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BRIEF REPORT

Impact of Comorbidity on Physical Function in Patients With Ankylosing Spondylitis and Psoriatic Arthritis Attending Rheumatology Clinics: Results From a Cross-Sectional Study

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Objective. To evaluate the impact of comorbidities on physical function in patients with ankylosing spondylitis (AS) and psoriatic arthritis (PsA).

Methods. This was a cross-sectional analysis of the baseline visit from the Cardiovascular in Rheumatology study. Multivariate models with physical function as the dependent variable (Bath Ankylosing Spondylitis Functional Index and Health Assessment Questionnaire for AS and PsA, respectively) were performed. Independent variables were a proxy for the Charlson Comorbidity Index (CCIp; range 0–27), sociodemographic data, disease activity (erythrocyte sedimentation rate [ESR] and Bath Ankylosing Spondylitis Disease Activity Index [BASDAI] in AS; Disease Activity Score in 28 joints [DAS28] using the ESR in PsA), disease duration, radiographic damage, and treatments. Results were reported as beta coefficients, 95% confidence intervals (95% CIs), and *P* values.

Results. We included 738 patients with AS and 721 with PsA; 21% of patients had >1 comorbidity. Comorbidity burden (CCIp) was independently associated with worse adjusted physical function in patients with PsA (β = 0.11). Also, female sex (β = 0.14), disease duration (β = 0.01), disease activity (DAS28-ESR; β = 0.19), and the use of nonsteroidal antiinflammatory drugs (β = 0.09), glucocorticoids (β = 0.11), and biologics (β = 0.15) were associated with worse function in patients with PsA. A higher education level was associated with less disability (β = –0.14). In patients with AS, age (β = 0.03), disease activity (BASDAI; β = 0.81), radiographic damage (β = 0.61), and the use of biologics (β = 0.51) were independently associated with worse function on multivariate analyses, but CCIp was not.

Conclusion. The presence of comorbidities in patients with PsA is independently associated with worse physical function. The detection and control of the comorbidities may yield an integral management of the disease.

INTRODUCTION

Physical function is a crucial consideration in patients with spondyloarthritis (SpA) and, along with health-related quality of life, is considered a major outcome in patients with ankylosing spondylitis (AS) and psoriatic arthritis (PsA). Furthermore, functional improvement is one of the ultimate goals of therapy for patients with AS and PsA. Patients with AS have increased comorbidity when compared to the general population, particularly with regard to some specific disorders, such as cardiovascular disease (CVD) and osteoporosis (1). Patients with PsA also have increased comorbidities, such as CVD, diabetes mellitus, metabolic syndrome, and depression, and more than 50% have >1 comorbidity (2).

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SIGNIFICANCE & INNOVATIONS

- A large number of comorbidities has been identified in a nation-wide cohort of patients with spondyloarthritis (SpA).
- Comorbidity burden was independently associated with physical function in patients with psoriatic arthritis (PsA).
- Associations between female sex and worse physical function and between higher education level and better function were identified in patients with PsA.
- Associations between physical function and some well-known related factors, such as age, disease activity, and radiographic damage, were confirmed in Spanish patients with SpA.

Although both conditions have an impact on physical function, which is directly related to disease activity and structural damage (3,4), other factors may also deteriorate physical function in patients with chronic inflammatory rheumatic diseases. For example, comorbidity has been found to be relevant in patients with rheumatoid arthritis (RA), where functional status becomes worse with increasing levels of comorbidity, independently of disease activity (5). However, fewer studies have focused on the impact of comorbidity on physical function in patients with AS and PsA, even though the physical function impairment and the quality of life limitations of such patients are similar to those with RA (6). Taking together all these considerations, the main purpose of the current study was to analyze the impact of comorbidities on physical function in Spanish patients with AS and PsA.

PATIENTS AND METHODS

Study design. This was a cross-sectional study drawing on baseline data from the Cardiovascular in Rheumatology (CARMA) project, an ongoing multicenter 10-year prospective national study of a cohort of patients with chronic inflammatory rheumatic diseases. It included patients with RA, AS, and PsA, along with age- and sex-matched subjects without chronic inflammatory rheumatic diseases from 67 randomly selected Spanish outpatient rheumatology clinics (recruited from July 2010 to January 2012). The patients' recruitment criteria have previously been published (7).

Patients. For this study, 738 patients with AS (modified New York criteria) and 721 with PsA (Moll and Wright criteria) were analyzed. The study was performed following the principles outlined in the Helsinki Declaration, and written informed consent was obtained from all subjects before their inclusion in the CARMA project. The study protocol was approved by the Ethics Committee for Clinical Research of Lugo, Galicia, Spain (protocol #2009/077).

Variables and operative definitions. *Dependent variable.* The main outcome was physical function, measured through the Spanish validated versions of the Bath Ankylosing Spondylitis Functional Index (BASFI) in patients with AS, and the Health Assessment Questionnaire (HAQ) in patients with PsA.

Independent variables. The independent variables included: 1) demographic data: age, sex, and education level; 2) disease activity: assessed in patients with AS by persistently raised erythrocyte sedimentation rate (ESR) or C-reactive protein and by the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), Spanish validated version; in patients with PsA, the Disease Activity Score in 28 joints (DAS28) using the ESR was used; 3) disease duration; 4) radiographic damage, defined in this study as "spinal radiographic changes" for AS and "presence of erosions" for patients with PsA, observed in standard radiographs; 5) treatments for the rheumatic disease and comorbidities; 6) comorbidities recorded as dichotomous variables and also quantitatively by using a proxy of the Charlson Comorbidity Index (CCI), which is a well-known validated index to measure comorbidity disease status (8). The CCI is a weighted score of 19 different comorbidities, selected according to their potential influence on mortality. The sum of the weights of each condition can range from 0 to 33, and the CCI score is an indicator of disease burden. The proxy we used (CCIp) consisted of a minor modification of the original CCI, made by pooling all of the tumors (solid, leukemia, and lymphoma) into a single item, named Cancer. The remaining comorbidities were collected and rated as in the original CCI. Consequently, the sum of the possible scores in our proxy ranged between 0 and 27.

Statistical analysis. Descriptive analyses were performed for the demographic and clinical variables. Afterward, bivariate analyses were conducted to investigate the associations between the independent variables and physical function. Numerical

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No potential conflicts of interest relevant to this article were reported.

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variables were assessed using Student's *t*-test or the Mann-Whitney U test. Qualitative variables were assessed by chi-square, Yates' correction, or Fisher's exact tests in 2 × 2 tables. To study the association between single comorbidities or CCIp scores and physical function, 2 different multivariate linear models were performed, with physical function as the dependent variable (BASFI and HAQ, respectively), adjusted for potentially confounding factors.

The selection of the independent variables in the multivariate models was based on those found to be statistically significant in the bivariate analyses and also on clinical judgement. Estimates for these associations are shown as beta coefficients, 95% confidence intervals (95% CIs), and *P* values. All analyses were performed using SPSS software, version 22.0. Statistical significance was assumed at a *P* value less than 0.05.

RESULTS

Clinical and demographic features of the patients and comorbidities. We analyzed 1,459 patients (738 AS and 721 PsA) whose demographic and clinical features are summarized in Supplementary Table 1, available on the *Arthritis Care & Research* web site at http://onlinelibrary.wiley.com/doi/10.1002/acr.23910/abstract. Briefly, patients with AS had an earlier disease onset and were younger at the time of study inclusion than those with PsA. In addition, the AS cohort had a higher percentage of men than that of patients with PsA. A similar percentage of patients in both groups were receiving biologic therapies, but more patients with AS received nonsteroidal antiinflammatory drugs (NSAIDs), whereas a higher number of patients with PsA used conventional synthetic disease-modifying antirheumatic drugs (DMARDs), combined therapies (synthetic plus biologic DMARDs), and glucocorticoids.

The comorbidities and CCIp percentages of the 2 groups are shown in Table 1. Regarding traditional CVD risk factors, patients with PsA had a higher body mass index (BMI) and hypercholesterolemia prevalence. In contrast, we found more current smokers among patients with AS. Apart from a higher prevalence of chronic obstructive pulmonary disease (COPD) among patients with AS and a nonsignificant increase of mild liver disease in patients with PsA, no other differences in the prevalence of the different comorbidities between the 2 groups were identified. Regarding the comorbidity burden, 21% of patients had >1 comorbidity (CCIp >1) in both groups; more specifically, patients with AS had a mean ± SD CCIp of 1.32 ± 0.73, whereas those with PsA had a CCIp of 1.30 ± 0.66.

Physical function and comorbidity. When we analyzed physical function distribution (using BASFI in the AS group and HAQ for patients with PsA) across different levels of comorbidity, we did not detect differences in patients with AS (median BASFI 3.3 [interquartile range (IQR) 1.6–5.6] for patients with CCIp >1 versus 3.0 [IQR 1.2–5.1] for those with CCIp = 1; $P = 0.353$). However, we observed that patients with PsA and more comorbidities had worse physical function (HAQ 0.75 [IQR 0.25–1.25] for CCIp >1) than patients with just 1 comorbidity (HAQ 0.25 [IQR 0.0–0.75]; $P < 0.001$).

Table 1. Comorbidities of the patients with ankylosing spondylitis and psoriatic arthritis*

Variable	AS (n = 738)	PsA (n = 721)	*P*
BMI, mean ± SD kg/m^2	27.4 ± 4.4	28.2 ± 4.7	<0.001†
Hypertension	190 (25.7)	213 (29.5)	0.105
Hypercholesterolemia	199 (27)	257 (35.6)	<0.001†
Obesity (BMI ≥30)	186 (25.2)	209 (29.1)	0.097
Current smokers	254 (34.4)	157 (21.8)	<0.001†
Past smokers	240 (32.5)	227 (31.5)	–
Never smokers	244 (33.1)	337 (46.7)	–
Myocardial infarction	21 (2.9)	11 (1.5)	0.085
Congestive heart failure	4 (0.5)	7 (1.0)	0.344
Peripheral vascular disease	8 (1.1)	7 (1.0)	0.830
Dementia	1 (0.1)	0 (0.0)	0.323
Chronic obstructive pulmonary disease	20 (2.71)	9 (1.3)	0.045†
Ulcer disease	32 (4.3)	26 (3.6)	0.476
Diabetes mellitus	52 (7.1)	61 (8.5)	0.312
Cerebrovascular disease	3 (0.4)	0 (0.0)	0.087
Mild liver disease	20 (2.7)	33 (4.6)	0.057
Hemiplegia	0 (0.0)	0 (0.0)	–
Moderate or severe renal disease	18 (2.4)	14 (1.9)	0.517
Diabetes mellitus with end-organ damage	3 (0.4)	5 (0.7)	0.458
Cancer‡	17 (2.3)	16 (2.2)	0.914
Moderate or severe liver disease	4 (0.5)	2 (0.3)	0.430
Metastatic cancer	1 (0.1)	0 (0.0)	0.323
CCIp, median (IQR)	1 (1–1)	1 (1–1)	0.912
CCIp = 1	585 (79.3)	567 (78.6)	–
CCIp >1	153 (20.7)	154 (21.4)	0.769

* Values are the number (%) unless indicated otherwise. AS = ankylosing spondylitis; PsA = psoriatic arthritis; BMI = body mass index; CCIp = Charlson Comorbidity Index proxy; IQR = interquartile range (25–75).
† Statistically significant.
‡ Solid tumors, leukemia, and lymphoma pooled.

Independent variables associated with physical function. *AS cohort*. On bivariate analyses (Table 2), physical function was associated with age, female sex, disease duration, disease activity (BASDAI and ESR), and spinal radiographic damage. In addition, treatment with NSAIDs and glucocorticoids was associated with physical function. In contrast, a higher education level was associated with less disability. We also identified an association between physical function and some individual comorbidities (obesity, hypertension, hiatal hernia, thyroid disease, or an increase in triglycerides) or the use of statins, on bivariate analyses. However, we did not identify an association between physical function and comorbidity burden (CCIp).

Table 2. Comorbidity and physical function: variables associated with BASFI in patients with AS and with HAQ in patients with PsA, unadjusted estimates*

	AS			PsA		
Variables	β	95% CI	*P*	β	95% CI	*P*
Age at inclusion	0.04	(0.03, 0.06)	<0.001†	0.01	(0.00, 0.01)	<0.001†
Sex (ref. male)	0.74	(0.34, 1.14)	<0.001†	0.36	(0.27, 0.44)	<0.001†
Disease duration	0.02	(0.01, 0.04)	<0.001†	0.01	(0.01, 0.02)	<0.001†
Education level (ref. primary)						
Basic	1.07	(0.08, 2.05)	0.03†	0.23	(0.04, 0.24)	0.02†
Secondary	–0.16	(–0.59, –0.26)	0.45	–0.17	(–0.28, –0.06)	<0.01†
University	–1.01	(–1.46, –0.56)	<0.001†	–0.24	(–0.35, –0.13)	<0.001†
CCIp	0.17	(–0.08, 0.41)	0.19	0.21	(0.14, 0.27)	<0.001†
Obesity	0.77	(0.36, 1.19)	<0.001†	0.19	(0.09, 0.29)	<0.001†
Statins	0.66	(0.17, 1.15)	0.01†	0.08	(–0.02, 0.19)	0.13
Hypertension	0.74	(0.33, 1.15)	<0.001†	0.20	(0.11, 0.30)	<0.001†
Triglycerides‡	0.40	(0.15, 0.65)	<0.001†	0.11	(0.05, 0.17)	<0.001†
GI bleeding	0.51	(–0.69, 1.71)	0.403	0.49	(–0.20, 1.19)	0.16
Hiatal hernia	1.39	(0.71, 2.07)	<0.001†	0.17	(–0.02, 0.36)	0.07
Thyroid disease	1.60	(0.44, 2.76)	0.01†	0.18	(–0.01, 0.37)	0.06
NSAID	0.78	(0.41, 1.14)	<0.001†	0.12	(0.03, 0.21)	0.01†
Biologic DMARD	0.21	(–0.14, 0.58)	0.240	0.12	(0.03, 0.21)	0.01†
GC	0.99	(0.33, 1.65)	<0.001†	0.25	(0.13, 0.36)	<0.001†
DAS28-ESR	–	NA	–	0.24	(0.21, 0.27)	<0.001†
BASDAI	0.82	(0.77, 0.88)	<0.001†	–	NA	–
ESR	0.03	(0.01, 0.04)	<0.001†	0.01	(0.00, 0.01)	<0.001†
Radiographic damage§	0.82	(0.31, 1.34)	<0.001†	0.03	(–0.07, 0.14)	0.499

* The dependent variable for patients with ankylosing spondylitis (AS) was the Bath Ankylosing Spondylitis Functional Index (BASFI; range 0–10) and for patients with psoriatic arthritis (PsA) was the Health Assessment Questionnaire (HAQ; range 0–3). 95% CI = 95% confidence interval; CCIp = Charlson Comorbidity Index proxy; GI = gastrointestinal; NSAID = nonsteroidal antiinflammatory drug; DMARD = disease-modifying antirheumatic drug; GC = glucocorticoids; DAS28-ESR = Disease Activity Score in 28 joints using the erythrocyte sedimentation rate; NA = not applicable; BASDAI = Bath Ankylosing Spondylitis Disease Activity Index.
† Statistically significant.
‡ Triglycerides analyzed per 100 mg/dl increase.
§ Defined as "spinal radiographic damage" in patients with AS and "presence of erosions" in patients with PsA.

In the multivariate model (Table 3), no association between physical function and comorbidity burden (CCIp) was found. Furthermore, age, disease activity (measured by BASDAI and ESR), and spinal radiographic damage were associated with higher disability. Also, treatment with biologic DMARDs was associated with physical function. At this point, no significant associations with sex or education level were identified in patients with AS.

PsA cohort. In patients with PsA, an independent association between comorbidity burden and physical function was observed (Table 2). In this regard, the increase in CCIp was significantly associated with higher disability (β = 0.11 [IQR 0.05–0.17]) on the adjusted multivariate model (Table 3). In addition, we identified an association between physical function and age, female sex, disease duration, disease activity (DAS28-ESR), and use of NSAIDs, biologic DMARDs, and glucocorticoids, on bivariate analyses. Apart from age, all of the above-mentioned associations were confirmed in the multivariate model. Also, some comorbidities, such as obesity, hypertension, or the increase in triglycerides, were associated with physical function on bivariate analysis. Interestingly, a higher education level was associated with less disability in these patients.

DISCUSSION

The present multicenter national survey indicates that the presence of comorbidities may decrease the reported physical function of the patients with SpA. Comorbidity burden was independently associated with physical function in patients with PsA. Moreover, the study confirmed that comorbidity is common among patients with SpA. However, some differences between AS and PsA were observed. In this regard, some CVD risk factors, such as high BMI and hypercholesterolemia, were more prevalent in patients with PsA. In addition, obesity was associated with worse function on bivariate analysis in such patients. Obesity negatively influences not only CVD risk but also other disease outcomes. In this regard, being obese and overweight reduces the chances to achieve minimal disease activity in patients with PsA receiving traditional or biologic DMARD therapy (9).

Smoking is known to be a harmful factor in patients with AS, leading to worse outcomes, including radiographic damage (10). In connection with that, in our survey we found that smoking habit and COPD were more common in patients with AS. Therefore, patients with AS should be encouraged to refrain from smoking as soon as a diagnosis of the disease is made.

Table 3. Comorbidity and physical function: variables associated with BASFI in patients with AS and with HAQ in patients with PsA, adjusted multivariate model*

Variables	AS			PsA		
	β	95% CI	*P*	β	95% CI	*P*
Age at inclusion	0.03	(0.02, 0.05)	<0.001†	0.00	(–0.00, 0.00)	0.906
Sex (ref. male)	–0.11	(–0.38, 0.16)	0.430	0.14	(0.06, 0.22)	<0.001†
Disease duration	0.01	(–0.00, 0.02)	0.095	0.01	(0.00, 0.01)	0.015†
Education level (ref. primary)						
Basic	0.21	(–0.45, 0.86)	0.532	0.14	(–0.03, 0.31)	0.096
Secondary	0.01	(–0.26, –0.29)	0.925	–0.08	(–0.17, –0.01)	0.093
University	–0.22	(–0.52, 0.08)	0.154	–0.14	(–0.24, –0.04)	0.004†
CCIp	0.03	(–0.13, 0.20)	0.701	0.11	(0.05, 0.17)	<0.001†
NSAID	0.11	(–0.14, 0.37)	0.390	0.09	(0.02, 0.17)	0.017†
Biologic DMARD	0.51	(0.27, 0.76)	<0.001†	0.15	(0.07, 0.23)	<0.001†
GC	0.03	(–0.40, 0.46)	0.899	0.11	(0.01, 0.21)	0.026†
DAS28-ESR	–	NA	–	0.19	(0.16, 0.22)	<0.001†
BASDAI	0.81	(0.75, 0.86)	<0.001†	–	NA	–
ESR	0.01	(0.00, 0.02)	0.013†	–	NI	–
Radiographic damage‡	0.61	(0.28, 0.95)	<0.001†	–	NI	–

* The dependent variable for patients with ankylosing spondylitis (AS) was the Bath Ankylosing Spondylitis Functional Index (BASFI; range 0–10) and for patients with psoriatic arthritis (PsA) was the Health Assessment Questionnaire (HAQ; range 0–3). 95% CI = 95% confidence interval; CCIp = Charlson Comorbidity Index proxy; NSAID = nonsteroidal antiinflammatory drug; DMARD = disease-modifying antirheumatic drug; GC = glucocorticoids; DAS28-ESR = Disease Activity Score in 28 joints using the erythrocyte sedimentation rate; NA = not applicable; BASDAI = Bath Ankylosing Spondylitis Disease Activity Index; NI = not included in the multivariate model.
† Statistically significant.
‡ Defined as "spinal radiographic damage" in patients with AS and "presence of erosions" in patients with PsA.

Interestingly, we identified a relationship between comorbidity burden and physical function in patients with PsA. The most commonly reported factors affecting physical function in patients with PsA are disease activity and radiographic damage (4). However, we believe that comorbidity may also exert some negative influence on the physical function of patients with PsA, and our results support this view. In this case, the measurement of physical function would reflect not only the disease process but also other factors related to the patients' general health. In this way, a recent study from the Assessment of Spondyloarthritis international Society Comorbidities in Spondyloarthritis cohort identified a relationship between comorbidity and functional status in patients with axial and peripheral SpA (11). The understanding of the different causes that impact the functional disability becomes more relevant now that remission-inducing therapies are available. However, the disability related to causes different from the disease itself may not be improved if they are not properly detected. Therefore, recognizing the comorbid conditions that overshadow the outcome of patients with SpA is important. In fact, recommendations for their identification and management have been recently published (12). However, to ascertain the impact of the comorbidity control on long-term outcomes such as function, longitudinal studies are needed.

A recent study showed an association between comorbidity burden and physical function in patients with SpA (11), but we could not confirm this association in our patients with AS. Methodologic differences, such as different populations and the use of different indexes to measure comorbidity burden, may explain such a discrepancy. Moreover, since comorbidity has been reported to be a major contributor to functional limitation in late AS (13), this association may be more evident in patients with longstanding AS, due to the increase of comorbidities with aging.

Our study also revealed an association between female sex and worse function in patients with PsA. This finding is in agreement with previous reports that showed an association of female sex with worse function and quality of life (14). In patients with AS, we identified an association between female sex and worse function, but the association was not confirmed on the adjusted multivariate model. The impact of sex on function is still unclear in patients with AS, with some cross-sectional studies reporting worse function among women with AS, whereas a prospective study did not identify sex differences in disease activity or physical function over time in AS (15). In our study, although the bivariate analysis showed worse function in women with AS, worse function was not confirmed by the multivariate model.

The association between higher education level and lower reported disability identified in our patients with PsA has already been reported in patients with SpA (11). The fact that the education level can influence the way in which the patients handle, or report, their disease process cannot be dismissed.

Finally, other well-recognized factors with an impact on physical function, such as age, disease activity, and radiographic damage in patients with AS (3), as well as disease duration and disease activity in patients with PsA (4), were also associated with

worse function in our study. Likewise, the association between the use of biologics in AS, and the use of NSAIDs, glucocorticoids, and biologics in PsA, with worse physical function, would probably indicate more severe disease.

Among the strengths of our study, we highlight the large nationwide sample of patients from daily clinical practice that, unlike patients included in clinical trials, had different levels of comorbidity and disability. Thus, the results are representative of Spanish patients with SpA (AS and PsA) attending rheumatology outpatient clinics.

Nevertheless, this study has several limitations. First, it had a cross-sectional nature, which precludes causal inferences. Second, we used a proxy of the CCI. However, we judged this proxy as a useful estimate of the comorbidity burden in our cohort, because the information collected was not complete to apply the original CCI. Since there is no standard comorbidity index currently used in rheumatology research, variations of the CCI are used because they have been extensively validated throughout different medical and research contexts. However, the CCI was primarily developed to predict mortality and not functional disability. Furthermore, our proxy was not able to overcome the fact that the CCI does not include osteoporosis or depression, highly prevalent comorbidities in patients with AS and PsA that may also be relevant to physical disability. Third, although definitions for radiographic damage in both diseases were used in the CARMA study protocol, quantification of radiographic damage by using validated scores was not performed. This fact may explain the lack of association between function and radiographic damage in patients with PsA. Nevertheless, since several studies have shown a close relationship between radiographic progression and disease duration, the multivariate models performed in our study were also adjusted for the effects of disease duration.

In conclusion, as shown in our large series of patients with SpA who were followed up at outpatient rheumatology units, the presence of comorbidities may decrease the reported physical function of patients with SpA. In this setting, a high prevalence of comorbidities has been shown. More importantly, as the comorbidity burden increases, the reported physical function of the patients with PsA decreases. The detection and control of the comorbidities may yield an integral management of the disease.

AUTHOR CONTRIBUTIONS

All authors were involved in drafting the article or revising it critically for important intellectual content, and all authors approved the final version to be submitted for publication. Dr. González-Gay had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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ROLE OF THE STUDY SPONSOR

AbbVie, Spain had no role in the study design or in the collection, analysis, or interpretation of the data, the writing of the manuscript, or the decision to submit the manuscript for publication. Publication of this article was not contingent upon approval by AbbVie, Spain.

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