Follow-up and prognostic value using magnetic resonance imaging in patients with spondyloarthritis treated with biologic agents

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ABSTRACT

Early diagnosis and assessment of the response to treatment in patients suffering from spondyloarthritis have always been challenging due to the lack of imaging techniques able to demonstrate spinal and sacroiliac inflammation.

The last 2 years have seen important advances in the use of magnetic resonance imaging (MRI) for the study of spondyloarthritis. The possibility of quantification of inflammatory lesions using different scoring systems allows not only an early diagnosis, but the assessment of the response to several therapeutic agents, especially those known as “biological therapies.”

A number of randomized controlled trials of anti-tumor necrosis factor agents have been published showing regression of inflammatory lesions in MRI. This review discusses briefly the techniques and scoring systems used and all the evidences that exist about assessing treatment in spondyloarthritis.

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Monitorización y valor pronóstico por resonancia magnética de los tratamientos biológicos en las espondiloartritis

RESUMEN

El diagnóstico precoz y la respuesta al tratamiento en los pacientes con espondiloartritis han supuesto, desde siempre, un reto dada la escasez de técnicas de imagen que demostrasen, de manera cuantitativa, la inflamación en columna y articulaciones sacroiliaicas.

Durante los últimos 2 años se han llevado a cabo importantes avances en el uso de la resonancia magnética (RM) para el estudio de las espondiloartritis. La posibilidad de cuantificar la inflamación que ocurre en estos pacientes mediante la utilización de diferentes sistemas de puntuación permite no sólo llevar a cabo el diagnóstico de forma precoz, sino además valorar la respuesta de los pacientes con espondiloartritis a diferentes agentes terapéuticos, en especial a las nuevas terapias biológicas.

Se han publicado varios ensayos controlados con dichos fármacos que muestran la disminución de las lesiones inflamatorias en RM. Esta revisión se centra, brevemente, en las técnicas y los sistemas de puntuación de RM utilizados, así como en los datos aportados por dichos estudios, que valoran la respuesta al tratamiento con terapias biológicas mediante las imágenes de RM.

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Introduction

In the past few years, early diagnosis and evaluation of response to treatment in spondyloarthritis has been undergoing very important changes due to the introduction of magnetic resonance (MR) as an imaging technique in these patients.

Osteomuscular affection in spondyloarthritis can be of 2 types: produced by inflammatory changes and structural changes that follow the former.

Traditionally, in order to diagnose and classify patients with suspected spondyloarthritis, sacroiliac and spinal column x-rays have been the first choice. These x-rays allow for the clear detection of structural changes while, in order to detect active inflammation, MR is becoming the technique of choice, after having demonstrated that it can show inflammatory changes at an early stage.
The use of MR has meant an incredible improvement in the evaluation of patients with spondyloarthritis, given its capacity to perform an early diagnosis at an early stage and the possibility it offers of detecting active inflammation (something that cannot be detected in a trustworthy manner using clinical or laboratory data). In addition, it allows for the measurement of spinal inflammation, making MR an ever more present tool used in the design of clinical trials of new therapeutic agents. This review centers on the role that MR can have in the evaluation of response to treatment through biologic therapy in patients with spondyloarthritis.

**Technique**

Sacroiliac joints are usually studied in MR using a semicoronal plane, oriented through the long axis of the sacral bone. This allows for the visualization of the cartilage component of the joint, which presents a convex form with its apex oriented antero-inferiorly. Occasionally, the sacroiliac joints can be studied in the axial plane, oriented in a perpendicular manner to the transaxial sections described above, allowing to study ligament structures of the postero-superior portion of the joint.

The spine is generally studied in a sagittal plane, and can be divided into 2 segments: one, superior, including the cervical spine and the dorsal vertebrae, (generally C1-T10) and the inferior one, which includes the last dorsal vertebrae and the lumbar vertebrae (T10-S2).

Currently there are 4 types of sequences for the study of patients with spondyloarthritis. A T1 potentiated sequence (used to evaluate structural changes and obtain images that serve as an anatomical guide), a T2 FSE sequence with fat suppression, a STIR (short tau inversion recovery) sequence or a T1 sequence with fat suppression and the administration of paramagnetic contrast. These last three are the ones that will demonstrate inflammatory changes, either by manifesting bone marrow edema (T2 and STIR) or by showing an increase in vascularity that occurs in areas with inflammation.

Inflammatory findings appear in the form of hyper intense lesions in the T2 and STIR with paramagnetic contrast (Figure 1). The sacroiliac joint affection can be unilateral at the beginning (predominantly on the iliac side of the joint), and then become bilateral and affect the sacral sector.

Signs on the spine are usually located in the cervico-thoracic and thoraco-lumbar transition zones, and affect the vertebral body as well as posterior vertebral elements and even the intervertebral disc.

**Scoring system**

The development of different systems that, through the use of MR, allow for the quantification of inflammation has been an interesting advance in the study of patients with spondyloarthritis. Thanks to them it is possible to evaluate change in inflammatory activity produced after the administration of determined therapeutic agents.

Currently, there are several systems which have been described for sacroiliac joints, both to evaluate the activity of sacroiliitis as for determining the structural abnormalities found.

There are six methods recognized by OMERACT for the evaluation of inflammatory sacroiliac lesions: MISS, Leeds, Aarhus, SPARCC systems, and two initiatives proposed by Sieper-Rudwaleit and Hermann-Bollow. Only the system developed in Aarhus has been published in a complete form, while MISS and SPARCC have appeared in abstract form. The rest remain unpublished. Of all of them, some use contrast (gadolinium) sequences, while other only use STIR sequences. Scores vary from a general form for the whole joint to a detailed joint quadrant score using several scans. Changes in scores through time and the capacity for discrimination of the scoring methods among patients have almost never been investigated. Intra-observer agreement was shown to be good or excellent, while between observers it was poor to moderate except in the case of the SPARCC system in which it was very good. In general, all of the observations were based on a limited number of images and readers and were obtained only in centers in which the systems were developed.

To evaluate the activity of the inflammatory process in the spine, 4 methods have been proposed so far: SPARCC, Leeds, Berlin and ASSpiMRI-a (Table). Of those, only ASSpiMRI-a uses gadolinium in a standardized form. The Berlin method is based on the ASSpiMRI-a, modified through the elimination of the use of gadolinium and not including erosions as part of the final score of each vertebral unit. These two methods score all of the vertebrae from C2 to S1, while the Leeds system includes only lumbar vertebrae and the SPARCC, only the 6 worse affected discovevertebral units. Only the SPARCC and ASSpiMRI-a systems provide data regarding their effectiveness. For both methods, intra and interobserver agreement was good to excellent.

In general, there is little information on reproducibility, effectiveness and sensitivity to change of all of these scoring methods (both in the sacroiliac joints as in the spine). The methods that evaluate inflammatory change seem to be more useful than those that evaluate structural change, and the capacity of MR to detect the latter has even been recently called into question.

**Evaluation of response to treatment**

Without a doubt, the introduction of what is now referred to as “biologic therapy” in the past years, with drugs that specifically inhibit cytokine pathways (for example, Tumor Necrosis Factor alpha [TNFα] antagonists) has extraordinarily modified the therapeutic management of the spondyloarthritides. There are three active antagonists of TNFα on whom studies have been performed: adalimumab, etanercept, and infliximab, with abundant evidence supporting the effectiveness of these agents in improving signs and symptoms of ankylosing spondylitis. In addition, recent data indicates that these drugs can also have disease modifying activity from a structural standpoint as well.

Infliximab has demonstrated to be clinically effective for ankylosing spondylitis. Baraliakos et al evaluated the radiological progression in the cervical and lumbar spine in patients with ankylosing spondylitis treated with both infliximab as well as conventional therapy. 41 patients from the first clinical randomized trial on the use of...
Table
Technical characteristics of the scoring systems evaluating spinal activity

<table>
<thead>
<tr>
<th>Method</th>
<th>Sequences</th>
<th>Plane</th>
<th>Thickness</th>
<th>Score by</th>
<th>Segments</th>
<th>Degrees</th>
<th>Interval</th>
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<tbody>
<tr>
<td>SPARC (Sieper)</td>
<td>T1 SE.</td>
<td>Sagital</td>
<td>3-4 mm</td>
<td>Discovertebral unit divided into 4 quadrants</td>
<td>6 units that show more significant alterations in STIR.</td>
<td>12 due to the presence of edema in a discovertebral unit; extra points for intensity and depth</td>
<td>0-108</td>
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<tr>
<td></td>
<td>T2 SPIR</td>
<td></td>
<td>(12 cuts in total)</td>
<td></td>
<td>Evaluate three consecutive scans for each lesion 5 lumbar vertebrae</td>
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<td>Bone marrow edema</td>
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<td>Number of lesions</td>
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<tr>
<td>Leeds</td>
<td>T2 SPIR</td>
<td>Sagital</td>
<td></td>
<td>Vertebral body spinous process, interapophiseal joints paraspinal soft tissue</td>
<td>23 vertebral units (C2-C3-L5/S1)</td>
<td></td>
<td>0-69</td>
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<td>Bone marrow edema (0-3)</td>
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<tr>
<td>Berlin (Sieper)</td>
<td>STIR</td>
<td>Sagital</td>
<td></td>
<td>Vertebral unit</td>
<td>23 vertebral units (C2-S1)</td>
<td></td>
<td>(0-6)</td>
</tr>
<tr>
<td>ASSpiMRI-a</td>
<td>STIR T1</td>
<td>Sagital</td>
<td></td>
<td></td>
<td>Bone marrow edema</td>
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<td></td>
<td>gadolinium</td>
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of the patients showed improvement in the ASSpiMRI-a scores and the inflammatory images in the sacroiliac joints (Figure 2).

Prognosis

As has been stated up to this point, MR has shown to be particularly useful for demonstrating the presence of early spondyloarthritides and can predict the development of radiological changes and significant sacroiliitis with 2-3 years of anticipation with respect to x-rays. This indicates that MR could be employed for early diagnosis, before developing radiographic changes and could possibly be included in future classification criteria for spondyloarthritis. However, the cost/effectiveness relationship of this technique has not been yet evaluated in this context.

There is very little data that shows a correlation between the inflammatory changes in the MR and the clinical and laboratory data that have been classically used to evaluate the prognosis of spondyloarthritis. The occasional presence, in small quantities, of residual inflammation in the images taken after treatment, as well as the little agreement seen between clinical activity and MR inflammation and the absence of long-term studies that evaluate the progression of the inflammatory lesions and their transformation into structural lesions ankylosis forces us to be prudent and wait for further information to be able to include MR as a method of prognostic value in spondyloarthritis.

Conclusions

MR is a very important advance in the diagnosis of spondyloarthritis. Currently, its larger use lies in its capacity to perform an early diagnosis that saves years in the diagnosis of spondyloarthritis. The capacity of MR for quantifying inflammation is of great help when evaluating response to treatment with biologic therapy; however, it is necessary to perform long-term studies to demonstrate the cost/efficacy relationship of this technique.

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