Hip involvement in ankylosing spondylitis: epidemiology and risk factors associated with hip replacement surgery

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Abstract

Objectives. Although clinicians recognize hip involvement, which frequently leads to hip replacement surgery, as an important feature of AS, data on the epidemiology, nature of the disease and therapeutic strategies are scarce. We aimed to describe the epidemiology of clinical and radiological hip involvement and define the risk factors for the hip replacement surgery in AS patients.

Methods. Data from 3 datasets were merged, including 847 Belgian (ASPECT database), 1405 Spanish (REGISPONSER database) and 466 Ibero-American (RESPONDIA database) AS patients. The ASPECT and REGISPONSER database (Dataset A) are used for exploratory analysis; the RESPONDIA database (Dataset B) is used for confirmative analysis. Factors associated with hip involvement and the hip replacement surgery were analysed.

Results. Twenty four (REGISPONSER) to 36% (RESPONDIA) of AS patients under rheumatologist’s care presented clinical hip involvement, including the 5% (Dataset A) of AS patients who needed hip replacement surgery. Patients with hip involvement had significantly worse overall Bath Ankylosing Spondylitis Functional Index (BASFI) scores compared with patients without hip involvement (mean difference = 1.6, P < 0.001) (Dataset A, confirmed in B). Corrected for disease duration, patients with early disease onset, enthesial and axial disease needed most frequently hip replacement surgery (Dataset A, confirmed in B).

Conclusion. Hip involvement is commonly recognized by rheumatologists in AS patients, and involves about one out of the three to four patients with AS and is associated with impaired functioning reflected by higher overall BASFI scores. Early onset of disease, axial and enthesial disease are associated with the hip replacement surgery in AS.

Key words: Ankylosing spondylitis, Hip, Hip replacement surgery, Risk factors.

Introduction

AS is the prototype of SpA and is characterized by inflammation of the sacroiliac joints and spine, resulting in changes (narrowing, sclerosis, erosions and ankylosis) which are eventually evaluable on conventional radiographs [1]. This may lead to a completely ankylosed spine in a substantial number of patients. Clinical observations of patients and a number of clinical reports [2–5] indicate that hip involvement increases the burden of the disease and its prognosis. To illustrate the prognostic value of hip disease, it has been reported that...
radiographic spinal progression in AS patients is more prevalent in patients with hip arthritis vs patients without hip involvement [6]. Due to the important and central function of the hip, impairment of hip functioning is clearly related to restricted body function in AS patients [7]. However, it seems that limited data are available regarding the epidemiology, the pathophysiological nature of hip involvement and its effects on function and disease activity.

Data on the effectiveness of treatment strategies are also scarce. A specific treatment option in patients with end-stage hip disease is hip replacement surgery. Hip prostheses have a limited life span, and revision surgery is often needed. Ideally, new systemic treatment strategies should be explored to prevent hip damage, while also reducing signs, symptoms and progression in other diseased areas.

In order to highlight the importance of and to prepare for focused research on this topic, we describe the epidemiology of hip involvement in patients with AS under rheumatologist’s care and the association of hip involvement with functionality and disease activity. We also identify factors that are associated with more severe destructive hip involvement, leading to the replacement surgery.

**Patients and methods**

**Description of the populations**

Population 1 comes from the Belgian ASPECT database. This is a nation-wide, cross-sectional database containing information on 1023 AS patients, 847 of whom fulfilled the definite New York modified criteria for AS. Patients were seen by 89 rheumatologists from different academic and non-academic centres covering 50% of all Belgian rheumatologists. The epidemiology of these patients has been previously described [8]. The second population comes from Spanish REGISPONSER database. From this database, only patients with definite AS (n = 1405) were entered into the merged dataset. The epidemiology of part of this second population has also been previously described [9].

The third population of definite AS patients (n = 466) comes from the RESPONDIA database [10]. This database used the same clinical record form and variable names as the REGISPONSER database and consisted of patients from Portugal and different Ibero-American countries (Chile, Argentina, Venezuela, Costa Rica, Mexico, Peru, Ecuador and Uruguay).

All patients were included consecutively and the participating centres were spread over the countries.

In ASPECT, every week’s first and fourth patient was evaluated and patients entered the registry between February 2004 and February 2005. For REGISPONSER, patients entered between April 2004 and March 2005. For RESPONDIA, patients were included between January 2006 and December 2007.

All patients fulfilled the definite New York modified criteria, and clinical data on hip involvement were available. They signed an informed consent form, and data were anonymously coded. Local investigational review boards or ethical committees approved the different studies.

**Description of the different definitions for ‘hip involvement’**

In the absence of a standard definition for hip involvement, three definitions for hip involvement were used.

‘Clinical hip involvement’ consisted of the rheumatologist’s clinical perception of hip involvement. In ASPECT, this was recorded in the case report form as ‘current or ever hip arthritis’. In REGISPONSER and RESPONDIA, this was recorded in the case report form as ‘pain or limitation of the hips’.

‘Radiological hip involvement’ was based on the BASRI-hip scoring system [11] assessed by the treating rheumatologists and applied to recent (not >1 year) radiographs of the hips. These data were available in REGISPONSER and RESPONDIA only.

‘The need for hip replacement surgery’ was based on the presence of one or two replaced hips. This item was recorded in all databases and was considered as the most objective proxy for severe end-stage hip involvement.

**Data recorded in the databases**

The databases consisted of at least the following variables: demographics, age at onset (of symptoms), disease duration (since symptom onset), extra-articular manifestations and the presence (current or past) of peripheral arthritis or enthesitis (according to the treating rheumatologists, mostly defined as present or past Achilles tendonitis or fasciitis plantaris). Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), Bath Ankylosing Spondylitis Functional Index (BASFI), HLA-B27, CRP, Shober index, occiput to wall distance, thorax expansion and cervical rotation were available in all databases. Shober index, occiput to wall distance, thorax expansion and cervical rotation were available in all databases. Complete BASMI (including inter-malleolar distance) was available in ASPECT only. Height and weight, necessary to calculate the BMI, and coxitis as first symptoms of the disease were available in REGISPONSER and RESPONDIA only.

In ASPECT, the radiographs of the pelvis were scored for sacroilitis (New York criteria) and the spine was classified into three exclusive categories: (i) no changes related to AS, (ii) syndesmophytes and (iii) spinal ankylosis, further referred to ‘severe axial disease’. In REGISPONSER and RESPONDIA, the radiographs of the pelvis and spine were scored according to Bath Ankylosing Spondylitis Radiology Index (BASRI) scoring system [11]. Severe axial disease was defined by a BASRI-spine score of 12. All radiographs were scored by the treating rheumatologists.

**Evaluation of heterogeneity between populations and merging of databases**

Databases were physically merged. Heterogeneity between the three populations and the different countries...
was analysed by the evaluation of all variables on differences in frequencies and means. Some relevant variables in the RESPONSEIA database showed significant differences (exceeding 10%) with the ASPECT and REGISPONSER database. Similar differences were found between countries and races in the RESPONSEIA database.

These analyses, together with initial aim to use the RESPONSEIA database for ‘validation’, suggested to analyse the RESPONSEIA dataset separate from the merged ASPECT–REGISPONSER dataset (further referred to as Dataset A), and to keep the RESPONSEIA dataset (further referred to as dataset B) for confirmative analyses, rather than trying to adjust for the different confounders (different countries, different races, etc.).

Statistics

Descriptive statistics and inference. Descriptive statistics were used to describe the data and differences between subgroups by the calculation of means with s.d. for continuous data. Dichotomous and ordinal data were described by frequencies. Descriptive statistics were given for the three databases (ASPECT, REGISPONSER and RESPONSEIA) separately in order to give the reader the opportunity to evaluate the heterogeneity between the databases.

Differences between subgroups and inference were calculated in the merged Dataset A (ASPECT and REGISPONSER) and Dataset B (RESPONSEIA) by the calculation of odds ratios (ORs) and mean differences with their 95% CIs. P-values were calculated in Dataset A only, as Dataset B was considered to be underpowered.

If the 95% intervals obtained from Datasets A and B were found to be overlapping, the estimate was considered as ‘confirmed’ [12]. Ordinal data were expressed in frequencies per subgroup and χ²-statistics [13].

Regression models. In order to explore the effect of one or more variables on several outcomes, corrected for potential confounders, generalized linear regression models were used. An identity link function was used if the dependent variable was continuous (BASFI, BASDAI models were used. An identity link function was used if the dependent variable was binary (hip replacement surgery). Logistic regression and included the confounders to correct for, based on univariate analysis of differences between the groups.

When needed, variable selection was performed with backward elimination based on the likelihood ratio tests and Akaiki’s information criteria. After the variable selection, interaction terms were evaluated.

Missingness completely at random was assumed. Missing cases were excluded, pair wise, for demographical explorations and list wise in the logistic regression model. All analyses were performed with SPSS 15.0 (SPSS, Chicago, IL, USA).

Results

Descriptive analysis of hip involvement

Clinical hip involvement. Twenty-four (REGISPONSER) to 36% (RESPONSEIA) of the patients with AS presented previous or current clinical hip involvement. Patients with clinical hip involvement had a significantly earlier age at disease onset compared with patients without hip involvement: 21% of the patients with hip involvement had a juvenile onset of the disease vs 9% without hip involvement (P < 0.001) [γ = −0.3 (s.e. = 0.1) in Dataset A] [γ = −0.2 (s.e. = 0.1) in Dataset B]. In ASPECT, patients with clinical hip involvement had a significant lower inter-malleolar distance than patients without clinical hip involvement (mean difference: 14, s.e. = 2, P < 0.001). Other differences are listed in Table 1.

Radiological hip involvement. Based on the BASRI-h scoring system, 56, 22, 11, 5 and 6% had no, suspicious, mild, moderate or severe damage on conventional radiography of the hip (n = 1359) in Dataset A, respectively [11, 15]. In Dataset B, these scores were observed in 45, 22, 11, 12 and 10% (n = 355). There was a significant association between radiological hip involvement and clinical hip involvement in Dataset A (γ = 0.71, s.e. = 0.03) and in Dataset B (γ = 0.66, s.e. = 0.06).

Hip replacement surgery. Overall, 5 (Dataset A) to 8% (Dataset B) of the AS patients had undergone hip replacement surgery of whom 47% underwent bilateral hip replacement. After >30 years of disease duration, 12 (Dataset A) to 25% (Dataset B) of the patients had at least one replaced hip.

Effect of hip involvement on BASFI and BASDAI

Patients with clinical hip involvement had a 1.6 (s.e. = 0.1) points worse overall BASFI score compared with patients without clinical hip involvement (Table 1). Figure 1 shows that patients with hip involvement had worse scores on all questions of BASFI compared with patients without hip involvement. Generalized linear regression analysis, corrected by propensity scores including those variables that significantly differed between patients with and without clinical hip involvement (disease duration, cervical rotation, lumbar flexion, country, CRP, sex and age at disease onset), showed that patients with hip involvement had significantly higher BASFI scores than patients
| Hip involvement | Dataset A | | Dataset B | | | Statistic | | Dataset B | | Dataset A | | Dataset B | | | Statistic |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | ASPECT | REGISPONSER | | | | | | | | | | | | |
| | No, n = 617 | Yes, n = 230 | OR = 1.2 (1.0–1.5) | | OR = 1 (0.7–1.6) | | OR = 1.4 (1.2–1.6) | | OR = 0.8 (0.6–1.1) | | OR = 1.1 (1.0–1.5) | | OR = 1.0 (0.7–1.5) | | OR = 1.0 (0.7–1.5) |
| Sex, male, % | 67 | 70 | 74 | 79 | | 69 | 70 | OR = 1 (0.7–1.6) | | OR = 1.2 (1.0–1.5) | | OR = 1.0 (0.7–1.5) | | OR = 1.0 (0.7–1.5) |
| Age, mean ± s.d., years | 44 ± 12 | 44 ± 12 | 47 ± 12 | 52 ± 12 | | 43 ± 14 | 47 ± 14 | Diff = 4.2 (1.5–7) | | Diff = 2.7 (1.6–4) | | Diff = 2.7 (1.6–4) | | Diff = 2.7 (1.6–4) |
| Disease duration, mean ± s.d., years | 16 ± 11 | 21 ± 12 | 20 ± 13 | 25 ± 13 | | 12/15/73 | 14/19/67 | Diff = 3.9 (1.7–6) | | Diff = 2.7 (1.6–4) | | Diff = 2.7 (1.6–4) | | Diff = 2.7 (1.6–4) |
| Age at disease onset, % | 10/21/69 | 30/21/49 | 8/25/67 | 15/27/58 | | Diff = 2.7 (1.6–4) | | Diff = 2.7 (1.6–4) | | Diff = 2.7 (1.6–4) | | Diff = 2.7 (1.6–4) | | Diff = 2.7 (1.6–4) |
| IBD diagnosis—ever, % | 10 | 11 | 5.1 | 5.4 | OR = 1.1 (0.8–1.6) | | 4.1 | 5.6 | OR = 1.4 (0.6–3.4) | | OR = 1.1 (0.8–1.6) | | OR = 1.1 (0.8–1.6) | | OR = 1.1 (0.8–1.6) |
| Uveitis—ever, % | 24 | 36 | 20 | 24 | OR = 1.5 (1.2–1.9) | | 23 | 22 | OR = 0.9 (0.6–1.4) | | OR = 1.5 (1.2–1.9) | | OR = 1.5 (1.2–1.9) | | OR = 1.5 (1.2–1.9) |
| Psoriasis—ever, % | 10 | 13 | 9 | 9 | OR = 1.1 (0.8–1.5) | | 12 | 14 | OR = 0.9 (0.5–1.6) | | OR = 1.1 (0.8–1.5) | | OR = 1.1 (0.8–1.5) | | OR = 1.1 (0.8–1.5) |
| HLA-B27, % | 83 | 83 | 84 | 79 | OR = 0.8 (0.6–1.1) | | 68 | 62 | OR = 0.8 (0.4–1.4) | | OR = 0.8 (0.6–1.1) | | OR = 0.8 (0.6–1.1) | | OR = 0.8 (0.6–1.1) |
| Current peripheral arthritis, % | 4/8/3 | 10/31/10 | 5/4/2 | 7/8/3 | | 10/11/7 | 9/17/17 | OR = 1.2 (1.0–1.5) | | OR = 1.2 (1.0–1.5) | | OR = 1.2 (1.0–1.5) | | OR = 1.2 (1.0–1.5) |
| Peripheral arthritis—ever% | 43 | 100 | 30 | 43 | | 62 | 70 | OR = 1.4 (0.9–2.2) | | OR = 1.4 (0.9–2.2) | | OR = 1.4 (0.9–2.2) | | OR = 1.4 (0.9–2.2) |
| Peripheral enthesial disease, % | 48 | 54 | 34 | 40 | OR = 1.3 (1.1–1.6) | | 61 | 64 | OR = 1.2 (0.8–1.7) | | OR = 1.3 (1.1–1.6) | | OR = 1.3 (1.1–1.6) | | OR = 1.3 (1.1–1.6) |
| Anti-TNF started, % | 11 (39) | 14 (56) | 15 | 25 | OR = 1.6 (1.2–2.1) | | 11 | 19 | OR = 1.8 (1.1–3.3) | | OR = 1.6 (1.2–2.1) | | OR = 1.6 (1.2–2.1) | | OR = 1.6 (1.2–2.1) |
| Lumbar flexion, % | 40/32/48 | 25/28/45 | 38/29/33 | 21/25/54 | γ = 0.5 (0.1) | | 40/25/35 | 30/20/50 | γ = 0.2 (0.1) | | γ = 0.5 (0.1) | | γ = 0.5 (0.1) | | γ = 0.5 (0.1) |
| Cervical rotation, % | 50/38/12 | 35/38/27 | 56/32/12 | 30/38/32 | γ = 0.4 (0.1) | | 41/43/16 | 22/44/34 | γ = 0.4 (0.1) | | γ = 0.4 (0.1) | | γ = 0.4 (0.1) | | γ = 0.4 (0.1) |
| BASDAI score, mean ± s.d. | 5.2 ± 2.1 | 5.6 ± 2 | 3.9 ± 2.3 | 4.6 ± 2.1 | | 4.4 ± 2.4 | 4.8 ± 2.4 | Diff = 0.5 (0.1–0.9) | | Diff = 0.6 (0.4–0.9) | | Diff = 0.6 (0.4–0.9) | | Diff = 0.6 (0.4–0.9) |
| BASFI score, mean ± s.d. | 4.8 ± 2.5 | 5.8 ± 2.5 | 3.4 ± 2.5 | 5.2 ± 2.5 | | 3.7 ± 2.9 | 5.7 ± 2.6 | Diff = 2 (1.5–2.5) | | Diff = 1.6 (1.3–1.8) | | Diff = 1.6 (1.3–1.8) | | Diff = 1.6 (1.3–1.8) |
| BASRI hip, mean ± s.d. | NA | NA | 0.5 ± 0.8 | 1.9 ± 1.4 | | 0.7 ± 1 | 2.3 ± 1.4 | Diff = 1.5 (1.3–1.8) | | Diff = 1.4 (1.3–1.5) | | Diff = 1.4 (1.3–1.5) | | Diff = 1.4 (1.3–1.5) |
| Severe axial radiology, % | 14 | 36 | 8 | 23 | OR = 3.3 (2.5–4.4) | | 11 | 18 | OR = 1.8 (0.9–3.5) | | OR = 3.3 (2.5–4.4) | | OR = 3.3 (2.5–4.4) | | OR = 3.3 (2.5–4.4) |

*Age at onset: frequencies are given for the following categories: before 16 years, between 16 and 21 years and after 21 years. *Current arthritis type: frequencies are given for the following categories: monoarthritis, oligoarthritis and polyarthritis. *Peripheral arthritis: ASPECT: including hip arthritis, REGISPONSER: excluding hip arthritis. 'Crude' ORs are mentioned in the table, adjusted ORs are mentioned in the text. NA: not available; Nap: not applicable.
without affected hips (mean difference in BASFI scores: 0.7; 95% CI 0.4, 1; \( P < 0.001 \)) (Dataset A). Similar estimates were obtained in Dataset B (mean difference in BASFI scores: 0.8; 95% CI 0, 1.7). Also questions that seem not to be directly related to the hip (such as Question 8: ‘Difficulty to look over your shoulder without turning your body’) had statistically significantly worse scores than patients without hip involvement (Fig. 1), also after correction with the propensity score.

In contrast to BASFI, the difference in BASDAI that was observed between patients with and without hip involvement was not statistically significant after correction with the propensity score.

These findings were also observed in Dataset B and if clinical hip involvement was replaced by radiological hip involvement (figures made available for review or online publication).

**Association of hip involvement with axial disease**

**Clinical.** Corrected for disease duration and age at onset, patients with clinical hip involvement were more prone to have severely limited (<20°) cervical rotation [Dataset A: OR = 2.9 (2.2–3.7), \( P < 0.001 \); Dataset B: OR = 2.7 (1.6–4.4)] and lumbar flexion (<2 cm) [Dataset A: OR = 1.9 (1.5–2.4), \( P < 0.001 \); Dataset B: OR = 1.8 (1.1–2.7)] than patients without clinical hip involvement (Table 1).

**Radiological.** Corrected for disease duration and age at onset, patients with severe radiological hip involvement are more prone to have severe axial disease [Dataset A: OR = 5.5 (3.1–9.5), \( P < 0.001 \); Dataset B: OR = 5.1 (1.7–15)].

**Modelling the need of hip replacement surgery**

Logistic regression analysis was performed with the need of hip replacement surgery as dependent variable and the variables that were significantly associated with hip replacement surgery (variables in bold letters from Table 2, and country) as explanatory variables. Variable selection with backward elimination by likelihood ratio testing was performed in Dataset A. This resulted in a model with the following variables: age at onset, disease duration, enthesial disease and severe axial disease (Table 3). Fitting a new logistic regression model with those variables in Dataset B resulted in similar estimates for the different variables (Table 3). None of the models showed significant interaction terms.

If axial disease was omitted from the model by removing the variable ‘severe axial radiological disease’ from
TABLE 2 Factors associated with hip replacement surgery

| Hip replacement surgery | ASPECT | REGISPONSE | RESPONDIA |
|-------------------------|--------|------------|-----------|
|                         | DATASET A | DATASET B | DATASET B |
|                         | No, \( n = 53 \) | Yes, \( n = 55 \) | Yes, \( n = 38 \) | Statistic | No, \( n = 53 \) | Yes, \( n = 55 \) | Yes, \( n = 38 \) | Statistic |
| Sex, male, %            | 68      | 74         | 85        | OR = 1.5 (0.9-2.4) | 68      | 76         | OR = 1.5 (0.7-3.2) |
| Age, mean, years        | 44      | 48         | 48        | OR = 5.7 (3.3-8.1) | 44      | 49         | OR = 4.8 (0.1-9.6) |
| Disease duration, mean, years | 17  | 27         | 35        | Diff = 11.5 (8.1-13) | 13  | 25         | Diff = 11.4 (7.5-15) |
| Age at onset, %         | 14/21/65 | 40/23/36 | 9/25/66  | 26/41/33 | \( \gamma = -0.6 \ (0.1) \) | 11/16/73 | 40/17/43 | \( \gamma = -0.6 \ (0.1) \) |
| IBD                     | 9       | 17         | 5         | OR = 1.7 (0.9-3.2) | 5       | 3          | OR = 0.6 (0.1-4.4) |
| Uveitis ever, %         | 27      | 32         | 21        | OR = 1.8 (1.2-2.7) | 22      | 35         | OR = 2 (0.9-4) |
| Peripheral enthesial disease ever, % | 49 | 60         | 35        | OR = 1.8 (1.2-2.6) | 61      | 66         | OR = 1.2 (0.6-2.5) |
| Peripheral arthritis ever, % | 55 | 100        | 35        | OR = 2.6 (1.5-4.5) | 63      | 71         | OR = 1.5 (0.7-3) |
| First sign coxitis, %   | NA      | NA         | 4         | OR = 3.8 (1.6-8.8) | 20      | 21         | OR = 1.1 (0.5-2.5) |
| Psoriasis ever, %       | 11      | 8          | 9         | OR = 1.2 (0.6-2.2) | 13      | 16         | OR = 1.2 (0.5-3.1) |
| Severe axial radiological disease, % | 18 | 47         | 11        | OR = 5.9 (3.9-9.2) | 12      | 25         | OR = 2.4 (0.9-6.4) |
| HLA-B27, %              | 82      | 90         | 83        | OR = 1.3 (0.7-2.5) | 66      | 71         | OR = 1.3 (0.4-4.3) |
| BMI, mean               | NA      | NA         | 27        | Diff = 2 (0.3-3.7) | 26      | 25         | Diff = 0.9 (-0.8-2.5) |

Age at disease onset: before 16 years, between 16 and 21 years and after 21 years. Severe radiological disease was defined as a radiological score of 3 in ASPECT or a BASRI score >10. Statistical significant differences between the groups are given in bold.

TABLE 3 Factors associated with hip replacement surgery from Datasets A and B

| Disease duration, years | OR, Dataset A | \( P \)-value | OR, Dataset B |
|-------------------------|---------------|---------------|---------------|
|                         | 1.04 (1.02-1.06) | <0.001        | 1.03 (1-1.1) |
| Enthesial disease       | 1.86 (1.13-3.07) | 0.016         | 1.19 (0.2-6.7) |
| Age at onset, years     | <0.001        |               |               |
| \( <16 \)               | 3.82 (2-7.33) | <0.001 | 5.92 (0.9-1.1) |
| 16-21                   | 2.072 (1.12-3.82) | 0.020 | 1.16 (0.1-10) |
| \( >21 \)               | Reference |               |               |
| Severe axial radiology  | 3.79 (2.23-6.42) | <0.001 | 2.24 (0.1-15) |
| Constant                | 0.006 | <0.001 | 0.022 |

The factors mentioned in the table result from a logistic regression analysis in Datasets A and B.

Discussion

This is the first large, international study that explores the impact of hip involvement in patients with AS. We confirm that hip involvement is a common disease manifestation in AS patients under rheumatologist’s care [16]. The exact estimate of the prevalence of hip involvement in AS patients largely depends on the used definitions. Three definitions were used: clinical hip involvement, radiological hip involvement and the end-stage hip disease. Any of these three definitions can be subject to bias when applied in daily clinical practice rheumatologist’s centres.

Nevertheless, the reported findings for any of the used definitions could be confirmed in an independent and more heterogeneous database making these findings robust.

Patients with hip involvement have worse BASFI scores than patients without hip involvement. These higher BASFI scores could be found not only in all BASFI questions of which many appear to be directly related to the hip (e.g. difficulty with getting up off the floor or out of a chair, tying shoes, climbing stairs), but also on questions related to functions with no hip involvement (e.g. Question 8 of the BASFI: looking over the shoulder without turning your body). This could indicate that a patient’s judgement of functional impairment is not necessarily only reflecting range of motion in the joints. Perhaps, hip involvement also hampers other activities related to spinal mobility.
An alternative explanation could involve the association of hip involvement with more severe axial disease in terms of ankylosis progression; however, as the model was also corrected for the Bath Ankylosing Spondylitis Metrology Index measurements that are related to axial disease, this explanation seems less likely. High disease activity (high BASDAI score) and worse physical function (high BASFI score) are closely related to health care utilization, work loss, sick leave and associated cost-of-illness [17–19].

Consistent in all datasets and analyses, and independent of disease duration, we confirm that early age at disease onset is associated with hip involvement [14]. Patients with juvenile onset (age at disease onset <16 years) of AS were at the highest risk of developing hip disease and the subsequent need for hip replacement surgery. Different factors that are associated with the end-stage hip disease could be defined. However, a true prediction model could not be constructed. The construction of a true prediction model for the need of hip replacement surgery would require that a large cohort of the patients would be followed up over 20–30 years in order to obtain sufficient cases that underwent hip replacement surgery resulting in robust estimates. The present cross-sectional analysis, taking into account disease duration, is the second best option to identify variables that are associated with the end-stage hip disease. They were: early age at onset, disease duration, enthesial disease, ankylosing disease and severe axial disease.

We confirm previous observation that clinical and radiological hip involvement is linked to more severe axial disease. From these findings, it has been suggested that hips can be as root joints, more linked to the spine than to other peripheral joints. However, it seems that the effect of age at onset, time and disease duration is somewhat different for the hip disease compared with the axial disease [11, 14, 16].

Future work should be dedicated to creating a better definition of hip involvement in AS (with emphasize on early detection) and the differentiation between primary inflammatory hip involvement and secondary degenerative hip involvement. Whether hip involvement can best be clinically evaluated by history taking, the measurement of the intermalleolar distance or by the hip internal rotation (or combinations) is still a matter of discussion [20]. Moreover, the histological characteristics of this hip involvement, including the definitions of ‘active hip disease’ vs damage, are not very well-known and may differ from what is seen in the sacroiliac joints or spine [21].

Further relevance of an appropriate way to detect early hip involvement is the emergence of new therapeutic options in AS, the effects of which are mainly focused on the spine and axial radiology and to some extent on peripheral arthritis or enthesitis. Little is known regarding their effects on the hip and later need for surgery. This holds true for the classic DMARDs such as SSZ and MTX which demonstrated little or no effect on axial disease and are recommended only in patients with peripheral arthritis [22, 23]. Their effect on hip involvement is uncertain. Similarly, TNF inhibitors have been shown to be highly effective in controlling disease activity for axial diseases, but their capability to reduce the incidence and activity of coxitis and their effect on the long-term need for hip surgery will be diminished is still to be investigated. TNF inhibitors reduce progression of erosive disease in RA. The chronic morphological changes that are seen in AS-related hip involvement are frequently of the erosive-destructive type. Further case reports suggest an effect of anti-TNF therapy [21, 24, 25]. This topic therefore certainly merits more attention.

To conclude, hip involvement is a common disease manifestation of AS, reflecting more severe disease that is associated with a functional impairment. Long-term studies are needed to evaluate the effect of therapeutic strategies that can prevent hip involvement and the need for hip replacement surgery, especially in patients with younger onset of disease.

### Rheumatology key messages

- One out of the three to four patients with AS suffer from hip involvement.
- Hip involvement has an important impact on clinical functioning, measured by BASFI.
- Juvenile onset, axial and enthesial disease are associated with hip replacements in AS.

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