OMERACT Magnetic Resonance Imaging Initiative on Structural and Inflammatory Lesions in Ankylosing Spondylitis — Report of a Special Interest Group at OMERACT 10 on Sacroiliac Joint and Spine Lesions

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ABSTRACT. The ASAS/OMERACT MRI group recently described and defined magnetic resonance imaging (MRI) findings in sacroiliac joints (SIJ) that are essential for the diagnosis of sacroiliitis in patients with axial spondyloarthritis, including ankylosing spondylitis (AS). At the Outcome Measures in Rheumatology Clinical Trials (OMERACT) 2010 meeting, a special interest group (SIG) was formed to design a research agenda for the definition and description of structural lesions in the SIJ and the spine in patients with established AS. During the SIG, a summary of the previous work of the group was presented to all participants, containing: (1) a description of the current definitions of structural SIJ changes; (2) available scoring methods for SIJ changes; (3) data from a previous pilot MRI exercise on chronic SIJ changes performed by members of the group; and (4) a proposal for a research agenda for OMERACT 11. The group agreed on the project's scientific merits and the need to evaluate all available scoring methods and to have clear definitions for all possible abnormalities that can be seen on MRI, prior to the start of the exercise. It was also agreed that the exercise should include scoring of both structural and inflammatory lesions, due to lack of agreement about the best scoring method for assessing both types of lesions in AS. Participants agreed that longitudinal MRI over a certain period are needed to learn about the time sequence of pathologic changes and to understand the course of the disease. Finally, participants asked the group to add the development of a scoring method for structural changes in the spine in a subsequent exercise. Further to these objectives, all experts who agreed to contribute in the exercise will collaborate to achieve consensus on definitions and to organize training in the different scoring systems prior to the start of the project, with the aim to finalize the multiple reader exercise by the end of 2011, in time for OMERACT 11. (J Rheumatol 2011;38:2051–4; doi:10.3899/jrheum.110423)

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Ankylosing spondylitis (AS) is the prototype of the group of the spondyloarthritides (SpA). The disease affects mostly young male patients and is usually characterized by involvement of the sacroiliac joints (SIJ) initially, spreading later to the spine in the majority of patients[1,2]. To date, classification of patients with AS has been based on the modified New York criteria[3]. These criteria require the presence of an advanced stage of chronic SIJ changes, which can be based on findings of conventional radiographs. However, clinical symptoms in AS may already be present about a decade earlier than definite signs of radiographic involvement[4]. Thus, use of the modified New York criteria may lead to a significant delay when diagnosing patients with AS. In spite of these drawbacks, the modified New York criteria have been used for decades for identification, diagnosis, and treatment decisions in patients presenting with clinical symptoms of AS.

Very recently, the Assessments in AS (ASAS) international society has developed new criteria for axial and peripheral SpA[5]. These criteria are based on new imaging modalities such as magnetic resonance imaging (MRI) for detection of sacroiliitis, since new studies have shown that MRI is able to reliably depict both inflammatory and structural changes in patients with AS[6,7].

Further, MRI has been shown to be reliable in documenting improvement of inflammatory disease activity in patients treated with clinically effective treatment modalities such as tumor necrosis factor-α (TNF-α) blockers[8,9,10]. In addition, MRI was found to be the only imaging technique that has a prognostic value for treatment efficacy in patients with AS[11].

There is need for appropriate measurement tools (scoring systems) for quantification and documentation of MRI lesions (regarding both activity and structural lesions) in patients with

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spondyloarthritis (SpA) in general and AS in particular. This was the starting point to establish a research group under the umbrella of ASAS and Outcome Measures in Rheumatology Clinical Trials (OMERACT), consisting of experts in the field of imaging and treatment of AS.

In a first step, which was initiated at OMERACT 6 (2002, Australia), it was agreed that the research activities of the group should focus on inflammatory lesions, since only short-term studies with TNF-blocker therapy including MRI were available at that time. At OMERACT 7 (2004, USA), the group met again and it was agreed to start a reading exercise in order to set definitions on the inflammatory changes of the SIJ in MRI of patients with established AS. The results of this exercise have been published[12] and served as a basis for identification of a "positive" MRI when dealing with the new ASAS classification criteria for SpA[5]. At OMERACT 8 (2006, Malta), the initiative for a similar exercise for the spine was started. The focus was the analysis of all available scoring methods for the measurement and quantification of spinal inflammatory lesions. The final report was recently published[13]. In parallel, the group has worked on the definition of spinal structural lesions in AS — these data were presented at the European League Against Rheumatism 2010 meeting in Rome[14] and have been submitted as a full paper.

At OMERACT 10 (2010, Malaysia), the group initiated a special interest group (SIG) with the aim of developing definitions for the different structural changes seen in the SIJ of patients with AS. In addition, agreement was sought on the differentiation of AS-related changes from pathologic changes seen in other diseases; and finally, on the choice of one of the available scoring systems for quantification of inflammatory and structural lesions in patients with AS, as depicted by MRI. During the SIG it was proposed to also continue with scoring of structural changes of the spine.

PROCEEDINGS DURING THE SIG

Presentation of Data

Background information and technical considerations. The meeting of the SIG included a short presentation, starting with emphasizing the complicated anatomy of the SIJ and reviewing the anatomy and structures (cartilaginous, ligamentous) of the joint. It was shown that, in order to assess the entire SIJ and both its structural components, semiaxial slices parallel to the upper vertebral plate of S1 and semicoronal slices perpendicular to the semiaxial slices should be used[15].

Since the aim of the SIG was the assessment of AS-related structural changes on MRI, the most recent data on this topic were presented. According to a recent publication[16], MRI has great diagnostic utility in SpA and can be used to differentiate patients with SpA from patients with nonspecific back pain and from healthy subjects. In another publication from a retrospective study[17], it was suggested that structural changes such as erosions (in combination with elevated C-reactive protein) or subcortical cysts in the MRI of the SIJ might be more characteristic and helpful than presence of bone marrow edema, in differentiating patients with AS or SpA from other diseases. Finally, a very recent publication was presented, showing that structural and inflammatory lesions on MRI of the SIJ were predictive of further structural deterioration in the long term[18].

Definitions of AS-related structural changes in the SIJ. In January 2007, the ASAS/OMERACT MRI group met in Toronto, Canada, for a first discussion of the definitions for changes in the SIJ. With respect to the technical aspects of performing MRI of the SIJ in SpA, it was decided that T1 MRI sequences are sufficient to detect structural changes, such as sclerosis, fat deposition, and ankylosis, while T1 fat-suppressed or T2 gradient-echo sequences might be more appropriate to detect erosions. During the SIG, a description of all definitions recorded at the Toronto meeting was presented; they will be a topic of discussion in future projects prior to the planned scoring exercise.

Available scoring methods for SIJ lesions in AS. In a next step, all available scoring methods for the SIJ in MRI of AS patients were presented during the SIG meeting. Four scoring methods were presented, 2 of which are unpublished and another 2 published recently[16,18]. Of those scoring systems, one evaluates both active and structural changes, while the other 3 describe structural changes only. All scoring methods evaluate each SIJ separately.

The first scoring system (unpublished) divides each SIJ into 4 quadrants. Two quadrants (upper and lower) are in the iliac portion and 2 quadrants (upper and lower) are in the sacral portion of the SIJ. Each quadrant can be scored between 0 and 4, according to extent of deterioration.

The second scoring method (unpublished) is similar to the first but assesses SIJ changes in more detail. Again, each single SIJ is evaluated and divided into 4 quadrants. However, each possible structural change (erosion, sclerosis, fat accumulation, entheseal mineralization) is assigned a separate score from 0 to 3.

The third scoring method was published recently from the Denmark group[18]. It also assesses SIJ in quadrants and scores for different MRI changes on a scale from 0 to 3. For fat deposition, the extent and depth are scored separately, while bone erosion and ankylosis are scored only in the cartilaginous portion of the joint (thus, in only 2 of the 4 quadrants).

The fourth scoring method, proposed by the Canadian/Swiss/Danish group, was also published recently[16]. It evaluates both structural (erosions) and/or inflammatory (bone marrow edema) changes, and assesses changes according to the ASAS definition of a positive MRI.

A fifth scoring system (published by the Leeds group[19]) was not presented during the SIG, but was considered thereafter as an additional scoring system to be included in the scoring exercise, since it also evaluates both structural and inflammatory lesions of the SIJ.

Conclusions from a preliminary exercise. In a final step, the data from a previous preliminary exercise of the group were presented, where overall 8 readers scored 16 sets of SIJ MRI from patients treated with anti-TNF agent (n = 7) or placebo (n = 9) by using the first 2 scoring methods described above. Briefly, intraclass correlation coefficients (ICC) for between-reader variation were regarded as acceptable for the general scoring method for erosions and for fat accumulation, but not for sclerosis and entheseal mineralization. There were insufficient data to test for sensitivity to change and discrimination between different treatments.

Conclusions of the presented data. The presentation concluded that, based on the present preliminary definitions data there is a need for a systematically performed scoring exercise for assessment of the structural and inflammatory changes by a broad range of experts in the field. This should be done after consensus of the group is reached about which lesions are AS-specific and add important information about the disease. It should also be based on the ability of the scoring systems to identify those lesions, and reliably differentiate between treatment regimes (e.g., anti-TNF vs placebo) if possible. The analyses of the results will be performed according to the OMERACT filter.

Discussion with participants. After the presentation of the data, participants agreed that this was a useful and important project with important scientific and clinical implications, and that the group should continue its efforts on this topic, as well as on assessing structural changes of the spine. It was suggested that, as a first step, definitions of all possible pathologic signs seen on MRI should be clarified and all readers should be made aware of these definitions.

After presentation of the structural lesions, participants agreed that no data were available yet to answer the question of whether inflammation or fatty degeneration occurs first in the course of the disease. However, this would be an interesting question to answer during this exercise. There was also consensus that all available scoring methods should be included in the scoring exercise, including scoring methods for inflammatory lesions, since agreement is lacking on the best scoring method for assessment of both types of lesions in AS. A meeting prior to the start of the exercise should also be held to provide training and discuss each scoring method.

For the entire exercise, a multireader comparison of at least 5 readers should be planned and an appropriate MRI study set of at least 30 patients with active (anti-TNF) treatment versus placebo, and at least 2 timepoints should be provided to the readers. Every reader should read the entire set of patients with every method. Finally, the participants of the SIG agreed that longterm MRI followup studies (more than 2 years) would be the best setting for such an exercise, since structural changes, which are the main outcome, require longer time periods to occur. Thus, at least 2 timepoints of followup should be presented to the readers, but additional assessment timepoints could also be of value to evaluate the course of structural changes over time. The interreader reliability, sensitivity to change, and discrimination between anti-TNF and placebo, as well as the feasibility of the scoring methods for capturing information (time to score each image, etc.) would then be provided as part of the results of the exercise and would be analyzed based on the OMERACT filter.

It was decided that a similar methodology be applied to further investigate the assessment of structural changes of the spine.

CONCLUSION

Experts in the field of imaging and treatment of AS will participate in a scoring exercise project for identification of the best scoring method for assessment of inflammatory and structural changes in the SIJ and the spine of patients with AS, as assessed by MRI. The available scoring methods will be tested against the OMERACT filter. Prior to that, all possible changes for AS will be defined by consensus of the participants of the group. Ideally, the study set will include at least 30 patients with longterm followup and at least 2 timepoints for each image set. Results of this exercise will be presented at the OMERACT 11 meeting and the data published as the ASAS and OMERACT contribution in the field of outcome measures in rheumatology.

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