Ref: Ro J Rheumatol. 2021;30(4)
DOI: 10.37897/RJR.2021.4.4

Managing comorbidities in spondyloarthritis patients – to what extent do rheumatologists carry the burden?

Claudia Cobilinschi[1,2], Cristian Cobilinschi[2,3], Alexandra Constantinescu[1], Adel Abu Abid[2], Ruxandra Ionescu[1,2], Daniela Opris-Belinski[1,2]

[1]Rheumatology and Internal Medicine Department, "Sf. Maria" Clinical Hospital, Bucharest, Romania
[2]"Carol Davila" University of Medicine and Pharmacy, Bucharest, Romania
[3]Intensive Care Unit, Clinical Emergency Hospital, Bucharest, Romania

ABSTRACT

Objective. The spondyloarthritis group comprises chronic inflammatory conditions that share clinical, genetic and radiographic features. The impact of comorbidities on disease activity is not entirely known. The aim of this study is to identify the frequency and management of comorbidities in SpA patients.

Materials and methods. A six-month retrospective study included 235 SpA patients for whom demographic, disease data and associated comorbidities were collected, according to EULAR's designated categories. Statistical analysis was performed using Microsoft Excel.

Results. 71% were males, with a mean age of 42.3, suffering from SpA for more than 15 years. 60% patients were overweight or obese, 25% had been diagnosed with hypertension, 28% were smokers. 18% suffered from dyslipidemia and 9% had type II diabetes. 16% had hepatitis B while 2% had C viral infection, 14% had previous mild to moderate urinary or pulmonary infections. Osteoporosis was confirmed in 6% and malignancies in 2.5% cases.

Conclusions. The most frequently encountered comorbidities were cardio-vascular events, followed by gastro-intestinal disorders. SpA patients require early comorbidity detection with the aid of their rheumatologist and a multidisciplinary care to avoid additional disease burden.

Keywords: COVID-19, rehabilitation therapy, psoriatic arthritis, psoriasis

INTRODUCTION

The term "spondyloarthritis" (SpA) refers to a group of inflammatory diseases with overlapping clinical and imaging features and pathogenic mechanisms but with differences in clinical outcome or response to treatment (1). Although pathogenesis is still not fully understood, SpA is considered to be induced mainly by genetic and environmental triggers (2).

The management of SpA patients represented a real challenge for rheumatologists in times where only non-steroidal drugs and physical therapy were available. The outcome of SpA patients was substantially influenced by the approval of biological therapies which are capable of producing a rapid and significant clinical improvement together with a reduction of the inflammatory process (3). Treatment should be individualized according to each patient's manifestations of the disease, articular and extraarticular symptoms, imaging results and comorbidities (4).

Apart from extra-articular manifestations, SpA patients may also suffer from other different entities referred to as "comorbidities", which may have existed or may occur during the disease course (5). These associated conditions worsen the SpA outcome by contributing to disease activity, physical disability and morbi-mortality (5) since they can be linked to the high inflammatory status in SpA, treatment-related and they have a different pathogenesis than that of SpA.

Studies have shown an increased association of comorbidities in patients with SpA than the non-

Corresponding author:
Cristian Cobilinschi
E-mail: claudia.cobilinschi@umfcd.ro

Article History:
Received: 15 December 2021
Accepted: 23 December 2021

SpA population, diminishing the quality of life in these patients (6). Thus, clinicians should be aware about the screening, the prevention and the treatment of these linked diseases.

The management of comorbidities in SpA can be done at different levels, namely reporting of comorbidities (personal history), screening for comorbidities (screening tools), screening for risk factors of comorbidities, prevention and treatment of comorbidities (7).

Management of comorbidities should be conducted by a specialist in the field but rheumatologists can lead the way in implementing specific recommendations issued by EULAR (8). Thus, comorbidities like CVD, malignancies, infections, osteoporosis, peptic ulcer and depression should be carefully assessed and managed in patients with inflammatory rheumatic diseases. Besides, all clinicians (nurses, rheumatologists) and patients should be involved in the screening and detection of comorbidities through self-administered questionnaires. Comorbidities should be revised periodically, at least every 5 years for patients with chronic inflammatory rheumatic conditions.

The present article aims to evaluate the frequency and management of comorbidities in patients diagnosed with SpA under biological therapy.

MATERIALS AND METHODS

The descriptive, retrospective clinical study reached over a period of six months (September 2020 to March 2021) and included 235 patients diagnosed with SpA in the Internal Medicine and Rheumatology Department of "Sf. Maria" Clinical Hospital.

Demographic (age, gender, disease duration), clinical and laboratory data (inflammatory markers – ESR, CRP) was collected together with the presence of comorbidities using patients' medical records. Disease activity was evaluated with traditional scores like BASDAI (Bath Ankylosing Spondylitis Disease Activity Index) and ASDAS (Ankylosing Spondylitis Disease Activity Score) using the CRP.

The data collection and graphical representations were done using Microsoft Office and Microsoft Excel 2010. The statistical tests used was the Chi square test. Significance of the analysis was expressed as a p value < 0.05.

Approval from the local Ethics' Committee was obtained in order to gather data from patient charts.

RESULTS

Demographic and disease data in the study group

Out of the 235 included patients, 71% were male and 29% were female, with an age distribution illustrated in figure 1.

39% of the patients had elementary education followed by 36% if the patients who had secondary education. 14% of the patients had higher education and 11% had no education.

The figure 2 illustrates the BMI distribution of the patients included in the analysis, indicating more than a half were overweight or obese.

Regarding disease duration, 29% of the patients had been dealing with SpA for 11 to 15 years, 21% for 21-30 years and 14% for a time period between 6 and 10 years. Only 3% of the patients have been dealing with this disease for more than 40 years.

54.9% of patients had axial and peripheral SpA, while 45.1% of the patients had axial SpA. HLA B27 was positive in 84% of the patients.

The presence of enthesitis was noted in 38% of the patients and 15.6% history of dactylitis. Psoriasis was present at only 3% of the patients, either as current or history of psoriasis. Two patients mentioned family history of psoriasis. Anterior uveitis was present at 18% of the patients, either as preceding episode of SpA or after the diagnosis was set. Crohn's disease was present at 3.8% of the patients and ulcerative colitis was present at 2% of the patients.

67% patients had a BASDAI score of under 4, suggesting an inactive disease at the moment of last evaluation which was no later than three months prior. The rest of 33% had BASDAI scores over 4, indicating a degree of disease activity.

The majority of the patients (34%) had their ASDAS-CRP at their last assessment smaller than 1.3, which showed that the disease was inactive, followed by those who had it between 1.3 and ≤ 2.1 (31%), which showed that the disease had a low activity. The rest had high or very high disease activity.

Distribution of patients according to their comorbidities

Cardiovascular disease (hypertension, smoking, ischemic heart disease, dyslipidemia, type 2 diabetes)

Only 25% of the patients had hypertension, but it comes as no surprise since the majority of patients in the study group are of young age and had no prior history of high blood pressure values. No staging of hypertension was possible at the moment of data collection because of variability of information in patient charts.

28% of the patients were smokers.

8% of the patients had ischemic cardiac disease diagnosed by a cardiologist and only 5 patients had documented myocardial infarction. 3.8% had documented atherosclerosis through carotid ultrasound performed during a cardiology check-up. No patient in the study group has registered event of stroke.

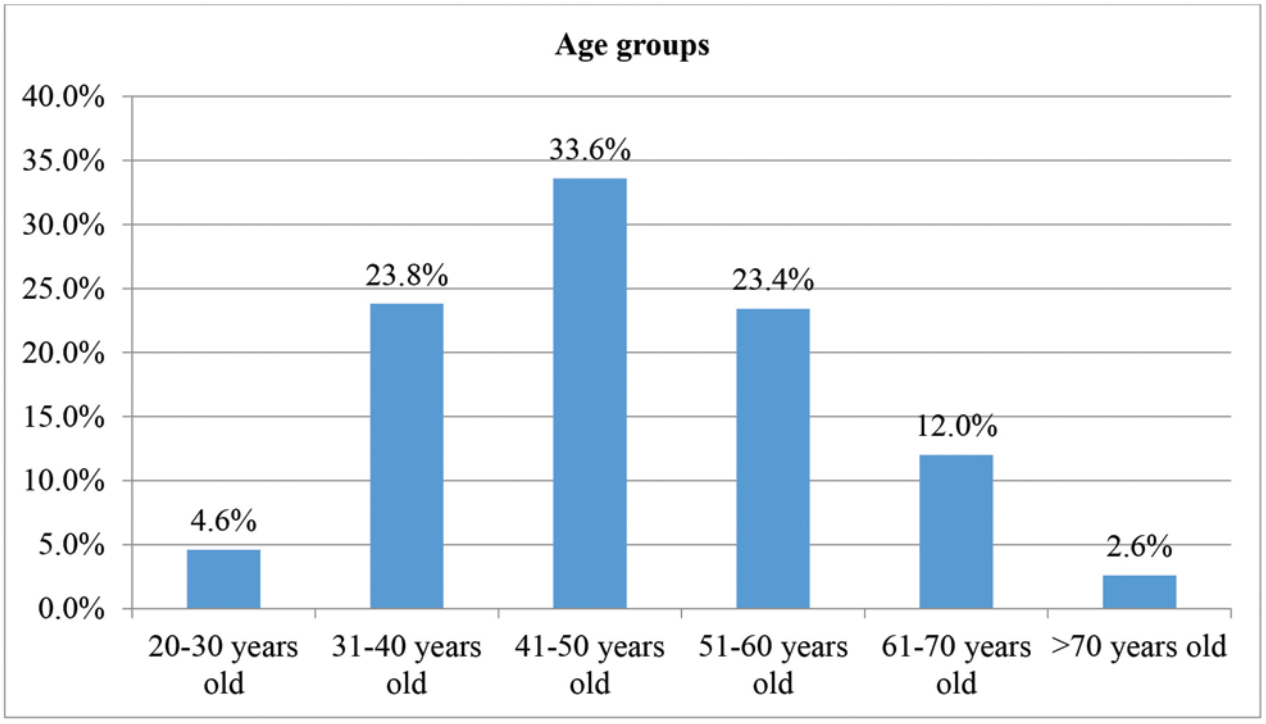

FIGURE 1. Distribution of patients according to age group

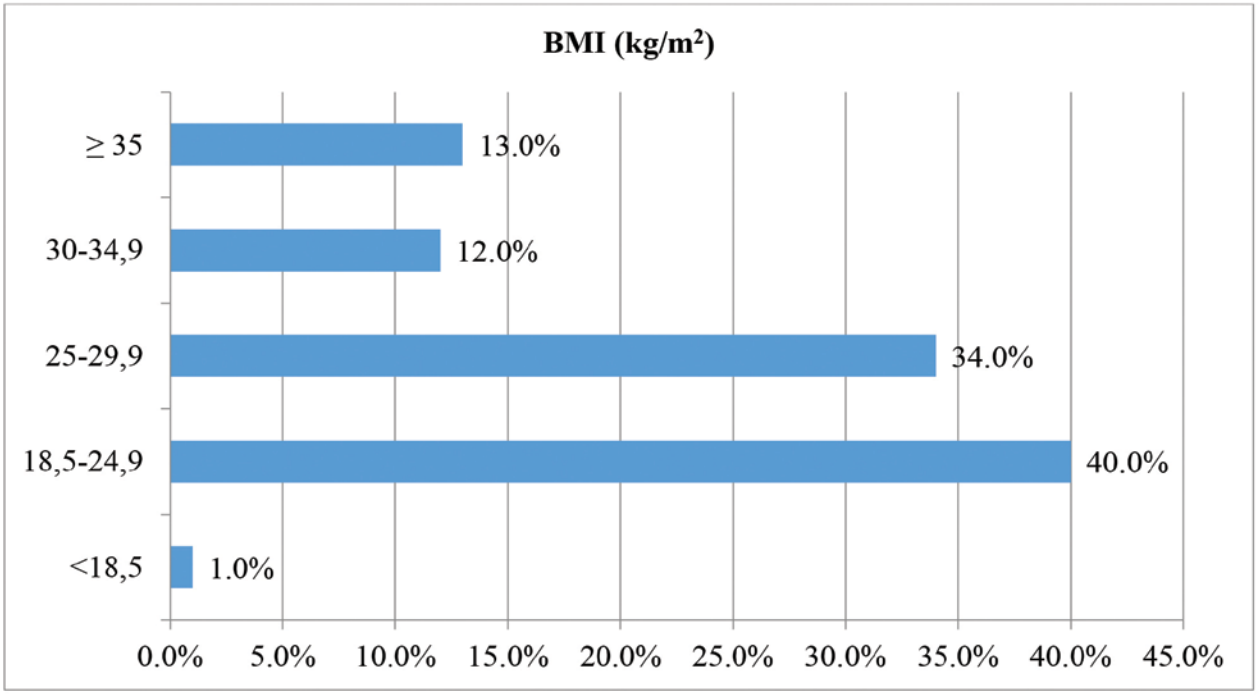

FIGURE 2. Body mass index (kg/m2) distribution in the study group

Dyslipidemia was present in 18% of the patients, with high LDL-cholesterol levels and low HDL-cholesterol values determined at least once in the past two years.

Diabetes mellitus was present at 9% of the patients. All patients had type 2 diabetes and 5.4% suffered from both hypertension and dyslipidemia, suggesting the presence of a metabolic syndrome.

Infections (latent tuberculosis, hepatitis B, C, other infections)

Patients' eligibility for biological therapy was tested at the certain point in disease history and out of the study group, the Quantiferon test was positive in 22% of the patients but no signs of active tuberculosis was noted, thus only chemoprophylaxis was considered necessary.

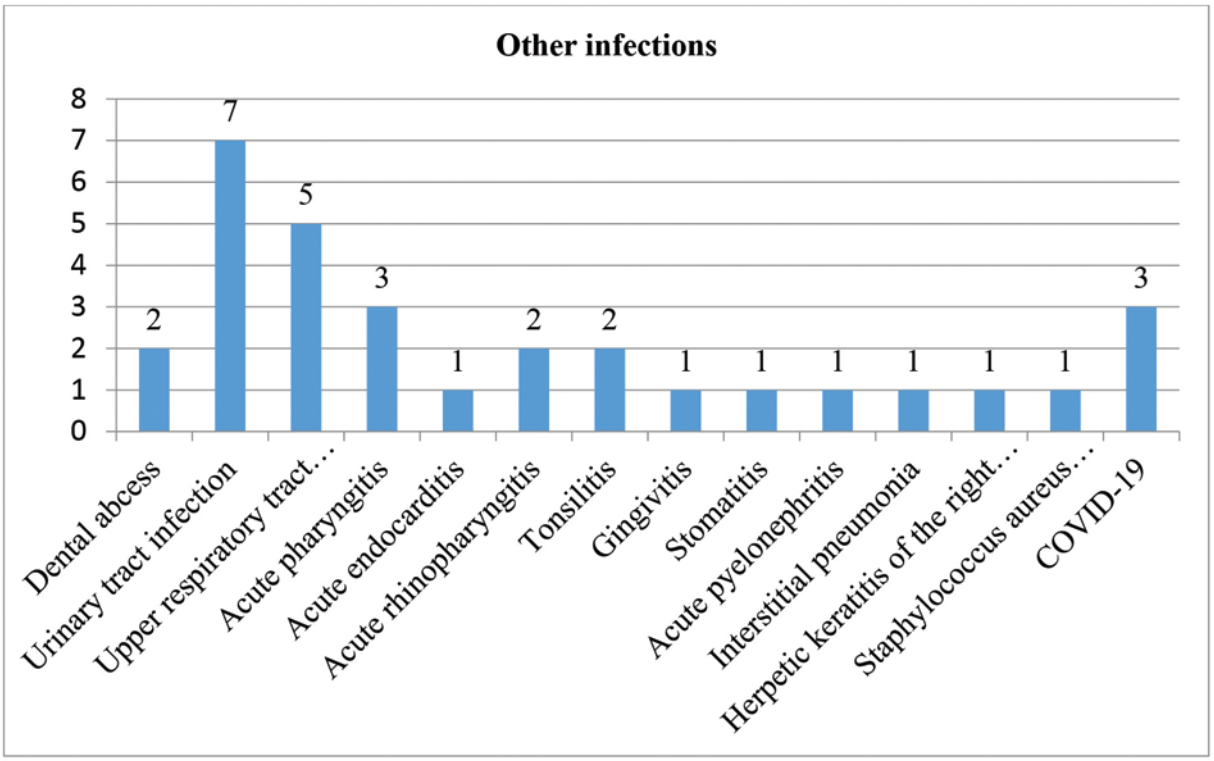

FIGURE 3. Other infections in the study group

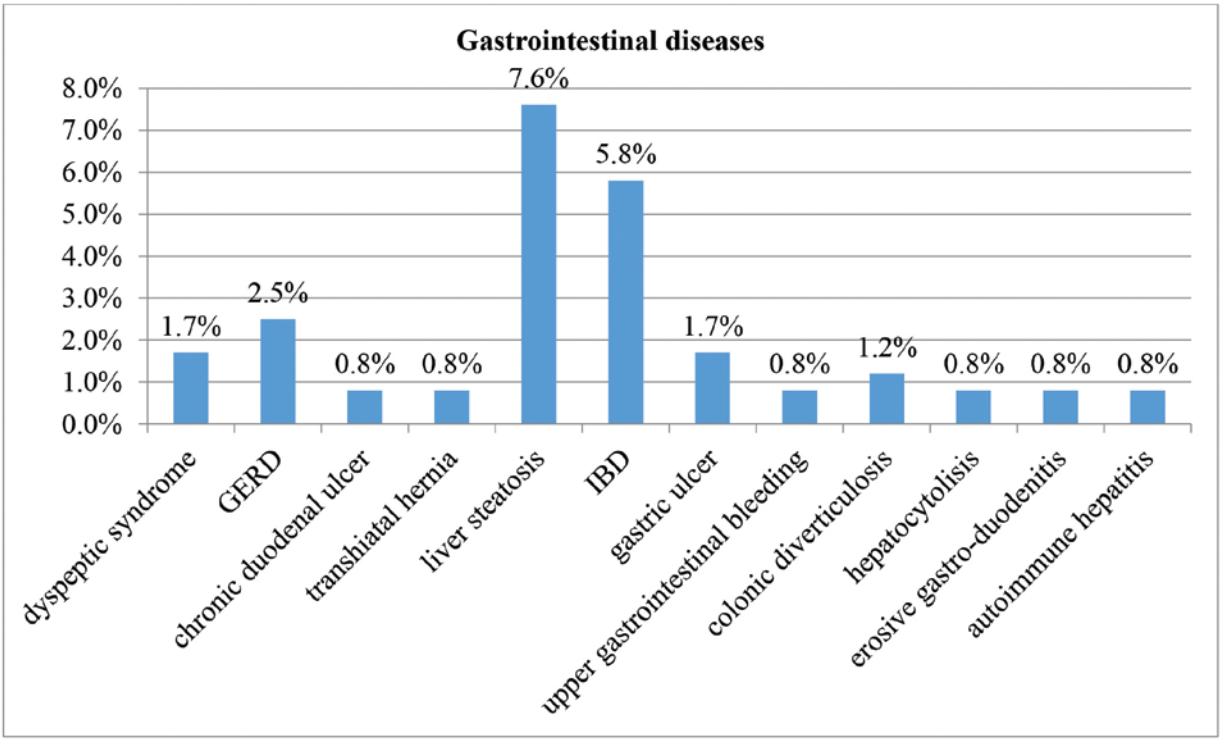

FIGURE 4. Gastrointestinal conditions in the study group

In the study group, 16% of the patients had viral hepatitis B. 15% had inactive hepatitis and 1% of patients had active infection, requiring antiviral therapy. Apparently, no patient suffered from cirrhosis. Only 2% of the patients had evidence of chronic hepatitis C and two patients were assigned to the cirrhotic stage but no specific treatment was mentioned.

Other encountered infections in the study group are briefly illustrated in figure 3.

At the moment of data collection and availability in the clinic, only three patients with SpA were reported as having COVID19, in mild forms. Later on, data gathering confirmed 81 rheumatic patients in the clinic who developed COVID19, out of which 56.7% had SpA with a mean age of 47.5 years old.

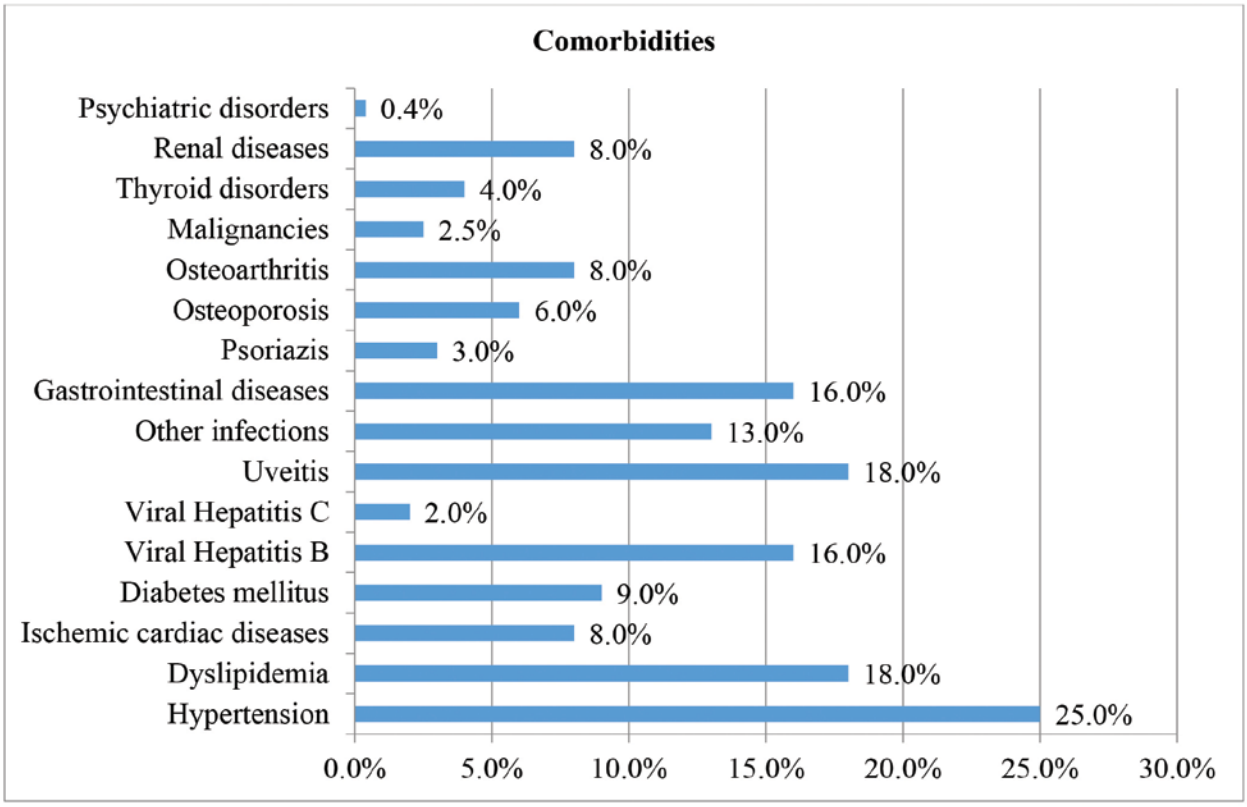

FIGURE 5. Representation of all comorbidities in the study lot

They developed mild and moderate SARS-COV2 infection while their disease was in remission or with low disease activity. The viral infection imposed treatment interruption in 51% of patients, either synthetic DMARDs or biological therapy, according to specialists' opinion.

Gastrointestinal diseases were present at 16% of the patients, including dyspeptic syndrome, gastro-esophageal reflux disease or liver steatosis, as seen in figure 4.

Regarding osteoporosis (OP), 6% of the patients had documented OP with a DXA investigation, having a T score of lower than -2.5SD. Only 2.5% of patients had history of hip or vertebral fractures in the previous 5 years.

8% of the patients had osteoarthritis confirmed through plain X-rays affecting hips, knees or spine. No prosthetic joints were documented for osteoarthritis, except the ones imposed in patients with hip fractures due to osteoporosis.

Malignancies were present at 2.5% of the patients, mentioning one patient with ovarian cancer, two patients with basal-cell carcinoma and one patient with papillary thyroid carcinoma in their medical history. Ovarian cancer, basal-cell epithelioma and papillary thyroid carcinoma were present at an equal percentage of patients, 0.8% each.

Patients suffered from other disorders like renal diseases present at 8% of the patients, mentioning lithiasis, amyloidosis, chronic kidney disease or solitary congenital kidney.

Thyroid disorders were encountered in 4% of the patients, namely autoimmune thyroiditis with hypothyroidism or multinodular goiter. Two patients had hyperthyroidism.

0.4% of the patients had psychiatric disorders like depression or anxiety confirmed by a specialist that required periodic visits (figure 5).

Management of comorbidities in patients with SpA – data from daily practice

Management of comorbidities in patients with SpA might be a difficult task for the clinician because of regular check-ups that are imposed by the main disease, the need for a multidisciplinary team and patients' compliance with treatment schemes and changes in lifestyle.

Using complete medical charts, we were able to gather information on treatment of different comorbidities identified in the study group.

As seen in the table 1, not all patients benefit from adequate comorbidity treatment or data summarization in patients' records is not feasible in daily practice.

No self-filled questionnaires was offered to SpA patients because of the lack of accessibility in the medical facility of both patients and students in the context of COVID-19 pandemic.

DISCUSSION

Treating patients with SpA might be a challenge for rheumatologists, but their task was made easier

TABLE 1. Main comorbidities and their treatment

Comorbidity	Percent diagnosed (%)	Percent treated (%)
Hypertension	25	-
Beta-blockers	-	68
ACE inhibitors	-	82
Angiotensin 1 antagonists	-	21
Diuretic drugs	-	40
Ischemic heart disease	8	-
Low dose aspirin	-	76
Oral anticoagulants	-	21
Dyslipidemia	18	-
Statins	-	59
Fibrates	-	18
Type 2 diabetes mellitus	9	-
Insulin	-	31
Oral hypoglycemics	-	75
Infections (hepatitis B, C)	18	-
Anti-viral treatment	-	10
Gastro-intestinal disorders	16	-
Proton-pump inhibitors	-	84
H2 blockers	-	13
Osteoporosis	6	-
Anti-osteoporotic treatment	-	34
Psychiatric disorders	0.4	-
Anti-depressants	-	56

by the approval of biological therapies targeting TNF alpha or IL-17 (9). The importance of early disease detection cannot be overstated since the window of opportunity for optimal treatment is in the first years from disease onset (10). Disease progression without adequate therapy leads to ankylosis, invalidity and altered quality of life.

Apart from the individual burden of the disease, SpA patients deal with coexistent disorders that can be linked to the high inflammatory status in SpA or related to treatment and they have a different mechanism of occurrence than that of SpA, so that they need to be differentiated from the concept of clinical features of the rheumatic disease. However, in both SpA and comorbidities, the genetic factor has an important role (6).

Significant data on SpA patients were collected and comorbidities were identified in various percentages in the study lot and classified according to EULAR's designated categories.

However, the percentage of patients that received targeted treatment for associated conditions was less than the number of diagnosed patients, emphasizing the idea of a broader medical approach during SpA patient follow-up and the importance of a multidisciplinary team. Thus, the burden of comorbidities should not impact the rheumatic disease at such a high level.

In order to correctly collect patient data, EULAR has issued recommendations for reporting, screening and preventing comorbidities in inflammatory rheumatic diseases that involves the entire medical staff (rheumatologists, nurses). This initiative was entitled "Points to consider for reporting, screening for and preventing selected comorbidities in chronic inflammatory rheumatic diseases in daily practice" (11).

Regarding patient self-administered questionnaires, a relatively recently published study from a work group in Spain aimed to approach comorbidities in SpA patients from a practical manner. Therefore, a group of clinicians established the most important comorbidities, taking after their frequency and impact and elaborated two checklists, one addressed to the physician and the other to the patient (12).

Another useful tool to assess the presence of comorbidities and their impact on SpA patients is the modified self-administered comorbidity questionnaire (mSCQ), adapted for SpA (SCQ-SpA). Results from the study show that data from patient knowledge is consistent with data from their medical records, apart from digestive conditions and depression that are more often reported by patients (13).

Regarding management of comorbidities in patients with SpA, there are three important axis to follow, namely reporting (comorbidity occurrence), screening for comorbidities or risk factors, prevention strategies like vaccination.

The latter point concerning vaccination is of high importance since vaccination in patients with autoimmune inflammatory rheumatic diseases can prevent a lower frequency of hospitalizations due to infections and highly infectious diseases (14). Despite repeated recommendation issuing, rheumatic patients have an insufficient vaccination scheme and show low rates of vaccination. The vaccination management should be a global effort from patients, general practitioners, rheumatologists and nurses and vaccines should be administered while disease is not active and best planned before initiating immunosuppressive therapy. Non-live vaccines are safe and provide immunity, except when administered while on B-cell depletion therapy (15). The co-existence of different comorbidities might

have several impacts on SpA such as a higher mortality, a greater functional impairment than SpA patients without comorbidities or treatment outcomes (16).

CONCLUSIONS

The issuing of European recommendations by EULAR brings us one step closer to the implementation and distribution, which becomes the hardest part, thus all practitioners should be available and encourage patients on the necessity of filling these points in order to expect better clinical outcomes and avoid unexpected prognosis.

The results of the present study emphasize the importance of early comorbidity detection by rheumatologists and the importance of a multidisciplinary approach when making decisions on patient management. Thus, SpA patients will avoid supplementary disease burden and improve their outcome, facilitating a better lifestyle and work force.

Conflict of interest: none declared
Financial support: none declared

REFERENCES

1. Sieper J, Rudwaleit M, Baraliakos X, Brandt J, Braun J, Burgos-Vargas R, Dougados M, Hermann KG, Landewé R, Maksymowych W, van der Heijde D. The Assessment of SpondyloArthritis international Society (ASAS) handbook: a guide to assess spondyloarthritis. *Ann Rheum Dis.* 2009 Jun;68 Suppl 2:ii1-44.
2. Akgul O, Ozgocmen S. Classification criteria for spondyloarthropathies. *World J Orthop.* 2011 Dec 18;2 (12):107-15.
3. Van Der Heijde D, Ramiro S, Landewé R, Baraliakos X, Van Den Bosch F, Sepriano A, et al. 2016 update of the ASAS-EULAR management recommendations for axial spondyloarthritis. *Ann Rheum Dis.* 2017;76 (6):978-91.
4. Smolen JS, Braun J, Dougados M, Emery P, Fitzgerald O, Helliwell P, et al. Treating spondyloarthritis, including ankylosing spondylitis and psoriatic arthritis, to target: recommendations of an international task force. *Ann Rheum Dis.* 2014 Jan;73(1):6-16.
5. Claudepierre P. Management of spondyloarthritis. *Rev Prat.* 2018;68 (7):740-6.
6. Gökşenoğlu G, Buğdaycı D, Paker N, Yıldırım MA, Etli Ö. The prevalence of comorbidity and predictors in ankylosing spondylitis. *Turkish J Phys Med Rehabil.* 2019;65 (2):132-8.
7. Ljung L, Sundström B, Smeds J, Ketonen M, Forsblad-d'Elia H. Patterns of comorbidity and disease characteristics among patients with ankylosing spondylitis – a cross-sectional study. *Clin Rheumatol.* 2018;37 (3):647-53.
8. Richette P, Doherty M, Pascual E, Barskova V, Becce F, et al. 2016 updated EULAR evidence-based recommendations for the management of gout. *Ann Rheum Dis.* 2017 Jan;76(1):29-42.
9. Cheung PP. Anti-IL17A in Axial Spondyloarthritis-Where Are We At? *Front Med* (Lausanne). 2017 Jan 18;4:1.
10. Robinson PC, Brown MA, Baraliakos X, Haibel H, Listing J, Sieper J, et al. The window of opportunity: a relevant concept for axial spondyloarthritis. *Arthritis Res Ther.* 2014;16(3):109.
11. Baillet A, Gossec L, Carmona L, De Wit M, Van Eijk-Hustings Y, Bertheussen H, et al. Points to consider for reporting, screening for and preventing selected comorbidities in chronic inflammatory rheumatic diseases in daily practice: a EULAR initiative. *Ann Rheum Dis.* 2016 Jun 1;75 (6):965-73.
12. Lindström Egholm C, Krogh NS, Pincus T, Dreyer L, Ellingsen T, Glintborg B, et al. Discordance of Global Assessments by Patient and Physician Is Higher in Female than in Male Patients Regardless of the Physician's Sex: Data on Patients with Rheumatoid Arthritis, Axial Spondyloarthritis, and Psoriatic Arthritis from the DANBIO Registry. *J Rheumatol.* 2015 Oct;42(10):1781-5.
13. Stolwijk C, Essers I, Van Den Bosch F, Dougados M, Etcheto A, Van Der Heijde D, et al. Validation of the self-administered comorbidity questionnaire adjusted for spondyloarthritis: Results from the ASAS-COMOSPA study. *Rheumatol* (United Kingdom). 2020;59 (7):1632-9.
14. Furer V, Rondaan C, Heijstek MW, Agmon-Levin N, Van Assen S, Bijl M, et al. 2019 update of EULAR recommendations for vaccination in adult patients with autoimmune inflammatory rheumatic diseases. *Ann Rheum Dis.* 2020;79(1):39-52.
15. Bijlsma JW. EULAR December 2020 View points on SARS-CoV-2 vaccination in patients with RMDs. *Ann Rheum Dis.* 2021 Feb 9;80(4):411-2.
16. Molto A, Sieper J. Peripheral spondyloarthritis: Concept, diagnosis and treatment. *Best Pract Res Clin Rheumatol.* 2018 Jun;32(3):357-368.