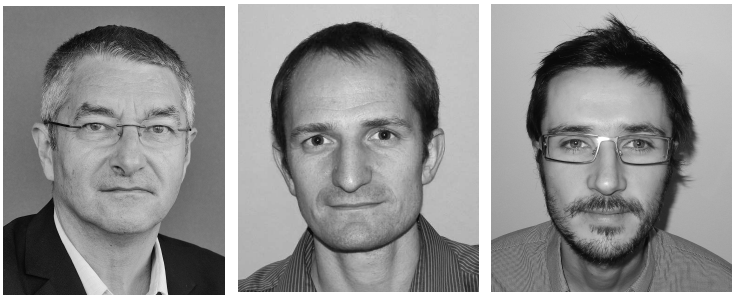
Editorial

Spondyloarthritis. Clinical Versus Imaging Assessment: And the Winner Is?



Spondyloarthritis (SpA) is a condition in which imaging plays an important part. Imaging findings are included in classification criteria, often for diagnostic purposes. Inclusion of a magnetic resonance imaging (MRI) definition of sacroiliitis has made it possible to individualize/recognize nonradiographic axial SpA[1]. But conventional MRI has not resolved all the problems in SpA, such as the possibility of overdiagnosis and low performance as an outcome measure or therapeutic evaluation tool[2]. Under these circumstances, new imaging tools may represent an advance in disease assessment, particularly for locations that are difficult to access using conventional imaging or (sometimes) during clinical examination. This may be the case for enthesitis, the hallmark of spondyloarthritis; imaging provides objective proof of inflammatory involvement, and allows the differential diagnosis with other painful disorders of the entheses, such as fibromyalgia[3,4].

In this issue of *The Journal*, Althoff, *et al*[5] compared whole-body MRI (wbMRI) imaging versus clinical examination of enthesitis in patients with early axial SpA (disease duration < 5 yrs) during 3 years of continuous anti-tumor necrosis factor (TNF) therapy. This design is interesting because it may give an idea of the performance of clinical and wbMRI enthesitis assessment in early disease (with potential diagnostic and prognostic implications) and during longterm anti-TNF therapy (and this may allow evaluation of the utility in assessment of therapeutic response). The first lesson of this study is the high frequency of enthesitis at baseline, detected by clinical examination (more than 50%), mainly located in the pelvis as expected, but also at the anterior chest wall (ACW; in 25% of patients). This is in accordance with previous studies. In the DESIR cohort of patients with recent inflammatory back pain suggestive of axial SpA, the prevalence of ACW pain was 44%[6], and was associated with enthesitis score and radiographic abnormalities of sacroiliac joints.

The second lesson is the relatively low performance of wbMRI for detection of enthesitis: MRI is supposed to be sensitive for detecting early inflammation; however, this technique detected enthesitis at baseline in 21% of patients, one-half of that detected clinically. This raises the question of a gold standard for enthesitis assessment. Clinical evaluation is investigator-dependent, with pain (yes/no) on pressure of the entheses. At the ACW, low correlations between clinical and imaging findings were also noted. Weber, *et al*[7] evaluated ACW involvement with wbMRI in 122 consecutive patients with SpA [95 with ankylosing spondylitis (AS) and 27 with nonradiographic SpA (nrSpA)] and 75 healthy controls. Among patients with SpA, 26% had clinical involvement of the ACW. ACW inflammation was found by wbMRI more frequently in patients with AS (49.5%) versus nrSpA (25.9%) and controls (9.3%). There was no association between clinical assessments of ACW, including the Maastricht Ankylosing Spondylitis Enthesitis Score, and MRI features. In the present study[5], a significant association of clinical and wbMRI was found at baseline for ACW and pelvis. Clinical and ultrasound evaluation of ACW was performed in 131 patients with established SpA and 49 control subjects[8]. Clinical and US involvement of ACW were found in, respectively, 39% and 35.5% of SpA and in 12% and 14.3% of controls; no association was found between clinical and US involvement. In the axial structures in early disease (DESIR cohort), even if the site of pain [thoracic spine, lumbar spine, or buttock(s)] was associated with MRI inflammation at the same site in patients with recent inflammatory back pain, there was no overlap between clinical and MRI location: Of the 648 patients, 61% had thoracic pain, 91.6% lumbar pain, and 79.2% buttock pain; and MRI inflammation was present in 19%, 21%, and 46% of patients at the thoracic, lumbar, and sacroiliac sites, respectively[9].

The third lesson is the reduction in the percentage of

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patients with enthesitis under continuous anti-TNF treatment, assessed either clinically or by wbMRI. This result confirms the potential efficacy of TNF blockade on enthesitis, so enthesitis may be a valuable outcome measure in some patients. Comparing clinical and wbMRI findings in the study by Althoff, *et al*[5], showed a reduction in enthesitis; and a slightly better standardized response mean was found for clinical evaluation.

Finally, when comparing clinical and wbMRI results to validated disease activity assessment tools such as the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) and the Ankylosing Spondylitis Disease Activity Score (ASDAS), a correlation was found only between BASDAI and clinical evaluation at year 2 and 3, but no correlation at baseline, or with MRI or with ASDAS–C-reactive protein. Evaluations of enthesitis, whether done clinically or by wbMRI, do not represent a potential proxy for global disease activity or therapeutic response assessment in this population.

The debate between clinical and imaging assessment of enthesitis in SpA remains open. Could wbMRI represent the "all-in-one" solution in this situation? This may be premature, considering the results of the study discussed[5]. The answer may arise from new imaging modalities in musculoskeletal diseases[10]. Besides wbMRI discussed here, other MRI techniques may bring accurate information. High-resolution MRI may provide more sensitive detection of bone erosions of the sacroiliac joints, whereas diffusion-weighted MRI could allow earlier detection of bone inflammation. Focusing on entheses, a key involvement for clinical and pathogenic understanding[11], ultrasound is currently used as a valid and reliable tool for assessing entheseal involvement in SpA[12]; novel modalities such as contrast-enhanced ultrasound or sonoelastography may bring additional information[10]. There are great expectations for positron emission tomography combined with computerized tomography[10] or MRI[13], and using several tracers: fluorodeoxyglucose for inflammation[14], and fluoride for osteoblastic activity[15]. But all these need to be evaluated in terms of sensitivity, specificity, as diagnostic tools, of sensitivity to change for disease activity and therapeutic response assessment, and compared to clinical data and classical instruments. Such an approach is indispensable to advancing and defining the optimal use of new imaging techniques. From this perspective, studies based on therapeutic evaluation are worthwhile, and papers such as the one from Althoff and colleagues[5] contribute to this process, taking into account feasibility and accessibility of these techniques in current practice.

To date there is no winner: Clinical and imaging assessment in spondyloarthritis remain complementary. In the meantime, as studies continue to look for awaited objective results, physicians should order imaging based on a precise question to be answered and only after conscientious clinical examination.

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REFERENCES

1. Wendling D, Prati C, Claudepierre P, Guillot X, Breban M. Non-radiographic spondyloarthritis: a theoretical concept or a real entity? Joint Bone Spine 2012;79:531-3.
2. Wendling D, Claudepierre P, Pham T, Loeuille D, Prati C. MRI in axial spondyloarthritis: From light to shadow? Joint Bone Spine 2015;82:302-4.
3. Salaffi F, De Angelis R, Carotti M, Gutierrez M, Sarzi-Puttini P, Atzeni F. Fibromyalgia in patients with axial spondyloarthritis: epidemiological profile and effect on measures of disease activity. Rheumatol Int 2014;34:1103-10.
4. Almodóvar R, Carmona L, Zarco P, Collantes E, González C, Mulero J, et al. Fibromyalgia in patients with ankylosing spondylitis: prevalence and utility of the measures of activity, function and radiological damage. Clin Exp Rheumatol 2010;28 Suppl 63:S33-9.
5. Althoff C, Sieper J, Song IH, Weiss A, Diekhoff T, Haibel H, et al. Comparison of clinical examination versus whole-body MRI of enthesitis in patients with early axial spondyloarthritis during three years of continuous etanercept treatment. J Rheumatol 2016;43:618-24.
6. Wendling D, Prati C, Demattei C, Loeuille D, Richette P, Dougados M. Anterior chest wall pain in recent inflammatory back pain suggestive of spondyloarthritis. Data from the DESIR cohort. J Rheumatol 2013;40:1148-52.
7. Weber U, Lambert RG, Rufibach K, Maksymowych WP, Hodler J, Zejden A, et al. Anterior chest wall inflammation by whole-body magnetic resonance imaging in patients with spondyloarthritis: lack of association between clinical and imaging findings in a cross-sectional study. Arthritis Res Ther 2012;14:R3.
8. Verhoeven F, Guillot X, Godfrin-Valnet M, Prati C, Wendling D. Ultrasonographic evaluation of the anterior chest wall in spondyloarthritis: a prospective and controlled study. J Rheumatol 2015;42:87-92.
9. Blachier M, Coutanceau B, Dougados M, Saraux A, Bastuji-Garin S, Ferkal S, et al. Does the site of magnetic resonance imaging abnormalities match the site of recent-onset inflammatory back pain? The DESIR cohort. Ann Rheum Dis 2013;72:979-85.
10. Eshed I, Hermann KG. Novel imaging modalities in spondyloarthritis. Curr Opin Rheumatol 2015;27:333-42.
11. Miceli-Richard C. Enthesitis: The clue to the pathogenesis of spondyloarthritis? Joint Bone Spine 2015;82:402-5.
12. Sakellariou G, Iagnocco A, Delle Sedie A, Riente L, Filippucci E, Montecucco C. Ultrasonographic evaluation of entheses in patients with spondyloarthritis: a systematic literature review. Clin Exp Rheumatol 2014;32:969-78.

13. Buchbender C, Ostendorf B, Ruhlmann V, Heusch P, Miese F, Beiderwellen K, et al. Hybrid 18F-labeled fluoride positron emission tomography/magnetic resonance (MR) imaging of the sacroiliac joints and the spine in patients with axial spondyloarthritis: A pilot study exploring the link of MR bone pathologies and increased osteoblastic activity. J Rheumatol 2015;42:1631-7.
14. Yamashita H, Kubota K, Takahashi Y, Minamimoto R, Morooka M, Kaneko H, et al. Similarities and differences in fluorodeoxyglucose positron emission tomography/computed tomography findings in spondyloarthropathy, polymyalgia rheumatica and rheumatoid arthritis. Joint Bone Spine 2013;80:171-7.
15. Darrieutort-Laffite C, Ansquer C, Maugars Y, Le Goff B, Bodere F, Berthelot JM. Sodium (18)F-sodium fluoride PET failed to predict responses to TNF-α antagonist therapy in 31 patients with possible spondyloarthritis not meeting ASAS criteria. Joint Bone Spine 2015;82:411-6.

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