Hip involvement in ankylosing spondylitis

What is the verdict?


In this issue of Rheumatology, van der Cruyssen et al. [1] report data about hip involvement in patients with AS from three registries. Their main results are that involvement of the hip is common in AS patients, and it is associated with impaired functioning. Furthermore, the authors claim to have identified three risk factors for hip replacement surgery in AS, early onset, axial and entheseseal disease manifestations.

The importance of hip involvement in patients with AS has been recognized for several decades as a common and disabling problem [2], whereas involvement of the other root joint, the shoulder, is less frequent and less severe. Histopathologically, hip involvement in AS seems to be largely based on inflammation of the subchondral bone marrow [3]. However, in contrast to the classical changes of AS in the spine, rheumatic inflammation in the hip does not lead to formation of new bones, but results in an erosive disease, which will often destroy the joint [3]. These changes might have already occurred in young patients, and total hip replacement is often the therapy of choice in this difficult clinical situation [4], which leads to dramatic improvements of function in most cases.

Hip involvement is an important prognostic factor associated with radiographic progression. In a French study [5], a severe outcome of SpA was predictable when the hip was involved or if three other (out of many) clinical factors were present at study entry (sensitivity 50%) and mild disease was practically excluded (specificity 98%). In North Africa, the risk of hip involvement was estimated at 40% after a 10-year disease duration [6]. A multivariate analysis identified the risk factors such as diagnostic delay, young age at onset and a combination of lower social class and no refrigerator at home [6].

In a Dutch–Belgian cooperative study [7], male sex, younger age at symptom onset and hip involvement were associated with radiographic changes; but HLA-B27, peripheral arthritis and extra-articular disease status (e.g. uveitis, psoriasis and inflammatory bowel disease) were not. In the same study, patients with older age, higher Bath Ankylosing Disease Activity Index (BASDAI), hip involvement and spinal change contributed to Bath Ankylosing Spondylitis Functional Index (BASFI); whereas, sex, disease duration, peripheral arthritis and extra-articular manifestations did not. Of course, depending on the cohort studied, other prognostic factors identified in AS are cervical and lumbar spine involvement and the presence of syndesmophytes at baseline, which were shown to predict future syndesmophytes in AS [8].

Is hip involvement in AS mainly associated with young age at onset or is it largely a consequence of disease duration and the burden of inflammation over time? Available evidence shows that both observations are correct. Reports of young AS patients with severe involvement of the hips were already published many years ago [2], and recent data from cohorts [9] suggested that patients with juvenile onset not only had higher frequencies of hip involvement but also had a greater need for total hip replacement, as compared with patients with adult-onset AS. However, radiographic damage of the spine seemed to be less severe in the patients with juvenile onset [10]. In other studies, an association of hip involvement with disease duration of AS was reported [11].

The data provided in this study [1] are from two merged European databases, whereas a third one from South America was used as a confirmative dataset. The motivation for the registries was triggered by the successes of anti-TNF therapy, but since all consecutive patients could be included, there may have been no bias towards the inclusion of more severe patients. Involvement of the hip was based on three different definitions: clinical perception, radiological involvement when the Bath Ankylosing Spondylitis Radiology Index (BASRI)-hip score was rated as at least suspicious (score of ≥1) and advanced (need for hip replacement surgery) when surgery had taken place. The use of three different definitions in this study already indicates that this is not an easy issue, and the BASRI has not been designed to serve as a dichotomous cut-off.

Depending on the datasets used, BASRI scores showed that ~30% of the patients had moderate (BASRI-hip Grade 3) and ~15–20% had severe (Grade 4) hip involvement. Hip replacement was reported by 5–8% of the patients, and about half of those had bilateral replacements. Confirming previous data, more patients with juvenile onset AS (age at onset <16 years) reported having undergone surgery. Whether this is, at least in part, due to ascertainment bias (patients are more likely to take part in the registry if they have severe disease) is not known. Furthermore, a patient with longstanding AS who
needs hip replacement may have been registered as having OA, which is indeed possible because there is no evidence that AS patients are protected against degenerative changes.

Radiographic and clinical signs of hip involvement showed significant positive correlation. Patients with hip involvement had generally higher BASFI scores than those without hip involvement. In contrast, no differences were reported between patients with and without hip involvement for disease activity (BASDAI). Patients with hip involvement also had higher radiographic spinal scores and limitations in cervical and lumbar mobility. This finding confirms that osteodestructive and osteoproliferative changes may occur in parallel at different sites in AS—an ongoing challenge for research.

This study should revitalize the discussion on radiographic outcomes in AS, especially in anti-TNF-treated patients, because despite convincing clinical efficacy of TNF blockers confirmed by MRI, radiographic progression was not found to be inhibited or decelerated when compared with historical controls [12]. However, in contrast, an AS patient treated with the anti-TNF-α antibody infliximab was reported to have a positive result on the joint space narrowing of the hip joint [13]. Such data suggest a positive effect of anti-TNF treatment on osteodestructive changes in SpA that is well-known from patients with RA or PsA. Preliminary cohort data suggesting a lower incidence of hip replacements over the past few years, potentially due to the effect of anti-TNF agents, would be in agreement with this hypothesis. There is a clear need for controlled studies which show that TNF inhibitors prevent osteodestructive changes in AS.

The recommendation for daily practice and clinical studies with AS patients is clear: hip involvement should be assessed routinely. International agreement should be made on how best to assess hip involvement, and controlled studies with effective therapies such as the TNF blockers need to be done to prove their effect on structural damage. Of course, waiting for total hip replacement is not an ideal therapeutic strategy for young AS patients. At the moment, however, it is still the main choice. Furthermore, there is an ongoing need for prospective cohort studies with long-term follow-ups to learn more about the course and the prognosis of juvenile and axial SpA (the early forms need, of course, to be included in such studies).

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