SPARTAN
Spondyloarthritis Research and Treatment Network

SPARTAN NEWS

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JOURNAL CLUB: Critical Review Of The Literature

2019 ACR abstract: "High Dimensional Flowcytometric Profiling Distinguishes Psoriasis and Psoriatic Arthritis"

Mulder M, van den Reek J, de Jong, E, van Cranenbroek B, Smeets R, Joosten R, He X, van den Hoogen F, Koenen H, Wenink M

Early detection of PsA is important for minimizing the negative impacts of psoriatic arthritis (PsA) on quality of life, function, and joint structure. Research for identifying patients at high risk for early PsA has largely focused on phenotypic and genetic predictors of PsA in psoriasis patients. This study explored a novel approach of using immunoprofiles in psoriasis patients to differentiate between people with and without psoriatic arthritis. With high dimensional flow cytometry, approximately 150 immune cell populations were analyzed from the peripheral blood of 25 patients with psoriasis only (PsO) and 33 patients with PsA. Investigators identified distinct patterns of immune cell populations in PsA vs. PsO patients using principal component analysis (PCA). Distinct patterns between PsO and PsA patients were appreciated with both semi-unsupervised analysis (humans marked the clusters of data points on the PCA plots for the PsO and PsA groups) and with unsupervised computational flow cytometry (computers identified the PsA and PsO data point clusters). Distinctions between PsO and PsA patterns were independent of demographics, PASI score, and treatment. While this study introduces a promising tool for PsA detection, additional work is required to validate the findings, explore the variability of immunoprofiles across time and

disease states, and determine the feasibility of immunoprofiling for PsA detection.

- Jessica Walsh, MD

2019 ACR abstract: MRI of the Sacroiliac Joints in Athletes: Do Semiaxial Slices Added to Standard Semicoronal Scans Facilitate Recognition of Non-specific Bone Marrow Edema?"

Weber U, JurikA, Zejden A, Larsen E, Jorgensen S, Rufibach K, Schioldan C, Schmidt-Olsen S

In a previous publication, Weber U et al. (Arthritis Rheum 2018;70:736) found with semicoronal MRI imaging that 30-41% of athletes had an average of 5-6 SIJ quadrants affected by BME, meeting the ASAS definition for active sacroiliitis without SIJ erosions. They theorized that BMD in young healthy active adults to be from mechanical stress and anatomical variations, suggesting SIJ erosions to have high specificity for recognition of early axial SpA. In a follow up study (ACR 2019 Abstract 0856 and Weber.et.al. Rheumatology, 10.1093/rheumatology/kez458,10/19) semi-axial SIJ MRI scans were combined with semi-coronal SIJ MRI scans in 20 recreational runners (12 women and 8 men) before/after running and 22 elite ice-hockey players to ascertain if adding semi-axial SIJ scans would facilitate recognition of non- specific BME. The MRIs were evaluated by 3 blinded readers (2 radiologists and a skilled rheumatologist) for BME and its association with 4 constitutional SIJ features: vascular partial volume effect, deep iliac ligament insertion, fluid-filled bone cyst, and lumbosacral transitional anomaly. ICC agreement among 3 readers for semi-axial SIJ BME was 0.86 (0.72-0.95). Perpendicular semi-axial and semi-coronal MRI scans confirmed SIJ BME in both cohorts consistently in 25% and 27% of athletes, preferentially in the anterior upper sacrum and posterior lower ilium. BME associated with 4 constitutional SIJ features was observed in 20-36% of athletes, clustering in the posterior lower ilium, the same region early sacroiliitis occurs in developing SpA in prior reports.
Regarding the issue of the specificity and hence utility of the ASAS definitions of BME used for clinical care (particularly the diagnosis of axSpA), the proportion of ASAS-positive sacroiliitis recorded on the semi-coronal plane alone decreased by 30-50% upon amending semi-axial scans from 30-35% to 20% in runners and from 41% to 18% in ice-hockey players. The proportion of false-positive ASAS assignments of sacroiliitis recorded on the semi-coronal plane alone was substantially reduced by combining semi-axial scans with semi-coronal MRI imaging of the SIJ.

However, according the Ulrich Weber, the main message is that roughly one-third of so called "BME" lesions in athletes visible as an intraosseous signal increase on semi-coronal orientation could later be uncovered as a vascular partial volume artifact caused by a venous plexus on the perpendicular semiaxial slices which showed no intraosseous signal change. Ulrich Weber feels, and he states in his publication, that "physically active healthy young subjects and in particular elite athletes in physically demanding sports may represent a model to refine the intersection between normal variation on SIJ MRI and incipient axial inflammation in SpA."The very revealing histologic slide he showed at his presentation where the deep iliac ligament insertion on pathology examination of a normal pelvis is associated with a rich vascular supply can be telling us something about the pathogenesis of sacroiliitis. After all, the pelvis is a very complicated structure with enormous forces acting in multiple directions related to movement of the upper and lower body segments during normal human activity (and presumed increased in athletes as well). All of this suggests that site specific inflammation can induce erosions which appear in response to mechanical stress. Maybe having HLA-B27 or some other gene makes this worse or perpetuates transient inflammation into bona fide axSpA. Who knows?

- Elizabeth Chang, MD

2019 ACR abstract: "What is Axial Spondyloarthritis? A Latent Class Analysis and Transition Analysis in the SPACE and DESIR Cohorts"

Sepriano A, Ramiro S, van der Heijde D, Hoonhour P, Molto A, Saraux A, Dougados M, Landewe R.

Because of the problem of circularity in the development of ASAS classification criteria (for example, circularity may have been present because the 'gold standard' was expert opinion yet the experts may have had a bias in placing "weights" on the importance of certain items), therefore the experts may have been simply validating their own biases. The example provided by the authors is that a clinician's view of the importance of MRI in early diagnosis may have been given greater prominence as a criterion when later validating it in a so-called independent validation exercise. The sophisticated technique called latent class analysis (LCA) does not need selection from experts as to item importance; therefore assumptions of the importance of each item or the combination of any set of Spondyloarthritis (SpA) features are absent.
Latent class analysis is a statistical attempt to discover the presence of latent classes, in this case a pattern of associations of signs and symptoms with the end result having the data be ultimately classified according to the maximum

likelihood of being in a specific class. It is a method by which patients (or research subjects) can be classified into mutually exclusive and exhaustive types based on their answers to categorical variables.

Two independent cohorts of patients, one with early onset of chronic back pain (called the SPACE cohort) and the other with inflammatory back pain (called the DESIR cohort) were studied. The LCA was used to estimate the latent (or "unobserved") 'Gestalt' of axSpA by modeling the covariance of the observed axSpA features without any 'a priori' assumptions of their weights or importance. The investigators then selected the best LCA model that splits axSpA into a number of exclusive yet clinically meaningful classes, and then label and name them according to the most prominent features. These classes were then used as a reference standard against which various ASAS classification criteria were tested. In addition, 5-year data was available from one of the cohorts to perform a latent transition analysis to determine if subjects changed classes over time.

The LCA recognized clearly that there is a syndrome that contained a high likelihood of axial imaging abnormalities, HLA-B27 positivity, and male predominance. This corresponds to the conventional rheumatologist belief in a standard clinical picture of axSpA. There was no difference observed between radiographic and non-radiographic axSpA. This is, of course, consistent with multiple other observations that radiographic axSpA and non-radiographic axSpA distinctions are artificial (potentially serving only a regulatory purpose) and that axSpA is one disease entity. In addition, the LCA recognized a separate entity with inflammatory back pain (IBP) associated with peripheral signs and symptoms; these patients were mostly female, HLA-B27 negative, and not likely to have positive imaging results. These patients do not fulfill the ASAS axSpA criteria, either the clinical arm (they lack HLA-B27) or the imaging arm (lack either a positive x-ray or MRI). They fulfill the peripheral SpA criteria; they had inflammatory back pain but did not have B-27 or imaging positivity. These results argue in favor of a broad spectrum of axSpA as identified by LCA.

A third phenotype was recognized with only risk factors for axSpA - patients with IBP and positive family history and positive B-27 - considered at best a grey zone because IBP has high sensitivity but very low specificity. This group is less likely to progress to real axSpA and should not be diagnosed as such.

In summary, there are three groups recognized by LCA - those with classical pure axSpA, axSpA with peripheral signs, and those at risk who will likely not ever get it. Finally, the follow-up study suggested strongly that patients keep their class over 5 years and transitions are very uncommon. The authors feel that the 'Gestalt' of axial SpA consists of these three fairly distinguishable groups - axial SpA, axial SpA with peripheral signs, and axial SpA at risk. They suggest that the axial and peripheral entities are best captured by combining them into one ASAS criteria.

One important finding did come out of this analysis - IBP with peripheral signs and symptoms is part of Spondyloarthritis. These patients, uncovered by LCA, are not often recognized because they have neither imaging nor B-27 positivity. However, these patients have a significant burden of disease (as recognized by the authors) and they do represent the spectrum of the disease called Spondyloarthritis. Finally, the authors caution against using classification criteria for diagnosis since there are subjects out there with chronic back pain, B-27 positivity, and a family history; these "at-risk" patients do not have clinical disease and have a small likelihood of progressing so. In this reviewer's opinion, the study reported herein was a valuable contribution to broadening our understanding of Spondyloarthritis.

- Michael Weisman, MD

CALL FOR ABSTRACTS

SPARTAN invites trainees from US, Canada, and Mexico to submit abstracts for presentation at our 2020 Annual Meeting in Madison, Wisconsin. The meeting will feature a wide range of exciting talks, discussions, and networking opportunities with experts, researchers, and up-and-coming leaders in our field. We welcome abstracts related to spondyloarthritis from any disciplinary background.All abstracts will be evaluated by members of the abstract selection committee. Scientifically sound abstracts with relevance to spondyloarthritis (basic, clinical or translational research) will be accepted for poster presentation. The highest ranked abstracts will be invited for oral presentation.

Information and Submission form

SPARTAN GRANT OPPORTUNITIES

The mission of SPARTAN is to advance research and education to improve the care of patients with spondyloarthritis. We feel strongly that laying the foundation for the next generation of researchers and leaders in SpA is an important portal to achieve this mission. The goal is to support the early stages of a research project to generate preliminary data that will support grant applications to funding agencies such as NIH.

Fellowship Grants for Pilot Projects
With the aim of encouraging fellows to take up research projects under mentors with expertise in SpA, SPARTAN will support up to 2 pilot projects. Applicants need to be a fellow in the 2020-21 academic year. A maximum of $10,000 will be allocated per project per year. The application deadline is April 12, 2020 12:00 noon EST. Read more >> here

Seed Grants for Junior Faculty
In line with SPARTAN's mision, this seed fund opportunity will support early career investigators who are working in the field of Axial Spondyloarthritis. Two new grants will be supported (one basic/translational project and one clinical project). A maximum of $10,000 will be allocated per project per year. The application deadline is March 31, 2020 12:00 noon EST. Read more >> here

UPCOMING SPONDYLOARTHRITIS EVENTS

SPARTAN Board Meeting
January 16
Houston

Annual ASAS Workshop
January 17-18
Houston

2020 SPARTAN-GRAPPA Symposium
February 2
Los Angeles
information and registration >> **here**

April 4
Cleveland

April 18
Chicago
information and registration >> **here**

October 21
Baltimore

SPARTAN Trainee Symposium
May 14, 2020
Madison

SPARTAN Annual Meeting
May 15-16
Madison

Registration open!

EULAR
June 3-6
Frankfurt

GRAPPA Annual Meeting
July 9-11
Brooklyn, New York

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