Different Clinical Expression of Patients With Ankylosing Spondylitis According to Gender in Relation to Time Since Onset of Disease. Data From REGISPONSER


A R T I C L E   I N F O

Article history:
Received 13 December 2011
Accepted 19 September 2012
Available online 1 May 2013

A B S T R A C T

Objective: To describe the differential characteristics by gender and time since disease onset in patients diagnosed with ankylosing spondylitis (AS) attending the Spanish rheumatology clinics, including those on the “Spanish Registry of spondyloarthritis” (REGISPONSER), as well as the diagnostic and therapeutic implications that this entails.

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**Resumen**

Objetivo: Establecer las características diferenciales según el sexo y el tiempo de evolución de la enfermedad en aquellos pacientes diagnosticados de espondilitis anquilosante (EA) asistidos en consultas de reumatología de toda España, incluidos en el Registro Españo de Espondiloartritis (REGISPONSER), así como la repercusión diagnóstica y terapéutica que ello conlleva.

**Materiales y métodos**: Estudio transversal y observacional de 1.514 pacientes con EA seleccionados de entre 2.367 espondiloartritis incluidos en REGISPONSER. En cada paciente se evaluaron y registraron de modo exhaustivo los datos demográficos, epidemiológicos, sociosanitarios, clínicos, analíticos, radiológicos y terapéuticos previstos en el protocolo de REGISPONSER que componen el Conjunto Mínimo Básico que identifica la enfermedad. La función física se evaluó mediante el Bath Ankylosing Spondylitis Functional Index. La actividad clínica mediante velocidad de sedimentación globular, proteína C reactiva y el Bath Ankylosing Spondylitis Disease Activity Index (BASDAI). A cada paciente se le realizaron radiografías anteroposterior de pelvis, anteroposterior y lateral de columna lumbar y lateral de columna cervical, y se puntuaron según el índice Bath Ankylosing Spondylitis Radiographic Index Spine (BASRI-Spine), que mide el daño estructural.

**Resultados**: De los 1.514 pacientes seleccionados, 1.131 (74.7%) eran hombres. Encontramos que existen diferencias significativas en la edad tanto al inicio de los síntomas como en el día de la inclusión entre ambos grupos, siendo menor en los hombres. También obtuvimos diferencias en el tiempo de evolución de la enfermedad, que fue menor en el grupo de las mujeres. En cuanto a la existencia de anquilosis, tanto en el grupo de hombres como en el de mujeres, también resultó superior en éstas la puntuación media del BASDAI, con independencia del tiempo de evolución. Por el contrario, la mejoría del dolor con la toma de antiinflamatorios no esteroideos fue mayor en el caso de los hombres, así como la severidad radiológica, ambas de forma significativa.

**Conclusiones**: Entre los pacientes con EA españoles existen algunas diferencias en las manifestaciones clínicas y cuando se controló según el tiempo de evolución, también encontramos diferencias radiológicas según el sexo; los hombres muestran más daño estructural, mientras que las mujeres presentan mayor actividad. Estos datos sugieren que el fenotipo de EA difiere entre géneros, lo que puede influir en el manejo diagnóstico y posterior elección terapéutica.

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19 provinces covering the spectrum of the Spanish population both from the demographic, social, labor and economic viewpoint. Today, it has more than 2000 patient’s data regarding disease characteristics, clinical and radiological presentation and therapeutic response. This registry has been the basis for describing the clinical, demographic, analytical, radiological and metrological parameters of patients with spondyloarthritis in Spain.1,9

This article establishes the differential characteristics by gender and duration of disease of patients diagnosed with AS, as well as the diagnostic and therapeutic implications that this entails. To do this we compared the clinical, radiographic and functional outcomes and possible differences in severity considering gender and time since onset of disease.

Patients and Methods

Patients

For this study we selected 1514 of 2367 patients with AS composing the REGISPONSER database, of which 1131 (74.7%) were men and 383 (25.3%) women. The full details on the methodology and comprehensive compilation of the data included in REGISPONSER1,9 have been published previously.

Compiled Data

Each center had a trained rheumatologist who was responsible for patient assessment, data collection and compliance with the inclusion criteria. For our study we considered the following variables: age (years), gender, ethnicity (caucasian/other), first-degree family history (yes, no), smoking status (smoker or former smoker/non-smoker), marital status (married/single), type of work (sedentary, moderate, severe), SA disability and presence of human leukocyte antigen HLA-B27. Likewise, we collected the prior and current medications used by each patient (including the use of methotrexate, sulfasalazine, leflunomide, infliximab and etanercept) and improvement in pain with non-steroidal antiinflammatory drugs (NSAIDs). Other data collected the prior and current medications used by each patient (including the use of methotrexate, sulfasalazine, leflunomide, infliximab and etanercept) and improvement in pain with non-steroidal antiinflammatory drugs (NSAIDs). Other data collected included the presence of symptoms such as peripheral arthritis, enthesitis, uveitis and coxitis, the presence of hip affection and systemic symptoms (cardiac, renal, neurological or pulmonary involvement, all categorized as yes or no). To measure disability, patients were asked to complete the “Bath Ankylosing Spondylitis Functional Index” (BASFI).

To measure disease activity, we considered the following quantitative variables: erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) and the self-completion of the “Bath Ankylosing Spondylitis Disease Activity Index” (BASDAI). Each patient underwent anteroposterior pelvic X-ray, anteroposterior and lateral lumbar spine and cervical spine X-ray, and were scored according to the “Bath Ankylosing Spondylitis Radiographic Index – Spinal” (BASRI-Spinal),12 which measures structural damage.

Statistical Analysis

We performed a descriptive analysis of the clinical, epidemiological, radiographic and laboratory variables by gender and duration of disease. To do that, variables were stratified into 4 groups (0–9 years, 10–19, 20–39 and 40 years or more of disease progression). Subsequently, the first subgroup was analyzed by creating a new variable (0–4 years, 5–7 and 8–10 years). We calculated the mean and standard deviation for quantitative variables and absolute frequencies and percentages for qualitative variables. A bivariate test was performed using the Student’s t test for independent data for quantitative variables and the chi-square test for qualitative variables. The values of “P” were adjusted by the Finner test. Subsequently, we performed a univariate factorial ANOVA with a Sidak adjustment for multiple comparisons to establish the differences in BASDAI, BASFI, BASRI, ESR and CRP by gender and duration of disease.

All contrasts were bilateral and those considered significant had a P<0.05.

Results

Demographic and Clinical Characteristics

Table 1 shows the sociodemographic and clinical differences between men and women with AS of the 1514 patients selected. We found that there were significant differences between both groups in the mean age and the onset of symptoms at inclusion, being lower, in both cases, in men. There were also significant differences in the mean duration of disease, again lower in women. Regarding the existence of a history of AS among first-degree relatives, family forms were more frequent in the female group. For other sociodemographic characteristics there were no differences between the two groups, as occurred in the clinical expression, except for the presence of low back pain, which was more common among men.

Regarding treatment, there was no significant differences between genders in the drugs used previously. At the onset of the disease, the proportion of men using sulfasalazine was greater 87.9% than women (95% CI, 86.26–89.54) vs 83.3% (95% CI, 81.73–84.87), P=0.03. The improvement in pain of those patients taking NSAIDs was significantly more favorable in men.

Disease Activity

To assess disease activity we considered BASDAI, ESR and CRP. Compared to men, women had a higher average BASDAI score, regardless of the time of disease progression, with significant differences in all cases, except in those patients whose disease had a mean time interval of 20–39 years. This difference was accentuated in the group of 40 or more years of disease progression, where we observed that both the average score of the BASDAI as well as ESR and CRP levels were significantly higher in the women than in the men: BASDAI (cm) 5.25 (2.06) (95% CI, 4.18–6.32) vs 4.01 (2.39) (95% CI, 3.62–4.40), P=0.033; ESR (mm/h) 36.56 (26.37) (95% CI, 29, 14–43.97) vs 17.85 (17.08) (95% CI, 15.01–20.70), P<0.001, and CRP (mg/l) of 19.60 (30.44) (95% CI, 13.39–25.81) vs 8.42 (10.69) (95% CI, 6.03–10.81), P<0.001.

Both the average BASDAI score and CRP levels were significantly increased in the men related to the years of disease progression.

Radiographic Results

Radiological findings were more severe in men, with a mean score of 6.66 in BASRI – spinal (3.47) (95% CI, 6.45–6.87) vs 4.60 (2.67) (95% CI, 4.33–4.87) in women, P<0.001. Adjusting for the duration of the disease, we found that the mean score of BASRI – spinal worsened significantly in both groups over the years, resulting in all cases in worse outcomes in men. In the subgroup of 0–10 years we saw that BASRI – spinal significantly increased over the years in men. When comparing both groups we confirmed that, from the early stages of the disease, the mean BASRI – spinal score was higher in men, except in the group of 5–7 years where there were no differences.

Functional Disability

Globally, the BASFI increased significantly with time of disease progression although we cannot say that there were gender differences.
This discrepancy between radiological damage and functional outcomes is the result of women having more peripheral arthritis and less axial radiographic changes.

### Discussion

The review of previously published studies showed that women have more peripheral arthritis and less axial radiographic changes. In our study, we found no differences in relation to the presence of peripheral involvement by gender, although it did occur relative to axial involvement, being higher in men with a better response to NSAID use. Although our study confirms that men have greater radiographic damage than women, there seems to be an apparent contradiction, since although the structural damage was significantly higher in men functional outcomes are the same in both groups. The study of Grand et al. showed no gender differences in mobility of the spine. Furthermore Dagfinrud et al. found that changes in the mobility of the spine did not explain the observed differences in function; furthermore, the relationship between the radiographic structural damage and loss of function remains unknown. Even in the rheumatoid arthritis studies that have examined this question more fully, the nature of the relationship between the radiographic damage and functional loss is controversial, and may vary over the time course of the disease.

### Ethical Responsibilities

#### Protection of People and Animals

The authors declare that they have followed the protocols of their workplace regarding the publication of data from patients and all patients included in the study have received sufficient information and gave their written informed consent to participate in this study.

#### Data Confidentiality

The authors declare that they have followed the protocols of their workplace regarding the publication of data from patients and all patients included in the study have received sufficient information and gave their written informed consent to participate in this study.

#### Right to Privacy and Informed Consent

The authors declare that they have followed the protocols of their workplace regarding the publication of data from patients and all patients included in the study have received sufficient information and gave their written informed consent to participate in this study.

#### Conflict of Interest

The authors have no disclosures to make.

#### Acknowledgments

This work was made possible through an unrestricted grant from Abbott, Schering-Plough (now MSD) and Wyeth Spain (now Pfizer), managed by the Spanish Foundation for Rheumatology (FER).
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