BioSCIENCE Original Article
DOI: https://doi.org/10.55684/2024.82.e00058

Obesity influence in disease activity in ankylosing spondylitis

O impacto da obesidade na atividade da doença em pacientes com espondilite anquilosante

Ana Luiza Shiomi[1], Anna Heloisa Tavares[1], Rebeca Loureiro Rebouças[1], Thelma Larocca Skare[1]

ABSTRACT

Introduction - Ankylosing spondylitis (AS) or radiographic ankylosing spondylitis is an axial spondyloarthritis with a male predominance, whose symptoms include low back pain associated with morning stiffness that can progress to ankylosis. Its inflammatory etiology is associated with structural changes, which can influence the clinical condition, functionality and response to treatment.

Objective: To study body composition and its influence on the inflammatory parameters of AS according to sex.

Method: Sixty-seven patients with AS had lean and fat body mass assessed by bioimpedance and Body Mass Index (BMI) assessment. Disease activity was measured by ASDAS PCR and physical function by BASFI.

Result: All patients had fat mass above predicted and lean mass below predicted, and the majority had a BMI above normal. There was a positive correlation between BMI and ASDAS PCR only in men, with no correlation in women.

Conclusion: Obesity contributed to the increase in inflammatory activity parameters in male AS patients.

KEYWORDS: Electric impedance. Ankylosing spondylitis. Body mass index.

RESUMO

Introdução: Espondilite anquilosante (EA) ou espondilite axial radiográfica é espondiloartrite axial com predominância masculina, cujos sintomas incluem dor lombar baixa associada com rigidez matinal podendo evoluir para anquilose. Sua causa inflamatória está associada à alteração estrutural, o que pode influir na clínica, funcionalidade e resposta ao tratamento.

Objetivo: Estudar a composição corporal de pacientes com EA e sua influência nos parâmetros inflamatórios dela de acordo com o sexo.

Método: Sessenta e sete pacientes com EA tiveram avaliação da massa corporal magra e gorda por bioimpedância, da atividade da doença e do IMC. A atividade da doença foi calculada pelo ASDAS PCR e a função física pelo BASFI.

Resultado: Todos os pacientes estavam com massa gorda acima do previsto e massa magra abaixo, e a maioria tinham IMC acima da normalidade. Houve correlação positiva entre o IMC e o ASDAS PCR apenas nos homens, sendo inexistente nas mulheres.

Conclusão: A obesidade contribuiu para o aumento dos parâmetros de atividade inflamatória nos homens com EA.

PALAVRAS-CHAVE: Impedância elétrica. Espondilite anquilosante. Índice de massa corporal.

Central Message

Ankylosing spondylitis is axial arthritis with male predominance, whose symptoms include low back pain associated with morning stiffness and can progress to ankylosis. Its inflammatory cause is associated with structural changes, which can influence the clinic, functionality, and response to treatment. Thus, studying the body composition of patients with the disease and its influence on the inflammatory parameters evolved in relation to the sexes is interesting for a better clinical approach to the patients.

Perspective

This study described the nutritional profile of patients with ankylosing spondylitis and sought to associate it with clinical manifestations, disease activity, functional limitations, and treatments offered. It was observed that men and women were overweight, had high inflammatory tests, peripheral arthritis, had a normal nutritional assessment by the NAM, clinically active disease, had little functional limitation, and had a highly active disease. It was observed that obesity contributed to the increase in the parameters of inflammatory activity of the disease only in men.

[1] Instituto Presbiteriano Mackenzie, São Paulo, SP, Brasil

Conflict of interest: None | Funding: Anna Heloisa Tavares (Pibic/CNPq scholarship) | Received: 17/07/2024 | Accepted: 22/10/2024 | Correspondence: analuizashiomi@gmail.com | Associate Editor: Gustavo Rassier Isolan

How to cite:
Shiomi AL, Tavares AH, Rebouças RL, Skare TL. O impacto da obesidade na atividade da doença em pacientes com espondilite anquilosante. BioSCIENCE. 2024;82:e058

INTRODUCTION

Spondyloarthritis is a group of autoinflammatory diseases, which have as a serological characteristic the absence of rheumatoid factor or antinuclear antibody. Of this class of diseases, a classic form is ankylosing spondylitis (AS) or radiographic axial spondylitis. It is characterized by compromising the joints of the axial or peripheral skeleton, causing pain and reduction of joint space in the bones of the spine and sacroiliac joints. It is defined by the criteria modified in New York in 1984, although much is being discussed about its replacement by the ASAS criteria for axial spondyloarthritis due to the rapid development of imaging evaluations and genetic discoveries. However, the universally accepted concept still requires objective demonstration of axial inflammation for the classification of AS.[1,2]

Among the joint findings, a characteristic symptom is pain in the sacroiliac joints with an inflammatory characteristic.[3] Its evolution can ascend to the cervical region, leading to the loss of lumbar and cervical lordosis due to the inflammatory process. This inflammatory pain does not improve with rest, but with movement. It is associated with morning stiffness, the intensity of which increases with the level of disease activity.[4] Initial findings include loss of lumbar lordosis, fatigue, fever, weight loss, psoriasis, and inflammation of the entheses.

Later, the calcification of the ligaments and the inflammation of the entheses in the spine lead the patient to lose mobility, bending the body forward and acquiring the "skier's position" to maintain balance. Regarding extra-articular manifestations, acute, unilateral and recurrent anterior uveitis affects 40% of patients and may precede joint involvement.[5] It is characterized by inflammation of the anterior chamber of the eye, resulting in redness, pain, tearing, and progresses with the presence of HLA-B27. There is also cardiac involvement, nonspecific inflammation of the large and small intestines, renal amyloidosis, and neurological involvement due to compression of the vertebrae by vertebral fractures.

In ankylosing spondylitis (AE), there is a preponderance of males and a higher prevalence among Caucasians. It usually occurs in the second decade of life and rarely after the age of 45; has a strong genetic factor related to the presence of the Human Leukocyte Antigen (HLA)-B27 gene, which is present in 90% of patients. In Brazil, it is estimated that the prevalence varies from 0.[1-6%] of the population.[6] As for pathogenesis, it is still unknown; however, there may be a trigger for inflammation in the immune reaction to a bacterial or environmental antigen, which can lead to overexpression of interleukin-12 (IL-12), IL-17, and tumor necrosis factor-alpha (TNF-α).[7] In addition, it is believed that the B27 heavy chain may misfold and interact with Natural Killer (NK) cells in those with AS, resulting in pro-inflammatory process of antigen presentation and cytokine responses.[8]

Patients with the disease have increased circulating levels of IL-17 and IL-23 compared to healthy people. Its degree of inflammatory activity score by the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) correlates with serum IL-17 levels.[2] The Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) questionnaire tracks the evolution of AS treatment with greater accuracy based on questions about fatigue, back pain, joint inflammation, areas of pain on palpation, and morning stiffness.[3]

In addition, laboratory findings in patients with AS can serve as markers of chronic diseases. These include increased erythrocyte sedimentation and C-reactive protein (CRP).[7] Ankylosing Spondylitis Disease Activity Score (ASDAS) is an index to assess disease activity, which combines C-reactive protein (CRP, mg/l) as an acute phase reactant with 4 additional self-reported items: back pain (0-10 on the visual analogue scale), morning duration stiffness, peripheral pain/swelling, and global assessment of the patient's disease activity. ASDAS PCR classifies 4 states of disease activity: inactive (<1.3), moderate (between 1.3 and 2.1), high (between 2.1 and 3.5) and very high (>3.5).[1,2]

The condition of chronic inflammation caused by long-term AS, and elevated disease activity, lead to the development of sarcopenia. The inflammatory state, especially in the joints, causing pain, joint dysfunction and arthrosis, implies a decrease in physical activity and impairment of quality of life. Decreased physical activity and chronic inflammation are risk factors for the loss of lean mass. Thus, it seems relevant to assess the prevalence of loss of lean mass and its association with inflammatory markers, course of rheumatic disease, and activity.[9] In the assessment of functional disability, the Bath Ankylosing Spondylitis Functional Index (BASFI) questionnaire stands out, which assesses the patient's degree of ability to perform activities.[10]

Currently, it is known that adipose tissue performs endocrine functions, producing adipokines with well-defined activities in the immune process.[4] TNF-α is a pro-inflammatory cytokine produced by adipose tissue that influences the specific and nonspecific immune process through the recruitment and activation of neutrophils and monocytes to the site of infection. There is a correlation between the increase in serum levels, subcutaneous adipose tissue and visceral tissue with obesity. In a European study, overweight patients (BMI >27 kg/m2) had higher serum values of TNF-α and TNFR-2 (tumor necrosis factor receptor 2) than in people with normal weight (BMI <25 kg/m2).[11]

The assessment of BMI alone is limited, because although there is a correlation between disease activity and sarcopenia, there is no correlation between BASDAI and ASDAS with BMI.[9,12] However, when visceral fat and disease activity are evaluated, there seems to be a

correlation. This is due to the condition of obese cachexia, since - although the patient has no change in BMI - there is a change in the constitutional proportion of the individual.[13]

Although there are increasing studies on nutritional assessment in rheumatological patients, there is still much to be elucidated.[9]

The spondylytic patient has good therapeutic prospects. Treatment should be multidisciplinary, with drug therapy, psychological support for good integration into society, and physical therapy at all stages of the disease for postural re-education and prevention of functional limitations. Non-steroidal anti-inflammatory drugs (NSAIDs) of continuous use at maximum dose are the only drug treatment that has been proven to prevent the progression of axial manifestations of AS and should be used from the beginning of treatment. For those at risk of gastrotoxicity, or who cannot tolerate NSAIDs, treatment with COX-2 anti-inflammatory drugs, such as etoricoxib and celecoxib, is initiated.[14]

If there is no response to anti-inflammatory drugs or with intense disease activity, anti-TNF agents are indicated, such as adalimumab, infliximab, golimumab, and secukinumab, which decrease acute phase tests and improve osteoarticular inflammation.[15]

The objective of this study was to describe the epidemiological, inflammatory, nutritional, and functional activity profile of patients with AS at an outpatient rheumatology service.

METHOD

This is observational, analytical, and cross-sectional research. The convenience sample consisted of 67 patients from the rheumatology outpatient clinic of the Mackenzie Evangelical University Hospital, Curitiba, PR, Brazil, who presented for routine consultations and were invited to participate in the study on a first-come, first-served basis and the inclusion and exclusion criteria were met. Data collection was carried out from December 2021 to May 2023. This study was approved by institutional Research Ethics Committee, under protocol number 5,096,190. All participants signed an informed consent form.

Inclusion criteria were: meeting the classification criteria of New York Modified in 1984 to AE and accepting to participate in the study by signing an informed consent form. Exclusion criteria were: patients under 18 years of age; medical records with incomplete data; malabsorptive syndromes, untreated hypothyroidism, and patients with overlap of other inflammatory diseases. Individuals with metal implants (plates, screws, and pacemakers) given interference with bioimpedance were also excluded.

Data collection was done through the application of questionnaires, analysis of medical records, interviews with the patient, measurement of anthropometric measurements and bioimpedance examination in patients.

The following data were collected from the medical records: 1) demographic and anthropometric: age, age at onset of the disease, gender, race, tobacco use, alcohol use, weight and height for BMI, waist and hip circumference measurements; 2) laboratory: ESR, CRP and presence of HLA B27; 3) clinical: articular and extra-articular clinical manifestations possible in AS, with its intensities and peculiarities being detailed, with emphasis on inflammatory low back pain, axial (shoulder and hip) and peripheral joint involvement of the upper and lower limbs, sacroiliitis and its symmetry, involvement of the thoracic and cervical spine, enthesitis or enthesopathies, uveitis, dactylitis, bursitis, synovitis, myositis, tenosynovitis, and eventual respiratory problems or intestinal; 4) rheumatologic disease-modifying drugs used, such as methotrexate, sulfasalazine, antimalarials, cyclosporine, leflunomide, adalimumab, etanercept, infliximab, secukinumab; 5) bioimpedance, performed with a Bodystat 1500 device, involving the percentage of lean mass, fat and water with the reference values of the device for the classification of each one; and 6) results of the questionnaires applied, i.e., BASDAI to assess the degree of disease activity, BASFI and ASDAS PCR and ESR to analyze the level of function still present in the participants.

The BASDAI result ranged from 0 to 10, with 0 having no disease activity and 10 being the maximum. The total calculated BASFI also ranged from 0 to 10, but 0 represented no impairment of activities of daily living and 10, the impossibility of performing them as a consequence of the disease. The ASDAS score categorized disease activity as inactive, moderate, high, or very high. The 3 cutoff points to differentiate these states are: 1.3, 2.1 and 3.5.

Statistical analysis

The data were collected and stored in a Microsoft Excel spreadsheet. The analysis was performed with the aid of the SPSS v.22.0 computer program. The results were expressed as means, medians, minimum values, maximum values, and standard deviations (quantitative variables) or as frequencies and percentages (qualitative variables). Correlations were made by the Spearman or Person correlation tests, depending on the distribution of the sample obtained. Inferential analysis was performed using the chi-square test, Fisher's exact test, Student's t-test or Mann-Whitney test); p-values lower than 0.05 were considered significant.

RESULT

Of the universe of 83 patients identified with AS, 67 who met the study criteria were studied, 33 men and 34 women. In general, they were middle-aged, Caucasian, overweight, and did not have alcohol or smoking habits. Most of them had clinical manifestations of peripheral arthritis and HLA B27 positive (Table 1)

Most patients had clinically active disease according to ASDAS PCR and had little functional limitation according to BASFI (Table 1). According to the bioimpedance reference values, all of them had a high percentage of fat and a low percentage of lean mass in the body composition of both sexes. There was a predominance of BMI above normal among all.

TABLE 1 — Epidemiological, inflammatory, functional, and nutritional activity profile in the sample studied

Demographics	
Age	19 to 78 years old Average of 49.5±12.2 years
Age at diagnosis	12 to 51 – average of 39.4±11.4
BMI (kg/m2)	18.30-44.9 median of 27.8 (24.3-30.4)
Waist-to-hip ratio	0.59 to 1.08; average of 0.90±0.09
Sex	Women = 33 Men = 34
Ethnicity	Euro-descendant = 57 Afro-descendant=10
Smokers	7/67
Alcohol use	5/66
Uveitis	23/67
Enthesitis	31/67
Peripheral arthritis	33/67
Skin manifestations	6/67
HLA B27	41/63
Treatment	
Non-hormonal anti-inflammatory	23/66
Methotrexate	11/67
Sulfasalazine	17/50
Biological	Secukinumab – 5/67 Anti-TNF – 38/67
Activity/Function Ratios	
VHS	2 to 90; median of 22.5 (6.0-42.7)
PCR	0,03-52,0; median of 2.88 (1.10-6.76)
BASDAI	0-8,7; average of 3.7±3.2
BASFI	0-9,7; median of 3.1 (1.6-5.6)
ASDAS PCR	0.64 to 5.02; average of 2.82±1.09
ASDAS VHS	0.51 to 5.56; average of 2.74±1.18
Nutritional Indices	
% fat	19 to 61.7; average of 40.1±9.28
% fat Men	19 to 58.3; median of 34.3 (0.6-36.2)
% fat women	37,0- 61,7; average of 47.0±6.04
% lean mass	38.4 to 81.0; average of 59.4±9.46
% of lean mass men	41.7 to 81.0; median of 65.5 (63.2-69.1)
% of lean body mass women	38,3-63,0; average of 52.4±6.28

ASDA = ankylosing spondylitis disease activity score; BASDAI = Bath ankylosing spondylitis disease activity index; BASFI = Bath Ankylosing Spondylitis Functional Index; ESR = erythrocyte sedimentation rate; CRP = C-reactive protein

Only in men was a positive correlation identified between BMI and ASDAS CRP levels; other parameters, such as % of fat mass and lean mass, showed a tendency for correlation. No correlations were observed among women (Table 2).

TABLE 2 — Correlation of ASDAS PCR values in the sample of men with spondyloarthritis

Men			
	r	95%CI	p
% fat	0,31	-0.05 to 0.48	0,08
% lean mass	-0,31	-0.61 to 0.05	0,08
BMI	0,67	0,40-0,83	<0.0001
Waist-to-hip ratio	0,12	-0.23 to 0.26	0,49
Nutritional questionnaire	-0,29	-0.58 TO 0.07	0,11
Women			
% fat	0,06	-0.29 to 0.41	0,72
% lean mass	-0,06	-0.41 to 0.29	0,72
BMI	0,08	-0.27 to 0.42	0,63
Waist-to-hip ratio	0,19	-0.18 TO 0.51	0,30
Nutritional questionnaire	-0,17	-0.50 TO 0.20	0,34

DISCUSSION

This study described the nutritional profile of patients with AS and sought to associate it with clinical manifestations, disease activity, functional limitations, and treatments offered. It was observed that men and women were overweight, had high inflammatory tests, peripheral arthritis, had a normal nutritional assessment by the NAM, clinically active disease, had little functional limitation, and had a highly active disease.

In this population, the bioimpedance evaluation showed that 100% of them (of both sexes) had fat mass above the expected and 100% lean mass below the expected. Men had approximately 60% more fat mass and 20% less lean mass than expected; women, on the other hand, had 50% more fat mass and 30% less lean mass.

There is a complex correlation between fat content and inflammation disease activity.[16] As for the patients in the sample, no relevant correlation was observed between the measures of disease activity and the percentage of body fat, both in women and men, although there is a tendency for men. BMI, on the other hand, was positively correlated with ASDAS CRP in men, that is, the higher the BMI, the greater the disease activity. No correlation was observed in women.

In the sample, there was an equal proportion between men and women (unintentional), corroborating the current concept that in AS there is an equal proportion between the sexes, instead of believing that this is a predominantly male disease, as when diagnostic tools were more limited in the past.[17] In common, the people were middle-aged - which is in line with the prevalence of disease onset between 20-45 years.[7] This involvement of young adults at the peak of their productive life brings social and economic losses due to the restrictions of AS in activities of daily living.[18]

The finding of HLA-B27 positive Caucasian patients suggests the dominant genetic subtype HLA-B*27:05 in this population. This genetic component was identified as the main predisposing factor for AS, leading to earlier onset of the disease, when compared to those who do not have this genetic factor.[7]

The fact that most of the patients in this sample did not have addictions, this absence is a protective factor (among the acquired factors), since smoking is associated with increased disease activity, worse rates of BASDAI and BASFI.[19] Exercise in SpA can be effective for rehabilitation, to maintain function and strength, as well as to decrease joint inflammation.[20] Men are more prone to physical activity than women, and have a better therapeutic response.[17]

An important point of the present study is that the participants were being diagnosed in time to have no irreversible limitations. Interestingly, these patients had a low BASDAI index, but a high ASDAS index, somewhat contradicting the assertion regarding disease activity. It should be noted that BASDAI is an exclusively subjective activity index, while ASDAS uses inflammatory activity tests (CRP), which may explain the differences found. This

finding questions the low BASDAI score alone as a good predictor of therapeutic efficacy for anti-TNF.[21]

In AS, patients may also present with constitutional symptoms, including anorexia and weight loss.[7] However, those in this sample did not have this type of problem through the nutritional assessment questionnaire, despite having nutritional problems, due to overweight, low percentage of lean mass and high percentage of fat.

The low amount of muscle mass, when associated with low skeletal muscle strength, generates a risk for secondary sarcopenia due to the systemic inflammation of AS, leading to the risk of physical disability, poor quality of life, and even increased mortality rates. Although it is possible that the activity does not generate sarcopenia immediately, disability, arising from structural damage secondary to ongoing inflammatory activity, may do so.[9,22]

The limitations of the study consisted in having a small sample, due to the low prevalence of the disease, despite the fact that the service is a large university hospital and considered a state reference in rheumatological treatment. Another limitation was that it did not evaluate the practice of physical exercise, as it is a major factor in the body composition of patients, suggesting a more comprehensive study that also evaluates this parameter. In addition, interventional studies, changing the exercise practice and diet of patients, are welcome in this context.

CONCLUSION

This study showed that obesity contributed to the increase in the parameters of inflammatory activity in patients with AS in men.

Authors' contributions

Conceptualization: Ana Luiza Shiomi
Research: Anna Heloisa Tavares
Methodology: Thelma Larocca Skare
Writing (original draft): All authors
Writing (proofreading and editing): All authors

REFERENCES

1. Robinson PC, Van Der Linden S, Khan MA, Taylor WJ. Axial spondyloarthritis: concept, construct, classification and implications for therapy. Nat Rev Rheumatol. 2021;17(2):109-118. https://doi.org/10.1038/s41584-020-00552-4
2. Voruganti A, Bowness P. New developments in our understanding of ankylosing spondylitis pathogenesis. Immunology. 2020;161(2):94-102. https://doi.org/10.1111/imm.13242.
3. Sampaio-Barros PD, Azevedo V, Bonfiglioli R, Campos WR. Carneiro SC da S, Carvalho MAP, et al. Consenso Brasileiro de Espondiloartropatias: outras espondiloartropatias diagnóstico e tratamento - primeira revisão. Rev Bras Reumatol. 2007;47:243-50. https://doi.org/10.1590/S0482-50042007000400002
4. Costa JV, Duarte JS. Tecido adiposo e adipocinas. Acta Med Port. 2006;19:251-6.
5. Sampaio-Barros PD, Keiserman M, Meirelles E de S, Pinheiro M de M, Ximenes AC, Azevedo VF, et al. Recomendações sobre diagnóstico e tratamento da espondilite anquilosante. Rev Bras Reumatol. 2013;53(3):242–57.
6. Simioni J, Skare TL, Campos APB, Kotze L, Messias-Reason I, Ioshii SO, et al. Fecal Calprotectin, Gut Inflammation and Spondyloarthritis. Arch Med Res. 2019;50(1):41-6. https://doi.org/10.1016/j.arcmed.2019.04.003
7. Ebrahimiadib N, Berijani S, Ghahari M, Pahlaviani FG. Ankylosing Spondylitis. J Ophthalmic Vis Res. 2021;16(3):462-9. https://doi.org/10.18502/jovr.v16i3.9440
8. Braun J, Sieper J. Ankylosing spondylitis. Lancet. 2007;369(9570):1379-90. https://doi.org/10.1016/S0140-6736(07)60635-7
9. Cruz-Jentoft AJ, Romero-Yuste S, Chamizo Carmona E, Nolla JM. Sarcopenia, immune-mediated rheumatic diseases, and nutritional interventions. Aging Clin Exp Res. 2021;33(11):2929-39. https://doi.org/10.1007/s40520-021-01800-7
10. Pimentel-Santos FM, Pinto T, Santos H, Barcelos A, Cunha I, Branco JC, et al. Portuguese version of the Bath indexes for ankylosing spondylitis patients: a cross-cultural adaptation and validation. Clin Rheumatol. 2012;31(2):341-6. https://doi.org/10.1007/s10067-011-1864-5
11. Winkler G, Kiss S, Keszthelyi L, Sápi Z, Ory I, Salamon F, et al. Expression of tumor necrosis factor (TNF)-alpha protein in the subcutaneous and visceral adipose tissue in correlation with adipocyte cell volume, serum TNF-alpha, soluble serum TNF-receptor-2 concentrations and C-peptide level. Eur J Endocrinol. 2003;149(2):129-35. https://doi.org/10.1530/eje.0.1490129
12. Rubio Vargas R, Van Den Berg R, Van Lunteren M, Ez-Zaitouni Z, Bakker PA, Dagfinrud H, et al. Does body mass index (BMI) influence the Ankylosing Spondylitis Disease Activity Score in axial spondyloarthritis? Data from the SPACE cohort. RMD Open. 2016;2(1):e000283. https://doi.org/10.1136/rmdopen-2016-000283
13. Aydin M, Aydin F, Yuksel M, Yildiz A, Polat N, Akil MA, et al. Visceral fat reflects disease activity in patients with ankylosing spondylitis. Clin Invest Med. 2014;37(3):e186. https://doi.org/10.25011/cim.v37i3.21385
14. Dagfinrud H, Kvien TK, Hagen KB. Physiotherapy interventions for ankylosing spondylitis. Cochrane Database Syst Rev. 2008;2008(1):CD002822. https://doi.org/10.1002/14651858
15. Ferreira ALM, Alvarenga CQ de M, Barcelos G de F, Polito ETL. Espondilite anquilosante. Rev Bras Reumatol. 2008:48:243-7. https://doi.org/10.1590/S0482-50042008000400008
16. Vodnizza SI, Visman IM, Van Denderen C, Lems WF, Jaime F, Nurmohamed MT, et al. Muscle wasting in male TNF-αblocker naïve ankylosing spondylitis patients: a comparison of gender differences in body composition, Rheumatology 2017;56:1566–72. https://doi.org/10.1093/rheumatology/kex187
17. Marzo-Ortega H, Navarro-Compán V, Akar S, Kiltz U, Clark Z, Nikiphorou E. The impact of gender and sex on diagnosis, treatment outcomes and health-related quality of life in patients with axial spondyloarthritis. Clin Rheumatol. 2022;41(11):3573-81. https://doi.org/10.1007/s10067-022-06228-6
18. Packham J. Optimizing outcomes for ankylosing spondylitis and axial spondyloarthritis patients: a holistic approach to care. Rheumatology (Oxford). 2018;57(suppl_6):29-34. https://doi.org/10.1093/rheumatology/key200.
19. Dülger S, Aykurt Karlibel İ, Kasapoğlu Aksoy M, Altan L, Şengören Dikiş. How does smoking cessation affect disease activity, function loss, and quality of life in smokers with ankylosing spondylitis? J Clin Rheumatol. 2019; 25(7):288-96. https://doi.org/10.1097/RHU.0000000000000851
20. Sang Y, Dong C, Fu T, Zhao R, Ge X, Zhou W, et al. Associated factors with adherence to standard exercise therapy and health-related quality of life in Chinese patients with ankylosing spondylitis. Mod Rheumatol. 2020;30(1):149-54. https://doi.org/10.1080/14397595.2018.1559966
21. Nam B, Koo BS, Lee TH. Low BASDAI score alone is not a good predictor of anti-tumor necrosis factor in ankylosing spondylitis: a retrospective cohort study. BMC Musculoskelet Disord. 2012;22:140. https://doi.org/10.1186/s12891-020-03941-8
22. Barone M, Viggiani MT, Anelli MG, Fanizzi R, Lorusso O, Lopalco G, et al. Sarcopenia in Patients with Rheumatic Diseases: Prevalence and Associated Risk Factors. J Clin Med. 2018; 7(12):504. https://doi.org/10.3390/jcm7120504