ORIGINAL ARTICLE

Cognitive Impairment in Patients with Ankylosing Spondylitis

Bruno Kusznir Vitturi, Enrico Stefano Suriano, Ana Beatriz Pereira de Sousa, Dawton Yukito Torigoe

ABSTRACT ***Background:*** Little is known about the potential systemic effects of ankylosing spondylitis (AS) on the nervous system. We designed a study aiming to assess the frequency and clinical predictors of cognitive impairment in AS patients. ***Methods:*** We carried out a cross-sectional case–control study composed of consecutive patients with AS. Trained and blinded interviewers registered clinical-epidemiological data and applied a standardized neurological assessment for each subject of the study. At baseline, functional limitations were characterized using the Health Assessment Questionnaire. Cognitive impairment was evaluated with the Brief Cognitive Screening Battery, the Montreal Cognitive Assessment, and the Clinical Dementia Rating, while neuropsychiatric symptoms were investigated with the Hospital Anxiety and Depression Scale. Healthy controls were matched for age, educational attainment, sex, and comorbidities. We compared the neurological outcomes between case and controls, and we determined the clinical predictors of cognitive decline. ***Results:*** We included 40 patients (mean: 49.3 years) with AS and 40 healthy controls (mean: 48.8 years) in our study. In Brief Cognitive Screening Battery, patients with AS presented a statistically significant poor performance in the clock drawing test and in the verbal fluency. The mean Montreal Cognitive Assessment (MoCA) scores were significantly lower in AS subjects compared to the control group. Also, the prevalence of subjects classified as cognitively impaired according to MoCA was significantly higher in the AS group (90.0% vs. 57.5%, $p = 0.02$). Moreover, neuropsychiatric symptoms were more prevalent in AS patients. Worse functional limitations were associated with poor cognitive performance as well. ***Conclusions:*** Patients with AS might be more vulnerable to cognitive decline.

RÉSUMÉ : Troubles cognitifs chez des patients atteints de spondylarthrite ankylosante. ***Contexte*** **:** On sait peu de choses au sujet des potentiels effets systémiques de la spondylarthrite ankylosante (SA) sur le système nerveux. Nous avons ainsi conçu une étude dont l'objectif était d'évaluer la fréquence et les prédicteurs cliniques des troubles cognitifs de patients atteints de SA. ***Méthodes*** **:** Notre étude transversale cas-témoins a inclus un certain nombre de patients qui ont été vus consécutivement. Préalablement formés, des intervieweurs en double insu ont tout d'abord compilé des données cliniques et épidémiologiques et ont ensuite soumis chaque patient à une évaluation neurologique standardisée. Au départ, leurs limitations fonctionnelles ont été décrites au moyen du *Health Assessment Questionnaire* (HAQ) ; leurs déficiences cognitives, elles, ont été évaluées au moyen de trois outils différents : le *Brief Cognitive Screening Battery* (BCSB), l'Évaluation cognitive de Montréal ou MoCA et le *Clinical Dementia Rating* ; enfin, leurs symptômes de nature neuropsychiatrique ont été analysés à l'aide de la *Hospital Anxiety and Depression Scale*. Quant aux témoins en santé, ils ont été appariés en fonction de leur âge, de leur niveau d'instruction, de leur sexe et de la présence de comorbidités. Nous avons enfin comparé entre eux les résultats neurologiques de nos patients et de nos témoins et établi les prédicteurs cliniques du déclin cognitif. ***Résultats*** **:** Nous avons inclus dans cette étude 40 patients atteints de SA (âge moyen : 49,3 ans) ainsi que 40 témoins en santé (âge moyen : 48,8 ans). Dans le cas du BCSB, les patients atteints de SA ont donné à voir de faibles résultats, significatifs sur le plan statistique, au test de l'horloge (*clock drawing test*) et en matière d'aisance verbale. Les scores moyens au MoCA des patients atteints de SA se sont aussi révélés notablement plus faibles en comparaison avec ceux des témoins. Mentionnons aussi que la prévalence, selon le MoCA, de troubles cognitifs était nettement plus élevée chez les patients atteints de SA (90,0 % contre 57,5 % ; $p = 0,02$). Enfin, des symptômes neuropsychiatriques se sont avérés plus fréquents chez ces patients tandis que des limitations fonctionnelles plus graves ont été associées à de faibles résultats sur le plan cognitif. ***Conclusions*** **:** En définitive, il semblerait que les patients atteints de SA sont peut-être plus vulnérables à un déclin cognitif.

Keywords: Ankylosing spondylitis, Neurological manifestations, Dementia, Rheumatic diseases, Cognitive impairment

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Introduction

Ankylosing spondylitis (AS) is a chronic, progressive inflammatory disease that classically affects the axial skeleton, especially vertebrae and sacroiliac joints.[1] Extra-articular manifestations vary in terms of frequency and severity.[2] The most common extra-articular manifestations are represented by uveitis, bowel disease, heart, lung, skin, bone, and kidney involvement.[3] Overall, the prevalence of AS is around 1%,[4] and its incidence is around 20 per 10,000 people per year in studies from different countries.[5]

Neurological impairment is not usually observed in AS. However, it is increasingly recognized that autoimmune rheumatological diseases can be accompanied by cognitive dysfunction, with demographic factors, medical comorbidities, and medical treatment acting as potential risk factors.[6,7] One hypothesis for dementia in AS is the neurodegeneration caused by systemic inflammation.[8] Long-term or high-dose treatments with anti-inflammatory drugs are commonly used in rheumatic diseases and may decrease the volume of the hippocampus, causing cognitive impairment as well.[9] Neuropsychiatric involvement has been suggested to be important in AS patients as well.[10] Besides, recent experimental studies found altered regional activity and neural networks between the brains of patients with AS and healthy controls.[11]

Little is known about the potential systemic effects of AS on the nervous system. Nevertheless, cognitive manifestations might be underestimated or even unknown in AS. In parallel, in 2012, the World Health Organization announced that dementia is one of the highest priority public health issues globally.[12] This study aimed to assess the frequency and clinical predictors of cognitive impairment in AS patients.

Methods

Study Design and Subjects

We carried out a cross-sectional case–control study composed of consecutive patients with AS who were under regular clinical follow-up in the Rheumatology Unit of a university-affiliated, tertiary referral hospital between January 2016 and December 2018. Patients were considered eligible for the study if they aged 18 years or older and had been diagnosed with AS. The diagnosis of AS was made based on the American College of Rheumatology diagnostic criteria.[13] Patients diagnosed with dementia before AS were excluded from this study. Participants completed questionnaires and cognitive testing on the day of enrollment. Volunteers from the control group were randomly selected from the healthy patient population enrolled in our hospital. No patient with any previous rheumatologic or neurological disease was included. Information regarding patients with AS were ranked in order to recruit the individual from the control group. It was matched at a 1:1 ratio according to a propensity score that considered age, sex, comorbidities, and level of education. Examiners who applied the cognitive tests with controls were blinded to data from patients with AS. All participants provided written informed consent before inclusion, and the research protocol was approved by our local ethics committee.

Baseline Measures and Comorbidities

Trained interviewers conducted structured and standardized in-person assessment interviews with questionnaires that captured socio-demographic and clinical characteristics including sex, date of birth, total years of formal education, comorbidities (e.g. hypertension, diabetes, hyperlipidemia, and smoking status), and use of medications. The previous diagnosis of a neurological or psychiatric disorder was also investigated. We obtained information on disease's characteristics such as disease duration, disease-related symptoms, and use of oral glucocorticoids, disease-modifying antirheumatic drugs and tumor necrosis factor inhibiting biological therapy. Disease activity was assessed using the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI)[14] and The Ankylosing Spondylitis Disease Activity Score (ASDAS-CRP/ASDAS-ESR).[15] BASDAI measures the severity of fatigue, spinal and peripheral joint pain, localized tenderness, and morning stiffness (both qualitative and quantitative). Additionally, ASDAS considers the values of CRP and ESR. Both scores are well validated in clinical practice, and they show good discriminative ability and high discriminatory assessment of AS disease activity. Functional limitations were assessed using the Health Assessment Questionnaire (HAQ), one of the most widely used measures of functioning in RA research. The HAQ includes 20 items covering physical actions in 8 domains: dressing and grooming, arising, eating, walking, personal hygiene, reaching, gripping, and outdoor activities. HAQ scores range from 0 to 3 with higher scores reflecting greater functional limitations.[16]

Outcomes

Neurological status was assessed by structured face-to-face tests performed by experienced physicians blinded to each subject's clinical status. The severity of current symptoms of depression and anxiety was determined via the Hospital Anxiety and Depression Scale (HADS), a 14-item questionnaire that assesses symptoms of depression (HADS-D) and anxiety (HADS-A). Total scores range from 0 to 21 on each scale.[17] The HADS has already been validated for use in AS and the general population.[18] While scores $\geq$ 11 indicated probable anxiety or depression, the specificity of the HADS-A and HADS-D is high (>90%) in AS at this threshold.

The cognitive assessment included Brief Cognitive Screening Battery (BCSB)[19] and the Montreal Cognitive Assessment (MoCA).[20] BCSB and MoCA are useful screening tools for global cognition that have already demonstrated its validity for detecting cognitive impairment and dementia. Both scores were translated and adapted for use in Brazil, and they presented good internal consistency, test–retest reliability, and content validity. Using the conventional validated cut points, subjects were classified as "impaired" or "unimpaired". The performance of each cognitive domain was registered as well.

The BCSB is a tool for assessing cognitive mental status which can be administered in less than 10 minutes by following simple instructions.[21] It evaluates visual perception (0–10 points for identification of 10 figures and 0–10 points for their nomination, where no mistakes are expected in healthy individuals), incidental memory (0–10 points), immediate memory (0–10 points, where < 5 points may indicate attention impairment), verbal fluency (where literate individuals are expected to list > 12 animal names, while illiterate unimpaired individuals are expected to list > 8), clock drawing (0–10 points), late memory (0–10 points, where healthy individuals are expected to score 5 > points), and

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recognition (0–10 points, where < 9 points is considered abnormal). The MoCA is a 30-point test administered in 10–15 minutes, and through 10 subtests it can evaluate visuospatial/executive skills (0–5 points), naming (0–3 points), attention (0–6 point), language (0–3 points), abstraction (0–2 points), delayed recall (0–5 points), and orientation to time and place (0–6 points). Cognitive impairment was defined by a MoCA score < 26, a cutoff previously validated in the general population. To control for educational status, we added 1 point to the MoCA score in patients with < 12 years of education.[20]

Furthermore, the Clinical Dementia Rating (CDR) test was used to assess cognitive impairment and dementia. CDR is a global rating device that was found to distinguish unambiguously and with good reliability among subjects with a wide range of cognitive functions.[22] It has been translated, adapted, and validated for use in Brazil.[23] CDR evaluates cognition and behavior, as well as the influence of cognitive losses in the subject's ability to perform adequately daily activities. It is divided into six cognitive-behavioral categories: memory, orientation, judgment or problem solving, community affairs, home and hobbies, and personal care. Each of these categories should be classified in: 0 (no impairment), 0.5 (questionable), 1 (mild dementia), 2 (moderate dementia), or 3 (severe dementia) – except for the category "personal care", for which the 0.5 level does not exist. Memory is considered the primary category, and all others are secondary. The global CDR is the sum of the scores of the six categories. Dementia was diagnosed according to DSM-IV criteria, with memory impairment defined by scores below the 95% confidence interval of healthy controls' performance in the delayed recall sections of both the MoCA and the BCSB, in conjunction with altered scores in at least one additional cognitive test and functional impairment.

Statistical Analysis

Categorical variables were analyzed using the chi-square test or Fisher's exact test, and differences in continuous variables were assessed using the student's *t*-test (parametric test) or the Mann–Whitney test (non-parametric test). Confounding variables included age, educational attainment, cardiovascular risk, smoking, alcohol abuse, and other comorbidities. Multivariate logistic regression and linear regression were also used to identify potential predictors of cognitive impairment and included variables that have been linked with cognitive impairment in previous studies. The limit for significance was set at two-tailed $p = 0.05$. All analyses were conducted using SPSS, version 23.0.

Results

We included 40 patients with AS and 40 healthy controls in our study. Both groups were homogeneous regarding age, educational attainment, sex, and comorbidities. All patients were under regular treatment for AS. No patients received any opioids or neurological drugs for pain management (e.g. antiepileptic drugs). Demographic and clinical characteristics are summarized in Table 1.

Among the BCSB variables, we found significant differences between AS patients and controls in clock drawing and verbal fluency ($p < 0.05$) (Table 2). The mean MoCA scores were significantly lower in AS subjects compared to the control group ($p < 0.05$). Detailed analysis of MoCA revealed that there was a statistical difference between cases and controls in almost all cognitive domains, except for nomination, orientation, and delayed recall. In the individual analysis, there were 36 (90.0%) patients classified as cognitively impaired according to MoCA compared to only 23 (57.5%) healthy controls ($p = 0.02$). One patient (age: 60 years; sex: female) met the diagnostic criteria for dementia. The mean HAD score was significantly higher in AS subjects ($p = 0.003$). Moreover, compared with controls, patients with AS were more likely to present an impaired HAD score (32.5% vs 10.0%, $p = 0.02$).

The mean CDR was significantly higher in AS patients (1.3 ± 1.0) compared to controls (0.4 ± 0.6) ($p < 0.001$). The distribution of study participants according to the CDR demonstrates a higher propensity for AS patients to be classified with pronounced cognitive decline (Figure 1). On multivariable logistic regression, there was no statistically significant clinical predictor identified (Table 3). Also, there was no correlation between cognitive impairment and BASDAI and ASDAS scores (Table 4). On the other hand, on linear regression, HAQ was correlated with MoCA ($r = -0.42$; $p = 0.006$) and HAD score ($r = 0.31$; $p = 0.05$).

Table 1: Demographics and clinical characteristics of AS patients and healthy controls at baseline

	AS patients ($n = 40$)	Controls ($n = 40$)	*p*-Value
Age	49.3 (SD 15.2)	48.8 (SD 15.4)	0.9
Female	19 (47.5%)	18 (45.0%)	1.0
Educational attainment			
≤ 4 schooling years	12 (30.0%)	9 (22.5%)	0.61
4–8 schooling years	1 (2.5%)	4 (10.0%)	0.35
9–12 schooling years	18 (45.0%)	12 (30.0%)	0.24
≥12 schooling years	19 (22.5%)	15 (37.5%)	0.22
Hypertension	16 (40.0%)	6 (15.0%)	0.02
Diabetes	3 (7.5%)	2 (5.0%)	1.0
Smoking	3 (7.5%)	1 (8.6%)	0.6
Alcohol	0 (0.0%)	1 (2.5%)	0.5
Dyslipidemia	4 (10.0%)	4 (10%)	1.0
Time since diagnose	13.2 (SD 10.2)		
First symptom age	34.3 (SD 12.7)		
Oral glucocorticoid use	9 (22.5%)		
Biological therapy	16 (40.0%)		
Immunosuppressors	14 (35.0%)		
Sulfasalazine	20 (50.0%)		
NSAID	14 (35.0%)		
Antidepressive	5 (12.5%)		
HAQ	1.0 (SD 0.6)		
BASDAI	1.2 (SD 1.5)		
ASDAS CRP	1.7 (SD 0.9)		
ASDAS ESR	1.9 (SD 0.9)		

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Table 2: Comparison of BCSB variables, MoCA, and HAD scores between AS patients and healthy controls. Data are expressed in means (standard deviation)

	AS Patients	Controls	*p*-Value
BCSB			
Visual percepetion	19.2 (3.2)	19.3 (3.2)	0.88
Incidental memory	5.5 (1.5)	5.8 (2.0)	0.44
Immediate memory	7.5 (2.0)	7.9 (1.8)	0.37
Delayed recall test	6.6 (2.1)	6.9 (2.1)	0.39
Clock drawing	6.3 (2.9)	8.1 (2.4)	0.005
Verbal fluency	16.3 (6.4)	19.5 (7.0)	0.03
Recognition	9.0 (3.5)	9.1 (2.7)	0.86
MoCA	19.0 (6.4)	22.9 (5.3)	0.004
Visuo-spacial	2.6 (1.7)	3.8 (1.4)	0.001
Nomination	2.5 (0.8)	2.8 (0.5)	0.07
Attention	3.2 (1.9)	4.2 (1.5)	0.008
Language	1.6 (1.05)	2.0 (0.9)	0.05
Abstraction	1.2 (0.8)	1.6 (0.6)	0.02
Delayed recall	2.2 (1.9)	2.6 (1.6)	0.26
Orientation	5.6 (1.1)	5.7 (1.0)	0.70
HADS	12.9 (9.4)	7.3 (6.9)	0.003

Discussion

We suggest that patients with AS might be vulnerable to cognitive decline and dementia. The only previous similar evidence that refers to a recent nationwide cohort study found that the prevalence of dementia in the AS group was significantly higher than those of the control group.[24] Also, cerebral functional deficits in patients with AS have already been observed in fMRI.[11]

There are several possible explanations for cognitive impairment in patients with AS. Over the last decade, the presence of sustained immune response in the brain has emerged as a core pathology in dementia.[25] Systemic inflammation during midlife, whose example is exactly AS, was recognized as an early risk factor for cognitive decline.[26] In another study, a subjective cognitive complaint was reported in a quarter of AS patients.[27] Furthermore, many previous studies demonstrated that patients with autoimmune rheumatic diseases are more likely to develop dementia.[28] Currently, there is a growing literature demonstrating the relationship of multimorbidity and dementia as well.[29]

Another explanation comes from the extracellular deposit of amyloid, which besides being known as one of the abnormalities observed in Alzheimer's Disease,[30] is also implicated in AS patients showing an increased level of serum amyloid.[31] Social and physical activity are severely affected by AS.[32] Disturbed sleep is a common finding of the disease as well.[33] These are all comorbidities known to have a significant effect on cognitive ability.[34,35] Patients with AS also present an increased cerebrovascular risk,[36] which is a known cause of vascular dementia. Furthermore, common medications used for AS treatment may be involved in the pathogenesis of cognitive impairment. Glucocorticoid therapy has already been associated with an immediate impact on memory and a possible cumulative influence on hippocampal function.[37] In contrast, other studies suggest the potential benefits of anti-TNF-α therapies to prevent or slow the progression of Alzheimer's Disease.[38]

Patients with AS were more likely to present neuropsychiatric symptoms. This finding is in line with previous studies that found a risk to mood disorders 2–3 times higher whether AS is diagnosed.[39] Furthermore, neuropsychiatric disorders are commonly related to dementia. The prevalence of depression in dementia has been reported to be between 9 and 68%. Depression has been both proposed to be a risk factor for dementia as well as a prodrome of dementia.[40]

Functional limitations were associated with worse neurological outcomes in our study. This finding indicates that either intense disease activity or chronic sequelae of AS can explain worse performance on the neurological assessment. Previously, functional limitations have already been linked with cognitive function in rheumatic diseases.[7] Apart from HAQ, we did not identify any other predictor of cognitive decline, despite evaluating a wide range of variables. This fact may perhaps be better

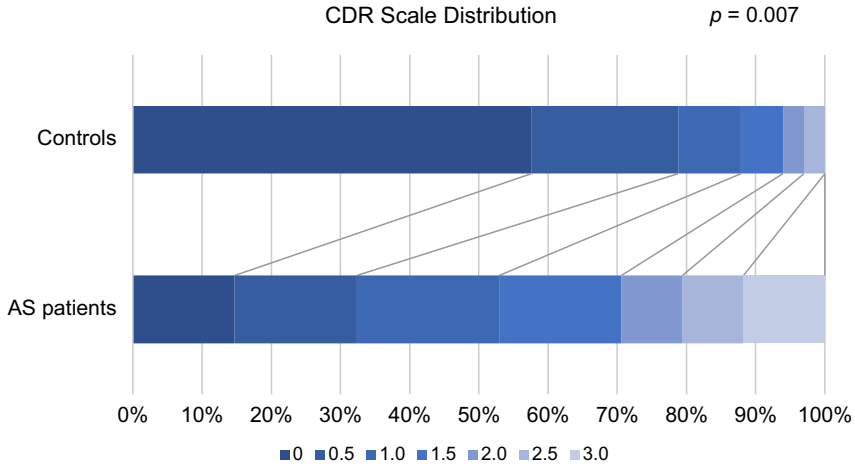

Figure 1: *Distribution of patients and controls according to CDR values.*

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Table 3: Multivariate analysis of possible clinical predictors of neurological impairment in patients with AS according to the MoCA and HADS

	MoCA			HAD		
	Impaired	Non-impaired	OR (95% CI)	Impaired	Non-impaired	OR (95% CI)
N	36 (100.0%)	4 (100.0%)		13 (100.0%)	27 (100.0%)	
Female sex	16 (44.4%)	3 (75.0%)	0.3 (0.02–2.8)	5 (38.5%)	14 (51.8%)	0.6 (0.1–2.2)
<8 schooling years	13 (36.1%)	0 (0.0%)	*	3 (23.1%)	10 (37.0%)	0.6 (0.1–2.3)
Hypertension	14 (38.9%)	2 (50.0%)	0.6 (0.08–5.0)	4 (30.8%)	12 (44.4%)	0.5 (0.1–2.2)
Diabetes	3 (8.3%)	0 (0.0%)	*	3 (23.1%)	0 (0.0%)	*
Smoking	3 (8.3%)	0 (0.0%)	*	1 (7.7%)	2 (7.4%)	1.0 (0.08–12.6)
Dyslipidemia	4 (11.1%)	0 (0.0%)	*	1 (7.7%)	3 (11.1%)	0.6 (0.06–7.1)
Oral glucocorticoid use	7 (19.4%)	2 (50.0%)	0.2 (0.02–2.0)	4 (30.8%)	5 (18.5%)	1.9 (0.4–9.0)
Biological therapy	15 (41.7%)	1 (25.0%)	2.1 (0.2–22.6)	6 (46.1%)	10 (37.0%)	1.4 (0.4–5.6)
Immunosuppressor	4 (11.1%)	2 (50.0%)	0.1 (0.01–1.1)	4 (30.8%)	2 (7.4%)	5.5 (0.9–35.7)
Sulfasalazine	17 (47.2%)	3 (75.0%)	0.3 (0.02–3.1)	6 (46.1%)	14 (51.8%)	0.8 (0.2–3.0)
NSAIDS	91 (44.4%)	2 (40.0%)	1.7 (0.2–18.0)	4 (30.8%)	10 (37.0%)	0.7 (0.2–3.1)

*Impossible to calculate the OR due to prevalence of 0% or 100%.

Table 4: Comparison of disease characteristics and neurological outcomes on multivariate logistic regression. Data are expressed in mean and standard deviation (SD)

	MoCA			HAD		
	Impaired	Non-impaired	*p*-Value	Impaired	Non-impaired	*p*-Value
N	36	4		13	27	
Age, years (SD)	51.6 (12.6)	43.0 (15.3)	0.2	50.0 (14.1)	51.0 (12.6)	0.8
Time of diagnose, years (SD)	13.4 (10.3)	12.5 (9.8)	0.9	34.8 (12.1)	35.2 (11.3)	0.9
First symptom age, years (SD)	35.6 (11.8)	30.8 (8.1)	0.4	14.6 (12.8)	12.6 (8.6)	0.55
ASDAS ESR	2.1 (0.7)	1.8 (1.1)	0.4	1.9 (0.5)	1.9 (1.0)	1.0
ASDAS CRP	1.7 (0.9)	1.5 (0.9)	0.7	1.3 (0.3)	1.9 (1.1)	0.06
BASDAI	1.2 (1.5)	1.6 (1.5)	0.6	0.8 (1.1)	1.4 (1.6)	0.2
HAQ	0.9 (0.8)	1.0 (0.8)	0.8	1.2 (0.8)	0.9 (0.7)	0.2

evaluated in longitudinal multicenter studies involving a large number of patients. ASDAS and BASDAI may not be sensitive enough to detect neurological manifestations of the disease and suffer acute/subacute variations according to the evolution and treatment of the disease, limiting its use as a marker for dementia in patients with AS. In addition, current data support that the inflammatory disease activity might be less prominent with aging, when dementia risk increases.

The strengths of this study include that our study cohort was prospectively followed up and details could be acquired by a comprehensive review of their medical records, by telephone interviews and by face-to-face assessments with trained neurologists who were blind to patients' clinical characteristics and AS severity. Our work is pioneering in demonstrating AS patients' susceptibility to cognitive decline. Furthermore, this the largest study performed to screen neurological dysfunction in patients with AS. The results of the study are for a matched population, which is a strength of the study as it minimizes potential confounding bias. Moreover, we were able to assess several possible risk factors that could explain cognitive impairment in RA.

The present study has a few limitations. First, because our research is a single-center, hospital-based study, rather than a community-based study, it is unclear to what extent findings can be generalized. Also, possible biases related to our method of patient and controls inclusion are also pertinent. Nevertheless, there are no restrictions to be admitted to our hospital, and we included all consecutive cases admitted. Besides, the single-center design allowed us to collect information systematically and to uniformly verify both the qualifying event as well as follow-up information in all patients, which reduces the risk of information bias. Second, the biases inherent in an observational study are also applicable to our research. Third, this was a cross-sectional study, and therefore, in spite of statistically significant findings regarding the relationship between the variables of interest, the causal pathway to

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cognitive impairment could not be determined. Fourth, we didn't use extensive batteries of neuropsychological tests to assess cognitive impairment. Nevertheless, we intended to evaluate the broadest spectrum of cognitive impairment in AS because even mild levels of impairment can disrupt daily functioning. Moreover, brief screening approaches hold value in that they may rapidly identify those at greatest need for services or facilitate large-scale research to study cognitive compromise in rheumatic diseases. In fact, in clinical practice, screening cognitive tests are commonly the first step in detecting cognitive impairment and in establishing the diagnosis of dementia, especially in the initial investigation of a possible newly discovered cause of dementia, like AS. Fifth, the low education of our population may decrease the sensitivity of MoCA. However, in addition to employing an adjustment for low education that has already been validated in other previous studies, we quantitatively compared the results of MoCA and controls and the education factor was included in the multivariate analysis. Anyway, we emphasize the need for future studies to define the best form of neurological investigation of patients with rheumatologic diseases, something that does not exist in the literature today. Finally, there may have been some degree of overlap between the CDR and the HAQ. However, each questionnaire has been developed and extensively validated for specific purposes, so that your questions are much more sensitive to their original purpose. Moreover, in our research, the application of these instruments was done at different times by blinded examiners. However, every test has disadvantages, and there is still no recommendation or specific tool for the cognitive assessment of patients with rheumatic diseases.

Conclusions

Patients with AS are more vulnerable to cognitive decline. Our findings enhance the understanding of the total burden for AS patients and may contribute to improved health assessment and treatment planning. Considering the severity of dementia, finding a high-risk group of vulnerable subjects based on various risk factors is a fundamental task in the prevention of disease in AS patients. Further longitudinal studies dedicated to diagnosing dementia in AS patients are encouraged.

Conflict of Interest

The authors have no conflicts of interest to declare.

Statement of Authorship

BKV designed the study, collected data, coordinated the study, performed the statistical analysis, interpreted the data, drafted the initial manuscript, reviewed and revised the manuscript. ESS and ABPDS collected data, identified patients for inclusion and drafted the initial manuscript. DYT supervised the study and reviewed and revised the manuscript.

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