patient controlled trial. The primary efficacy endpoint was ACR20 in the total PsA joints at Week 24 in pts meeting entry criteria. Additional endpoints at Week 24 and 28 included ACR50 and ACR70, and PASI 75, 90, and 100.

P72

WEIGHT-LOSS IMPROVES DISEASE ACTIVITY IN PATIENTS WITH PSORIATIC ARTHRITIS AND OBESITY

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Introduction/Aim. Psoriatic arthritis (PsA) is highly associated with obesity. This study aimed to determine the effects of weight-loss treatment with Very Low Energy liquid Diet (VLED) on disease activity in patients with PsA (Caspar criteria) and obesity (inclusion criterion: body mass index BMI ≥33 kg/m²).

Methods. VLED, giving a daily energy intake of 640 kcal, was taken during 12 or 16 weeks, depending on BMI. Afterwards an energy restricted diet was successively reintroduced. The treatment was given within a structured framework for support and medical follow-up during twelve months. Treatment with DMARDs and/or biologics was held constant from 3 months before baseline until 6 months after. The patients were assessed with 66/68 joints count, back-mobility tests, psoriasis body surface area (BSA), questionnaires, ESR, CRP and BMI at baseline, 3 and 6 months. The number of patients reaching Minimal Disease Activity (MDA), Psoriatic Arthritis Response Criteria (PsARC) and American College of Rheumatology (ACR) response criteria was calculated.

Results. Totally 41 patients, 63% women, with median age 54 years (IQR 48-62), completed the study. The median weight-loss was 18.7 kg (IQR 14.6-26.5) or 16.8% (IQR 14.7-26.3) of the baseline weight. A majority of the disease activity parameters improved significantly. The number of patients with MDA increased from n=12 (29%) to n=22 (54%) (p=0.002). 70% of (n=21), 53% (n=14) and 73%(n=3) respectively.

Conclusions. Weight-loss treatment with VLED had significant positive effects on disease activity in joints, spine, entheses and skin in patients with PsA and obesity. The study provides proof of the concept that obesity is involved in the pathophysiology of PsA.
P73


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Introduction. Vedolizumab is a humanized monoclonal antibody binding to α4β7 integrin and blocking the interaction between α4β7 integrin and mucosal cell adhesion molecule-1. Vedolizumab is used in moderate to severe Crohn disease (CD) as an alternative to TNF inhibitor therapy. While there are some case reports on beneficial effects of vedolizumab on both inflammatory bowel disease and spondyloarthropathy (SpA), some authors have submitted exacerbations of arthritis or sacroiliitis. Herein, we present a case with CD and SpA experiencing a flare of musculoskeletal symptoms under vedolizumab therapy.

Case Presentation. A 35 year-old female patient applied to our rheumatology outpatient clinic with complaints of right heel and low back pain. She had been diagnosed with CD in 2009 and with SpA in 2010. After treatment failure with mesalazine, azathioprine, prednisolone, and budenoside she commenced infliximab. Due to allergic reaction with infliximab, she was prescribed adalimumab until she became pregnant. After delivery, on not responding sufficiently to reinitialization of adalimumab, she received vedolizumab therapy within an international project. Her physical examination revealed tenderness in right Achilles tendon insertion and plantar fascia. Sacroiliac compression test was positive at the right, and FABER test was bilaterally positive. The MASES score was 3. BASDAI score was 7.2, and ASDAS-CRP was 3.1. Laboratory analyses were within normal limits (CRP:2.2 mg/l, ESR:7 mm/h, HLA B27:(−)). Right ankle ultrasound was unremarkable except for calcaneal spur (no effusion and Doppler sign). However, sacroiliac joint MRI reported bilateral early sacroiliitis characterized with irregularity, sclerosis and bone marrow edema which was noted on SpA in the literature, other reports indicate flares of sacroiliitis. This may be a paradoxical effect which may also be observed with TNF inhibitors (1).

Conclusion. Vedolizumab is a novel integrin blocker used for the treatment of active inflammatory bowel diseases. Although some improvements with vedolizumab was noted on SpA in the literature, other reports indicate flares of sacroiliitis. This may be a paradoxical effect which may also be observed with TNF inhibitors (1).

Reference

Fig. 1. STIR coronal MRI of the sacroiliac joint, focal bone marrow edema of the left sacral facet.

Fig. 2. T1 coronal MRI of the sacroiliac joint, bilateral focal erosive changes and minimal sclerosis.

P74

PREDICTING PERSISTENCE, DISCONTINUATION AND SWITCHING PATTERNS OF NEWLY INITIATED TNF INHIBITOR THERAPY IN ANKYLOSING SPONDYLITIS PATIENTS

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Aim. The objective of this study was to analyze treatment patterns in the 2 years following the initiation of TNF inhibitors (TNFi) in AS patients.

Methods. Adult patients with ≥2 AS diagnostic codes were included in this retrospective analysis of data from the Truven MarketScan Commercial Claims database. Patients who newly initiated a TNFi from 01/01/2009-12/31/2013 were indexed on their first TNFi. Patients were required to have a 1-year pre-index clean period of TNFi and continuous enrollment 1-year pre-index and 2-years post-index. Demographic, clinical, and treatment patterns were analyzed. Treatment patterns included switching to a new TNFi, discontinuation (≥90-day gap in therapy), or persistence (no gaps in therapy ≥90-days) during the 2-year follow-up period. Logistic regression analyses predicting persistent vs. non-persistent and switching vs. discontinuation were conducted.

Results. 1,372 AS patients (846 males/526 females) met the inclusion criteria for this study. Adalimumab was the first biologic for the majority of patients (44.6% males/43.3% females), followed by etanercept (40.4% males/41.6% females), infliximab (10.4% males/10.8% females), golimumab (4.6% males/3.8% females), and certolizumab pegol (0.0% males/0.4% females). During the follow-up period, 32.6% of male patients were persistent on their first TNFi, while only 22.8% of female patients were persistent. The majority of male (67.4%) and female (77.2%) patients discontinued their first TNFi. Patients pre-scribed cDMARDs (p=0.0482) were more likely to be persistent, while females (p=0.0005) and opioid users (p=0.0002) were less likely to be persistent on their first TNFi. Among those that discontinued their first TNFi, 32.8% (n=187) of males and 43.6% (n=177) of females switched to a second TNFi. Non-opioid analgesic users (p=0.0002), cDMARD users (p=0.0438), and females (p=0.0129) were more likely to switch to a second TNFi.

Conclusion. This study suggests that the majority of AS patients do not remain on their index TNF inhibitor 2 years post initiation.

Fig. 1. STIR coronal MRI of the sacroiliac joint, focal bone marrow edema of the left sacral facet.
P75

LEVELS OF ADHERENCE TO BIOLOGIC THERAPY OF SPONDYLOARTHRITIS PATIENTS

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Introduction. In clinical practice, knowledge about patients’ levels of adherence to medication is important. Our purpose is to evaluate our Spondyloarthritis (SpA) patients’ adherence to biologic therapy.

Material and Methods. Observational and cross-sectional study which included patients with SpA according to 2009 Assessment of SpondyloArthritis interna
tional Society (ASAS) classification criteria (CC) for axial spondyloarthritis or to 2011 ASAS CC for peripheral spondyloarthritis (including psoriatic arthritis), on biologic therapy, able to complete questionnaires autonomously and who agreed to participate. Demographic and clinical data were collected. To assess adherence, the Morisky Medication Adherence Scale (MMAS-8) was used and the patients were asked to apply it only to biologic therapy. Based on the MMAS-8, 3 levels of adherence were considered: 0 to <6 (low); 6 to <8 (medium); 8 (high).

Results. 55 patients were included; 54 on anti-TNF, 1 on Ustekinumab. Table 1 reports the variables collected. The mean MMAS-8 score was 6.9±1.1, the median 7.0 (6.5–8.0), the minimum 3.5 and the maximum 8. The adherence was medium in 52.7%, high in 27.3% and low in 20.0% patients. No significant differences were found in levels of adherence for gender, current age, disease duration, time on treatment with the current biologic, BASDAI, BASMI, ASAS, HADS-A, HADS-D and FACIT-F (p>0.05).

Conclusion. The adherence to biologic was at least medium for 80.0% of patients. Demographic and clinical variables, including disease activity do not seem to influence it.

Table 1. Means and medians of demographic and clinical variables.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Mean±SD</th>
<th>Median (IQR)</th>
</tr>
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<tbody>
<tr>
<td>Current age - years</td>
<td>49.9±12.3</td>
<td>49.1 (40.8-57.7)</td>
</tr>
<tr>
<td>Disease duration – years</td>
<td>18.0±11.1</td>
<td>14.1 (10.3-21.9)</td>
</tr>
<tr>
<td>Time on treatment with the current biologic therapy - years</td>
<td>4.2±2.6</td>
<td>4.3 (2.0-6.0)</td>
</tr>
<tr>
<td>BASDAI</td>
<td>2.9±2.2</td>
<td>2.8 (0.9-4.7)</td>
</tr>
<tr>
<td>BASMI</td>
<td>3.4±1.4</td>
<td>3.4 (2.4-4.2)</td>
</tr>
<tr>
<td>BASFI</td>
<td>5.2±3.2</td>
<td>2.2 (0.5-3.7)</td>
</tr>
<tr>
<td>ASAS</td>
<td>2.1±0.9</td>
<td>2.2 (1.4-2.8)</td>
</tr>
<tr>
<td>HADS-A</td>
<td>5.8±4.1</td>
<td>5.0 (1.0-9.0)</td>
</tr>
<tr>
<td>HADS-D</td>
<td>5.2±4.2</td>
<td>4.0 (1.0-9.0)</td>
</tr>
<tr>
<td>FACIT-F</td>
<td>37.3±10.1</td>
<td>36.0 (30.4-70.4)</td>
</tr>
</tbody>
</table>

P76

SECUKINUMAB DEMONSTRATES A CONSISTENT SAFETY PROFILE OVER LONG-TERM EXPOSURE (UP TO 4 YEARS) IN PATIENTS WITH ACTIVE ANKYLOSING Spondylitis – UPDATED POOLED ANALYSIS OF THREE PHASE 3 TRIALS

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Aim. To report updated long-term (up to 4 years of treatment) pooled safety and tolerability data for secukinumab (SEC) from three phase 3 studies in AS.

Methods. 371, 219, and 226 patients with active AS were randomised in the MEASURE 1, 2 and 3 studies, respectively. Study design, efficacy, and safety results have been previously reported.12 SEC doses included intravenous 10 mg/ kg or subcutaneous (s.c. 75–300 mg) loading, followed by s.c. maintenance dosing (75, 150, or 300 mg). Analysis included pooled patient (pt)-level data from all patients who received any dose (≥1) of SEC up to the date of the last pt attending the Week 156 study visit in MEASURE 1, and for all pts up to the Week 156 in MEASURE 2 and the Week 104 in MEASURE 3. Exposure adjusted incidence rates (EAIR) were calculated for differences in treatment exposure.

Results. 794 patients were included in the analysis (representing 1943.1 patient-years of SEC exposure). The most frequently reported AE was viral upper respiratory tract infection (Table). EAIRs for serious infections, Candida infections, inflammatory bowel disease (IBD), uveitis, neutropenia and major adverse cardiac events (MACE) were low (Table).

Conclusions. SEC was well tolerated during long-term treatment (up to 4 years) in patients with AS, with a favourable safety profile consistent with previous reports (1, 2).

References

Table. Summary of pooled safety: Entire safety period.

<table>
<thead>
<tr>
<th>Any secukinumab dose</th>
<th>N=794</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Total exposure, patient-years [minimum–maximum exposure (years)]</td>
<td>1943.1 (1-5000)</td>
<td></td>
</tr>
<tr>
<td>Death, n</td>
<td>5 (0.5)</td>
<td></td>
</tr>
<tr>
<td>EAIR per 100 patient-years (95% CI)</td>
<td>6.3 (2.7-17.6)</td>
<td></td>
</tr>
<tr>
<td>Most Common AEs</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urticarial rash</td>
<td>8 (0.4; 1.5)</td>
<td></td>
</tr>
<tr>
<td>Uveitis</td>
<td>5 (1.3; 3.3)</td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td>5 (1.3; 3.3)</td>
<td></td>
</tr>
<tr>
<td>Upper respiratory tract infection</td>
<td>6 (0.4; 1.5)</td>
<td></td>
</tr>
<tr>
<td>Selected AEs of interest</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sensible infections</td>
<td>12 (0.6; 1.9)</td>
<td></td>
</tr>
<tr>
<td>Infections</td>
<td>12 (0.6; 1.9)</td>
<td></td>
</tr>
<tr>
<td>Pelvic infection</td>
<td>12 (0.6; 1.9)</td>
<td></td>
</tr>
<tr>
<td>Uveitis</td>
<td>12 (0.6; 1.9)</td>
<td></td>
</tr>
<tr>
<td>Confirmed</td>
<td>12 (0.6; 1.9)</td>
<td></td>
</tr>
<tr>
<td>Neutropenia</td>
<td>7 (0.3; 1.3)</td>
<td></td>
</tr>
<tr>
<td>Poisons</td>
<td>6.3 (2.7-17.6)</td>
<td></td>
</tr>
</tbody>
</table>

1AEs in any SEC group with an EAIR >5 during entire safety period; Rates are for system organ class; Rates are for high level term; Rates are for preferred term (PT) (IBD PT data are reported for unspecified IBD); 8 cases of Crohn’s disease, 3 were flares in patients with history at baseline; 4 cases of ulcerative colitis, 1 was a flare with a history at baseline; 26 cases of uveitis, 14 were flares in patients with a history at baseline; Values are based on Novartis MedDRA query, which comprises 1) any AE; 2) any CVA; 3) all other CV events that are fatal, of a listing of 2200+ terms; CI: confidence interval; N: number of patients in analysis; n: number of patients with event.

Disclosure of interest
A. Deodhar Grant/research support from: AbbVie, Amgen, Eli Lilly, GSK, Janssen, Novartis, Pfizer, and UCB, Consultant for: AbbVie, BMS, Celgene, Chugai, Merck, Novartis, Pfizer, UCB, and Werfen, Speakers bureau: AbbVie, BMS, Celgene, Chugai, Merck, Novartis, Pfizer, UCB, and Werfen, H. Marzo-Ortega Grant/research support from: Janssen and Pfizer, Consultant for: AbbVie, Celgene, Janssen, Novartis, Pfizer, and UCB, X. Baraliakos Consultant for: AbbVie, BMS, Celgene, Chugai, Merck, Novartis, Pfizer, UCB, and Werfen.

P77

SECUKINUMAB SUSTAINS IMPROVEMENTS IN SIGNS AND SYMPTOMS IN PATIENTS WITH PSORIATIC ARTHRITIS THROUGH 2 YEARS (FUTURE 4)

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Aim. To assess long-term efficacy of subcutaneous secukinumab 150mg through 104 weeks in patients with active psoriatic arthritis (PsA) in the FUTURE 4 study (NCT02294227). Additionally, to explore efficacy of increasing 150mg dose to 300mg.

Methods. The study design has been described elsewhere.1 Secukinumab 150mg was increased to 300mg as early as Week-36 if active signs of disease were observed based on physician’s judgement; secukinumab 300mg was maintained thereafter. Clinical responses were analyzed as observed-pretreatment or post-escalation (12-16, 20-24 weeks) ACR and PASI responses were also evaluated.

Results. Of 341 randomized patients, 272 completed 104 weeks. Both secuki-
numab 150mg doses were superior to placebo with numerically greater and sustained efficacy through 2 years in both groups. In BLE patients, greater magnitudes of improvement were observed with SEC-300mg than 150mg in both unadjusted and adjusted analyses.

Conclusions. Although patients with BLE had more severe BL characteristics than patients with No BLE, SEC showed higher efficacy than placebo at Week 16 and maintained efficacy through 2 years in both groups. In BLE patients, greater magnitudes of improvement were observed with SEC-300mg than 150mg in both unadjusted and adjusted analyses.

Table. (Efficiency results with secukinumab in PA patients with or without baseline enthesitis defined by Leeds Enthesitis Index by gender and Enthesitis Status)

<table>
<thead>
<tr>
<th>Enthesitis Status</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>BLE</td>
<td>300mg</td>
<td>150mg</td>
</tr>
<tr>
<td>No BLE</td>
<td>300mg</td>
<td>150mg</td>
</tr>
</tbody>
</table>

P78

SECUKINUMAB EFFICACY IN PSORIATIC ARTHRITIS PATIENTS WITH OR WITHOUT ENTHESITIS AT BASELINE – POOLED ANALYSIS FROM TWO PHASE-III TRIALS OVER 2 YEARS

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Lund University, Lund, Sweden; University of Erlangen-Nuremberg, Erlangen, Germany; University of Glasgow, Glasgow, UK; Novartis Pharma AG, Basel, Switzerland; RTH Health Solutions, Barcelona, Spain; Novartis Pharmaceuticals Corporation, East Hanover, USA; Novartis Sverige AB, Täby, Sweden

Aim. The impact of secukinumab (SEC) treatment on efficacy outcomes in active psoriatic arthritis patients with or without baseline (BL) enthesitis by post-hoc analysis of pooled data from the FUTURE-2 (NCT01752634) and FUTURE-3 (NCT01989468) studies.

Methods. Efficacy outcomes (ACR20/50/70, PASI 90, HAQ-DI, SF-36 PCS, and DAS28-CRP) were assessed in patients with BL enthesitis (BLE; N=466) or without BL enthesitis (No BLE; N=246). Given imbalance in some baseline clinical and demographic characteristics, logistic regression/ANCOVA was performed as a function of the BL characteristics (enthesitis status, gender, DAS28, HAQ-DI, TNFi-status), treatment groups, and the interaction between treatment groups and enthesitis status. Binary variables are presented as observed proportions and continuous variables as least-square means. Estimates for the adjusted binary outcomes represent predicted probabilities from the logistic regression model applied to the given analysis set based on the estimated coefficients from the following terms in the model: treatment group, enthesitis at BL, and the interaction between treatment group and enthesitis at BL.

Results. Overall, 65% of patients had BLE. BLE demographic were balanced between BLE and No BLE groups except for a higher proportion of females, higher tender joint count, DAS28-CRP disability (HAQ-DI), and lower physical function (SF-36 PCS) in BLE than No BLE patients. At Week 16, improvements were observed in both groups treated with SEC-300mg, but were lower (except for PASI 90) in SEC-150mg treated BLE patients (Table). Improvements in these outcomes followed similar trends at Week 104. Unadjusted and adjusted results are presented (Table).

Conclusions. Although patients with BLE had more severe BL characteristics than patients with No BLE, SEC showed higher efficacy than placebo at Week 16 and maintained efficacy through 2 years in both groups. In BLE patients, greater magnitudes of improvement were observed with SEC-300mg than 150mg in both unadjusted and adjusted analyses.

Reference

P80
SIX-MONTH TREATMENT RESULTS FOR USTEKINUMAB (UST) AND TNF INHIBITORS (TNFi) IN PSORIATIC ARTHRITIS (PsA) IN EUROPE (PsABio-STUDY)

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Introduction. PsABio (NCT02627788) investigates efficacy, tolerability, and persistence of UST and TNFi as 1st, 2nd or 3rd line biologic therapy in PsA in routine care in 8 European countries. We present 6-month joint-related outcomes.

Methods. As-observed data for joint-related outcomes were available for 152 UST and 151 TNFi-treated patients. Baseline and 6-month data were compared within the treatment cohorts.

Results. UST was used as 1st, 2nd or 3rd line DMARD in 40%, 2nd in 36%, and 3rd in 24% of patients to distinct pathogens as well as to stimuli targeting selected immune responses to a broad range of microbial stimuli or agonists targeting specific monocyte/macrophage populations. Our findings suggest that TNF-blockers impact monocyte/macrophage polarization and break TNF- and IL-1-dependent feed-forward loops of NFkB activation. We also tested if induced immune responses in patients before initiation of therapy could predict therapeutic responses. Using machine-learning algorithms, we found that the expression of several molecules regulating key steps of leukocyte migration and invasiveness was significantly higher in patients responding to TNF-blockers, while expression of cytotoxic and TNF-cell genes was higher in non-responders. The random forest model that we trained and validated using 13 selected biomarkers has a predictive power of 83%. We propose that immune response profiling of patients before therapy is a powerful new strategy to help guiding clinical decisions.

Conclusion. Biosimilar drugs intend to be as effective and safe as their originators and would increase patients’ access to biological therapies. There is emerging evidence from randomized controlled trials concerning this issue, but data from real world clinical practice is still lacking. The decision of switching is not always promoted by physicians, as in this case.

P82
SWITCHING TO BIOSIMILARS: WHAT HAVE WE LEARNED?

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1Hospital de Egas Moniz (CHLH), Rheumatology, CEDOC, NOVA Medical School (FCM), Lisbon, Portugal

Introduction. PsA patients treated in a tertiary referral rheumatology center, who were switched from IFX and ETN originators to biosimilars were included. Disease activity and adverse events 3 months before and after switching were assessed (A means the difference between 3 months before and after the switch). A standardized questionnaire was applied to patients concerning the switching process. Hospital savings were calculated.

Results. Overall, 27 patients (15 males) were included, 4 switching to IFX biosimilar and 23 to ETN biosimilar. There were no significant changes in efficacy for both biosimilars compared to their originators in all disease subgroups [e.g. ∆BASDAI: 2.1 (IQR:5.4) and 0.6 (IQR:2.2), ∆ASDAS0.99 (IQR:3.2) and 0.19 (IQR:1) in ixSPA, results presented for IFX and ETN, respectively]. Similar results were found in terms of VAS (0-10). There were 3 mild to moderate adverse events reported with ETN and none with IFX. There were approximately 2300 euros savings! Although globally, most patients didn’t change the degree of satisfaction with the switch, they considered it to be made by economic reasons and believed they had no other choice.

Conclusion. In this case-study, where a non-medical switch has occurred, disease activity was largely unaffected and there were no safety major problems. Despite the savings and patients’ positive opinion, switching should remain a case-by-case clinical decision made primarily by both the physician and the patient on an individual basis.

P83
MONOTHERAPY WITH BIOLOGICS VS COMBINED THERAPY IN PATIENTS WITH PSORIATIC ARTHRITIS (APSOR) PERIPHERAL

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Background. In Apsor, adding methotrexate to biological treatment (BT) has not shown clinical superiority against monotherapy, although it could improve survival in the records of some biologics. Our findings suggests that TNF-blockers improve survival in the records of some biologics.

Objective. To assess the clinical response and the duration of the BT depending on the type of drug and whether it is combined with DMARD or not. Identify predictors that advise prolonged maintenance of DMARD.

Methods. Retrospective study of 75 patients with peripheral Apsor in BT seen from Dec 2016 to Dec 2017 in our center. We collected clinical, epidemiological and activity data of the disease by DAPSA in both groups.

Results. 64 patients. Evolved disease (mean 133 (63) months). 76.6% had received previous biological tx. 76.6% had received previous FAMES. 34.4% have received one (15.6%) or more previous biological tx.

Conclusion. This is the first quality improvement project that has demonstrated an actual reduction in measured biologic drug wastage. It represents a simple, reproducible and sustainable intervention which carries high satisfaction through a collaborative effort between patients and health care providers and offers potential significant savings in a time of austerity.
P84

IS THE CLINICAL AND THERAPEUTIC PROFILE RELATED TO SATISFACTORY RESPONSE TO APREMILAST IN PSORIATIC ARTHRITIS?

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1Hospital Clínico de Valencia, Valencia; 2Hospital Puerta de Hierro, Madrid; 3Hospital Doctor Peset, Valencia; 4Hospital Virgen de los Lirios, Alcoy; 5Hospital General de la Ribera, Alcira; 6Hospital Arnau de Vilanova, Valencia; 7Hospital Rafael Méndez, Lorca; 8Hospital General de Castellón, Castellón; 9Hospital General de Valencia, Valencia, Spain

Aim. To identify the factors that are related with response to Apremilast (APR) in Psoriatic Arthritis (PsA).

Materials and Methods. An observational and analytical multicenter retrospective study. There are included PsA patients treated with APR after two years of commercialization. Clinical and demographic data were collected: disease duration, previous treatments, cutaneous and joint involvement pattern defined as: joint exclusively, non joint and mixed (by several domains combination). It was collected: duration of treatment, tolerance, adverse events, and reason for APR choice: intolerance or toxicity to csDMARD, preference before bDMARD contraindication or caution to bDMARD, csDMARD and bDMARD inefficacy, csDMARD and bDMARD intolerance. The effectivesness was considered as a dicotomic variable (Yes/No) by clinical criteria.

Results. There were included 89 patients, 46(51.7%) males, the mean age was 53.9±12.3 years, and the PsA disease duration was 7.28±25 years. The PsA pattern was: joint 28/32.6%, non joint, 12/13.5% and mixed 48/53.9%. The reason for APR choice was: intolerance or toxicity to csDMARD 13 patients, preference before BT 28, contraindication or caution to BT 22, inefficacy to cDMARD or BT 18, intolerance to cDMARD and BT 1, and due to clinical profile 1. After a mean treatment duration with APR of 8.13±2.3 months a total of 33 withdrawals were found (17 due to inefficacy and 16 due to intolerance), treatment was maintained on them a mean of 4.3±0.12 months. 56 patients keep with APR a mean of 10.4±2.3 months, 22 of them among 1 and 2 years of evolution. The treatment was effective in 61 (68.5%) patients. Comparisons of the different variables analyzed did not show significant differences among the responders and non responders patients.

Conclusions. We have not found a specific profile that relates with a satisfactory response to APR.

P85

IMPACT OF BIOLOGICS ON IMMUNE CELLS IN AXIAL SPONDYLOARTHRITIS

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Introduction. Biologics (anti TNF and anti IL-17A) are revolutionizing the management of Axial Spondyloarthritis (AxSpA). However, the impact of these treatments on the immune system and in particular on immune cells is unknown. The objective was to identify cells affected by biologics using spectral cytometry and an unsupervised analysis.

Patients and Methods. 1 control group and 2 groups of patients with AxSpA (according to the ASAS criteria) were recruited: patients treated with anti-TNF and anti IL-17A. We have designed 2 panels of 14-color cytometry allowing analysis of the main immune cells (T cells, B cells, NK cells and monocytes) and analysis of T cell subpopulations (naive, memory, “Th1”-like, “Th2”-like, “Th17”-like, “Thb”-like, Tγ and MALT). To perform the unsupervised analysis, we used the ViSne algorithm.

Results. ViSNE represent in 2D a n-dimensional distribution of m events isolated unrevealed clusters of m-sizes. The comparison of the 2 groups of patients, 59 with the control group showed a cluster of monocytes specific to the two treatments and a cluster of B cells specific to the patients treated with anti-TNF. A second analysis showed 2 T-cell signatures (TCR Vβ7.2+ CD8+ CD45RAint CD27+ CCR6+ CD161+) specific to patients under anti-TNF and (TCR γδ+ CD4+ CD45RA− CD161int CD27− CXC3R3+) specific to patients under anti IL-17A. Conclusion. The combination of spectral cytometry associated with an unsupervised analysis allowed us to identify clusters of T cells, B cells and monocytes specific to biologics suggesting a modification in phenotype profiles according to the treatment.

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A CROSS-SECTIONAL EVALUATION OF A BRAZILIAN SPONDYLOARTHRITIS SINGLE-CENTER TERTIARY COHORT: CLINICAL AND TREATMENT DATA

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Background. The use of synthetic DMARDs (sDMARDs) in spondyloarthritis (SpA) has being increasingly questioned and restricted to peripheral disease, on the other hand, the use of immunobiological agents for the treatment of SpA has been further improved by anti-TNF and the release of new drugs with other mechanisms such as secukinumab (anti-IL17, SEC) and ustekinumab (anti-IL12 / 23, UST). The objective of our study is to describe clinical and treatment data of a SpA patients cohort followed at the outpatient clinic of a Brazilian single center.

Methods. 516 SpA patients evaluated from January 2017 to January 2018. Data from electronic medical records assessed including diagnosis, disease characteristics, treatment and disease activity at the last visit.

Results. Among all patients 195 (37.8%) were classified as Ankylosing Spondylitis (AS), 196 (38.3%) psoriatic arthritis (PsA), 66 (12.8%) axial non-radiographic or peripheral SpA, 42 (8.1%) PsA related to inflammatory bowel disease and 15 (3.0%) as reactive arthritis patients. From all SpA patients 190 (36.8%) have no axial disease, with isolated peripheral SpA. Among all patients 195 (37.8%) were classified as Ankylosing Spondylitis (AS), 196 (38.3%) psoriatic arthritis (PsA), 66 (12.8%) axial non-radiographic or peripheral SpA, 42 (8.1%) PsA related to inflammatory bowel disease and 15 (3.0%) as reactive arthritis patients. From all SpA patients 190 (36.8%) have no axial disease, with isolated peripheral arthritis. Regarding treatment, 321 (62.2%) patients were under sDMARDs as monotherapy or in association [156/321 (48.6%) methotrexate (MTX); 125/321 (38.9%) sulfasalazine (SSZ)]; 298 (57.7%) patients used NSAIDs. Concerning biological therapy 204 (39.5%) received biological DMARDs (bDMARDs) (infliximab (IFX), adalimumab (ADA), 35 etanercept (ETA), 6 golimumab (GOL), 2 cetolizumab pegol (CTZ), 23 secukinumab (SEC), 10 ustekinumab (UST), 1 rituximab (RTX)). Concerning disease activity, 25/125 (20%) of AS patients had ASDAS ≥2.1 and 42/198 (21%) of PsA patients had active arthritis in the last visit.

Conclusions. The description of epidemiological and clinical data of this cohort reinforces high prevalence of peripheral disease in Brazilian SpA patients. This fact could explain the wide use of sDMARDs in these patients. The frequency use of sDMARDs is in parallel with literature data including non-antiTNF drugs as SEC and UST.
Clinical and Experimental Rheumatology 2018

P87

PERSONALISING CARE: USING INFILIXIMAB DRUG TROUGH AND ANTI-DRUG ANTIBODY LEVELS IS A SAFE AND COST EFFECTIVE TREATMENT STRATEGY IN AXIAL SPONDYLOARTHRITIS

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Introduction/aim. Personalised medicine tailors treatment to the individual. Biologic drug dosing is standardised and there is paucity of data about the rationale and efficacy of dose adjustment. We conducted a service evaluation to measure serum infliximab trough level (DL) and anti-drug antibody (ADA) in our axial spondyloarthritis (axSpA) and psoriatic arthritis (PsA) patient cohort receiving bio-originator infliximab with the aim of 1) informing clinical decisions before possible switch to biosimilar, 2) assessing the impact of this approach to our clinical practice within the Leeds SpA Service.

Materials and Methods. Patients provided consent and were counselled on the measurement of DLs and ADBs to infliximab including possible treatment outcomes. A treatment algorithm was developed to guide the treating physician on treatment changes. Clinical and outcome data were recorded as per routine practice.

Results. A total of 53 patients were identified. Based upon the disease activity, DL and ADA/Ab, bio-originator infliximab was discontinued in 3 (6%) patients, the infliximab dose interval was extended in 8 (15%) and reduced in 3 (6%). The infliximab dose was reduced in 3 (6%) patients with no change in frequency interval. Four patients (8%) changed to an alternative biologic, either TNFi or alternative mode of action due to persistent high disease activity on infliximab. ADBs were absent in 20 (42%) patients on concomitant methotrexate (MTX). Very high titre ADBs were identified in 8 (15%) patients with corresponding very low (n=2) or undetectable (n=6) DLs suggesting a likely drug-neutralising effect. A total of 24 (45%) patients switched to biosimilar (CT-P13).

Discussion/conclusion. These data from a small cohort suggest that measuring ADBs and DLs personalises treatment and is a cost-effective strategy in infliximab-treated SpA. This approach unlocks the potential of ‘personalised medicine’ which supports individualised treatment and brings significant savings to the healthcare provider.

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THE EFFECT OF BIOLOGIC DISEASE-MODIFYING ANTIRHEUMATIC DRUGS (bDMARDs) IN TARGETING DISEASE REMISSION IN AXIAL SPONDYLOARTHRITIS (axSpA): A SYSTEMATIC LITERATURE REVIEW (SLR)

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Introduction. The treat-to-target concept is currently recommended in axSpA and remission is the main objective of treatment. Although conventional definitions of remission are lacking, ASAS-Partial Remission (ASAS-PR) and ASDAS-Inflammatory Disease Activity Score (ASDAS) have gained wide acceptance as clinical remission-like definitions in current practice.

Objectives. In this review we assessed the efficacy of different bDMARDs in achieving ASAS-PR or/and ASDAS-ID as remission-like outcomes. Data from placebo-controlled phases of randomised controlled trials (RCT), conducted in radiographic axSpA (r-axSpA) and non-radiographic axSpA (nr-axSpA) patients were included.

Methods. A SLR was performed using the MEDLINE database (May 1 2018). The PICO (P: population; I: intervention; C: comparison; O: outcome) concept was used according to Patients - adults with r-axSpA or nr-axSpA; Inclusion criteria - any bDMARD; Outcome - placebo and/or any different drug; Outcomes: ASAS-PR and ASDAS-ID.

Results. After screening 152 references, 19 RCTs fulfilled the inclusion criteria concerning tumor necrosis factor inhibitors (TNFi), 3 secukinumab (anti-IL17A) and 1 sarilumab (anti-IL6R). Only 1 RCT used these remission-like endpoints as primary outcomes, in the remaining, ASAS-PR or ASDAS-ID were studied as secondary measures. ASAS-PR was the preferred remission-like definition, used in 18 of the trials. Concerning TNFi, all the 15 trials provide evidence of efficacy in achieving remission – ASAS-PR and ASDAS-ID varying between 16-61.9% and 24-40.2%, respectively. Secukinumab was effective in achieving ASAS-PR when an initial intravenous loading dose was applied (MEASURE 1). Sarilumab was not effective in inducing remission in axSpA.

Conclusions. Clinical trials addressing remission-like concepts as outcomes are limited. Considering nowadays aimed treatment targets, these data raise the need for improved treatment options favoring optimized remission rates in axSpA patients.

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THE GO-DACT PROTOCOL: A RANDOMIZED CONTROLLED TRIAL TO COMPARE THE EFFICACY OF GOLIMUMAB IN COMBINATION WITH METHOTREXATE (MTX) VERSUS MTX MONOTHERAPY, IN IMPROVING DACTYLITIS AND ENTHESALGIA IN MTX NAÏVE PSORIATIC ARTHRITIS PATIENTS

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Introduction. Dactylitis is a hallmark manifestation of psoriatic arthritis (PsA) and a key feature for PsA diagnosis. Active dactylitis is associated with a higher risk of erosions and can severely impact function. Therapeutic strategies for dactylitis are largely empirical, with absence of properly designed trials assessing dactylitis as primary endpoint.

Methods. GO-DACT is an investigator-initiated multicentric trial, involving 13 sites. Patients older than 18 years, with PsA diagnosis and active dactylitis (tenderness score 3), refractory to NSAIDs, for 3 months, were included. Patients were randomized on a 1:1 ratio, to either MTX in combination with golimumab or placebo, for a period of 24 weeks. The primary aim of this trial is to determine differences of efficacy between the two treatment arms, in improving dactylitis (and enthesis), as assessed by the dactylitis severity score (DSS) at 24 weeks. Key secondary outcomes include: Leeds dactylitis index (LDI), Leeds enthesis index (LEI), joint counts, psoriasis area and severity index (PASI) and nail psoriasis severity index (NAPSI), health assessment questionnaire (HAQ), Dermatology life quality index (DLQI) and composite indexes for disease activity. The effect of treatment arms, on different tissue compartments, will be analysed by contrast-enhanced magnetic resonance imaging (MRI), with high resolution images for dactylitis, at baseline and 24 weeks.

Results/Conclusions. The results from GO-DACT are expected to have implications in clinical practice, bringing robust and valid data for the definition of dactylitis treatment stratification and algorithm. GO-DACT will also contribute to understand dactylitis pathogenesis through the assessment of treatment efficacy, namely in distinct tissue compartments as defined by MRI. https://www.clinicaltrials.gov (NCT02063713)

Acknowledgments. This investigator-initiated trial was supported by a research grant from Merck Sharp and Dohme.
Results. 750 PsA patients were identified, with a mean age of 47.6 years; 50.3% female. The overall retention of TNFi was 49±40 months when treated with a 1st TNFi, decreasing to 36±33 months for the 2nd TNFi, and 23±23 months for the 3rd TNFi. After being treated with a 1st TNFi, 35.8% discontinued therapy, 53.5% due to lack or loss of effectiveness and 24.4% due to adverse events. The rates of discontinuation for the 2nd and 3rd TNFi were of 39% and 54%, respectively, with similar proportions for lack/loss of effectiveness and adverse events for the 2nd (62.3%; 21.6%) and 3rd TNFi (63.0%; 22.2%).

Conclusions. The overall persistence of a 1st TNFi was high in PsA patients reg- istered at Reuma.pt, decreasing on average 13 months, in those who switched to a 2nd TNFi or a 3rd TNFi. Lack of loss of response were the main reason for TNFi discontinuation, independently of TNFi position.

Acknowledgement. Financial support for statistics and report writing was pro- vided by Novartis, S.A.

P91 REMISSION RATES OF BIOLOGIC-TREATED SPONDYLO- ARTHRITIS AND PSORIATIC ARTHRITIS PATIENTS

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Introduction. Biologic disease-modifying drugs (bDMARD) have revolution- ized the treatment of non-psoriatic spondyloarthritis (SpA) and psoriatic arthritis (PsA), allowing clinical remission to become a realistic goal.

Aim. To characterize bDMARD-treated SpA and PsA patients in remission from a single-center cohort.

Methods. Register data (Reuma.pt) from Hospital de Santa Maria was extracted on August/2017 for patients with SpA and PsA treated with bDMARDs. Remis- sion was defined as ASDAS ≤1.3 for SpA and DAS28 ≤2.6 for PsA. The number of patients in remission at the last consultation and at every assessment during the previous year was determined. These patients were further characterized regard- ing disease duration, time to bDMARD, type of bDMARD, previous switches, co-medications, persistence in remission and labour situation.

Results. From a cohort of 168 SpA and 117 PsA patients treated with bDMARDs, 23.8% of SpA and 29.9% of PsA patients were in remission at the last visit. Mean age (±SD) was 44.0 (±10.1) years for SpA and 52.4 (±10.7) years for PsA. Disease duration was 18.2 (±10.1) years for SpA and 16.2 (±8.5) years for PsA. Time from diagnosis to first bDMARD was 7.2 (±5.7) years for SpA and 6.6 (±5.5) years for PsA. 6.7% were retired because of their disease, 50.7% were active. 80% of patients had never switched a bDMARD, 13.3% had switched once, 6.7% had switched twice or more. Persistence on current bDMARD (±SD) was 82 (±49) months in SpA and 62 (±53) months in PsA patients. Persistence on each biologic was roughly proportional to the drug’s commercialization time. Persistent (12 month) remission was ob- served in 12 SpA and 23 PsA patients (respectively, 7.1% and 19.7% of patients treated with bDMARDs).

Conclusion. Remission is a feasible target in a small proportion of patients in real-life clinical setting. Even patients with longstanding disease can reach sus- tained remission after starting bDMARDs. Most patients in remission persisted in their first bDMARD for several years.

P92 DISPENSAÇÃO DE IMUNOBIOLOGIÇOS EM MODELO DE ASSISTÊNCIA TÉCNICO-MEDEIRIA EM SÃO PAULO

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Introduction. In the 2000s, immunobiologics were introduced as a treatment option in rheumatologic conditions, including Ankylosing Spondylitis (AS). The incorporation of these medications by the Public Health System in Brazil (SUS) brought clinical advances in the effective control of the inflammatory process and the quality of life of patients. With the increase in indications and the volume of patients attended, the impact on the SUS budget has increased, requiring a rational and efficient dispensation process.

Materials and Methods. All the visits were included in the center responsible for the model of assisted therapy, with medication provided by the Ministry of Health for patients presenting in the year 2015. In each of the consultations were recorded: medication, number of bottles, prescribed dose, dose received, cancel- lations, faults and estimates of bottles that would have been dispensed by the direct system. The financial value was calculated according to the acquisition value by the Ministry of Health in 2015. Results and Discussion. A total of 1688 consultations were performed for pa- tients with AS by the model of assisted therapy. 669 (23.26%) bottles of a total volume of 2876 prescribed vials of all medications intended for the treatment were no longer used, reducing expenses by € 109.369,57 (23.78%). Based on the same savings percentage of the model in question for the whole SUS and accord- ing to data from DATASUS for AS in 2015, the reduction of immunobiological expenses for the treatment would be € 11.503.979,10.

Conclusion. The model of assisted therapy considerably reduces the volume of dispensed bottles compared to the model of direct dispensing bringing significant reduction of expenses to the SUS.

P93 DEMYELINATION ASSOCIATED WITH ANTI-TNFα TREATMENT IN SPONDYLOARTHRITIS PATIENTS – A SINGLE-CENTER EXPERIENCE

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Introduction. Demyelination is a rare, but potentially severe adverse event as- sociated with anti-TNFα treatment. There are only scarce data regarding the inci- dence and long-term neurological outcome of this complication in cohorts of Spondyloarthritis (SpA) patients.

Objective. To assess the incidence, correlation with disease activity and total exposure to anti-TNFα treatment in SpA patients who developed CNS demy- elination.

Methods. Retrospective, case-control series from a tertiary care hospital. We reviewed all medical records of patients with SpA treated with at least one anti-TNFα agent(s) during 2003–2015 and developed clinical and radiologic features consistent with CNS demyelination. Patients were evaluated through multidisci- plinary approach.

Results. A total of 9 patients (7 women, 2 men) out of 530 (1.69%) developed demyelinating disease following anti-TNFα therapy. Two patients had peripheral SpA associated with psoriasis and 7 axial SpA (5 related to inflammatory bowel disease, 1 to psoriasis, 1 ankylosing spondylitis). There are only scarce data regarding the in- cidence of CNS demyelination.

Conclusion. Demyelinating disease is a rare complication of anti-TNFα treat- ment in SpA, which may occur when the disease is in remission or low disease activity. Despite anti-TNFα discontinuation, some cases will evolve into definitive MS, suggesting possible a priori predisposition.

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PSORIASIS AND INFLAMMATORY BOWEL DISEASE MODELS CO-OPERATE WITH BIOMECHANICAL STRESS IN TRIGGERING MILD JOINT INFLAMMATION

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Introduction. Spondyloarthritis (SpA) and Psoriatic arthritis (PsA) is a chronic inflammatory skeletal disease associated with psoriasis (PsO) and inflammatory bowel disease (IBD). Being the attachment sites of tendons and ligaments into the bones, entheses are a site of biomechanical stress and are considered as a primary disease localization. Increasing evidence supports the hypothesis that biomechanical stress, together with inflammatory triggers from distant sites such as the skin or the intestine, can contribute to the onset of SpA and PsA.

Objectives. We aim to understand early events leading to SpA and PsA by combining a protocol of forced exercise in mice with simultaneously locally-induced cutaneous or intestinal inflammation.

Methods. Eight weeks old C57/Bl6 male mice were treated with imiquimod cream (IMQ) on a shaved area of the back skin or with dextran sodium sulphate (DSS) dissolved in the drinking water. Control mice were left untreated. Afterwards, half of the mice were subjected to a forced treadmill running protocol to increase biomechanical stress. Control mice with or without IMQ or DSS treatment did not run. Severity of cutaneous or intestinal inflammation was assessed clinically and by histology, knees and paws were evaluated with microCT and histological analysis.

Results. Assessment of the skin and intestine confirmed the presence of local inflammation in the treated mice. Subsequently, systemic inflammation developed as demonstrated by the presence of trabecular bone loss and changes in spleen size. In the joints, histological assessment revealed mild synovitis and enthesitis as demonstrated by the presence of trabecular bone loss and changes in spleen size. In the joints, histological assessment revealed mild synovitis and enthesitis.

Conclusion. In the IMQ- or DSS-treated mice, slightly boosted by the forced exercise regimen.

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THE JAK1 SELECTIVE INHIBITOR FILGOTINIB REGULATES BOTH ENTHESIS AND COLON INFLAMMATION IN A MOUSE MODEL OF PSORIATIC ARTHRITIS


Introduction/Aim. The JAK1-selective inhibitor filgotinib (GLPG0634, GS-6034) displayed efficacy and safety in phase 2 studies in rheumatoid arthritis (RA) patients. Psoriatic arthritis (PsA) is a heterogeneous chronic inflammatory disease sharing features with RA in addition to syndromes such as psoriasis and Inflammatory Bowel Disease. We evaluated the efficacy of filgotinib in an IL-23-induced mouse model of PsA.

Methods. Overexpression of IL-23 was induced by hydrodynamic delivery of miIL23 enhanced Epithelial Expression Vector (SBI) to B10.RII mice. Paw and finger inflammation was assessed by clinical scoring and in vivo molecular imaging. Enthesis, colon and fingers were collected for transcriptomic analysis. Infiltration of inflammatory cells and pSTAT3+ positive cells were analyzed in Achilles’ enthesis, subcutaneous area, skin and gut.

Results. High levels of IL-23 were maintained during the time-course of the study and were correlated with severity of the inflammation in paws, fingers and enthesis. Filgotinib significantly improved clinical scores, strongly decreased immune cell infiltration in the skin and tended to prevent neutrophil/granulocyte infiltration in paw. Transcriptional analysis of enthesis, fingers and colons showed that filgotinib reversed the effect of IL-23 for a consistent number of genes. Filgotinib also significantly counteracted pSTAT3 induction in the subcutaneous area and in the epidermis, further demonstrating target engagement in the diseased tissue.

Conclusions. In a mouse model of PsA, filgotinib improved global clinical scores and decreased signs of inflammation in hindlimbs. Target engagement both in hindlimbs and colon was also demonstrated. These data support the evaluation of filgotinib in patients with PsA.

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mTOR BLOCKADE BY RAPAMYCIN DECREASES ARTHRITIS AND SPONDYLITIS DEVELOPMENT AND SEVERITY IN HLA-B27 TRANSGENIC RATS

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Introduction/Aim. HLA-B27 misfolding is thought to play a important role in the pathogenesis of spondyloarthritides (SpA), possibly through triggering of ER stress and the unfolded protein response. One of the mechanisms that regulates the unfolded protein response is autophagy. Autophagy is a process that degrades proteins, cytoplasmatic particles and organelles in lysosomes and is regulated by protein kinases, mechanistic target of rapamycin (mTOR) and AMP activated protein kinase. The aim is to study whether blockade of mTOR will affect spondyloarthritis development and/or severity in the Mycobacterium tuberculosis (M. tub.)-induced disease HLA-B27tg rat model.

Methods. HLA-B27/HuB2m transgenic rats were immunized with heat-inactivated M. tub in IFA and treated with 1.5 mg/kg rapamycin or vehicle intraperitoneally. Rats were clinically scored for SpA development and afterwards histology and mRNA measurements were performed.

Results. In the prophylactic experiment 72.7% and 18.2% rapamycin treated rats developed arthritis and spondylitis compared to respectively 100% (p=0.0225) and 92.3% (p=0.0001) control animals. Also severity of SpA was significantly decreased in rapamycin treated animals compared to control treated animals; mean arthritis severity of diseased rats was respectively 0.45 versus 7.15 on a scale from 0-12 (p=0.0001) and mean spondylitis severity was respectively 0.18 versus 2.07 on a scale from 0-3 (p=0.0001). Clinical findings were confirmed by histology with a significant decrease of inflammation, bone- and cartilage destruction and new bone formation in peripheral joints of treated rats compared to vehicle treated rats and a similar trend was observed in spinal joints. Also in a therapeutic setting rapamycin treatment decreased arthritis severity (p=0.0317) and spondylitis severity (p=0.0159). Histology for the therapeutic experiment is currently being performed as well as mRNA analyses for autophagy genes and pro-inflammatory cytokines.

Conclusion. mTOR blockade significantly suppressed SpA in the M. tub.-induced disease HLA-B27tg rat model of PsA.

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CERTOLIZUMAB PEGOL LIKE MICE EQUIVALENT REDUCES INFLAMMATION AND BONE DAMAGE IN TRANSMEMBRANE TNF TRANSGENIC MICE

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Introduction. Transmembrane (tm)TNF (TgA86) mice is a transgenic line that spontaneously develops peripheral arthritis and spondylitis, mimicking human spondyloarthritis (SpA). The aim of this work is to study the effect of TNF blockade in the mice SpA-like phenotype, focusing on histological inflammation and bone damage.

Methods. tmTNF (TgA86) mice were treated with certolizumab pegol like product (Ab501), 100mg/kg twice weekly intraperitoneal or vehicle, for 12 weeks, in a preventive (4 weeks of age) and therapeutic (10 weeks of age) settings. A semi-quantitative score for the severity of histologic inflammation and bone damage, was applied to paws and spine.

Results. 15 tmTNF (TgA86) mice at 4 weeks of age (prevention group) and 14 tmTNF (TgA86) mice at 10 weeks of age (therapeutic group) were treated with Ab501; and 30 tmTNF (TgA86) mice with vehicle, for 12 weeks. A statistically significant reduction in inflammatory infiltrate (p=0.001), lining cells layers (≤0.05), erosions (p=0.05) and global inflammatory scores (p=0.05) of the paws, was observed in Ab501 treated group, when compared with vehicle group, both for 4 and 10 weeks of age treatment groups. In the spine, statistically significant reductions in inflammation (p=0.001), intervertebral disc destruction (p=0.05), cartilage damage (p=0.001), bone erosion (p=0.05), and ectopic chondrocytes/ chondrocytephore scores (p=0.001) was also depicted in Ab501 treated group in comparison with vehicle.

Conclusions. Certolizumab pegol like product mice equivalent reduced histologic inflammatory infiltrate in paws and spine of tmTNF (TgA86) mice. Bone damage, as defined by erosions in the paws and spine and ectopic chondrocytes/chondrocytephore formation in the spine, also significantly improved.

Acknowledgments. Leonie M van Duivenvoorde and Dominique Baeten (AMC) for providing tmTNF (TgA86) mice for breeding and colony establishment. George Kollias from Flemming Institute for authorization to use this mice line.
1. Understanding
The University of Texas-Health McGovern Medical School, Dept. of Medicine, compared 49.4% of those with NICBP (p=0.005). HLA-B27 occurred in 57% of FDR's with CIBP com-
 versus 55.6 years, p=0.0002)), and had a higher frequency of heel pain (52.7%

2. Exploring the Ankylosing Spondylitis-Associated Regulatory SNPs at the RUNX3 locus
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Introduction/Aim. Of the >100 genetic associations with ankylosing spondylitis (AS), the RUNX3 transcription factor (TF), involved in diverse immu-

2. Intracellular Activity of Protein Phosphatase Magnesium-Dependent 1A Regulates Bone Metabo-
Lism in Ankylosing Spondylitis
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Introduction and Aim. Increased level of protein phosphatase magnesium-dependent 1A (PPM1A) in the synovium and serum of ankylosing spondylitis (AS)
has been implicated in the bony ankylosis through the regulation of osteoblast (OB) differentiation, yet little is known about potent mechanisms regulating the osteoclast (OC) differentiation involving the abnormal bone metabolism. Here, we reduced the expression of PPM1A in the macrophages known as OC proc-

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EXPLORELING THE ANKYLOSING Spondylitis-ASSOCIATED REGULATORY SNPS AT THE RUNX3 LOCUS
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Materials and Methods. We used publicly available datasets (including “Road-
map”) to define the RUNX3 epigenetic landscape and in vitro functional studies to characterize the effects of specific genetic variants, providing critical func-
tional evidence for their role in AS.
Results. (1) Roadmap data revealed a robust peak for open chromatin, TF bind-
ing and interaction of RUNX3 with different genomic loci (chromosome 1), in GM12878 lymphoblastoid cells; (2) preliminary DNA pull-down affinity capture experiments, followed by Mass Spectrometry, identified the whole range of TF’s (DNA/protein “interaction”) binding to a 50bp probe including rs4648889 in the
RUNX3 locus, in CD8+T-cells; (3) initial gene/pathway analysis highlighted a dis-
tinct contribution from the Ikars TF and associated chromatin-remodeling proteins.
Discussion. We provide strong evidence the 2kb region upstream the RUNX3 gene
has a plausible functional role in AS, probably by regulating gene transcription.
Conclusions. These observations are critically important not only in identifying specific cell types that play a pathogenic role in AS, but also in defining dysregu-
lated pathways and potential therapeutic drug targets.

References
1. IGAS et al.: Nat Genet. 2013 Jul; 45(7): 730-8
3. VECELLIO M et al.: EMD Open 2018 Feb 4; 1(1): e000628

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CHRONIC BACK PAIN (CBP) IN FIRST DEGREE RELATIVES (FDR’s) OF PATIENTS WITH ANKYLosing Spondylitis – PREDICTIVE VALUE OF HLA-B27 AND PERSISTENCE OF THE INFLAMMATORY BACK PAIN OVER TIME
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Introduction/Aim. We examined FDR’s of ankylosing spondylitis (AS) patients with chronic inflammatory back pain (CBP), non-inflammatory CBP (NICBP) and no CBP for clinical features, HLA-B27 alleles and persistence of IBD over time.
Materials and Methods. 548 FDRs of AS patients were divided into three groups, excluding those with a diagnosis of AS at baseline visit and, within each group, blood relatives: 1) No CBP (only subjects >40 years of age who never had CBP (n=79), and 3) No AS.
Results. FDRs with CBP were younger than those with NICBP (45.1 years versus 55.6 years, p=0.0002)), and had a higher frequency of heel pain (52.7% versus 43.4%, p=0.005). HLA-B27 occurred in 57% of FDR’s with CBP com-
pared 49.4% of those with NICBP (p=0.005), and 39.6% of those <40 years of age had CBP (p=0.005, OR=1.91; C.I. 1.2, 2.97). Of 23 patients with CBP at baseline seen again 67.04±31.02 months later, 16 (72.7%) still had CBP, whereas on four (33%) of 13 NICBP patients (33%) seen 61.23±31.84 months later were still asymptomatic. Of the remaining nine, three developed CBP and six had CBP.
Conclusions. These data suggest FDR’s of AS patients with CBP have a young-
er age at onset, a higher frequency of heel pain, and higher frequency of HLA-
B27 than those who do not develop CBP. The CBP phenotype remains stable and chronic over time in most, suggesting a need for long term treatment approaches in this group.

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INTRACELLULAR ACTIVITY OF PROTEIN PHOSPHATASE MAGNESIUM-DEPENDENT 1A REGULATES BONE METABO-
LISM IN ANKYLOSING Spondylitis
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Introduction and Aim. Increased level of protein phosphatase magnesium-depen-
dent 1A (PPM1A) in the synovium and serum of ankylosing spondylitis (AS)
has been implicated in the bony ankylosis through the regulation of osteoblast (OB) differentiation, yet little is known about potent mechanisms regulating the osteoclast (OC) differentiation involving the abnormal bone metabolism. Here, we reduced the expression of PPM1A in the macrophages known as OC proc-

Materials and Methods. Bone phenotypes of wild-type (WT) and PPM1A +/- mice were evaluated by micro-computed tomography. OC differentiation was induced by culturing bone marrow-derived macrophages (BMMs) in the pres-
ence of receptor activator of nuclear factor kapp-a B (RANK) ligand and mac-
rophage colony-stimulating factor (M-CSF) and evaluated by counting trarrete-
resistant acid phosphatase (TRAP)-positive multinucleated cells. The mRNA expres-
sion of PPM1A, RANK and OC-specific genes was examined by reverse transcription-polymerase chain reaction. Protein levels of PPM1A and MAPKs in BMMs of WT and PPM1A +/- mice were determined by Western blotting. The surface expression of RANK on BMMs was analyzed by fluorescence-activated cell sorting.
Results. Mice with conditional PPM1A knockout display reduced bone density and increased OC differentiation as well as expression of OC specific genes (OC-
STAMP, OC-STAMP, OC-STAMP, OC-STAMP). With WT littersmates. Mecha-
nistically, reduced PPM1A function in OC precursors from seen in PPM1A+/+
 mice increased and mediated OC lineage commitment by up-regulating RANK expression dependently of p38 MAPK activation in response to M-CSF. The expression of PPM1A mRNA and PPM1A were down regulated in OC prec-
ursors when stimulated by lipopolysaccharide. Similarly, in the PBMCS from AS patients, the ratio of RANK/PPM1A expression was correlated positively with disease activity score.
Conclusions. These results demonstrated that loss of PPM1A function in OC precursors in response to inflammatory signals contributes to the OC lineage commitment and differentiation via elevation of RANK expression through ac-

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IL-23 INDUCTION OF MDL-1+ MYELOID CELLS IS CRITICAL IN THE PATHOGENESIS OF PSORIATIC ARTHRITIS
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Background/Purpose. Interleukin-23 (IL-23) and its cognate receptor interleu-
kin-23R (IL-23R) play a critical role in the pathogenesis of many autoimmune diseases, including EAE, rheumatoid arthritis, psoriasis and psoriatic arthritis. Herein we show that IL-23 induces myeloid cell activation via the engagement of MDL-1/CLEC5A receptor a member of C-type lectin superfamily, exclusively expressed in myeloid cells.

Methods. To define the role of MDL-1 in IL-23 signaling and its contribution to pathogenesis of psoriatic arthritis, we performed in vivo gene transfer. IL-23 in WT, IL-23R+/- reporter mice and MDL-1 deficient mice. We investigated the joint and skin inflammation in the presence or absence of IL-23+/- MDL-1- cells and assayed inflammation using H&E and immunofluorescence staining, in conjunc-
tion with various tissue specific biomarkers assayed by qRT-PCR, western blot, and ELISA to analyze gene expression, protein, and cytokine levels, respectively. Results. In vivo gene transfer of IL-23 induced skin inflammation with increased number of CD11b+Ly6G, CD11b+Ly6C, CD11b+IL23R+ cells in skin and enhanced epidermal MDL-1+ cells. We further demonstrated that IL-23-induced pathology was impaired in IL-23R−/− (non-functional IL-23R) and MDL-1− mice with less epidermal hyperplasia and skin (ears and dorsal skin) inflammation, compared with wild-type (WT) mice. Expression of skin inflammatory markers Ki67, S100A7-9, CXCL-1, and CXCL-2, phosphorylation of NFκB and AKT as well as nuclear p65 were also lower than WT counterparts.

Conclusion. Our data show that MDL-1 is a critical component of IL-23 signaling that dictates synovial and skin inflammation in vivo. Our data suggest that activation of myeloid cells via MDL-1 could be effectively targeted for the treatment of spondylarthropathies.

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PROTEOMIC AND TRANSCRIPTOMIC PROFILING OF CELLS IN ANKYLOSING SPONDYLITIS PATIENTS IDENTIFIES A NOVEL, SYNOVIAL-RESIDENT CD8+ T CELL

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Introduction. Current data suggests that immune events in the gut may impact on joint inflammation in ankylosing spondylitis (AS) but what directs cells in the gut-joint axis is undefined. For this reason, we examined the expression of trafficking molecules on immune cells using Cytometry by Time-of-flight (CyTOF), and the expression of differentially regulated genes using RNA-seq. Our objectives are to utilize proteomic and transcriptomic analysis to 1) assess differential expression patterns of trafficking molecules between patients and controls, 2) generate joint-specific cellular signatures, and 3) obtain genetic profiles of noteworthy cell subpopulations.

Materials and Methods. Male subjects under 40 years of age fulfilling the mNY criteria were recruited. The following cells were surface stained using a 36-marker antibody panel: (i) Peripheral blood mononuclear cells (PBMC) from AS patients and the expression of differentially regulated genes using RNA-seq. Our objectives are to utilize proteomic and transcriptomic analysis to 1) assess differential expression patterns of trafficking molecules between patients and controls, 2) generate joint-specific cellular signatures, and 3) obtain genetic profiles of noteworthy cell subpopulations.

Results. Mature CD8+ T cells were increased in frequency in AS SFMC, with significant changes in their phenotype: β7+, CD103+, CD29+ and CD49α+ integrin expression was increased in CD8+CD45RO+ cells in AS SFMC vs paired AS PBMC (mean 7.51% vs 0.87%, p=0.0035). RNA-seq data analysis of CD103+CD49α+ cells in SFMC revealed elevated GZMA, GZMB, PRF1 and IL-10 cytokines, in addition to a cytotoxicity regulation profile.

Conclusion. We identified a novel integrin-expressing mature CD8+ T cell subpopulation from the synovial fluid.

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MicroRNAs Deregulation in Monocytes and CD4+ T-Lymphocytes from Patients with Axial Spondyloarthritis

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Introduction. Deregulation of microRNAs has been poorly studied in spondyloarthritides with published studies using diverse methodologies on small numbers of samples. Because CD4+ T-lymphocytes and monocytes are important cells in SpA pathophysiology, we wanted to assess the miR expression profile in these two cell types sorted from axial SpA patients.

Materials and Methods. Two independent cohorts of 22 and 59 SpA patients were compared to 17 and 38 age and sex-matched controls. Both SpA patients and controls were recruited in the department of rheumatology at Cochin Hospital in Paris, France. All SpA patients had an active disease (mean BASDAI score of 49±19) and were free of any biologic treatment. T-lymphocytes and monocytes were isolated from PBMC by direct isolation with magnetic microbeads (CD4+ and CD14+). 372 miRs were screened by qPCR on the exploratory cohort and only miRs showing a significant differential expression in the first cohort were analyzed in the validation cohort. An unpaired t-test was used for comparison of miR expression level.

Results. In the exploratory cohort, 51 (CD14+) and 70 miRs (CD4+) were found to be differentially expressed between patients and controls. Among these, 15 miRs (in CD14+), and 12 miRs (in CD4+) were replicated in the second cohort. These validated miRNAs were found to play a key role in physiological pathways such as NFκB or TGFβ, Wnt signalling and monocyte differentiation, that have been involved in the pathophysiology of the disease.

Conclusion. We found a deregulation of miR expression in monocytes and CD4+ T-lymphocytes from patients with axial spondyloarthritis, which could contribute to the pathophysiology of the disease and be of interest from a therapeutic perspective.

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TYK2 PROMOTES IL-23-INDUCED TYPE 3 IMMUNITY AND DISEASE PROGRESSION IN SPONDYLOARTHRITIS

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Introduction. While current therapeutics for ankylosing spondylitis (AS) generally provide symptomatic control, their ability to prevent disease progression remains uncertain. The genetics and animal models of AS support a central role for Type 3 (IL-17) immunity driven in part by IL-23. Tyk2, a janus kinase, is a genetic risk factor for AS and is crucial for the intracellular signaling of IL-23 via STAT3 phosphorylation, making it a potential therapeutic target for AS.

Methods. In a cohort of AS patients, TYK2 AS risk SNPs (rs1270356, rs34536443, rs35164067) were assessed by Taqman assay, TYK2 mRNA expression was assessed in whole blood by qPCR and at the cellular level in PBMC by Primeflow FACS. IL-23 and IL-6 induced pSTAT3 in human CD4+ T cells was assessed by FACS, with or without a selective Tyk2 inhibitor (NDI-031407). NDI-031407 was tested in the SKG and IL-23 minicircle murine models of SpA.

Results. Serum levels of IL-10 cytokines, in addition to a cytotoxicity regulation profile. Further experiments are ongoing to provide evidence of gut-joint trafficking capacities and to examine the arthritogenic potential of these cells.

Conclusion. Pharmacologic (NDI-031407) or genetic (Tyk2-KO23E mice) inhibition of Tyk2 was assessed in IL-23-stimulated, murine T cells. Results. TYK2 expression in whole blood or PBMC did not differ in AS patients vs controls. TYK2 expression did not stratify by risk SNPs, however the loss of function risk SNP, rs1270356, was associated with lower radiographic progression in the AS cohort. NDI-031407 potently inhibited STAT3 phosphorylation induced by IL-23, but not IL-6. In murine SpA models, NDI-031407 reduced dermatitis/arthritis and lowered Th17 cell frequency in popliteal lymph nodes. Both NDI-031407 and kinase-dead Tyk2-KO23E blocked IL-23 induced pSTAT3 and IL-17A/IL-22 production in vitro.

Conclusion. AS-associated TYK2 risk variants promote disease through altered Tyk2 function. Genetic and pharmacologic inhibition of Tyk2 kinase activity blocks Type 3 immune cell activity and protects against experimental SpA.
We demonstrate in this study that ILC3s are absolutely and rela-
tively more capable of expressing IL-22 in vitro, but not IL-17A, as tested by antibody-dye combinations. Several staining protocols were optimized to reduce receptor downregulation upon PMA/ionomycin stimulation. The final panel was applied to specimens from healthy individu-
als demonstrating variable expression of KIR3DL1 and KIR3DS1/DL1 in all 8 lymphocyte subsets.

Conclusions. We have developed a 19-parameter flow cytometry panel that reli-
ably distinguishes 8 lymphocyte subsets in PBMCs stimulated with PMA/ionomycin and permits the analysis of multiple KIRs and cytokines in a single sample. This panel will be used to study the relationship between KIR and cytokine ex-
pression in HLA-B27- and HLA-B27+ healthy individuals and patients with AS.

IL-22-EXPRESSING BUT NOT IL-17A-EXPRESSING GROUP 3 INNATE LYMPHOID CELLS ARE EXPANDED IN THE INFLAMED SPONDYLOARTHRITIS JOINT

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Objective. Clinical trials of the anti-IL-17A antibody secukinumab demonstrated a crucial role of the IL-17A cytokine in the pathogenesis of spondyloarthritis (SpA), however its cellular source in this condition remains controversial. Group 3 innate lymphoid cells (ILC3s) have been recently identified in a number of differ-
ent tissues as potent producers of proinflammatory cytokines, including IL-17A and IL-22. In this study we set out to characterize the presence and composition of ILC3s and investigate whether these cells are an important source of IL-17A in the synovial tissue of patients with SpA.

Methods. Matched synovial tissue (ST), synovial fluid (SF) and peripheral blood (PB) were obtained from SpA patients with actively inflamed knee joints. ILC subsets were characterised by flow cytometry. Gene expression analysis at the single-cell level was performed directly ex vivo and after stimulation with PMA ionomycin. IL-17A ELISPOT assay was used to detect IL-17A-secreting cells.

Results. Analysis revealed that ILCs, and particularly NKp44-positive ILC3s, are expanded in inflamed arthritic joints. Single-cell expression analysis demon-
strated that ST ILCs are clearly distinguishable from ST T cells and from their PB counterparts. We detected expression of Th17 signature transcripts RORC, AHR and IL-23R in a large fraction of ST ILC3s. These cells were capable to induce IL-22, but not IL-17A expression in response to in vitro re-stimulation.

Conclusions. We demonstrate in this study that ILC3s are absolutely and rela-
tively enriched in the synovial joint of patients with SpA, however are not a significant source of IL-17A cytokine in this pathology.

HISTOLOGICAL EVIDENCE THAT MAST CELLS ACT AS PRO-
MOTORS RATHER THAN REGULATORS OF IL-17A-MEDIATED TISSUE INFLAMMATION IN SPONDYLOARTHRITIS

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Background. Synovial mast cells contain IL-17A, a key driver of chronic tis-
seau inflammation in spondyloarthropathy (SpA). Recent in vitro studies showed that tissue-derived mast cells can capture, store, and release exogenous IL-17A. The present study aimed to investigate if this mechanism promotes rather than regu-
lates chronic tissue inflammation in SpA.

Methods. Potential activation of mast cells by IL-17A was assessed by gene expression analysis of the LAD2 mast cell line. The presence of IL-17A-positive mast cells was assayed by immunohistochemistry in synovial tissue obtained before and after secukinumab treatment, as well as in skin and gut tissues from SpA-related conditions.

Results. IL-17A did not induce a pro-inflammatory response in human LAD2 mast cells according to the canonical IL-17A signaling pathway. Using well validated anti-IL-17A antibodies, immunohistochemical staining of synovial biopsies obtained before and after secukinumab treatment indicated that the percent-
age of IL-17A-positive synovial mast cells increases rather than decreases upon anti-IL-17A therapy in SpA. IL-17A-positive mast cells were also readily detectable in barrier tissues such as skin and intestines, even in non-inflamed conditions. Although both total mast cells and IL-17A-positive mast cells were increased in psoriatic skin dermis and in submucosa from inflammatory bowel disease gut in comparison to non-
inflamed tissues, the proportion of IL-17A-positive mast cells was strikingly de-
creased in the inflamed BID gut surface area lamina propria.

Conclusions. The presence of IL-17A-positive mast cells across different SpA target tissues and the inverse correlation between their IL-17A content and inflam-
mation suggest that tissue-resident mast cells could act as sentinel cells preloaded with IL-17A, which can be released to amplify inflammatory responses.

RORγt INHIBITION SELECTIVELY TARGETS PATHOGENIC SUBSETS OF HUMAN INK T AND γδ-T CELLS ENRICHED IN SPONDYLOARTHRITIS WHILE PRESERVING IL-22 RESPONSES

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Dysregulated IL-23/IL-17 responses have been linked to inflammatory diseases including psoriasis, psoriatic arthritis and other forms of spondyloarthropathies (SpA). IL-23/IL-17 inflammation is controlled by RORγt, the key Thelper17 (Th17) cell transcriptional regulator. RORγt is also expressed by subsets of innate-like T cells, including invariant natural killer T (iNKT) and γδ-T cells, but how this contributes to disorders such as SpA is still unclear. Here we describe a unique population of RORγt+Tbet+PLZF iNKT and γδ-T cells present in healthy peripheral blood. iNKT and γδ-T cells showed profound IL-23 mediat-
ed Th17-like immune responses and were clearly enriched within inflamed joints. Moreover, selective depletion of iNKT and γδ-T cells in synovial fluid mononu-
clear cell samples led to a significant decrease (>70%) in IL-17A responses under-
scored by the pathogenic features of these cells in SpA. Interestingly, we have used clustered analyses by FlowSOM iterations revealed a marked heterogeneity of human blood iNKT and γδ-T cells which seemed skewed in SpA patients. Strik-
ingly, RORγt inhibition blocked γδ17 and iNKT17 cell function while selec-
tive depletion of γδ-T and iNKT subsets. Overall, these findings highlight a unique diversity of human RORγt T cells and underscore the potential of RORγt antagonism to modulate aberrant type 17 responses.
SCREENING FOR ANTIBODY REACTIVITY IN EARLY AXIAL SPONDYLOARTHRITIS IDENTIFIES NOVEL ANTIGENIC TARGETS
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Aim. Diagnosis of axial spondyloarthritis (axSpA) is challenging since clinical manifestations often overlap with other disorders and an appropriate serological test is still lacking. Although autoantibodies are not considered to be a hallmark of axSpA, emerging evidence suggests the involvement of plasma cells and autoantibodies in the disease. Therefore, we aim to identify novel (auto)antibodies specific for early axSpA patients.

Materials and Methods. An axSpA cDNA phage display library was constructed and screened for antibody reactivity to pooled plasma of early axSpA patients (n=10) with validation in additional pooled plasma of early axSpA patients (n=60) and healthy controls (HC, n=80) and in individual plasma samples of early axSpA patients (n=79), patients with non-specific chronic low back pain (NSCLBP, n=40), rheumatoid arthritis (RA) patients (n=60) and HC (n=94) using phage-ELISA.

Results. Antibody reactivity against 9 novel peptide targets was increased in pooled axSpA plasma. Further validation revealed antibody reactivity against at least one of these targets in 53% of early axSpA patients (42/79) compared to 35% of NSCLBP (14/40, p=0.0083), 38% of RA (23/60, p=0.0894) and 26% of HC (24/94, p=0.00033). By combining our 3 best targets, 20% of axSpA patients (16/79) were detected and screened for antibody reactivity with pooled plasma of early axSpA patients. Antibody reactivity against these targets will be further validated in an independent cohort of early axSpA patients.

Conclusion. The increased antibody reactivity against several novel antigenic targets in early axSpA patients compared to NSCLBP, RA and HC further supports the involvement of the humoral immune response in axSpA.

A PROBABLY ROLE OF HSP60 IN THE PATHOGENESIS OF SPONDYLOARTHRITIS
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Introduction. The cause of SpA is unknown, although there is an important relationship with gut enterobacteria and the HLA-B27 molecule. This later can misfold during its synthesis causing an altered proteinostasis with inflammatory consequences. We identified that patients with ankylosing spondylitis (AS) have serum antibodies against a 60kDa molecule of Kibrisella pneumoniae. This molecule was cloned and characterized as the heat shock protein 60 of K. pneumoniae (HSP60Kp). Later, we found high titers of plasma and synovial fluid antibodies against the HSP60Kp and the HSP60 of other enterobacteria accompanied by antibody responses against 9 novel peptide targets, each one contributing to the detection of a portion of axSpA patients. Antibody reactivity against these targets will be further validated in an independent cohort of early axSpA patients.

Conclusion. The increased antibody reactivity against several novel antigenic targets in early axSpA patients compared to NSCLBP, RA and HC further supports the involvement of the humoral immune response in axSpA.

AN ENTHESAL INNATE IMMUNE CELL BIOLOGICAL BASIS FOR DIFFERENTIAL EFFICACY OF PDE4 AND IL-23 PATHWAY BLOCKADE BETWEEN PSORIATIC DISEASE AND RHEUMATOID ARTHRITIS
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Introduction. Both IL-23 and PDE4 inhibition are ineffective in RA but show efficacy in PsA related synovitis despite similar cytokine and molecular profiles between synovitis in both disease settings. We hypothesized that resident innate immune cells, especially myeloid cells, might be capable of IL-23 production that could be modulated by PDE4 pathway blockade.

Materials and Methods. Human entheses (n=6) were digested and myeloid cells (CD14+) sorted from both the adjacent bone (EB) and soft tissue (ST) fractions. Both CD14+ sorted and CD14- unsorted cells were stimulated with bacterial and fungal adjuvants (TLR and CLR agonists) in the presence and absence of a PDE4 inhibitor and analyzed by ELISA and flow cytometry.

Results. Antibody reactivity against several novel antigenic targets was increased in pooled axSpA plasma. Further validation revealed antibody reactivity against at least one of these targets in 53% of early axSpA patients (42/79) compared to 35% of NSCLBP (14/40, p=0.0083), 38% of RA (23/60, p=0.0894) and 26% of HC (24/94, p=0.00033). By combining our 3 best targets, 20% of axSpA patients (16/79) were detected and screened for antibody reactivity with pooled plasma of early axSpA patients. Antibody reactivity against these targets will be further validated in an independent cohort of early axSpA patients.

Conclusion. The increased antibody reactivity against several novel antigenic targets in early axSpA patients compared to NSCLBP, RA and HC further supports the involvement of the humoral immune response in axSpA.

REGULATION OF CYTOKINE PRODUCTION BY INKT CELLS REQUIRES IRE1α
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Introduction. iNKT cells represent a prototypic example of innate like T cells which produces large amount of immunomodulatory cytokines. As such they are important in regulation of several forms of inflammatory diseases including PsA and inflammatory bowel diseases. It is currently unclear what determines the unique features of these cells in producing such large quantities of immunoregulatory cytokines. We reasoned that ER stress sensors might be involved as such the Insolvent requiring enzyme 1α (IRE-1α), a transmembrane protein which gets activated upon stress. Activated IRE1α results in the splicing of X box binding protein 1 (Xbp1) mRNA, which in turn transactivates genes involved in cellular homeostasis. Recent studies have shown that IRE1α also regulates the development and function of B cells, dendritic cells, and eosinophils. We therefore aimed to investigate whether iNKTs require IRE1α to regulate cytokine production following activation both in vitro and in vivo.

Methods. To assess steady-state IRE1α activity in INKT cells by flow cytometry, we utilized ERA147 transgenic mice as they express Vernox7 fused at the sites at which IRE1α splices XBPI. QPCR was performed in in vitro expanded INKT cells to examine the role of TCR-dependent signalling in regulating IRE1α activity within iNKT cells and effector cytokine production. ELISA, flow cytometry and QPCR were performed in CD4+, CD19+ mice were used to study the role of IRE1α in regulating the cytokine production by activated INKT cells. Intravital

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microscopy was done on iNKT cells by backcrossing CXCR6-GFP reporter mice with CD4-specific IRE1-deficient animals versus controls.

Results and Discussion. We show that TCR-dependent activation of iNKT cell results in splicing of Xbp-1 mRNA, much more than in mainstream T cells. In line with this, IRE1α reporter activity at steady state was selectively abundant in iNKT cells rather than other T cell subsets. A subsequent analysis in CD4+ IRE1α-mice revealed that TCR-dependent cytokine production by the iNKT cells was severely impaired in the absence of IRE1α. In this context, diminished cytokine production by IRE1α-deficient iNKTs was due to reduced mRNA stability for cytokines such as IL-2, IL-4, IL-6, IL-13, IL-17A TNF-α and IFNγ. As a result, lack of IRE1α profoundly affected iNKT cell functions in vivo.

Conclusion. The findings showed that NeP component in AS was associated with age, high disease activity, presence of current enthesitis, and depression.

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ASSOCIATION OF NEUROPATHIC-LIKE PAIN CHARACTERISTICS WITH CLINICAL AND RADIOGRAPHIC FEATURES IN PATIENTS WITH ANKYLOSING SPONDYLITIS

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Introduction/Aim. Ankylosing spondylitis (AS) is a chronic, progressive, inflammatory disorder and causes chronic back pain. It is not unusual for patients with AS to have symptoms similar to neuropathic pain. We aimed to investigate the neuropathic pain (NP) component in patients with AS using the painDETECT questionnaire (PD-Q) and to assess the relation between NeP and the disease characteristics of AS.

Materials and Methods. A single-center prospective study was performed, including 105 patients. Patients with AS completed three questionnaires: PD-Q, Beck Depression Inventory (BDI), and Euro Quality of life (EQ-5D) questionnaires. Patients were classified into three groups according to the PD-Q scores: nociceptive pain (NoP), mixed pain (MP) (score 13-18), and NeP (score ≥19). Fifteen patients (14.2%) were classified into the NeP group, 21 (21.0%) in the MP group, and 68 (64.8%) in the NoP group. The questionnaires and clinical and radiographic findings were analyzed.

Results. Patients with NeP and MP scored worse on the Bath ankylosing spondylitis disease activity index (BASDAI); BDI; modified Stoke Ankylosing Spondylitis Spine Score; pain–visual analogue scale (VAS); and EQ-5L index and showed an increased prevalence of enthesitis and peripheral arthritis. There were no differences in objective inflammatory markers. PD-Q scores were positively correlated with pain-VAS, BASDAI, BDI, and inversely correlated with EQ-5L index. Age, BASDAI, presence of current enthesitis, and BDI score were independently associated with PD-Q scores.

Conclusion. The findings showed that NeP component in AS was associated with age, high disease activity, presence of current enthesitis, and depression.

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PERFORMANCE OF REFERRAL STRATEGIES FOR SPONDYLOARTHRITIS: A POPULATION-BASED NATIONWIDE STUDY

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Introduction/Aim. Several referral strategies (RS) have been proposed to promote early referral of patients with axSpA, but consensus on the ‘best’ RS is yet to be achieved. We aimed to evaluate the performance of the RS for SpA of a nationwide epidemiological study (EpiReumaPt), as compared to previously proposed RS.

Materials and Methods. EpiReumaPt was a three-stage national survey where, in the first phase, 10,661 participants were randomly selected and interviewed using a face-to-face questionnaire that included screening for rheumatic diseases (RD). In the second phase, positive screenings plus 20% negative screenings were invited for an assessment by the rheumatologist. Finally, 3 rheumatologists (RD) revised all the information and defined the final diagnosis. All participants of the second phase were included (N=3,877). Each RS (table) was tested against the SpA diagnosis using the following metrics: sensitivity, specificity, positive predictive value (PPV), and post-test probability given a negative test (1-NPV).

Results. From the total 3,877 participants, 92 received a SpA diagnosis, 3,107 other RD diagnosis and 678 no RD diagnosis. The ASAS RS was the most sensitive (85.4%), followed by the EpiReumaPt strategy (72.1%). The ASAS and EpiReumaPt RS had the lowest post-test probabilities of SpA if negative (0.4% and 1.0%, respectively), thus, yielding a marked decrease in the probability of disease (1.0-0.4)/1.0*100=96%; (1.0-0.0)/1.0*100=100% respectively). On the other hand, the likelihood of SpA increased by 38% (2.2-2.6)/1.0*100=19% and 119% (3.1-6.1)/1.0*100=56% in case of a positive ASAS and EpiReumaPt RS, respectively. Conclusion. For the first time, a wide range of SpA RS were tested in a population-based setting. The ASAS and EpiReumaPt RS were shown to be the most sensitive, suggesting that these strategies are effective screening tools for SpA.

Table. Performance of the referral strategies against the rheumatologist clinical diagnosis (N=3,877; pre-test probability: 1.0% - weighted national SpA prevalence)

<table>
<thead>
<tr>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>PPV (%)</th>
<th>1-NPV (%)</th>
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<tbody>
<tr>
<td>ASAS</td>
<td>85.4</td>
<td>38.8</td>
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</tr>
<tr>
<td>EpiReumaPt</td>
<td>72.1</td>
<td>67.6</td>
<td>3.5</td>
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<td>Caffalda one</td>
<td>56.3</td>
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<td>3.7</td>
</tr>
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<td>Braun i</td>
<td>47.5</td>
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<td>3.5</td>
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INTEGRATED LONGITUDINAL ANALYSIS INCREASES PRECISION AND REDUCES BIAS: A COMPARATIVE 5-YEAR ANALYSIS IN THE DESIR COHORT

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Introduction/Aim. Evaluation of imaging is important in SpA research, but loss to follow-up often jeopardizes interpretation. Interpretation may further be challenged by the fact that often different readers contributed to scores, in multiple ‘read-waves’. A common approach is to evaluate patients with complete follow-up (completers analysis), but this approach is not assumption-free and may cause non-random data loss. We aimed to investigate if the use of all data in an assumption-free manner (‘integrated analysis’) affects the precision of estimates for imaging outcomes, compared to the completers analysis.

Table. Change per year in the percentage of positive cases for binary imaging outcomes over 5-years of follow-up, according to 3 different analytical methods, in early axSpA patients fulfilling the ASAS axSpA criteria from the DESIR-cohort

<table>
<thead>
<tr>
<th>Imaging outcomes</th>
<th>% change per year (95% CI) (n=398-411)</th>
<th>% change per year (95% CI) (n=342-364)</th>
<th>% change per year (95% CI) (n=218-236)</th>
</tr>
</thead>
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<td>SACROILIAC JOINTS</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sacroiliitis on MRI (SpA criteria)</td>
<td>-7.4 (11.7; -3.1)</td>
<td>-4.8 (-6.9; -2.7)</td>
<td>-3.1 (-5.1; -1.2)</td>
</tr>
<tr>
<td>&gt;1 flaky erosions on MRI SpA</td>
<td>4.7 (2.6; 6.8)</td>
<td>3.3 (1.8; 4.9)</td>
<td>3.1 (1.9; 4.3)</td>
</tr>
<tr>
<td>mXSpA on X-ray (positive/negative)</td>
<td>1.0 (0.7; 1.3)</td>
<td>0.8 (0.5; 1.2)</td>
<td>1.2 (0.5; 1.8)</td>
</tr>
<tr>
<td>SPINE</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BMI ≥ 3 erosions on MRI SpA (ASAS criteria)</td>
<td>-0.8 (-3.0; 1.4)</td>
<td>-0.4 (-4.4; 3.6)</td>
<td>-0.1 (-12.1; 1.0)</td>
</tr>
<tr>
<td>≥ 5 flaky erosions on MRI SpA</td>
<td>-0.1 (-5.0; 4.0)</td>
<td>-0.1 (-5.0; 4.0)</td>
<td>-0.1 (-5.0; 4.0)</td>
</tr>
<tr>
<td>≥ 1 syndesmophyte on X-ray</td>
<td>0.8 (0.1; 1.5)</td>
<td>0.8 (0.1; 1.5)</td>
<td>0.8 (0.1; 1.5)</td>
</tr>
</tbody>
</table>

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**Methods.** axSpA patients from the DESIR cohort were included (N=416). Radiographs and MRIs of the SIJ and spine were obtained at baseline, 1, 2 and 5 years. Each film was scored by 2-3 readers in 3 ‘read-waves’. Each outcome was analyzed: i. according to a ‘combination algorithm’ (‘2 out of 3’); and ii. per reader. The change of each outcome was analyzed by GEE using three approaches: i) ‘integrated analysis’ (including patients with ≥ 1 score from ≥1 reader from all waves); ii) completers-only analysis (including only patients with complete follow-up, using scores from individual readers from wave 3); iii) aggregated complete analyses (similar to ii but using combined-scores).

**Results.** An analysis with all data from different readers and ‘read-waves’ (‘integrated analysis’) was more inclusive with no meaningful loss of precision of the change-estimates compared to both complete analyses (Table). In fact, for low-incidence outcomes (e.g. % mNY), a similar incidence was ‘captured’, with more precision, by the ‘integrated analysis’ compared to the complete analysis.

**Conclusion.** An efficient and assumption-free usage of data does not compromise the precision of change estimates in imaging parameters and may yield increased statistical power for detecting changes with low incidence.

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**P116**

**HIGH PREVALENCE OF AXIAL SPONDYLOARTHRITIS IN PATIENTS WITH ANTERIOR UVEITIS AND CHRONIC BACK PAIN – PRELIMINARY RESULTS OF THE Sp-EYE STUDY**

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**Aim.** Axial spondyloarthritis (axSpA) patients still suffer an important diagnostic delay. Previous studies described a high proportion of undetected axSpA in patients with anterior uveitis (AAU). We hypothesized that referral of all patients with AAU and chronic back pain results in a high prevalence of newly diagnosed axSpA patients.

**Methods.** In 2017 a prospective observational study was started including all patients with noninfectious AAU and back pain (≥3 months, started < age of 45 years) referred from nine Ophthalmology clinics to our Rheumatology department. Exclusion criteria were: history of a rheumatic or other known systemic disease associated with uveitis. Sociodemographic, clinical, laboratory and radiographic parameters and patient questionnaires were collected. The axSpA diagnosis was made by the rheumatologist and classified following the ASAS criteria for radiographic or non-radiographic axSpA.

**Results.** In the first year, 42 patients were referred to the Rheumatology department, of whom 32 (age 35 years; 47% female) met all the inclusion criteria. Sixty-three percent had a history of more than one AAU and the median back pain duration was 11 years. AxSpA was diagnosed in 10 patients (31%, all HLA-B27 positive), of whom four fulfilled the criteria for radiographic and six for non-radiographic axSpA. Another 11 patients (34%, six HLA-B27 positive) were suspicious for early axSpA. A high disease activity score (ASDAS≤2.1) was present in 57% of the patients with a new diagnosis or suspicion of axSpA. Treatment with non-steroidal anti-inflammatory drugs was started in 20 patients, and a tumor necrosis factor inhibitor in one patient.

**Conclusion.** The referral of AAU patients with chronic back pain led to a notably high number of new axSpA diagnoses and patients suspicious for beginning axSpA, requiring further follow up. These results stress the importance of systematic referral of AAU patients in order to improve early recognition of axSpA.

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**P117**

**COMPUTER TOMOGRAPHY DEFINED SACROILIITIS IN INFLAMMATORY BOWEL DISEASE – A SERVICE EVALUATION OF REPORTING STANDARDS**

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**Introduction/Aim.** A joint rheumatology-radiology service evaluation was undertaken to explore the prevalence and reporting standards of Computer Tomography-defined Sacroiliitis (CTSII) in patients with Inflammatory Bowel Disease (IBD) imaged for non-musculoskeletal indications.

**Materials and Methods.** CT abdomen/pelvis of patients with verified IBD (Crohn’s disease (CD) or Ulcerative Colitis (UC)) were identified retrospectively from the radiology imaging system (RIS) between Jan 2010 and Dec 2017. The results were filtered to 18-55 year olds: considered to be the population with the highest diagnostic yield for axial spondyloarthritis (axSpA). For patients who have undergone multiple scans, the most recent CT scan was used as the index scan. CT review was undertaken by 3 radiology trainees (trained and under supervision of a senior musculoskeletal radiologist) in order to identify incidental CTSII, highly suggestive of axSpA.

**Results.** 301 unique scans of verified IBD patients (mean age 36; female 50.8%) were included. The prevalence of CTSII using the highest sensitive criterion of a validated CT screening tool was 19.9% (60/301). In 248 CD and 53 UC patients, the percentage of CTSII was 20.6% CD (51/248) and 17.6% UC (9/53) respectively. Of 60 positive reports 15/60 were reported as sacroiliitis but no recommendation was made for onward rheumatological evaluation: 7/15 had no prior diagnosis of axSpA. Of the remaining 45 CTSII, 26 were unrecongised despite a bone review having apparently been undertaken, 17 did not mention a bone review, 2 were unrecongised despite the SI joints having apparently been reviewed. **Discussion/Conclusion.** In 5 selected IBD patients have sacroiliitis suggestive of axSpA but this is not reported in 3 out of 4 scans. Raising the awareness of this association and using a validated CT tool may improve reporting quality. Future evaluation of this population may differentiate between asymptomatic sacroiliitis and a potential hidden burden of axSpA among IBD patients undergoing CT scanning for non-musculoskeletal indications.

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**P118**

**COMPARISON OF WORK DISABILITY, DEPRESSION, AND QUALITY OF LIFE IN ANKYLOSING Spondylitis VS Psoriatic Arthritis: INTERIM RESULTS FROM THE COMPLETE STUDIES**

Krhaishi M.1, Bessette L.1, Harasso B.1, Florica B.1, Setty Y.1, Teo M.1, Remple V.1

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**Introduction/Aim.** AS and PsA are chronic inflammatory diseases associated with severe pain and joint damage which may impact patient reported outcomes (PROs), such as ability to work, depression and quality of life. This analysis aimed at assessing PRO differences between anti-TNFα-naïve adults with active AS or PsA failing initial treatment. Here, baseline data from patients enrolled between Jul/2011-Jun/2017 were included. Disease activity was classified as active/severe vs low/moderate based on BASDAI (≤4 vs <4), and DAS28 (≥5.1 vs <5.1). PsA patients were further stratified as BSA≥3% vs <3%.

**Results.** 528 AS and 317 PsA (41% with BSA≥3%) patients were included. Upon multiple imputation adjustment, AS patients showed a trend towards higher scores in SF-12 Physical Functioning compared to PsA patients with BSA≥3% (46.1 vs 38.2, p=0.009). PsA patients with BSA≥3% had significantly higher scores in SF-12 Role Functioning (47.9 vs 39.1, p=0.031) and a trend towards higher scores in SF-12 Mental Health (58.6 vs 52.2, p=0.085) compared to those with BSA<3%. No differences were observed in the remaining SF-12 subdomains, WLQ, or BDI. Regarding other PRO determinants, active/severe disease was associated with higher BDI and worse scores in all WLQ and SF-12 dimensions, and female gender was associated with higher BDI scores and lower scores in the SF-12 Physical Functioning, Vitality, Social Functioning and Mental Health subdomains.

**Discussion/Conclusion.** AS and PsA affect multiple aspects of patients’ lives without significant differences. Higher disease severity is associated with depressive symptoms and greater impairment in daily activities and work productivity.
P119 IMPACT OF EXTRA-ARTICULAR MANIFESTATIONS ON PATIENT-REPORTED OUTCOMES IN ANKYLOSING SPONDYLITIS AND PSORIATIC ARTHRITIS: INTERIM RESULTS FROM THE COMPLETE STUDIES

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1Laval University, CHUL, Quebec; 2Memorial University of Newfoundland, St. John’s; 3University of Toronto, Toronto; 4Grey Bruce Health Services, Owen Sound; 5University of British Columbia, Penticton; 6AbbVie Corporation, Montreal, Canada

Introduction/Aim. Extra-articular manifestations (EAMs) in rheumatic diseases negatively impact health outcomes including quality of life and work capacity. Although EAMs may directly affect response to treatment, differences in patient-reported outcomes (PROs) based on EAM presence could be an important contributory variable. This analysis aimed at assessing the impact of EAMs on PROs among patients with active AS or PsA failing initial treatment. Here, baseline data from patients enrolled between July/2011-June/2017 were included.

Methods. Patients eligible for the COMPLETE studies are anti-TNF-α-naïve adults with active AS or PsA failing initial treatment. Here, baseline data from patients enrolled between July/2011-June/2017 were included. EAMs were defined as presence of: enthesitis, uveitis, IBD or psoriasis (EAM1 for AS); enthesitis, uveitis, or IBD (EAM2 for AS); enthesitis or dactylitis (EAM3 for PsA). PROs (SF-12, WLQ, BDI) were compared between patients with vs without EAMs using generalized linear models adjusting for disease state (high/very high vs. inactive/low/moderate disease based on the BASDAI and the DAS28), disease type, and ever smoking.

Results. 609 AS and 406 PsA patients were included with a mean age of 43.1 and 51.3 years, respectively. EAM1, EAM2, and EAM3 prevalence were 33.9%, 25.9%, and 5.0%, respectively. Upon multivariate adjustment, EAM1/EAM2 presence in AS/PsA patients was associated with significantly higher BDI (14.0 vs. 12.6, p=0.046) and lower SF-12 physical function (38.4 vs. 44.8, p=0.047). When evaluating the impact of EAM3 on AS/PsA patients, no significant differences were observed in PROs; however, BDI was notably higher among patients with EAMs (14.1 vs. 12.7, p=0.056).

Discussion/Conclusion. In Canadian real-world, a substantial proportion of AS and PsA patients requiring a change in treatment report EAMs. Presence of EAMs, particularly psoriasis for AS patients, was a significant independent predictor of depressive symptoms and reduced quality of life due to worse physical functioning.

P120 ASAS CONSENSUS ON SPANISH NOMENCLATURE FOR SPONDYLOARTHRITIS

Navarro-Compaín V.1, Otin T.2, Loza E.3, Almodóvar R.1, Ariza-Ariza R.4, BAustista-Molano W.5, Burgos-Vargas R.5, Collantes-Estévez E.6, de Miguel E.7, González-Fernández C.7, Gratacos J.7, Ibáñez S.8, Juanola X.9, Maldonado-Cocco J.7, Mello A.10, Pacheco-Tena C.11, Roman-Ramos C.12, Soya, Córdoba; H. Gregorio Marañón, Madrid; H. Parc-Taulí, Sabadell, Spain; 13C. Alemana, Santiago, Chile; 14H. Bellvitge, Barcelona, Spain; 15F. Medicina, Uni. Buenos Aires, Buenos Aires, Argentina; 16F. Cochin, Paris, France; 17H. Paular Hierro, Madrid, Spain; 18U. Autónoma, Chihuahua; 19Univ. Autonoma de GDL, GDL, Mexico; 20Clinica-Salud Reinun, Colombia; 21NIHR LBRC and EAMPsA for PsA). PROs (SF-12, WLQ, BDI) were compared between patients

Aim. To characterize clinical phenotypes of nr-axSpA patients enrolled in the ABILITY-3 study in terms of ASAS classification criteria and parameters of objective inflammation at baseline.

Methods. ABILITY-3 enrolled adult nr-axSpA patients fulfilling ASAS classification criteria but not modified New York radiologic criteria for ankylosing spondylitis (AS). Minimum-baseline disease activity, objective evidence of inflammation and inadequate response to ≥2 NSAIDs was required. Patients received open-label alimumab 40mg every other week for 28-weeks during period 1. Patients achieving sustained remission (weeks 16–28) were randomized into double-blind period 2. We analyzed whether enrolled patients fulfilled the imaging arm of ASAS classification criteria, clinical arm, or both arms, and which objective parameters of inflammation were present.

Table. Baseline characteristics and parameters of objective evidence of inflammation.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Total Population</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (y)</td>
<td>37.3±11.1</td>
</tr>
<tr>
<td>Male</td>
<td>370 (48.9)</td>
</tr>
<tr>
<td>White</td>
<td>651 (96.7)</td>
</tr>
<tr>
<td>Symptom duration, mean (y)</td>
<td>7.1±7.7</td>
</tr>
<tr>
<td>Positive HLA-B27 status</td>
<td>515 (76.6)</td>
</tr>
</tbody>
</table>

Elevated hsCRP: 451 (67.8)

NRA evidence of inflammation:
- SI joint and/or spine: 458 (68.4)
- Elevated hsCRP: 297 (42.6)
- Normal hsCRP: 211 (31.4)
- Elevated MRI: 216 (47.6)
- Normal MRI: 250 (56.6)
- SI joint only: 316 (46.7)
- Spine only: 50 (7.4)
- SI joint AND spine: 120 (39.3)
- Elevated hsCRP only (MRI normal): 162 (24.1)
- Positive MRI for SI joint AND spine AND elevated hsCRP: 90 (13.4)
- Negative MRI for SI joint AND spine AND normal hsCRP: 11 (1.6)

HLA-B27: human leukocyte antigen B27; hSACP: high-sensitivity C-reactive protein; MRI: magnetic resonance imaging; SI: sacroiliac.

1) pt had missing HLA-B27 data from the central laboratory.

2) 4 patients had missing MRI imaging (spine only, n=1; SI joint only, n=2; SI joint and spine, n=1).

3) Elevated hsCRP > greater than the upper limit of normal for the lab.

Results. 673/1506 screened patients were enrolled. Overall, 98.7% fulfilled the ASAS criteria, of which 67.6% fulfilled the imaging arm, 77.4% the clinical arm, and 44.0% both arms. 46% of both categories described in the Table. Conclusions. Objective measures of inflammation were not present in an important broadervations to name or classify the disease, and for 6 terms and 4 abbreviations related to SpA. It was agreed not to translate into Spanish 15 acronyms. However, when mentioning these, it was recommended to follow this structure: type of acronym in Spanish and acronym and expanded form in English. With regards to 7 terms or abbreviations attached to acronyms, it was agreed to translate only the expanded form and a translation was also selected for all of them.

Conclusions. Through this standardisation, it is expected to establish a common use of the Spanish nomenclature for SpA. The implementation of this consensus across the community will be of substantial benefit, avoiding misunderstandings and time-consuming processes.
Aim. To investigate 1) which spinal mobility measures (SMMs) are most frequently impaired and in which order; 2) which SMMs are most discriminative of impairment in patients ever treated with biologics, with higher disease activity and severity in early axSpA.

Methods. All SMM measurements of patients from the DESIR (5-year data) and SPACE (data from LUMC, 2.6 (1.9) years of follow-up) cohorts and with a clinical diagnosis of axSpA (level of confidence ≥7/10) were analysed. SMMs were considered impaired when falling below pre-defined cut-offs, derived from normal individuals (1). The proportion of patients with each of the SMMs impaired was calculated, for both baseline and all observations. The same analysis was conducted in subgroups to contrast patient and disease characteristics potentially influencing spinal mobility, like treatment with biologics (ever/never), disease activity (with/without low disease activity over time, i.e., ASDAS-C2.1 in ≥2/3 of visits) and the presence of baseline syndesmophytes (yes/no).

Results. We included 328 and 148 patients from the DESIR and SPACE cohorts, respectively. Considering patients in whom all SMMs were assessed, in DESIR, the most frequently impaired SMM (below 2.5th percentile) was mSchober (42%), followed by Lateral Spinal Flexion (36%), mSchober (14%), Chest expansion (13%), Cervical rotation (11%), and with ≥1SMM impaired (86% and 78% for DESIR and SPACE, respectively).

Conclusions. LSF and mSchober are the most impaired SMMs, together allowing the identification of the majority of patients with impaired spinal mobility in early axSpA. LSF and BASMI discriminate best between subgroups of patients, reflecting a worse spinal mobility in patients with more active and severe disease.

Reference

Figure 1. Measurements of 10-cm Schober’s test and Lateral Spinal Flexion in DESIR cohorts of axSpA patients in function of age: A) 10-cm Schober’s test in all axSpA patients; B) 10-cm Schober’s test in axSpA patients with low disease activity in at least 2/3 of visits; C) Lateral Spinal Flexion in all axSpA patients; D) Lateral Spinal Flexion in axSpA patients with low disease activity in at least 2/3 of visits.

Poster Presentations

P123

MEASURING SPINAL MOBILITY OVER TIME IN EARLY AXIAL SPONDYLOARTHRITIS: CAN WE DO IT RELIABLY?

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AIM. To investigate the longitudinal use of spinal mobility measures (SMMs) and the relation with mobility curves of healthy individuals in patients with early axSpA.

Methods. All SMMs of patients from the DESIR (5-year data) and SPACE (data from LUMC, 2.6 (1.9) years of follow-up) cohorts and with a clinical diagnosis of axSpA (level of confidence ≥7/10) were analysed. All available SMMs were plotted for each patient in function of age, and together with the percentile curves derived for healthy volunteers, the mobility curves (1). A subgroup analysis was performed in patients with low disease activity over time (ASDAS-C2.1 in ≥2/3 of visits), in order to control for the influence of disease activity on spinal mobility.

Intra- and inter-observer reliability were analyzed using Intraclass Correlation Coefficients (ICC) and the Smallest Detectable Change (SDC) in the SPACE cohort.

Results. We included 328 and 148 patients from the DESIR and SPACE cohorts, respectively. A high variability in SMMs within the same patient over time was observed, even when restricting the analysis to patients with low disease activity. Figure 1 shows the results for 10-cm Schober’s test and Lateral Spinal Flexion (LSF) in the DESIR cohort. The results were strikingly similar for all the SMMs and in both cohorts. The reliability of SMMs was only “fair” to “good” (inter-reader ICC (2,1): 0.55–0.84; intra-reader ICC (2,1): 0.49–0.72). The obtained SDs reflect that large variations in SMMs are needed to capture a true change beyond measurement error (e.g. 1.4 cm for 10-cm Schober’s test; 5.1 cm for LSF).

Conclusion. There is a high variation of SMMs from visit to visit, which impairs the use of spinal mobility measures, at the individual level in the follow-up of patients with axSpA. It should be tested if reliability can be improved to reduce at least part of the variability.
P124

INFLUENCE OF INFLAMMATION AND STRUCTURAL DAMAGE ON GLOBAL FUNCTIONING IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS – USING THE ASAS HEALTH INDEX IN ROUTINE CARE

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Aim. To investigate the relationship between spinal mobility and self-report global functioning as assessed by the ASAS HI, and to study the influence of structural and inflammatory spinal changes on global functioning.

Material and Methods. Patients from the outpatient clinic of our hospital suffering from axial or peripheral SpA completed self-report questionnaires assessing disease activity and functioning. Axial inflammation as detected by MRI was assessed by Berlin score, structural damage by mSASSS and spinal mobility by BASMI.

Results. Correlations between the ASAS HI and other health outcomes were analysed by Spearman’s test. Logistic regression analyses were performed to investigate the association between functioning and other clinical characteristics.

Conclusions. The influence of obesity on functioning is remarkable in patients with SpA. In contrast, the influence of structural damage and spinal inflammation on global functioning was limited in this study, probably due to the relatively low mSASSS and MRI scores.

P125

OSTEOPOROSIS COMMONLY OCCURS IN AXIAL SPONDYLOARTHROPATHY

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Background. Osteoporosis, a consequence of inflammatory arthritis, is frequently overlooked in axSpA, a condition with male predominance. Osteoporosis prevalence figures are therefore uncertain. To understand the impact of low BMD in axSpA, accurate epidemiology is crucial.

Aims. 1. Investigate the prevalence of low BMD in an axSpA cohort
2. Explore relationships between BMD and axSpA.

Materials and Methods. A detailed assessment was performed on axSpA patients. Disease severity was assessed using ASAS-DRP, BASDAI, BASMI and BASFI. BMD was assessed using DXA of the spine, hip and radius. The WHO criteria were used to classify low BMD.

Results. One hundred patients with axSpA were recruited: 78% (n=78) male, mean (SD) age 51 (12) years, disease duration 26 (13) years, median (IQR) mSASSS 10 (33). Low BMD was more prevalent at the spine than men when measured by lateral DXA (32% vs 12%, p<0.01), but not by AP DXA. A higher mSASSS, reflecting more syndesmophyte formation, was associated with a raising AP spine BMD (n=0.5, p=0.01), but had no effect on lateral spine BMD. The gap between AP and lateral spine BMD, i.e. when AP BMD was higher than lateral BMD, increased significantly (p=0.05) with increasing age (r=0.38), disease duration (r=0.37) and mSASSS (r=0.52). mSASSS was the strongest predictor of a difference between AP and lateral BMD measurements, suggesting syndesmophyte formation interferes with AP DXA of the spine.

Conclusion. AP DXA of the spine is affected by a higher burden of syndesmophytes, raising concerns traditional DXA may miss cases of osteoporosis. We suggest lateral DXA of the spine may be more accurate in axSpA patients.

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SYNDESMOPHYES PREVENT ACCURATE DXA ASSESSMENT OF THE SPINE IN AXIAL SPONDYLOARTHROPATHY

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1Rheumatology Dept., St. James’s Hospital; 2Gerontology Dept., St. James’s Hospital, Dublin, Ireland

Background. Axial spondyloarthropathy (axSpA) causes syndesmophytes and ankylosis of the spine. Osteoporosis is therefore difficult to diagnose, as traditional dual-energy x-ray absorptiometry (DXA) in the antero-posterior (AP) projection of the spine can overestimate bone mineral density (BMD) due to syndesmophytes. Lateral DXA of the lumbar spine is unaffected by syndesmophyte formation.

Aims. 1. Investigate different projections of DXA of the lumbar spine
2. Assess effect of syndesmophytes on spine BMD.

Material/Methods. AxSpA patients were assessed with clinical exam, questionnaires and laboratory investigations. The burden of syndesmophytes was scored using mSASSS, which ranges from 0-72. DXA was performed in the spine in both the AP and lateral projections.

Results. One hundred patients with axSpA were recruited: 78% (n=78) male, mean (SD) age 52 (12) years, disease duration 26 (13) years, median (IQR) mSASSS 10 (33). Spine BMD was lower by lateral DXA than AP (0.76 vs 1.11 g/cm², p<0.01). Lateral DXA detected more cases of low BMD than AP (21% vs 44%, p<0.01). Lateral spine BMD reduced with longer disease (r=0.3, p=0.02), whereas AP spine BMD increased with age (r=0.33, p=0.01). Men had osteoporosis at the spine than men when measured by lateral DXA (32% vs 12%, p<0.02), but not by AP DXA. A higher mSASSS, reflecting more syndesmophytes, was associated with a rising AP spine BMD (n=0.5, p=0.01), but had no effect on lateral spine BMD. The gap between AP and lateral spine BMD, i.e. when AP BMD was higher than lateral BMD, increased significantly (p=0.05) with increasing age (r=0.38), disease duration (r=0.37) and mSASSS (r=0.52). mSASSS was the strongest predictor of a difference between AP and lateral BMD measurements, suggesting syndesmophyte formation interferes with AP DXA of the spine.

Conclusion. AP DXA of the spine is affected by a higher burden of syndesmophytes, raising concerns traditional DXA may miss cases of osteoporosis. We suggest lateral DXA of the spine may be more accurate in axSpA patients.

P127

ADD-ON EFFECT OF AEROBIC EXERCISE TO STRETCHING IN PATIENTS WITH ANKYLOSING SPONDYLITIS

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Introduction. Unlike stretching exercise, the effect of aerobic exercise in patients with ankylosing spondylitis (AS) is not well known. We aimed to evaluate the additional benefits of aerobic exercise to stretching in patients with AS.

Subjects and Methods. This prospective study recruited 34 patients classified as AS according to the 1984 modified New York criteria and randomly assigned into aerobic and stretching-exercise group (n=16) and stretching-exercise-only group (n=18). All participants performed instructed group-exercise guided by a physiatrist and physical therapists and then performed a home exercise for 12 weeks using an exercise booklet with detailed photos. The outcome measurements, including visual analogue scale (VAS), AS Disease Activity Score (ASDAS), Bath AS Disease Activity Index (BASDAI), Bath AS Functional Index (BASFI), and AS Quality of Life Questionnaire (ASQoL) were performed before instructed group-exercise and after 12 weeks of home exercise. Bath AS Metol- index (BASMI) was examined before and 30 minutes after the instructed group-exercise and 12 weeks after a home exercise.

Results. Baseline epidemiologic and baseline outcome parameters showed no significant differences between two groups. After exercise, significant improvement in BASMI was observed in both groups. Significant improvement in BASDAI was observed only in the combination-exercise group. Otherwise, the changes of other outcome measurements at 12 weeks did not show significant differences between the groups; ΔVAS (p=0.59), ΔASDAS (p=0.86), ΔBASFI (p=0.49), ΔASQoL (p=0.82).

Discussion/Conclusion. The aerobic exercise in patients with AS did not show a significant add-on effect to stretching alone in terms of pain, functional level, quality of life, and disease perception. Although addition of aerobic exercise showed beneficial effect on BASDAI, exercise with an emphasis on stretching seems sufficient for management of AS.
Results. Age and sex distribution were not different between groups. Some demographic and disease related characteristics were shown in the table. BAS-DAO, BASFI, global assessment of disease activity and ASAS-HI scores were matched 27 patients with nr-axSpA (63% male) and 30 healthy control subjects (63% male) were included in the analysis. Patients with hypertension, diabetes and known cardiac disease were excluded. All patients underwent detailed echocardiographic examination including M-mode, pulsed-wave Doppler imaging, pulsed-wave tissue Doppler imaging and 2D speckle tracking.

Radiographic Non-radiographic Control

Table. The demographic and disease related characteristics of study groups.

<table>
<thead>
<tr>
<th>Radiographic</th>
<th>Non-radiographic</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>axSpA patients</td>
<td>axSpA patients</td>
<td>subjects</td>
</tr>
<tr>
<td>(n=64)</td>
<td>(n=27)</td>
<td>(n=50)</td>
</tr>
<tr>
<td>Age, years (mean ± SD)</td>
<td>40.9 ± 10.2</td>
<td>37.6 ± 9.4</td>
</tr>
<tr>
<td>Duration of disease, years (mean ± SD)</td>
<td>14.1 ± 7.8</td>
<td>10.6 ± 8.1</td>
</tr>
<tr>
<td>BASDAI (mean ± SD)</td>
<td>2.7 ± 2.1</td>
<td>3.0 ± 1.8</td>
</tr>
<tr>
<td>BASFI (mean ± SD)</td>
<td>2.5 ± 2.3</td>
<td>2.6 ± 2.0</td>
</tr>
<tr>
<td>Ejection fraction, (mean ± SD)</td>
<td>58.9 ± 5.2</td>
<td>60.1 ± 4.7</td>
</tr>
<tr>
<td>Global Longitudinal Strain, (mean ± SD)</td>
<td>20.4 ± 3.3</td>
<td>21.3 ± 3.8</td>
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</table>

Conclusions. The results of the present study showed that left ventricular function had impaired in r-axSpA patients and speckle tracking echocardiography may be a useful tool for early demonstration of left ventricular dysfunction.

P129

ASSESSMENT OF EARLY MYOCARDIAL DYSFUNCTION USING SPECKLE TRACKING ECHOCARDIOGRAPHY IN PATIENTS WITH RADIOGRAPHIC AND NONRADIOGRAPHIC AXIAL Spondyloarthritis

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Background. Axial spondyloarthritis (axSpA) is a chronic inflammatory disease that mainly affects axial skeleton. Although some differences like sex and objective signs of inflammation were described between these two subgroups, overall disease burden was found to be similar in radiographic (r-) and non-radiographic (nr-) axSpA patients. The association of chronic inflammation with cardiac dysfunction was well documented in many inflammatory rheumatic diseases. However it was not assessed in the subgroups of axSpA patients. Advanced two-dimensional (2D) speckle tracking echocardiographic analysis is more sensitive and accurate method of early detection of myocardial dysfunction than the conventional 2D transthoracic echocardiography (TTE).

Objectives. To evaluate the left ventricular function by using speckle tracking echocardiography in patients with both r- and nr-axSpA.

Methods. In total 64 patients with r-axSpA (70% male) and age- and sex-matched 27 patients with nr-axSpA (63% male) and 30 healthy control subjects (63% male) were included in the analysis. Patients with hypertension, diabetes and known cardiac disease were excluded. All patients underwent detailed echocardiographic examination including M-mode, pulsed-wave Doppler imaging, pulsed-wave tissue Doppler imaging and 2D speckle tracking.

Results. Age and sex distribution were not different between groups. Some demographic and disease related characteristics were shown in the table. BAS-DAO, BASFI, global assessment of disease activity and ASAS-HI scores were found to be similar between r- and nr-axSpA patient groups. Although ejection fraction (EF) (p=0.019) and other echocardiographic variables were similar between groups, global longitudinal strain (GLS) (p=0.045) was found to be different among groups (table). Post-hoc analysis showed that GLS was similar in r-axSpA patients. In univariate analysis GLS was correlated with age (p=0.032), peripheral arthritis (p=0.047) and smoking (p=0.019). However in regression only peripheral arthritis (p=0.032) and EF (p=0.015) were found to be the independent predictors of GLS.

Conclusions. The results of the present study showed that left ventricular function had impaired in r-axSpA patients and speckle tracking echocardiography may be a useful tool for early demonstration of left ventricular dysfunction.

P129

ASAS, BASDAI AND ASAS REMISSION IN SECUKINUMAB TREATED PATIENTS WITH ACTIVE ANKYLOSING SPONDYLITIS: 3-YEAR RESULTS FROM A POOLED ANALYSIS OF TWO PHASE 3 STUDIES

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Introduction/Aim. Secukinumab (SEC), a fully human mAb that selectively neutralises IL-17A, has demonstrated significant improvement in the signs and symptoms of active ankylosing spondylitis (AS) up to 3 years (yrs).1-3 This post-hoc analysis evaluated the effect of SEC in achieving clinical remission (REM) criteria in patients (pts) with AS: 3-yr data pooled from the phase 3 MEASURE 1 and 2 studies.

Materials and Methods. Study designs have been reported previously.1 REM was defined as meeting one or more of these criteria: ASAS ID (score ≤1.3), ASAS PR (score ≤2 in each of the 4 main ASAS domains) or BASDAI score ≤2 (non-validated cut-off). Pt-reported outcomes (PROs) in pts with and without REM were also explored.

Results. In the overall population, proportion of REM states at Wk16 were higher in SEC versus PBO and further increased through 156 Wks (Table). In INF-NAIVE and TNF-NAIVE pts, proportion of REM states were higher with SEC versus PBO at Wk16 and further improved through Wk 156 (Table). Pts with REM response reported greater improvement in PROs compared to pts without REM (Figure).

Table. Proportion (%) of patients in remission at Weeks 16 and 156

| Table. Proportion (%) of patients in remission at Weeks 16 and 156
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<tr>
<td></td>
<td>Wk 16</td>
<td>Overall</td>
<td>TNF-NAIVE</td>
<td>INF-NAIVE</td>
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<td></td>
<td>16</td>
<td>20.4</td>
<td>21.3</td>
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<td>19.8</td>
<td>21.3</td>
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<tr>
<td>ASAS ID ≤1.3</td>
<td>16</td>
<td>19.8</td>
<td>21.3</td>
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<td>19.8</td>
<td>21.3</td>
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<tr>
<td>ASAS PR ≤2</td>
<td>16</td>
<td>16.1</td>
<td>18.2</td>
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<td>16.1</td>
<td>18.2</td>
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<td>16.1</td>
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<tr>
<td>BASDAI ≤2</td>
<td>16</td>
<td>16.1</td>
<td>16.1</td>
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</table>

Conclusion. SEC treated pts maintain ASAS inactive disease, ASAS PR or BASDAI remission up to 3 yrs in this completers’ analysis. Pts who achieved remission, reported greater improvement in physical function, health-related quality of life, work productivity and less fatigue than pts without remission.

References
THE EUROPEAN MAP OF AXIAL SPONDYLOARTHRITIS (EMAS) – LIVING WITH THE CONDITION

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Conclusions. The European Map of Axial Spondyloarthritis (EMAS) aims to describe how patients diagnosed with axSpA experience the disease from a physical, psychological, and everyday life perspective and how they are managed within the healthcare systems.

Methods. EMAS employed a cross-sectional survey adapted from the Spanish Atlas of Axial Spondyloarthritis 2017, and containing 120 items on sociodemographics, diagnosis, comorbidities, psychological distress (General Health Questionnaire- GHQ-12), healthcare utilization, pharmacological treatments, disease activity (BASDAI), physical activity and limitations, productivity loss, and patient perspective. Patients from Austria, Belgium, France, Germany, Italy, Netherlands, Norway, Russia, Slovenia, Sweden, Switzerland and UK were included. Data from Spain was retrospectively added. A scientific steering committee, formed by 9 leading axSpA experts was selected to validate the results.

Results. 2,846 axSpA patients participated in the survey: mean age was 44 years, 61.3% were female, 67.9% were married and 79.2% were HLA-B27 positive. Almost half were university educated (48.1%), working (51.5%) and members of a patient support group (38.9%). Participants reported a diagnostic delay of 7.2 years with a disease duration of 16.8 years. Active disease (BASDAI >4) was detected in 70.9%; while 33.5% had received biological therapy. High GHQ-12 (≥3) was observed in 57.1%, and patients reported diagnosed anxiety (37.2%) or depression (33.2%).

Conclusions. In this sample of non-selected patients, long diagnostic delay and high patient burden, including self-reported active disease and psychological distress, indicate important unmet needs in axSpA. As the first snapshot of issues relevant to European axSpA patients and disease management, EMAS results may contribute to increasing disease awareness and improving the standard of care.

P132

ASSESSING FUNCTIONAL DISABILITY AND GENERAL HEALTH SITUATION IN PATIENTS WITH ANKYLOSING SPONDYLITIS BY ASAS HEALTH INDEX

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Introduction/Aim. Ankylosing Spondylitis can cause physical dysfunction and reduce patients health quality and thus can cause disability. Ankylosing Spondylitis Quality of Life (ASQoL) index is widely used to assess patients with ankylosing spondylitis. ASAS health index and environmental factors index are easy to use and show us the disease from patients perspective. We aimed to assess general health status, dysfunctions by using ASAS health index and environment factors and other doctor and patient related scales.

Materials and Methods. 94 patients covered ASAS diagnostic criteria were included. ASAS Health index (ASAS-HI), Bath ankylosing spondylitis disease activity index (BASDAI), Bath ankylosing spondylitis functional index (BASFI), patient related health assessment questionnaire (HAQ) and ankylosing spondylitis quality of life (ASQoL) questionnaires were filled by participants.

Results. 45 of 91 (%50) patients were male, mean age was 35.6 (10.6) and average disease duration was 25.7 (40.5) months. 50% of patients BASDAI score was more than 4 (0-10) and had active disease. When ASAS health index result was evaluated patients (%33) had normal function, 44.6% had light disability, 19.8% moderate disability and 29% had severe disability. BASFI results showed that 29 patients (%33) had normal function and 32 patients had (%36.4) moderate function.

Discussion. ASAS health index and environmental factor index results showed positive correlations with BASFI, BASDAI, spatial pain and HAQ. Although ASQoL is only used to assess health quality, ASAS health index and environmental factor index are used to assess general health status, functional disability degrees, pain levels, social participation and emotional and sexual function status.

Conclusion. ASAS health index is a easy, fast and reliable scale in patients with axial spondyloarthritis.

EMPOWERING ANKYLOSING SPONDYLITIS (AS) PATIENTS THROUGH AN ONLINE PERSONAL HEALTH SYSTEM

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Introduction. Patient empowerment integrates multiple concepts that allow a patient to self-manage his disease, which are accessing to health information, education, bi-directional communication between patients and healthcare professionals, self-care support, chronic disease management support and shared decision making.

Methods. In order to evaluate whether an online personal health platform improves AS patients’ health and enhances their effectiveness in managing their health, an online personal health platform is developed for AS patients in Turkey within the positive European Commission supported PALANTE project. Share them with healthcare professionals, messaging module which allows patients to ask questions to healthcare professionals without getting any appointment, exercise module which allows patients to follow the exercise plan specified by physical therapist, videos module which allows patients to learn how to do exercises correctly.

Results. The system has been used by 131 patients and 3 healthcare professionals in Turkey. In order to evaluate the success of the system, a questionnaire was sent to the patients after they used the system for 6 months.

Discussion. Questions are categorized in three groups as communication, educational, and informational features. For each group, same set of questions were asked to patients. Using the functionalities enabled me to accomplish my health tasks more quickly, Communication 70%, educational 74%, Informational 67%. Using the functionalities enhanced my effectiveness in managing my health; Communication 66%, educational 73%, Informational 67%. I want this service to continue; Communication 86%, educational 76%, Informational 66%. I found the … functionalities enhanced my effectiveness in managing my health; Communication 70%, educational 74%, Informational 67%. I want this service to continue.

Conclusion. As it can be seen from the table, majority of patients reacted positively and want the services to continue. Patients found educational features, which contains videos module that allows patients to do their daily exercises correctly without consulting physical therapist, as the most useful functionality of the system. Consequently, the system improved AS patients’ health and enhanced their effectiveness in managing their health.
P134
PREVALENCE AND CHARACTERIZATION OF PSORIATIC ARTHRITIS MUTILANS PATIENTS FROM A SINGLE TERTIARY CENTER

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Introduction. Psoriatic arthritis mutilans (PsAM) is the most serious and uncommon form of psoriatic arthritis (PsA) described in about 5% patients. Data about PsAM subtype are scarce. Therefore, the aim of our study is to describe the clinical characteristics of PsAM patients from a unique tertiary rheumatology center in Brazil.

Materials and Methods. All patients ≥18 years who met CASPAR criteria for PsA followed at our rheumatology division between 2002 and 2017 were actively searched for PsAM deformity of hands and feet.

PsAM was considered in the presence of shortened fingers, digital telescoping, and anteroposterior radiography showing at least one joint with severe erosive arthritis (for example pencil-in-cup or gross osteolysis of the bones) without osteophytes. Demographic, clinical, laboratory and radiographic data were collected.

Results. Roughly 8.2% PsA patients had PsAM (17/207), 12 were males and 5 females with mean age 59±9.9 years and mean age at arthritis onset 34±12.6 years. Most prevalent PsAM comorbid conditions were hypertension in 13 patients (76%), dyslipidemia in 10 (59%), metabolic syndrome in 9 (53%), osteoporosis in 6 (35%), psychiatric disorders in 4 (24%), diabetes in 2 (12%). Interestingly 3 (18%) patients had colorectal cancer (colon, breast and multiple myeloma). Axial radiographic imaging showed syndesmophytes in 9/16 (56%) patients and sacroiliitis in 7/16 (44%). Remarkably 9 of 13 (69%) patients tested positive for HLA-B27 were positive. According to therapy, 9/17 PsAM patients (53%) were on biologic agents (adalimumab, infliximab, etanercept, secukinumab).

Conclusion. We have shown a slightly higher prevalence of PsAM in 8.2% of our PsA Brazilian patients. The enhanced positivity of HLA-B27 and radiographic axial involvement in PsAM shown herein for the first time is striking. Moreover, use of biologic therapy in more than half PsAM patients reinforces the aggressive nature of mutilans involvement.

P135
HEALTH STATUS IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS MUTILANS AS DETERMINED BY THE ASSESSMENT OF SPONDYLOARTHRITIS INTERNATIONAL SOCIETY HEALTH INDEX (ASAS-HI)

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Background. AxSpA, mainly ankylosing spondylitis is a disease that affects and ultimately health related quality of life (HRQoL), as consequence of inflammation in the initial years and bone proliferation throughout the course of the disease. The ASAS-HI is a new instrument to assess the impact of axSpA based on the International Classification of Functioning, Disability and Health, which has been validated in Mexican patients.

Objective. To investigate the status of health of Mexican patients with axSpA using the ASAS-HI.

Methods and Materials. This is a multicenter cross-sectional study of 323/358 patients with axSpA (ASAS criteria) referred by 55 rheumatologists private or institutional practice across the country through six months. Sociodemographic and clinical data were collected at each site and analyzed centrally.

Results. The ASAS imaging arm were fulfilled 87% and the clinical by 82%; HLA-B27 was positive in 82.4%; 70% were males; 56% received bDMARDs. Mean ages at onset and diagnoses were 26.1 (10.3) and 33.1 (12.1) years. Median age was 42 (18-72) years. ASAS-HI correlation with BASDAI, BASFI, and EQ-5D values below meant good health; 176 (54.5%) patients had good health and 147 (45.5%) bad. Univariate analysis disclosed significant differences between the two groups in variables that were significant in the regression models (see below) and sex, NSAID, sacrolitits, and ASDAS. The two models that were associated ASAS-HI in the multivariate analysis were: 1) education, comorbidities, enthesitis, and physician global assessment; 2) BASDAI, BASFI, and EQ-5D. Univariate analysis found a number of differences between the two groups, but the multivariate analysis found significant association with BASDAI, BASFI, and EQ-5D.
P136

IS THE DELAY FROM RECOGNITION OF SEVERE ACTIVE AXIAL SPONDYLOARTHRITIS TO BIOLOGIC DISEASE MODIFYING THERAPY INITIATION IMPROVING?

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1Royal National Hospital for Rheumatic Diseases, Bath; 2College of Liberal Arts, Bath Spa University, Bath, UK

Introduction/Aim. Axial Spondyloarthritis (axSpA) is characterised by chronic inflammatory disease affecting spinal and peripheral joints, entheses and extra-articular manifestations. Since 2000, biological disease-modifying therapy (bDMARD) has been available to treat severe active axSpA. In the United Kingdom, access to bDMARD is heavily influenced by National Institute for Health and Care Excellence (NICE) guidelines, with the first axSpA guideline issued in 2008. Previous studies have demonstrated substantial delay to bDMARD initiation in severe active axSpA, potentially resulting in worse long-term outcomes. Our aim was to establish whether the time from identifying severe active axSpA to bDMARD initiation is improving.

Materials and Methods. We performed a retrospective analysis of patients prescribed bDMARDs for axSpA at the Royal National Hospital for Rheumatic Diseases, Bath. Dates of diagnosis, first bDMARD initiation and the first recorded BASDAI and back pain VAS scores >4, were included in order to calculate the delay between identifying severe active axSpA and bDMARD treatment. The trend in this delay over time was tested by Spearman’s correlation coefficient. Patients with incomplete data or were diagnosed before the availability of bDMARDs in 2000 were excluded from analysis.

Results. 39 patients met the inclusion criteria. The mean delay to initiation of the first bDMARD in this cohort was 3.95 years. There was a slight tendency towards shorter mean delay in recent years, though this did not reach statistical significance (Spearman’s correlation coefficient 0.18, p=0.27).

Discussion. Delays in initiating bDMARDs for patients with severe active axSpA continue to exist, potentially yielding worse long-term outcomes. It is unclear whether these delays are improving despite innovations such as early back pain clinic and increased use of imaging. Further work could include prospective data collection to establish why such delays occur.

Conclusions. It remains unclear whether the delay from recognition of severe active axSpA to bDMARD initiation is improving.

P137

AXIAL SPONDYLOARTHRITIS-RELATED QUALITY OF LIFE IMPROVES SIGNIFICANTLY FOLLOWING INITIATION OF BIOLOGICAL DISEASE-MODIFYING THERAPY

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Introduction/Aim. Axial Spondyloarthritis (axSpA) is characterised by chronic inflammatory disease affecting spinal and peripheral joints, entheses and extra-articular manifestations. Patients with axSpA also suffer worse quality of life with increased levels of ill-health, functional impairment and work-related disability. Our aim was to establish whether initiation of biological disease-modifying therapy (bDMARDs) significantly improved these outcomes.

Materials and Methods. We performed a cross-sectional, retrospective analysis of patients prescribed bDMARDs for severe active axSpA at the Royal National Hospital for Rheumatic Diseases, Bath. ASQoL measurements immediately prior to the nearest to six months after initiation of the first bDMARD were included, with percentage change calculated. The percentage of patients achieving 20%, 40% and 70% reduction in ASQoL was established (described as ASQoL20/ASQoL40/ASQoL70). Patients were excluded from analysis where we failed to establish both pre- and post-treatment scores or where data was incomplete.

We also looked at changes in BASDAI, BASFI, BASMI, WPAI (overall work impairment due to health), FACIT, Jenkins sleep scale and EQ5D for comparison. Recruits 38 patients met the inclusion criteria. Following initiation of the first bDMARD, 63.2%, 55.3% and 34.2% achieved ASQoL20, 40 and 70 responses respectively. Statistically significant improvements following initiation of the first bDMARD were also detected in BASFI (p=0.001, n=21), WPAI percentage activity impairment due to health (p=0.000002, n=35), FACIT (p=0.002, n=19), EQ5D (p=0.002, n=25) and mean Jenkins sleep scale score (p=0.0002, n=24).

Discussion. Significant improvement in axSpA-related quality of life was achieved by the majority of patients treated with their first bDMARD in this cohort, reflecting corresponding improvements in function, work-related disability, fatigue, sleep, depression and anxiety scores. Future analysis could include identification of factors for quality of life improvement with bDMARD treatment.

Conclusion. Treating severe axSpA with bDMARDs significantly improves quality of life outcomes for patients.

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WORK PRODUCTIVITY AMONG WORKERS WITH AXIAL SPONDYLOARTHRITIS

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Background: Axial Spondyloarthritis (axSpA) usually starts in early adulthood and the lifetime impact of the disease can be considerable. Absenteeism and presenteeism are still responsible for high costs associated with the disease. Objectives: Assess absenteeism, presenteeism, work and daily-activities impairment and their related associated factors in patients with axSpA. Methods: Cross-sectional postal, uncenter, non-interventional study. Patients fulfilling the ASAS criteria for axSpA under working age were included. Two groups were defined: A) patients under current anti-TNF; B) patients under conventional therapy. Quantitative and qualitative surveys were performed: Work Productivity and Activity Impairment Questionnaire in SpA (WPAI); participants’ experiences of working and their perceptions of how their condition had affected their work capacity and workplace relationships were recorded. The questionnaires were applied through a telephone call, after consent of the participant and respecting anonymity. Results: 60 patients were included. Mean absenteeism, presenteeism, work and activities impairment were 6.8%, 32%, 35% and 41%, respectively. The univariate analysis showed correlations between absenteeism and phVAS (p=0.027); presenteeism and ASDAS-CRP (p=0.002), BASDAI (p=0.03), BASFI (p=0.02); patient VAS and phVAS (p=0.01, p=0.006), ESR (p=0.03), CRP (p=0.024); percent overall work impairment and ASDAS-CRP (p=0.002), BASDAI (p=0.019), BASFI (p=0.03), patient VAS and phVAS (p=0.016, p=0.01), ESR (p=0.01) and CRP (p=0.03); percent activity impairment and BASDAI (p=0.006), BASFI (p=0.004), phVAS (p<0.0004) and phVAS (p=0.007). BASDAI, BASFI, phVAS, patient VAS and CRP accounted for 63% of the variance of presenteeism, with 10 points increase in phVAS resulted in an increase of 17% in presenteeism (p=0.046). Over time, 95% had already gone to work sick; economic reasons (60%) were the major reasons to presenteeism. 63% considered that the disease can limit their projects or career progression and 15% stated that had already felt discriminated.

Conclusions: Presenteeism, impairment of work productivity and activity were correlated with disease activity and physical functioning, with the increase of VAS physician resulting in increase in presenteeism.

P139

IMPROVEMENT OF CYTOLOGICAL GRADE AND TEAR PRODUCTION IN ANKYLOSING SPONDYLITIS PATIENTS UNDER ANTI-TNF THERAPY: A LONG-TERM FOLLOW-UP

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Introduction/Aim. Clinical expression and pathophysiology of dry eye disease (DED) have recently changed and pro-inflammatory cytokines, such as TNF-α, may play a role in the multifactorial mechanism of DED. Few studies evaluated the effect of TNF blockage in DED and there are no data regarding this complication in ankylosing spondylitis (AS). The aim of the study is to analyze the ocular surface (OS) in AS patients according to the DED severity grade and conjunctival impression cytology (IC) and the effect of anti-TNF therapy in a subgroup of patients with a one-year follow-up.

Methods. Thirty-six AS patients and 39 controls with strict exclusion criteria for DED were enrolled at study entry, and 14 were followed prospectively post-anti-TNF therapy at 3months (3M), and 12 months (12M). AS disease parameters were performed for all patients. Ocular evaluation included OS Index Disease questionnaire, Schirmer I test, break-up time, vital staining, and conjunctival IC. DED severity grade was also applied.

Results. AS patients presented higher frequency of DED (80.5% vs. 43.6%, p=0.01), a worse score of severity [10-3 vs. 0-0.1], p=0.001], and a higher frequency of altered IC (55.3% vs. 12.8%, p=0.007) when compared to controls. The 14 patients under anti-TNF therapy presented an improvement in all clinical AS disease activity parameters throughout the one-year treatment (p=0.05). A concomitant increase in the Schirmer test was also observed [BL.102-35 mm, 3M:17.5(4-35) mm and 12M:20(4-30) mm, respectively, p=0.04] as well as a significant amelioration in the altered IC to a normal IC was noticed (p=0.006). The questionnaires were applied through a telephone call, after consent of the participant and respecting anonymity. The result of the questionnaire is presented as mean±SD. 63% considered that the disease can limit their projects or career progression and 15% stated that had already felt discriminated.

Conclusions: Presenteeism, impairment of work productivity and activity were correlated with disease activity and physical functioning, with the increase of VAS physician resulting in increase in presenteeism.

Poster Presentations

Eleventh International Congress on Spondyloarthritides

Clinical and Experimental Rheumatology 2018

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EMERGENCE OF SEVERE SPONDYLOARTHRPATHY RELATED ENTHESAL PATHOLOGY IN VEDELIZUMAB TREATED INFLAMMATORY BOWEL DISEASE


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Introduction/Aim. Vedolizumab (VDZ) therapy for inflammatory bowel disease (IBD) has been associated with mild spondyloarthrits (SpA) related features including sacroiliitis and syndesmophytes. Following presentation of an index case, we collaborated with other centres to determine if severe SpA had occurred after IBD therapy with VDZ. Herein, we report a series of cases demonstrating the emergence of severe SpA associated enthesitis/osteoitis following successful IBD treatment with VDZ.

Materials and Methods. We evaluated 11 VDZ treated patients with IBD across 7 centres that developed severe SpA and/or enthesopathy with the aim of characterising the VDZ associated SpA or enthesal flares.

Results. De novo SpA developed in 9 of 11 patients in total and flare of established SpA in 2 patients. Four patients required hospitalisation due to disease severity. Available data showed that 1/7 were HLA-B27 positive. The median time from VDZ initiation to flare was 12 weeks with IBD activity ameliorated in 7/10 (no data 1 case) at flare. Severe SpA enthesitis/osteoitis was evident on magnetic resonance imaging (MRI) or ultrasound including acute sacroiliitis (n=5), extensive vertebral osteitis (n=1), peri-facetal oedema (n=1), and isolated peripheral enthesitis (n=3). Due to SpA/enthesitis severity, VDZ was discontinued in 9/11 cases and changes in therapy were initiated including alternative anti-TNF.

Discussion. As we anticipate increasing use of α4β7 inhibition, awareness of this paradoxical reaction and specific phenotype amongst rheumatologists and gastroenterologists alike, can facilitate combined management decisions for effective treatment of IBD and SpA or enthesitis. These cases also tell us about the disease process and why in the face of quiescent gut disease do patients develop a severe SpA/enthesitis? We believe that α4β7 bound to adhesion molecules MADCAM-1/VCAM-1 for T-cell transportation into mucosal or vascular tissue, may offer an explanation for these severe SpA/enthesitis flares. This proposed model of pathogenesis offers an explanation for these severe SpA/enthesitis flares.

Conclusion. Severe SpA, predominantly HLA-B27 negative, with osteitis/enthesitis, may occur under successful VDZ treatment for IBD.

VITAMIN D DEFICIENCY IS ASSOCIATED WITH GREATER PRESENCE OF VERTEBRAL FRACTURES, IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS

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Introduction/Aim. Vitamin D (25(OH)D) insufficiency has been associated with disease activity in axial spondyloarthritis (axSpA). There are no studies in these patients that associate it with vertebral fractures (VF), as in postmenopausal women.

Objective. To evaluate the association between 25(OH)D, insufficiency and presence of VF in axSpA, as well as the risk in ten years time (FRAX) and low bone mineral density (BMD).

Methods. Cross-sectional study. 25(OH)D insufficiency if <30ng/mL. BMD measured with DXA in lumbar spine and femoral neck (FN). Low BMD if T/z score < -1. Evaluation of VF with semiquantitative method (Genant) in thoracolumbar radiographs. Bivariate and multivariate analysis. Significant p value =0.05.

Results. 206 patients (69.9% male), 86.4% radiographic AxSpA. 44.6% had 25(OH)D <30ng/mL. 34% had VF. Prevalence low BMD: FN 28.9%, lumbar 59.7%. These differences were even greater in insufficiency subgroup (Table I).

Differences depending on 25(OH)D levels (all p<0.05)

<table>
<thead>
<tr>
<th>25(OH)D, insufficiency</th>
<th>Normal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients</td>
<td></td>
</tr>
<tr>
<td>85.6%</td>
<td>14.36%</td>
</tr>
<tr>
<td>VF</td>
<td>38.7%</td>
</tr>
<tr>
<td>Major FRAX</td>
<td>8.7±6.7</td>
</tr>
<tr>
<td>BASDAI</td>
<td>4.2±2.2</td>
</tr>
<tr>
<td>BASFI</td>
<td>3.8±2.5</td>
</tr>
<tr>
<td>ASDAS-CRP</td>
<td>2.2±0.1</td>
</tr>
<tr>
<td>ASDAS-ESR</td>
<td>2.7±0.2</td>
</tr>
<tr>
<td>Low FN BMD</td>
<td>56.4%</td>
</tr>
</tbody>
</table>
VALIDITY OF PROMIS MEASURES IN ANKYLOSING SPONDYLITIS PATIENTS

Hwang M.C., Ogdie A.R., Reveille J.D.
McGovern Medical School at The University of Texas Health Science Center at Houston, Dept. of Internal Medicine, Houston; Hospital of the University of Pennsylvania, Dept. of Internal Medicine, Philadelphia, USA

Aim. To evaluate the validity of selected Patient-Reported Outcome Information Measurement (PROMIS) measures in Ankylosing Spondylitis (AS) patients across self-reported Assessment in Spondyloarthritides International Society core set and patient-identified domains.

Materials and Methods. Patients in the Prospective Study of Outcomes in Ankylosing Spondylitis, a longitudinal, prospective, AS cohort from the Houston, Texas study-site from Sept 2017-May 2018 (n=82) completed PROMIS short forms (SFs) assessing global health, depression, fatigue, pain and physical function. PROMIS SFs ranged from 3-12 questions. We assessed internal consistency using Cronbach’s alpha. Content validity was assessed by asking patients if the PROMIS SF questions related to their disease. We assessed construct validity through examination of score distributions, floor effects and through examination of the Spearman’s correlation coefficients between PROMIS measures and existing legacy AS measures (e.g. BASDAI, BASFI, Global Numeric Rating Scale (NRS), Pain NRS and CES-D) of similar domains. We hypothesized that there would be moderate to strong correlation (e.g., 0.6-1) between the PROMIS measures and the target legacy measures.

Results. Participants were mostly male (75%), white (84%), with a mean age of 55 years (Table I). All 82 patients felt the PROMIS SFs addressed AS disease aspects. Legacy measures demonstrated a floor effect that was not present in the PROMIS SFs (Fig. 1). Strong internal consistency was noted in the PROMIS.

Table I. AS Patient characteristics (N=82).

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (Mean SD; years)</td>
<td>53.1 ± 14.2</td>
</tr>
<tr>
<td>Male Gender (n, %)</td>
<td>62 (75.6%)</td>
</tr>
<tr>
<td>Caucasian Race (n, %)</td>
<td>69 (84.1%)</td>
</tr>
<tr>
<td>College Education (n, %)</td>
<td>67 (81.7%)</td>
</tr>
<tr>
<td>Current Employment (n, %)</td>
<td>58 (70.7%)</td>
</tr>
<tr>
<td>Disease Duration (Median, IQR; years)</td>
<td>20.33 (8.4, 28.8)</td>
</tr>
<tr>
<td>Biologic Therapy (n, %)</td>
<td>12 (14.6%)</td>
</tr>
</tbody>
</table>

SFs ranging from 0.843–0.973 (Table II). PROMIS Global, Depression, Fatigue, Pain, Physical function correlated moderately-strongly (rho .684–.865) with the appropriate legacy measures (Table III). Patients reported time to complete the entire PROMIS SFs packet was <10 minutes overall.

Conclusions. This study demonstrates the content and construct validity of PROMIS SFs to assess AS symptoms from a single-center sample of AS patients. Further research is needed to assess discrimination (the ability of PROMIS SF to distinguish disease activity groups), responsiveness, feasibility/resource burden, and translations for AS patients.

(Figure 1 and Tables II and III are on the following page)
Table II. PROMIS and legacy measure scores in AS patients.

<table>
<thead>
<tr>
<th>Measure</th>
<th>N</th>
<th>Mean</th>
<th>Median</th>
<th>Std. Deviation</th>
<th>Range</th>
<th>Minimum</th>
<th>Maximum</th>
<th>Cronbach's alpha (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient Global</td>
<td>82</td>
<td>46.3256</td>
<td>46.3000</td>
<td>8.5506</td>
<td>44.20</td>
<td>23.50</td>
<td>67.70</td>
<td>.843 (.787, .889)</td>
</tr>
<tr>
<td>Global NRS</td>
<td>82</td>
<td>25.67</td>
<td>20.00</td>
<td>23.462</td>
<td>100</td>
<td>0</td>
<td>100</td>
<td>.938 (.916, .957)</td>
</tr>
<tr>
<td>Depression</td>
<td>82</td>
<td>43.9451</td>
<td>38.2000</td>
<td>8.05124</td>
<td>33.10</td>
<td>38.20</td>
<td>69.30</td>
<td>.970 (.958, .979)</td>
</tr>
<tr>
<td>PROMIS Emotional Distress - Depression</td>
<td>80</td>
<td>50.375</td>
<td>47.2000</td>
<td>9.64216</td>
<td>51.80</td>
<td>26.00</td>
<td>77.80</td>
<td>.973 (.963, .981)</td>
</tr>
<tr>
<td>Center for Epidemiologic Studies - Depression</td>
<td>80</td>
<td>50.375</td>
<td>47.2000</td>
<td>9.64216</td>
<td>51.80</td>
<td>26.00</td>
<td>77.80</td>
<td>.973 (.963, .981)</td>
</tr>
<tr>
<td>Fatigue</td>
<td>82</td>
<td>48.768</td>
<td>48.6500</td>
<td>10.64216</td>
<td>51.80</td>
<td>26.00</td>
<td>77.80</td>
<td>.973 (.963, .981)</td>
</tr>
<tr>
<td>Bath Ankylosing Spondylitis Disease Activity Index - Fatigue</td>
<td>82</td>
<td>3.7805</td>
<td>3.0000</td>
<td>2.5530</td>
<td>9.00</td>
<td>0</td>
<td>9</td>
<td>.973 (.963, .981)</td>
</tr>
<tr>
<td>Pain</td>
<td>82</td>
<td>44.8171</td>
<td>43.5000</td>
<td>9.14456</td>
<td>33.40</td>
<td>30.70</td>
<td>64.10</td>
<td>.925 (.902, .949)</td>
</tr>
<tr>
<td>PROMIS Pain Intensity</td>
<td>82</td>
<td>50.375</td>
<td>47.2000</td>
<td>9.64216</td>
<td>51.80</td>
<td>26.00</td>
<td>77.80</td>
<td>.973 (.963, .981)</td>
</tr>
<tr>
<td>PROMIS Pain Interference</td>
<td>82</td>
<td>50.375</td>
<td>47.2000</td>
<td>9.64216</td>
<td>51.80</td>
<td>26.00</td>
<td>77.80</td>
<td>.973 (.963, .981)</td>
</tr>
<tr>
<td>Bath Ankylosing Spondylitis Function Index</td>
<td>82</td>
<td>2.8549</td>
<td>2.2000</td>
<td>2.62279</td>
<td>9.40</td>
<td>0</td>
<td>40</td>
<td>.973 (.963, .981)</td>
</tr>
</tbody>
</table>

Table III. Correlations between PROMIS and legacy measures in AS patients.

<table>
<thead>
<tr>
<th>Measure</th>
<th>PROMIS Global</th>
<th>Global NRS</th>
<th>PROMIS Emotional Distress-D</th>
<th>CESD</th>
<th>PROMIS Fatigue</th>
<th>BASDAI-Fatigue</th>
<th>PROMIS Pain Intensity</th>
<th>PROMIS Pain Interference</th>
<th>Pain NRS</th>
<th>PROMIS Physical Function</th>
<th>Bath Ankylosing Spondylitis Functional Index</th>
</tr>
</thead>
<tbody>
<tr>
<td>PROMIS Global</td>
<td>1.00**</td>
<td>.938**</td>
<td>.949**</td>
<td>.949</td>
<td>.941**</td>
<td>.942**</td>
<td>.964**</td>
<td>.988**</td>
<td>.760**</td>
<td>.741**</td>
<td></td>
</tr>
<tr>
<td>Global NRS</td>
<td>-.838**</td>
<td>1.00</td>
<td>.405**</td>
<td>.465</td>
<td>.495**</td>
<td>.662**</td>
<td>.651**</td>
<td>.752**</td>
<td>.717**</td>
<td>.794**</td>
<td></td>
</tr>
<tr>
<td>PROMIS Emotional Distress - Depression</td>
<td>-.494**</td>
<td>.405**</td>
<td>1.000</td>
<td>.684</td>
<td>.401**</td>
<td>.223**</td>
<td>.347**</td>
<td>.477**</td>
<td>.271**</td>
<td>-.313**</td>
<td>.283**</td>
</tr>
<tr>
<td>Center for Epidemiologic Studies - Depression</td>
<td>-.592**</td>
<td>.465**</td>
<td>.684**</td>
<td>1.000</td>
<td>.429**</td>
<td>.441**</td>
<td>.442**</td>
<td>.504**</td>
<td>.381**</td>
<td>-.388**</td>
<td>.395**</td>
</tr>
<tr>
<td>PROMIS Fatigue</td>
<td>-.572**</td>
<td>.495**</td>
<td>.401**</td>
<td>.429</td>
<td>1.000</td>
<td>.574**</td>
<td>.376**</td>
<td>.474**</td>
<td>.333**</td>
<td>-.464**</td>
<td>.413**</td>
</tr>
<tr>
<td>BASDAI - Fatigue</td>
<td>-.706**</td>
<td>.662**</td>
<td>.223**</td>
<td>.441</td>
<td>.574**</td>
<td>1.000</td>
<td>.620**</td>
<td>.589**</td>
<td>.672**</td>
<td>.653**</td>
<td>.627**</td>
</tr>
<tr>
<td>PROMIS Pain Intensity</td>
<td>-.712**</td>
<td>.651**</td>
<td>.347**</td>
<td>.442</td>
<td>.376**</td>
<td>.620**</td>
<td>1.000</td>
<td>.753**</td>
<td>.861**</td>
<td>-.474**</td>
<td>.498**</td>
</tr>
<tr>
<td>PROMIS Pain Interference</td>
<td>-.761**</td>
<td>.752**</td>
<td>.477**</td>
<td>.504</td>
<td>.474**</td>
<td>.589**</td>
<td>.753**</td>
<td>1.000</td>
<td>.757**</td>
<td>-.688**</td>
<td>.680**</td>
</tr>
<tr>
<td>Pain NRS</td>
<td>-.688**</td>
<td>.717**</td>
<td>.271**</td>
<td>.381</td>
<td>.333**</td>
<td>.672**</td>
<td>.861**</td>
<td>.757**</td>
<td>1.000</td>
<td>-.558**</td>
<td>.586**</td>
</tr>
<tr>
<td>PROMIS Physical Function</td>
<td>-.760**</td>
<td>.779**</td>
<td>.313**</td>
<td>.388</td>
<td>.464**</td>
<td>.563**</td>
<td>.474**</td>
<td>-.688**</td>
<td>-.558**</td>
<td>.1000</td>
<td>-.865**</td>
</tr>
<tr>
<td>Bath Ankylosing Spondylitis Function Index</td>
<td>-.741**</td>
<td>.794**</td>
<td>.283**</td>
<td>.395</td>
<td>.413**</td>
<td>.627**</td>
<td>.498**</td>
<td>.680**</td>
<td>.586**</td>
<td>.865**</td>
<td>1.000</td>
</tr>
</tbody>
</table>

**Correlation is significant at the 0.01 level (2-tailed), * Correlation is significant at the 0.05 level (2-tailed).
Results. Thoracic kyphosis angle showed negative correlations with dominant side shoulder flexion active range of motion (AROM) (p<0.001; rho=-0.711), abduction AROM (p=0.007; rho=-0.545), external rotation AROM (p=0.008; rho=-0.536) and non-dominant side shoulder flexion AROM (p<0.001; rho=-0.768), abduction AROM (p<0.008; rho=-0.540), external rotation AROM (p<0.005; rho=-0.563). There was no correlation between thoracic kyphosis angle and shoulder abduction and flexion muscle strength.

Discussion. As a result of our study, it was determined that in patients with male AS, thoracic kyphosis angle was correlated with shoulder flexion AROM, abduction AROM and external rotation AROM. There are muscular and mechanical connections between the spinal column, scapula, clavicle and humerus. The position changes of these bone structures biomechanically affect each other. We think that as the thoracic kyphosis angle increases, the shoulder mobility decreases in male patients with AS because of this reason. In light of this knowledge, therapeutic approaches to thoracic hyperkyphosis will benefit for the shoulder mobility in AS patients.

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RELATIONSHIP BETWEEN THORACIC KYPHOSIS AND SHOULDER MUSCLE STRENGTH AND SHOULDER JOINT MOTION IN MALE PATIENTS WITH ANKYLOSING SPONDYLITIS

Mete O.1, Saraç D.C.2, Baglan Yentur S.2, Tore G.2, Sarı F.2, Ataç N.2, Göker B.3, Oksay D.2

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Introduction. Ankylosing Spondylitis (AS) is a rheumatologic disease that primarily affects the axial skeleton. Spinal inflammation, increased ossification of the ligaments and syndesmophytes in the spinal column can cause an increase in thoracic kyphosis in the AS patients. Negative effects of thoracic kyphosis on shoulder functions have been reported in studies performed in different populations. The aim of our study is to determine the relationship between thoracic kyphosis angle and shoulder motion.

Methods. Twenty-three (23) male participants (age:41.18±11.89, 89 year, body mass index:26.25±5.02 kg/m2) diagnosed with AS according to the Modified New York criteria were included in the study. Thoracic kyphosis angle and shoulder motion were measured with digital inclinometer. Strength of shoulder muscles were evaluated with digital hand-held dynamometer. Pearson correlation test and Spearman correlation test were used for statistical analysis.

Results. Thoracic kyphosis angle showed negative correlations with dominant side shoulder flexion active range of motion (AROM) (p<0.001; rho=-0.711), abduction AROM (p=0.007; rho=-0.545), external rotation AROM (p=0.008; rho=-0.536) and non-dominant side shoulder flexion AROM (p<0.001; rho=-0.768), abduction AROM (p<0.008; rho=-0.540), external rotation AROM (p<0.005; rho=-0.563). There was no correlation between thoracic kyphosis angle and shoulder abduction and flexion muscle strength.

Discussion. As a result of our study, it was determined that in patients with male AS, thoracic kyphosis angle was correlated with shoulder flexion AROM, abduction AROM and external rotation AROM. There are muscular and mechanical connections between the spinal column, scapula, clavicle and humerus. The position changes of these bone structures biomechanically affect each other. We think that as the thoracic kyphosis angle increases, the shoulder mobility decreases in male patients with AS because of this reason. In light of this knowledge, therapeutic approaches to thoracic hyperkyphosis will benefit for the shoulder mobility in AS patients.

P147

DIAGNOSTIC PERFORMANCE OF POWER DOPPLER ULTRASONIC OF THE ENTHESES IN PATIENTS WITH UNCERTAIN DIAGNOSIS OF SPONDYLOARTHRITIS: THE ECHO-SPA PROSPECTIVE MULTICENTER FRENCH COHORT

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Objectives. To evaluate the performance of PDUS-detected enthesis for the diagnosis of SpA in patients with suggestive symptoms.

Methods. Prospective, multicenter French cohort. Outpatients consulting for suspected SpA (inflammatory back pain, arthritis or inflammatory arthralgia, enthesitis or dactylitis, HLA-B27+ uveitis, familiarity for SpA) were recruited and followed up (2yrs). At baseline, patients underwent to standardized physical examination, pelvic x-ray, sacroiliac MRI, HLA-B27 typing, and other tests judged useful for diagnosis. A blinded PDUS examination of 14 entheses was also performed. Table I shows demographic, clinical and imaging data.

Table I. Total number of AS-IBP parameters in patients with axSpA diagnosis
diagnosis and classified according to the ASAS criteria in the Be-Giant and SPACE cohort.

Be-Giant cohort
n=228

<table>
<thead>
<tr>
<th>All (%)</th>
<th>All (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 IBP parameters</td>
<td>0 IBP parameters</td>
</tr>
<tr>
<td>1 IBP parameters</td>
<td>2 (0.9%)</td>
</tr>
<tr>
<td>2 IBP parameters</td>
<td>12 (5.3%)</td>
</tr>
<tr>
<td>3 IBP parameters</td>
<td>31 (13.6%)</td>
</tr>
<tr>
<td>4 IBP parameters</td>
<td>59 (25.9%)</td>
</tr>
<tr>
<td>5 IBP parameters</td>
<td>124 (54.4%)</td>
</tr>
<tr>
<td>axSpA, axial spondyloarthritis; IBP, inflammatory back pain. IBP parameters: Age onset back pain ≤40 years, insidious onset of back pain, improvement with exercise, no improvement with rest, pain at night.</td>
<td></td>
</tr>
</tbody>
</table>

Sex ratio, men/women 0.6
Symptoms duration at inclusion (any) in years, mean [sd] 39.6 [10.48]
Primary inclusion criterion, no (%) IBP 195 (51.3)
Arthritis/arthralgia 102 (26.8)
Enthesitis/dactylitis 33 (8.7)
HLA-B27+ AUA 33 (8.7)
Psoriasis 85 (22.4)
IBD 20 (5.3)

Radiological and laboratory findings
HLA-B27, no. positive/no. performed (% positive) 193/460 (42)
Pelvic x-ray, no. doubtful/no. performed (% doubtful) 132/351 (37.1)
Pelvic MR scan, no. positive/no. performed (% positive) 58/234 (25)
Pelvic MRI, no. positive/no. performed (% positive) 81/451 (21)
PDUS of entheses 470 (100)
Abnormal entheses (any), no (%positive) 334 (87.7)
At least 1 vascularised enthesis, no (%positive) 140 (42)
RDASAI (median [IQR]) 44.50 (28.20, 58.73)
SpA diagnosis (experts opinion at 2 years), no (% positive) 186 (48.9)
SpA diagnosis (LCA at 2 years), no (% included) 125/300 (42)

Diagnosis of SpA was performed after 2 years, using a latent class analysis (LCA) stratified on initial presentation. In the LCA, SpA diagnosis, performed by a group of experts using a DELPHI method, considering clinical, laboratory and imaging findings (except PDUS) retrieved during follow up, and the baseline PDUS evaluation, were entered as independent variables.
Results. 489 patients were included (96% of the target), and 470 followed over 2 yrs (380 with complete follow up). After 2 years, the experts classified 186 (49%) patients as SpA, of which 46 had at least 1 vascularized enthesitis (Ses-25) vs 15 of the 194 non-SpA (Ses-8). LCA classified 125 patients as SpA, and the diagnostic performance of baseline PDUS enthesis (at least 2 vascularized enthesis, with minimal inflammation, or 1 highly inflamed enthesis), was estimated through 500 bootstrap replications (stratified by centre) and resulted in: median sensitivity=0.57, median specificity=0.87, median RVP=4.39, median RVN=0.5, median diagnostic odds-ratio=8.8.

Conclusion. This multicenter study confirms the accuracy of vascularized PDUS enthesis, to ascertain an early diagnosis of SpA in suspected patients.

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INTER-OMIC ANALYSIS REVEALS FUNCTIONAL RELATIONSHIP BETWEEN DIVERSE GUT MICROBIOTA AND DYSREGULATED HOST IMMUNE RESPONSE IN HLA-B27-MEDIATED EXPERIMENTAL SPONDYLOARTHRITIS
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Aim. HLA-B27 has been hypothesized to alter gut microbiota to promote spondyloarthritis (SpA). In HLA-B27 transgenic (HLA-B27 Tg) rats with experimental SpA, we reported divergent effects of HLA-B27 on gut microbiota despite similar immune dysregulation on different host backgrounds. Inter-omic analysis was employed to determine the relationship between diverse microbes and common host immune dysregulation.

Material and Methods. We correlated the relative frequency of microbes (16S rRNA gene sequencing), with host genes expression levels (RNAseq), from cecum and colon of HLA-B27 Tg and wild-type rats on Dark Agouti, Lewis and Fischer backgrounds. Microbes with a maximum relative abundance >1%, and genes with maximum expression value (reads per kilobase million; RPKM)>1 and coefficient of variation >0.8 were included. Significant correlations (r, FDR q<0.1).

Results. Inter-omic analysis determined several microbes whose relative frequency significantly associated with dysregulated cytokines driving Th17 and Th1 pathways in both cecum and colon. While some microbes were differentially abundant (HLA-B27 Tg vs. wild-type) on both Lewis and Fischer backgrounds (Clostridium), most were unique to either LEW (e.g. Prevotella) or Fischer (e.g. Akkermansia). Interestingly, many microbes that strongly correlated with immune dysregulation (e.g. Lachnospiraceae) were not identified by analyzing effects of HLA-B27 alone. PICRUSt revealed perturbed metabolic pathways (e.g. glycogen biosynthesis, steroid biosynthesis) during inflammation, despite dramatic differences in dysbiotic microbes.

Conclusions. Inter-omic analysis reveals the complexity of HLA-B27-associated microbial dysbiosis. Perturbation of common metabolic pathways by divergent gut microbiota during inflammation on different genetic backgrounds suggest important functional overlaps that maybe key to evoking similar host immune dysregulation, and that microbial communities and their function may be more important than individual microbes.

P150
A STUDY OF THE HLA-B27-ASSOCIATED MICROBIOTA IN HEALTHY INDIVIDUALS REVEALS INTESTINAL DYSBIOSIS AND AN ALTERED MICROBIOTA-SPECIFIC IMMUNE RESPONSE MAY BE PREDISPOSING EVENTS IN THE PATHOPHYSIOLOGY OF SPONDYLOARTHRITIS
Asquith M.1, Sternes P.2, Costello M.E.3, Schleisman M.1, Davin S.1, Diamond S.1, Karstens L.2, Brown M.A.3, Rosenbaum J.T.2,3
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Introduction. Mechanisms that underpin the substantial contribution of HLA-B27 to spondyloarthritis susceptibility remain incompletely understood. In this study we tested the hypothesis that HLA-B27 expression, even in healthy individuals, was sufficient to drive intestinal dysbiosis.

Methods. Intestinal biopsies and feces were collected from healthy HLA-B typed individuals (n=107) and subject to 16S rRNA gene sequencing. Global and taxon-specific IgA responses to the intestinal microbiota were established by flow cytometry and IgA-SEQ.

Results. HLA-B27+ve individuals exhibited a distinct intestinal microbiota to those individuals that were HLA-B27 -ve. This included significantly increased carriage of the genera Roseburia and Oscillibacter and decreased carriage of the species Blautia obeum. These taxa are all members of the broader Clostridium XIVa/XIV cluster. HLA-B27 expression in healthy individuals was also associated with a significantly enhanced total frequency of IgA-coated bacteria. Interestingly, IgA-SEQ analysis revealed the Blautia genus was specifically enriched for IgA coating.

Discussion. Our findings provide evidence that microbial dysbiosis in HLA-B27 individuals, and a perturbed microbiota-specific IgA response are not merely secondary to SpA disease. Future studies will examine whether over-represented taxa or those targeted by maccos IgA responses in this study may functionally contribute to SpA pathogenesis.

Acknowledgements. M.A. and J.T.R. are supported by the Rheumatology Research Foundation and the Spondylitis Association of America.

P149
A STUDY OF THE HLA-B27-ASSOCIATED MICROBIOTA IN HEALTHY INDIVIDUALS REVEALS INTESTINAL DYSBIOSIS AND AN ALTERED MICROBIOTA-SPECIFIC IMMUNE RESPONSE MAY BE PREDISPOSING EVENTS IN THE PATHOPHYSIOLOGY OF SPONDYLOARTHRITIS
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1Dept. of Medicine, Oregon Health & Science University, Portland, USA; 2Institute of Health and Biomedical Innovation, Queensland University of Technology, Brisbane, Australia; 3Dept. of Medical Informatics and Clinical Epidemiology, OHSU, Portland; 4Casey Eye Institute and Dept. of Ophthalmology, OHSU, Portland; 5Legacy Devers Eye Institute, Portland, USA

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P150
A STUDY OF MICROBIAL TRANSLOCATION IN AN ANIMAL MODEL OF SPONDYLOARTHRITIS
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Introduction. The mechanism through which enteric microbes contribute to peripheral inflammation in spondyloarthropathy (SpA) remains uncertain. The primary objective of this study was to determine whether microbial translocation can be observed to extra-intestinal tissues in the HLA-B27/Ila2 transgenic rat - a foremost translational model of SpA. We also compared translocation in HLA-B27 transgenic animals with and without arthritis.

Methods. Intestinal (cecal) contents, mesenteric lymph nodes, spleen, serum, liver, lung, ankle joint and eye were collected from age matched HLA-B27/Ila2 transgenic rats with or without arthritis and WT controls (n=20-45/group). DNA was extracted under sterile technique and the 16S rRNA V4 region subject to 16S rRNA sequencing. Extraction blanks were run throughout sample processing and amplification (every 12 samples) to control for environmental contamination. Sequencing data was first processed through DADA2 pipeline prior to identifying and removing contaminant sequences with the recently developed Decomant (v0.8) algorithm.

Results. Our study revealed a polymicrobial DNA signature in extra-intestinal tissues irrespective or rat genotype or disease state. The most abundant microbial 16S DNAs in joint tissue included Prevotella spp. and Roseburia faecis. Blautia obeum DNA was significantly over-represented in arthritic joint tissue. Arthritis was also associated with a marked decrease in intestinal colonization by flavone-producing bacterium Eubacterium osidoreducens.

Conclusions. We propose translocation of microbes/microbial products from the gut to extra-intestinal tissues may be a contributory mechanism to SpA pathogenesis, although alone is not sufficient to elicit inflammatory disease. Specific changes in microbial community DNA profile in the gut or elsewhere may serve as useful biomarkers of disease state in either patient populations or disease models. This approach may yield useful candidates for further study such as Eubacterium osidoreducens. Future studies will verify our findings using PCR-independent methods.

Acknowledgement. M.A. and J.T.R. are supported by the Rheumatology Research Foundation and the Spondylitis Association of America.
THE RESPONSE TO TNF-BLOCKERS TREATMENT OF SpA PATIENTS IS INFLUENCED BY THE INTERPLAY BETWEEN HLA-B27 AND GUT MICROBIOTA COMPOSITION AT BASELINE

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Introduction. The response to TNF-blockers in axial spondyloarthritis (AxSpA) is at least partially influenced by HLA-B27 through a still poorly understood mechanism. Given that HLA-B27 regulates the gut microbiota composition in rats, we seek to evaluate the predictive value of the gut microbiota composition in AxSpA patients at baseline on their subsequent responsiveness to TNF-blockers.

Methods. 58 patients were recruited according to the following criteria: active disease despite NSAIDs intake; no history of inflammatory bowel disease; no antibiotics intake within 3 months prior recruitment. Bacterial 16S rDNA gene sequencing region was performed on stools samples before and after TNF-blocker treatment. Diversity metrics and custom LeSe were used to explore the relationship between the composition of the intestinal microbiota and the efficacy of TNF-blockers.

Results. A lower alpha diversity at baseline was unexpectedly associated with better treatment response, HLA-B27 genotype and smoking behavior. Meanwhile, beta diversity was associated with smoking behavior and HLA-B27 genotype before and after treatment. Beta diversity at baseline was associated with the BASDAI index after treatment, and the response to the treatment. These results indicate a potential regulatory role for the gut microbiota on the underlying mechanisms involved in the response to TNF-blockers. Moreover, a LeSe-like approach identified 6 bacterial species as potential biomarkers for the treatment response, despite the absence of global changes (beta diversity) in the microbiota composition following a 3-month TNF-blocker intake.

Conclusions. The baseline composition of the gut microbiota from AxSpA patients could be associated with treatment efficacy. Further functional studies will be conducted to assess which of the aforementioned bacteria could be used as predictors of the treatment efficacy and potentially as probiotics promoting treatment efficacy among non-responders patients.

FUNGI OVERLOOKED: THE MYCOBIOME AS A CAUSE OF SPONDYLOARTHRITIS (SpA)

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We and others have strongly implicated the bacterial microbiome in the pathogenesis of SpA. Although bacteria or bacterial products contribute to the pathogenesis of SpA, the role of bacteria is incompletely understood. In addition, very little attention has been focused on the potential contribution of fungi. The hypothesis that the mycobiome contributes to the pathogenesis of SpA is based on: 1) Two genetic loci affect susceptibility to spondylitis (CARD9 and IL23R) and also regulate the immune response to fungi; 2) Antibodies to Saccharomyces cerevisiae antigens (ASCAs) or antibodies against conserved fungal cell wall glycans (mannan, beta-glucan, and chitin) are used to diagnose Crohn’s disease, and are elevated in SpA and psoriasis; 3) Bacterial cell wall components mimic fungal cell wall components (cortical, dimeric, and adhesin) activate innate immune cells that can re-circulate from the gut to the site of extra-intestinal inflammation. Emerging data indicate that the fungal component of the microbiome, termed the virome, can also profoundly influence host physiology and modify host immune responses (Handley et al., 2012; Norman et al., 2014; Virgin, 2014). In this study, we evaluated whether alterations in intestinal virome occur in the gut of AS and may modulate intestinal immune responses.

Methods. Immunohistochimistry and electronic microscopy was used to identify viral infection in AS ileal samples. Recent and lytic EBV infection was investigated in AS and normal controls by RT-PCR, in situ hybridization and immunohistochimistry/immunofluorescence. To quantify miRNA levels, stem-loop qRT-PCR was performed with TaqMan MicroRNA Reverse Transcription Kit (Thermo Fischer Scientific) and TaqMan Universal Master Mix II (Thermo Fischer Scientific) according to the manufacturer’s protocols. RNU6B was used for normalization. Following TaqMan MicroRNA assays, specific primers (Thermo Fischer Scientific) were used for detection: ebre-miR-BART2: 197238_mat; ebre-miR-BART3: 004578_mat; ebre-miR-BHRF1-3 197221_mat; RNU6B: 197238_mat. The EBV-encoded homologues of IL-10 (viral or vIL-10) and the latent BHRF1 transcripts encoding bcl-2 homologue and the EBH-3 protein that forms heterodimers with p28 to form intercelluskin-27 (IL-27) were assessed by RT-PCR and immunohistochimistry. The effect of the IL-27 on the differentiation of Th17 cells was assessed in vitro studies.

Results. Big viral inclusion were observed in the context of Paneth cells of patients with AS but not in the ileal samples of normal controls. EBV dysregulation was observed exclusively in AS ileal samples but not in healthy controls, as revealed by presence of EBV latent (LMP2A, EBV-encoded small RNA (EBER)) transcripts, EBER+ cells and immunoreactivity for EBV latent (LMP1, LMP2A) and lytic (BHRF1) antigens in B cells and plasma cells, respectively. The presence of EBV in AS ileal samples was associated with the strong down-regulation of HLA class II surface levels on epithelial cells. Analysis of CD4+ and CD8+ T-cell localization and granulocyte B expression suggests that EBV persistence in AS ileal samples might be favored by exclusion of CD8+ T cells from B-cell follicles and impaired CD8-mediated cytotoxicity. Over-expression of EBV derived miRNA, BART1, BART2 and BART10 were over-expressed in the ileal samples of AS patients with more severe gut inflammation and their expression was inversely correlated with the expression levels of IL-6, TNF, and IL-12p40. EBV-encoded homologue of IL-10 (viral or vIL-10) and the latent BHRF1 transcripts encoding bcl-2 homologue and the EBH-3 protein that forms heterodimers with p28 to form intercelluskin-27 (IL-27) were assessed by RT-PCR and immunohistochimistry. The effect of the IL-27 on the differentiation of Th17 cells was assessed in vitro studies.

Conclusions. We demonstrated alteration of intestinal virome in AS gut characterized by the presence active EBV infection. EBV infection in AS is associated with profound virus-mediated alterations of innate immunity such as down-regulation of IL-12p40, IL-6, TNF-α and increased expression of vIL-10 and IL-27.
**IS CALPROTECTIN A USEFUL DIAGNOSTIC TOOL IN DIAGNOSING Spondyloarthropathies?**

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**Introduction.** Spondyloarthropathies (SpA) are characterized by clinical and radiographic features on which the ‘Assessment of SpondyloArthritis’ (ASAS) classification criteria are based. The use of the ASAS criteria in the diagnosis of SpA is hampered by a relative low sensitivity of 79.5%. In more than 40% of the patients, SpA is associated with clinically (in)over Cohn’s Disease (CD).

The aim of this study is to investigate, if the currently used diagnostic biomarker for CD, fecal calprotectin (FC), has a role in the diagnostic process of SpA.

**Patients and Methods.** A total of 99 first diagnostic patients with differential diagnosis of SpA were included in the study. From these patients, 99 fecal samples (n SpA= 52) and 60 serum samples (n SpA= 25) could be retrieved for calprotectin analysis. SpA diagnosis was based on expert opinion. Fecal (FC) and serum calprotectin (SC) were quantified in adult patients with clinical suspicion of SpA. Patients were asked to discontinue intake of NSAIDs 2 weeks before sample collection. Patients previously diagnosed with inflammatory bowel disease were excluded. Three commercially calprotectin assays (Quantum Blue Calprotectin, Bühlmann; QUANTA® Calprotectin Extended Range, Inova Diagnostics; LIASON® Calprotectin, DiaSorin) were performed on each sample.

**Results.** FC levels were significantly higher in the SpA group versus non SpA group, which was not seen for serum calprotectin (SC). Diagnostic performance among FC assays did not differ significantly, but there was a significant difference in diagnostic performance characteristics when using the manufacturer’s cut-offs (Table I). FC significantly improved diagnostic sensitivity if added to the diagnostic bilan of SpA patients, based on radiology and HLA-B27 analysis (Table II). The likelihood for SpA increased, with increasing FC (Fig. 1).

**Conclusion.** The dosage of FC significantly improved the diagnostic sensitivity for SpA.

### Table I. Diagnostic performance of different fecal calprotectin assays in SpA diagnosis.

<table>
<thead>
<tr>
<th>Manufacturer</th>
<th>Bühlmann</th>
<th>DiaSorin</th>
<th>Inova</th>
</tr>
</thead>
<tbody>
<tr>
<td>AUC [95 CI]</td>
<td>0.658 [0.556-0.750]</td>
<td>0.684 [0.583-0.774]</td>
<td>0.661 [0.559-0.754]</td>
</tr>
<tr>
<td>Median [95 CI] in SpA (n=52)</td>
<td>59.0 μg/g [39.9 – 82.0]</td>
<td>25.4 μg/g [15.8 – 38.7]</td>
<td>24.6 μg/g [15.2 – 32.6]</td>
</tr>
<tr>
<td>Median [95 CI] in non-SpA (n=47)</td>
<td>32 μg/g [15.0 – 45.4]</td>
<td>11.5 μg/g [7.9 – 16.6]</td>
<td>13.0 μg/g [10.9 – 15.6]</td>
</tr>
<tr>
<td>Manufacturer’s cut-off</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sensitivity for SpA [95 CI]</td>
<td>50 μg/g</td>
<td>50 μg/g</td>
<td>50 μg/g</td>
</tr>
<tr>
<td>Specificity for SpA [95 CI]</td>
<td>56% [41-70]</td>
<td>94% [83-99]</td>
<td>96% [86-100]</td>
</tr>
<tr>
<td>Specificity for SpA [95 CI]</td>
<td>68% [53-81]</td>
<td>98% [89-100]</td>
<td>98% [89-100]</td>
</tr>
<tr>
<td>Cutoff at 98% specificity for SpA</td>
<td>50 μg/g</td>
<td>200 μg/g</td>
<td>120 μg/g</td>
</tr>
<tr>
<td>Sensitivity for SpA [95 CI]</td>
<td>157 μg/g</td>
<td>62 μg/g</td>
<td>60 μg/g</td>
</tr>
<tr>
<td>Likelihood ratio for SpA [95 CI]</td>
<td>6.3 [0.8-49.5]</td>
<td>9.9 [1.3-74.1]</td>
<td>3.6 [0.4-31.2]</td>
</tr>
<tr>
<td>Odds ratio for SpA [95 CI]</td>
<td>7.2 [0.8-60.5]</td>
<td>12.3 [1.5-99.8]</td>
<td>3.8 [0.4-35.6]</td>
</tr>
<tr>
<td>Sensitivity (%)[95 CI]</td>
<td>36% [95-79]</td>
<td>74% [59-85]</td>
<td>71% [57-82]</td>
</tr>
<tr>
<td>LR [95 CI]</td>
<td>0.2964§§</td>
<td>3.808§§</td>
<td>0.0985**</td>
</tr>
<tr>
<td>OR [95 CI]</td>
<td>8.8 [1.9-41.3]</td>
<td>10.5 [3.02-36.5]</td>
<td>8.6 [3.1-23.8]</td>
</tr>
</tbody>
</table>

* McNemar test (paired proportions) versus R + HLA-B27; ** McNemar test (paired proportions) versus R.

**Table II.** Diagnostic performance of different diagnostic tests used for SpA diagnosis.

<table>
<thead>
<tr>
<th>Test</th>
<th>R n=80</th>
<th>R + HLA-B27 n=67</th>
<th>R+HLA-B27+FC n=67</th>
<th>FC n=99</th>
<th>HLA-B27+FC n=81</th>
<th>R + FC n=80</th>
</tr>
</thead>
</table>

With n= number of patients for which the test(s) was/were performed; R= Radiology (RX and/or MRI); HLA= HLA-B27 analysis; FC= fecal calprotectin analysis DiaSorin performed at cutoff of 62 μg/g, corresponding to a 98% specificity for SpA; ** McNemar test (paired proportions) versus R + HLA-B27. ** McNemar test (paired proportions) versus R.

* § odds ratios calculated using the method of Altman et al. in MEDCALC®; §§ McNemar test (independent samples).

**Fig. 1.** Likelihood ratio for SpA in function of fecal calprotectin concentrations (DiaSorin).
P155

FEATURES OF CHRONIC PAIN SYNDROME IN PATIENTS WITH ANKYLOSING SPONDYLITIS

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Describing their painful sensations, patients with ankylosing spondylitis often use the following qualitative characteristics of pain in their complaints: numbness, burning, tingling, pain intensification when exposed to pain stimuli. These characteristics are neuropathic pain descriptors resulting from chronic inflammation leading to changes in the central nervous system.

Objective. To detect dysfunction of the pain component (DPC) in patients with ankylosing spondylitis (AS).

Materials and Methods. 150 patients were examined, 127 men and 23 women. The average age of 35, and 52±10.53, mean disease duration of 7.19±9.63. All bol was examined by deny design: Clinic-rheumatology survey (index BASDAI, BASFI), the assessment of pain intensity on VAS, clinical-neurological examination with the use of pros tend DN4 and PainDETECT pain, as well as assessment of emotional-attachment disorders (HADS).

Results. 22 patients (14.7%) scored 4 or more points in the DN4 questionnaire, however, no somatosensory nervous system lesions were detected in these patients, therefore, 14.7% of patients had DCP. Comparison of patients with CKD group 1 (22 patients) and absence of DCP group II (128 patients) showed: in group I, statistically significant higher back pain intensity in the VAS (6.0±1.85 vs 4.5±2.02, p=0.001, respectively); the disease is more active according to the BASDAI index (7.0±1.58 vs 4.8±2.16, p=0.001, respectively); expression of functional disturbances by the BASFI index (6.4±2.24 vs 4.0±2.81, p=0.001); the parameters of the HADS questionnaire in group I corresponded to the presence of clinically significant anxiety and its absence in group II (10.0±2.86 vs 6.1±2.32, p=0.001). However, for the duration of the disease, there were no significant differences in the groups (9.4±1.49 vs 8.6±1.63, p=0.07).

Discussion. The study showed that in 22 patients the presence of neuropathic pain descriptors in conjunction with anxiety disorders, as a result of which, we concluded that along with the nociceptive component of pain, CKD was detected in 14.7% of cases.

Conclusion. Thus, in a number of patients with AS, the pain syndrome is mixed, which can serve as a rationale for complex therapy including drugs from the group of antidepressants (TCAs, SSRIs).

P156

EFFICIENCY OF LONG TERM EDUCATIONAL PROGRAMS FOR PHYSICIANS IN EARLY DIAGNOSIS AND TREATMENT OF AXIAL SPO NDYL ARTHITIS IN KAZAN

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In recent years, there have been cardinal changes in terminology, understanding of pathogenesis of axial spondylitis (AxSpA) and ankylosing spondylitis (AS), early diagnosis has improved. An important role is played by the level of awareness of primary care physicians in the early diagnosis of AxSpA and AS.

Aim. To evaluate the effectiveness of educational activities for primary contact physicians in AxSpA (including AS) diagnosis.

Material and Methods. From 2012 to the present time, educational activities are conducted for primary care physicians in diagnostics and tactics of managing patients with AS with discussion of the criteria for inflammatory back pain, options for onset and the algorithm for diagnosis and examination of patients with AxSpA for primary contact physicians in Kazan. Since 2014, educational modules have been integrated into the system of continuous education of doctors. The results of educational schools were carried out according to the analysis of reports of outpatient admission to rheumatologist of the City Rheumatology Center in Kazan (Clinical Hospital # 7) and the analysis of medical records of patients sent to a rheumatologist in 2011 (base year) in comparison with 2012-2017 in the process of schools.

Results. In the process of conducting schools (2012–2017) the number of patients with AxSpA and AS significantly increased for the first time this year. In 2012–2013, the number of patients almost doubled (575 pts in 2012, 765 in 2013) compared to 2011 (378 pts). The second sharp increase in the number of patients was observed in 2016 (1178 pts) and in 2017 (1298 pts). The same dynamics was observed for AxSpA patients (including AS) who applied for the first time to the rheumatologist with a significant increase in patients in 2012–2013 (2012 - 218 pts, 2015 - 290 pts), 2016 - 506 pts, 2017 year - 711 patients.

“Peak” increase in the number of patients in 2012–2013 can be explained by the beginning of educational activities for doctors; in 2016–2017 - an increase in the number of activities (including remote ones), the amount of information, increased availability of MRI examinations for patients with AxSpA.

Primary care physicians were more likely to refer patients with suspected AxSpA or the number of patients coming from the primary contact physician to the rheumatologist with the required volume of examination (description of back pain, laboratory tests, HLAB27 determination, radiographs and/or MRI) increased significantly from 23.7% in 2012 to 87% in 2017, which allows to verify diagnosis without repeated consultations.

Conclusion. Educational programs for primary care physicians (lectures, schools, remote programs) have great importance for the timely diagnosis of AxSpA, reducing the number of consultations before the diagnosis and with the subsequent appointment of adequate therapy.

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PRELIMINARY RESULTS OF DEVELOPMENT AND 12 MONTHS FOLLOW UP TEST OF THE MOBILE APPLICATION FOR PATIENTS WITH AXIAL SPO NDYLA RTHITIS

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Background. According to the recommendations for management of axial spondylarthropathies (axSpA) - the treatment to target by measuring disease activity, and adjusting therapy accordingly, improves outcomes.

Authors together with patient organization developed the mobile application (app) for Android platforms, which allows patients (pts) to self-control and remote control of the rheumatologist on axSpA disease activity, symptoms and treatment.

Aim. To develop and to test the mobile application «ASpine» for pts with axSpA.

Materials and Methods. The «ASpine» consists of two parts: mobile app for pts and website for rheumatologists. For a test of the first version of the mobile app included 30 patients (pts) with axSpA (ASAS criteria, 2009) at least 12 months (mo) follow up (FUP). In the mobile app, pts fills indexes BASDAI, BASFI, im port their laboratory, instrumental tests, notes which drugs they take. The doctor has an opportunity to observe dynamics of his pts disease activity online. If the patient’s condition worsens the doctor receives a notification about the incident and decides to correct therapy or call the patient for visit.

Results. Only 5 (16.6%) from 30 pts for 12 mo of FUP required correction of therapy. Average BASDAI score at baseline and after 12 mo were 3.2±1.6 vs. 1.9±1.3 (p<0.05), average BASFI score at baseline after 12 mo were 1.4±1.1 vs. 1.2±1.0 (p<0.05). An analysis by a doctor of the health status of patients takes about 1 minute every day in absence of adverse events. Analysis of one case of notification by the patient on average lasts nearly 5-8 minutes. Thus, according to this research with a five-day workweek in 12 months, 30 pts were monitored by the rheumatologist for about 5 hours, which corresponds to an average of 30 minutes per month and 1 minute a day.

Conclusions. The mobile app is a new convenient method for pts self-control and remote control axSpA disease activity for rheumatologists and effectively as our practice shows.

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PAIN BELIEFS AND DISABILITY IN CHRONIC “INFLAMMATORY” AND “NON-INFLAMMATORY” LOW BACK PAIN

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Background. Biopsychosocial factors make important contributions to chronic disability from “non-inflammatory” low back pain (LBP). Patients beliefs about the nature and cause of their pain influence uptake and response to treatment. Changes in those beliefs that follow participation in a pain management programme are associated with improvements in disability.

Hypothesis: Pain beliefs differ between patients with chronic LBP attributed to inflammatory or non-inflammatory medical diagnoses.

Methods. Outpatients with disability attributed to inflammatory LBP were recruited from an ankylosing spondylitis (AS) clinic (n=31, 19 males), those with ‘non-inflammatory’ LBP were recruited through a pain management programme (n=65, 25 male). Participants completed a questionnaire booklet addressing pain beliefs (PBQ), coping strategies(CSQ), pain and disability(SF-36) and psychological distress (STAI-SSF, CDI).

Results. Participants with AS were more likely to be male and reported less bodily pain and disability and slightly lower psychological distress than patients with ‘non-inflammatory’ LBP. Participants with AS less frequently endorsed ‘organic’ pain beliefs (p<0.005) and reported less catastrophising (p<0.001). Diff-

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Early and sustained improvements in the symptoms of PsA correlated positively with improved HRQoL. The greatest HRQoL improvements were achieved when both skin and musculoskeletal symptoms improved early and were sustained.

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**HEALTH UTILITY ESTIMATES IN ECONOMIC EVALUATIONS IN AXIAL SPONDYLOARTHRITIS – DIFFERENT METHODS, DIFFERENT RESULTS**

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Introduction/Aim. A common method for assessing health utility in economic evaluations is the EQ-5D questionnaire – five questions each with three possible responses (EQ-5D-3L) or five responses (EQ-5D-5L). In axial spondyloarthritis (AxSpA), cost-effectiveness analyses have often used indirect measures of health utility, estimated from disease activity or function. Several algorithms have been proposed to convert one scoring method to another, although their validity is unknown. The aim of the current study was to compare directly measured EQ-5D health utility values with those estimated from published mapping algorithms.

Materials and Methods. The British Society for Rheumatology Biologics Registry (BSRBR-A5) recruits patients with AxSpA, native to biologic therapy, across the UK. Annual questionnaires collect information on health utility (EQ-5D-5L), disease activity (BASDAI), and function (BASFI).

Health utility values were:

1. Derived directly from questionnaire responses (EQ-5D-5L value set for England);
2. Estimated from the ‘crosswalk’ value set, mapping EQ-5D-5L to EQ-5D-3L scores; and
3. Computed using two published algorithms incorporating patient age, gender, BASDAI and BASFI.

Differences in the mean and distribution of utility scores were compared between the different methods.

Results. 1981 patients completed 4384 questionnaires (males=71%; mean age=51yrs; mean BASDAI=4.4). Mean (5th/95th percentile) utility scores for the 5L and 3L valuation sets were 0.67 (0.15,0.94) and 0.53 (-0.01,0.88) respectively. Using published algorithms, estimates were 0.63 (0.30,.0.89) and 0.56 (0.20,0.87). The discrepancy between the three estimations, versus the directly measured (5L) score, varied with disease activity.

Discussion/Conclusion. Health utility scores calculated directly, differ from those obtained by extrapolating data on disease activity and function. Where EQ-5D can be measured directly, this should be done. Elsewhere, given that small differences in health utility can influence the results of cost-effectiveness analyses, consideration should be given to how values are computed. There are important implications for both historic and future economic evaluations.
Remission is the goal of axial spondyloarthritis (axSpA) treatment, but until now the definition of remission is unclear. Remission is established only in case when patient fulfills all the criteria. Due to results of voting process was decided to indicate clinical - laboratory and MRI types of remission. Drug-free remission or drug-dependent types of remission also should be note. Remission with or without structural progression has to be marked.

The remission criteria due to opinion of SPA group members are:
1. The values of the ASDAS index (the Ankylosing Spondylitis Disease Activity Score) ≤1.3 (agreement 80%).
2. The values of the BASDAI index ≤1.0 (100% agreement).
3. The duration of morning stiffness is less than 30 minutes (agreement 85%).
4. Absence of swollen joints (agreement 80%).
5. Absence of enthesitis (agreement 93%).
6. The mean values of nocturnal back pain estimated by the NRS for the last week ≤ 1.0 (agreement 83%).
7. Average back pain over the past week ≤1.0 for NRC (agreement 92%).
8. Absence of clinical and instrumental signs of coccyx (100% agreement).
9. Absence of active extra-articular manifestations (uveitis, aortitis, carditis, etc.) (agreement 92%).
10. Normal levels of CRP and ESR (agreement 92%).

Remission is established only in case when patient fulfills all the criteria.

Conclusions. The developed definition and criteria of remission have to be adapted in clinical practice and validated in further studies.
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THE PREVALENCE OF RHEUMATOLOGICAL DISEASES AND PSORIASIS IN THE FIRST-DEGREE RELATIVES OF PsA PATIENTS

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Introduction/Aim. Psoriatic arthritis is a chronic, inflammatory disease associated with psoriasis. Both psoriasis and PsA have a strong genetic/hereditary basis and cumulation in the family. The studies based on the family, some alleles were shown to increase the tendency to PsA when compared to psoriasis. Hence, we aim to define the frequency of psoriasis and other rheumatological diseases in the relatives of PsA patients.

Materials and Methods. Patients fulfilling CASPAR (Classification Criteria for Psoriatic Arthritis) criteria for PsA were recruited. Demographic and clinical findings of the patients were recorded. First-degree relatives of PsA patients were questioned for psoriasis and rheumatologic diseases and recorded in patient forms. The most of first-degree relatives of recruited PsA patients were the patients with rheumatological disease whom followed up by our rheumatology clinic. Form of the disease (psoriasis) at the beginning, either with cutaneous or joint findings, were questioned and recorded on the patient’s file.

Results. A total of two hundred sixty-three patients with PsA (170 female and 93 male patients, mean age: 44.39±12.36 years) were included into our study. In the questionnaire of the first-degree relatives of PsA patients; psoriasis in 60 patients (%22.8), rheumatoid arthritis (RA) in 6 (%2.3), ankylosing spondylitis (AS) in 9 (%3.4), psoriatic arthritis (PsA) in 21 (%8), connective tissue disease (SLE, Sjögren, SSC) in 3 (%1.1), Crohn’s/ulcerative colitis in 2 (%0.8), Familial Mediterranean fever (FMF) in 2 (%0.8) and more than one rheumatological diseases in 2 (%0.8) patients were detected. In 63.9 % of the PsA patients, skin lesions begin earlier than arthritis; joint problems seen earlier than skin lesions in 19.8% and in 16.3% of the patients appeared joint problems and skin lesions at the same time. The results of this study demonstrated that fatigue and depressive symptoms had negative effect on work instability beside pain, disease activity, and functionality in patients with AS. The recognition and improvement of fatigue and depression may lead to reduced risk of job loss in these patients.

Conclusion. In the first-degree relatives of PsA patients, the possibility of psoriasis and PsA was mostly increased due to genetic inheritance and cumulation in the family. Therefore, the prevalence of AS was not significantly increased. Further studies are necessary to evaluate whether other inflammatory rheumatic diseases including spondyloarthopathies increase or not.

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ASSOCIATION OF WORK INSTABILITY WITH FATIGUE AND EMOTIONAL STATUS IN PATIENTS WITH ANKYLOSING SPONDYLITIS – COMPARISON WITH HEALTHY CONTROLS

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Introduction/Objective. Ankylosing spondylitis (AS) is usually seen in among younger person of working age and carries a significant economic burden. It was aimed to explore the relation of work instability with fatigue, depression and anxiety in working AS patients comparing with healthy controls.

Methods. Actively working 61 patients with AS and 40 sex and age matched working healthy controls were enrolled. In patients; pain was assessed by Visual Analogue Scale, disease activity by the Bath AS Disease Activity Index, functional capacity by the Bath AS Functional Index, and spinal mobility by Bath AS Metrology Index. Emotional status, fatigue level, and work instability of all participants were evaluated by Beck Depression Inventory, Beck Anxiety Inventory, Multidimensional Assessment of Fatigue, and AS Work Instability Scale, respectively. Data were analyzed by SPSS, using Chi-square test, Mann-Whitney U test, Kruskal-Wallis test, Spearman correlation analysis, and Multivariate linear regression analysis.

Results. Depression, fatigue, and work instability scores were significantly higher in patients than controls (p<0.05). Clinical parameters (except spinal mobility) showed a significant worsening across the levels of work instability in patients (p<0.05) and work instability scores were positively correlated with all clinical parameters except spinal mobility (p<0.001). There was a weak correlation between work instability and spinal mobility (p<0.05). Fatigue (p<0.001), pain, and functional capacity scores (p<0.05) were found to be influential variables on work instability scores.

Conclusion. The results of this study demonstrated that fatigue and depressive symptoms had negative effect on work instability beside pain, disease activity, and functionality in patients with AS. The recognition and improvement of fatigue and depression may lead to reduced risk of job loss in these patients.