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Axial Spondyloarthritis in the Era of Precision Medicine: Biomarkers, Microbiota, and Multimodal Therapy

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Abstract

Introduction and Purpose

Axial spondyloarthritis (axSpA) is a chronic inflammatory rheumatic disease affecting the axial skeleton. It includes both radiographic (r-axSpA) and non-radiographic (nr-axSpA) forms. This study aims to compare the clinical characteristics, disease burden, and treatment outcomes of r-axSpA and nr-axSpA and evaluate the role of biomarkers, microbiota, and physical therapy in disease management.

Materials and Methods

A systematic review of the literature was conducted, analyzing clinical studies comparing r-axSpA and nr-axSpA, focusing on disease activity indices (ASDAS, BASDAI), inflammatory markers, microbiome alterations, and treatment approaches, including NSAIDs, TNFi, IL-17 inhibitors, and JAK inhibitors. The impact of exercise programs on disease progression was also assessed.

Results

Patients with r-axSpA had longer disease duration, higher CRP levels, and more structural damage, while those with nr-axSpA had a higher prevalence of peripheral manifestations. ASDAS was found to be superior to BASDAI for monitoring disease activity. Biologic therapies, particularly TNFi and IL-17 inhibitors, showed efficacy in symptom control. Physical therapy, especially aquatic and workplace-home combined exercises, significantly improved mobility, quality of life, and pulmonary function.

Conclusion

AxSpA requires a multidisciplinary approach combining pharmacological treatment, exercise, and lifestyle modifications. Biologic drugs remain the mainstay of treatment for refractory cases, while ASDAS is the preferred disease activity measure. Future research should explore microbiome-targeted therapies and personalized treatment strategies.

Key Words

Axial spondyloarthritis, ankylosing spondylitis, non-radiographic axSpA, biologic therapy, TNF inhibitors, IL-17 inhibitors, JAK inhibitors, microbiota, exercise therapy, disease activity indices.

1. Introduction

Axial spondyloarthritis (axSpA) is a chronic, inflammatory rheumatic disease of the musculoskeletal system that primarily affects the axial skeleton. It is often accompanied by peripheral manifestations such as arthritis, enthesitis, and dactylitis, as well as extramuscular manifestations, including acute anterior uveitis, inflammatory bowel disease (IBD), and psoriasis. AxSpA includes both patients with radiographic changes in the sacroiliac joints (radiographic axSpA – r-axSpA, also known as ankylosing spondylitis) and those who do not (nonradiographic axSpA – nr-axSpA). [1,2]

Studies have shown that r-axSpA and nr-axSpA are part of the same disease spectrum, and patients with both types have similar clinical features, disease burden, comorbidities, and response to treatment. Therefore, the term “axSpA” was considered the most appropriate and was adopted in these recommendations. [1]

In a study by Clementina López-Medina et al, the aim of which was to compare clinical features, disease burden (disease activity, functioning, quality of life), treatment methods, and treatment outcomes in patients with radiographic and nonradiographic spondyloarthritis (r-axSpA and nr-axSpA), it was shown that patients with r-axSpA were more likely to be male (69.6% vs 53.6%), smokers (37.7% vs 31.1%), and had a longer mean disease duration (8.6 vs 5.0 years) and a longer time to diagnosis (6.1 vs 4.2 years) compared to patients with nr-axSpA. Peripheral manifestations were more common in the nr-axSpA group, whereas uveitis and structural damage on MRI of the sacroiliac joints were more common in r-axSpA. C-reactive protein level and AS mobility index (BASMI) were higher in r-axSpA, whereas disease activity index (BASDAI), function index (BASFI) and AS quality of life were similar in both groups. No significant differences in treatment effects were found.

Thus, patients with r-axSpA and nr-axSpA have a similar clinical presentation, except for the more frequent occurrence of peripheral changes in the nr-axSpA group. Apart from the more

impaired mobility in r-axSpA, both groups showed similar disease burden, treatment methods, and treatment outcomes.[3]

The Ankylosing Spondylitis Disease Activity Score (ASDAS) has become the best tool for assessing disease activity and is recommended for monitoring patients with axSpA. The ASDAS, preferentially calculated using C-reactive protein (CRP), is a well-balanced index, in contrast to the previously more widely used BASDAI (Bath Ankylosing Spondylitis Disease Activity Index), which shows some redundancy. Furthermore, ASDAS takes into account the patient's perspective and includes CRP as an objective indicator of inflammation, whereas BASDAI relies only on the patient's subjective assessment. The ASDAS has also been validated using a rapid CRP test, which improves its use in daily clinical practice. Furthermore, the ASDAS shows an association with syndesmophyte formation, whereas the BASDAI alone did not show such an association unless used with CRP, which had a weaker effect than the ASDAS. Specific thresholds for the ASDAS have also been established to define disease activity states and criteria for improvement and deterioration. The ASAS core set of indicators for monitoring in clinical practice remains an important tool.[1,2,4]

Ankylosing spondylitis (AS) is associated with several autoimmune diseases, such as inflammatory bowel disease (IBD), anterior uveitis, and psoriasis, suggesting common genetic and immunological mechanisms. Alterations in immune cells and cytokine levels in AS patients suggest a significant role of the immune system in disease development.[2] The mechanism by which HLA-B27 contributes to disease development is still not fully understood. Genetic factors play a key role as pathogenic elements, accounting for more than 90% of the population variance in AS symptoms. One of the most important genetic risk factors is the HLA-B27 allele, which belongs to class I of the major histocompatibility complex (MHC). Although the exact mechanism of pathogenesis remains unclear, HLA-B27 shows a strong association with the incidence of AS in various populations worldwide. Studies indicate that 90%–95% of AS patients are HLA-B27 positive, while only 1%–2% of people with this allele develop the disease. This risk increases to 15%–20% in people with a first-degree relative with AS. [5,6] The pathogenesis of AS is also associated with the activation of the immune system, especially the IL-23/IL-17 axis and the Th1 cell pathway, which leads to the overproduction of TNF-α.

Chronic activation of T lymphocytes and the imbalance of their subsets, including the decrease in the number of regulatory T cells (Tregs), may play a role in the development of

the disease. Although the function of B cells, especially regulatory B cells (Bregs), in AS is not well understood, some studies suggest that their impaired function may contribute to the pathology. [7]

In patients with AS, as well as in healthy individuals with a positive HLA-B27 result, the levels of T lymphocytes secreting TNF-α and IFN-γ are lower in studies, while CD8+ T cells in patients with AS tend to produce increased IL-10. [5]

The discovery of the IL-23/IL-17 axis shed new light on the role of Th17 cells in the pathogenesis of AS. Th17 cells, which produce IL-17, play a key role in the inflammation of entheses, or the sites where tendons attach to bones, that is characteristic of AS. IL-23, produced by myeloid cells, activates Th17 cells, which in turn secrete IL-17, contributing to the inflammatory process. IL-17 may also affect bone damage by inducing the production of RANKL, which leads to the activation of osteoclasts. [8] In the meta-analysis Dong Liu et al. Imbalance of Peripheral Lymphocyte Subsets in Patients With Ankylosing Spondylitis: A Meta-Analysis, an attempt was made to explain the lymphocyte imbalance in peripheral blood in patients with ankylosing spondylitis (AS), comparing them to a group of healthy donors. A significantly increased percentage of CD4+ T lymphocytes was found. Analysis of individual subpopulations of these lymphocytes showed a significant increase in the percentage of Th17 and Tfh cells, as well as an increased Th1/Th2 ratio.Moreover, the increase in the percentage of Th17 cells was independent of the disease classification and its activity, which underlines the credibility of this result. At the same time, a significant decrease in the percentage of regulatory T lymphocytes (Treg) was observed. However, no significant differences were found in the numbers of Th1 and Th2 subpopulations. Further analysis of subgroups suggested that the increase in the number of T lymphocytes was particularly pronounced in patients with high disease activity. Another interesting observation was the increased number of Th1 lymphocytes in patients with high disease activity, although the previous analysis did not show general differences in this population. Still, no significant changes were observed in the percentage of Th2 and CD8+ T lymphocytes.[8]

2. Microbiome

Changes in the gut microbiota (dysbiosis) may contribute to the development or occurrence of various rheumatic diseases. Since the gut microbiota can be modified, it is

considered a potential target for the treatment or prevention of these diseases. However, knowledge about the relationship between the gut microbiota and rheumatic diseases is still limited.[23] The gut microbiota acts as a defense layer against pathogenic organisms and maintains the homeostasis of different T lymphocyte populations in the gastrointestinal tract.[9] Bacteria, which constitute the majority of the microbiota, participate in many functions such as digestion and absorption of food, but also prevent the adhesion of pathogenic bacteria to the mucosa, ensuring its integrity, and play a key role in modulating the innate and adaptive immunity of the host [10].

In HLA-B27 transgenic rats, spondyloarthropathy features were not observed in a sterile environment, but symptoms of the disease developed after exposure to commensal bacteria, indicating possible interactions between HLA-B27 and the gut microbiome.

Analysis of the composition of the gut microbiota revealed significant differences between AS patients and healthy individuals, especially with regard to bacteria from the families Lachnospiraceae, Veillonellaceae, Prevotellaceae, Porphyromonadaceae, and Bacteroidaceae. Klebsiella pneumoniae, a naturally occurring opportunistic pathogen in the human intestine, may play a role in the enhancement of autoimmunity in AS. Although the results of studies on the effect of this bacterium on disease activity are ambiguous, some scientists suggest that its interaction with HLA-B27 may indirectly contribute to the development of AS. Furthermore, infection of the gut microbiome may be associated with immune deficiencies, leading to more intense and prolonged immune responses.[5]

In the study by Yilun Wang et al. the analysis of mean differences in microbiota diversity (α) between patients with rheumatic diseases and healthy individuals was performed using a random effects model. The differences in β diversity were also compared, and the relative number of microorganisms was analyzed.

In the analysis of β diversity, including 64 studies, more than half of them showed significant differences between patients with various rheumatic diseases, such as rheumatoid arthritis, systemic lupus erythematosus, systemic sclerosis, ankylosing spondylitis, gout, Sjögren's syndrome, and IgG4-related diseases. It was noted that the differences in β diversity were particularly pronounced in ankylosing spondylitis and IgG4-related diseases.[11]

In the Gut microbiota dysbiosis in ankylosing spondylitis: a systematic review and meta-analysis by Qin-Yi et al. observed a significant reduction in gut microbiota diversity in AS

patients, manifesting as a decrease in both richness and evenness. In addition, AS patients who received combined antirheumatic drug therapy showed a more pronounced decrease in a-diversity compared to untreated patients, highlighting the potential impact of this treatment on the balance of the gut microbiota. changes in a-diversity and relative abundance of specific bacteria in AS patients. This suggests that targeting the gut microbiota may provide new therapeutic options for AS treatment.[12]

3. Pharmacological treatment

The goals of pharmacological treatment of AS are to improve and maintain spine flexibility, maintain proper posture, alleviate symptoms, reduce functional limitations, and reduce complications. The main drugs used in therapy are nonsteroidal anti-inflammatory drugs (NSAIDs) and TNF-α inhibitors (TNFi). Additionally, biologic drugs are used in treatment: IL-17 and IL-23 inhibitors. Oral JAK inhibitors, such as tofacitinib and filgotinib, have also shown promising results in clinical trials.[5,13]

3.1 Patients with pain and stiffness should use nonsteroidal anti-inflammatory drugs (NSAIDs) as the first line of treatment, taking into account the risks and benefits, up to the maximum dose. [11] Current recommendations support continuous NSAID therapy with good response to medication and symptom control. However, it is worth remembering that adverse effects may reduce the quality of life. The decision to use NSAIDs should be justified by symptom control and not by the desire to prevent structural changes.[1,14]

Physical activity, defined as the average recommendation in the treatment of SA disease [1], is also possible in many cases thanks to the relief of symptoms by first-line drugs. In the study described by Iulia Rahela Marcu et al. disease activity was assessed using the BASDAI index, and patient functioning using BASFI. Quality of life was assessed using the HAQ questionnaire. Patients were divided into three groups: the first: taking drugs (etoricoxib 90 mg daily), the second group: performing physical exercises (individual exercise program for 3 months, then at home for a year) and the third group: combined (drugs and exercises). The study lasted a year, and monitoring took place every 3 months. After 12 months of therapy, a significant reduction in inflammatory markers (ESR and CRP) was observed in the groups

taking drugs and exercising, especially in the combined group. The greatest improvement in disease activity (BASDAI) and functioning (BASFI) was achieved in the etoricoxib and exercise group, which showed a statistically significant difference ($p < 0.05$). The greatest effect on quality of life (HAQ) was seen in the combined therapy, suggesting that the combination of medication and exercise provides better results than medication or exercise alone. This study has shown the importance of an interdisciplinary approach to treatment, and recommendations to use NSAIDs as first-line pharmacological treatment, in this study etoricoxib, support the use of individual exercise programs in the treatment of AS, improving disease activity, functioning, and quality of life for patients.[15]

However, not all patients respond equally well to NSAIDs. At least one third of patients do not have adequate symptom control or experience serious side effects. Therefore, in addition to symptom-relieving therapy, medications that adequately control the disease in as many patients as possible are necessary. There is no evidence that conventional synthetic disease-modifying antirheumatic drugs (csDMARDs) are effective in treating axial AS[4], although sulfasalazine may be effective in treating peripheral joint symptoms but not axial disease.[16]

3.2 Local glucocorticosteroid injections may be an effective treatment option for enthesopathy and arthritis. Glucocorticosteroid injections into the affected peripheral joints, sacroiliac joints, may provide rapid symptomatic relief. However, long-term systemic glucocorticosteroid therapy is relatively contraindicated due to the increased risk of osteoporosis, hyperlipidemia, and insulin resistance. Studies have shown that patients with AS have achieved symptomatic relief with short-term high-dose glucocorticosteroid therapy (50 mg/day). In patients with peripheral arthritis as a comorbidity, conventional synthetic disease-modifying antirheumatic drugs (csDMARDs) such as methotrexate, leflunomide, and sulfasalazine should be considered, but not in patients with isolated sacroiliac arthritis. Methotrexate treatment has not been shown to be effective in patients with AS without peripheral arthritis, even with the use of TNF inhibitors. [5]

3.3 “TNFi, IL-17i or JAKi should be considered in patients with persistently high disease activity despite conventional treatments; current practice is to start a TNFi or IL-17i.” [1]. In the case of ineffective or intolerant treatment with NSAIDs, patients with AS have limited therapeutic options. Additionally, because bDMARDs are administered parenterally, there is a need to develop oral therapies with an alternative mechanism of action.[13,14] The complex etiology of the disease, in which proinflammatory cytokines play a key role, such as:

IL-17, IL-12, IL-23 and IL-6, has influenced the development of targeted therapies, which have revolutionized treatment, offering patients more effective methods of disease control.[17,18]

TNF-α inhibitors – e.g. adalimumab, infliximab, etanercept – effectively inhibit inflammation, but are not sufficiently effective in all patients. Adalimumab is a fully human IgG1 monoclonal antibody that selectively blocks tumor necrosis factor alpha (TNF-α) – a key element of inflammatory processes in autoimmune diseases, including ankylosing spondylitis (AS). By binding TNF-α, adalimumab inhibits its interaction with TNFR1 and TNFR2 receptors, which results in a reduction of inflammatory reactions. [19]

In the context of AS, adalimumab is an effective biologic drug that reduces inflammation in the spine joints and improves the motor function of patients. Its action leads to symptom relief, slowing the progression of the disease, and improving the quality of life of patients. This drug is approved by the FDA for the treatment of AS, which confirms its effectiveness in reducing symptoms and limiting joint damage resulting from the chronic inflammatory process.[20] However, due to the high cost of adalimumab, a search for cheaper biosimilar equivalents has begun. Researchers in the study "Evaluation of adalimumab biosimilar candidate (HS016) in Chinese patients with active ankylosing spondylitis based on a health survey: sub-analysis of a phase 3 study" described by Jinmei Su et al showed that both HS016 and adalimumab led to rapid improvement of symptoms within the first two weeks of treatment. The results suggest that HS016 may provide a more cost-effective therapeutic alternative for Chinese patients with AS, providing rapid symptom relief and improving quality of life.[19,20] The study by Erye Zhou et al. Comparison of biologics and small-molecule drugs in axial spondyloarthritis: a systematic review and network meta-analysis suggests that NSAIDs such as celecoxib may not provide significant additional benefit when combined with TNFi in patients with well-controlled disease. However, they may be useful in high-risk patients who have persistent symptoms or inflammation despite TNFi therapy. The study found no major differences in clinical outcomes between groups, suggesting that TNFi alone can effectively control disease activity in most patients and that NSAIDs are needed only when necessary.[21]

IL-17 inhibitors, such as secukinumab, ixekizumab, brodalumab, work by blocking IL-17A or its receptor (IL-17RA), reducing inflammation and delaying the progression of structural changes.[18] Secukinumab is a fully human IgG1-kappa monoclonal antibody that blocks

interleukin 17A (IL-17A), which plays a key role in inflammatory processes. Clinical trials have shown it to be effective in the treatment of moderate to severe psoriasis (PsO), psoriatic arthritis (PsA), and ankylosing spondylitis (AS). It is characterized by a rapid onset of action and long-lasting therapeutic effect, while also having a favorable safety profile.[22]

Deodhar et al. Arthritis Research & Therapy[2019] presented safety data for secukinumab. The studies included patients from 21 phase 2, 3 and 4 clinical trials and post-marketing surveillance reports. The most frequently reported adverse event was upper respiratory tract infection. Complications such as severe infections, Candida infections, inflammatory bowel disease, and serious cardiovascular events were reported at a low incidence. There were no cases of tuberculosis reactivation. The analysis confirmed that secukinumab has a stable safety profile even with long-term use, supporting its continued use in the treatment of chronic inflammatory diseases such as AS. [18]

IL-12/23 inhibitors – e.g. ustekinumab – are potentially effective in modulating the immune response, but require further study in axSpA. JAK inhibitors – e.g. tofacitinib, upadacitinib – block signaling pathways responsible for inflammatory cell activation, representing a new therapeutic option for patients who are insensitive to TNFi and IL-17i. [17] Tofacitinib is an oral Janus kinase (JAK) inhibitor that is being studied as a potential treatment option for adult patients with AS. JAK inhibitors act directly on the catalytic activity of JAK enzymes, which play a key role in signaling pathways regulating the cytokine response of the innate and adaptive immune system. Activation of these pathways leads to the proliferation of inflammatory cells in the joints and outside the musculoskeletal system, contributing to joint destruction—one of the main symptoms of AS. Therefore, blocking JAKs may help alleviate both joint and extra-joint symptoms of the disease.[13] In Tofacitinib for the treatment of ankylosing spondylitis: a phase III, randomised, double-blind, placebo-controlled study, the results of the phase III study showed that in patients with active AS who were not responding to NSAIDs, tofacitinib 5 mg twice daily provided rapid, long-lasting, and clinically meaningful benefits. In addition, no new safety concerns were identified, suggesting a favorable benefit-risk ratio for the treatment of active AS with this drug.

It is recommended to use TNFi (TNF inhibitors) as the first biologic agent, before secukinumab or ixekizumab. In case of failure to respond to the first TNFi, secukinumab or ixekizumab is recommended instead of the second TNFi. TNFi, secukinumab, and

ixekizumab are preferred over tofacitinib. Concomitant use of low-dose methotrexate with TNFi, nor a strict treatment-to-target strategy, nor interruption or reduction of biologics in patients with stable disease is recommended. Sulfasalazine is recommended only for persistent peripheral arthritis when TNFi are contraindicated. In patients with unclear inflammation, magnetic resonance imaging of the spine or pelvis is recommended. Regular monitoring of radiographic changes with spine X-rays is not recommended. [23]

4. Therapeutic exercises

Exercise plays a key role in the treatment of patients with AS, especially in the context of improving pulmonary function, which can deteriorate as a result of changes in the chest and as a result of inflammatory disease. AS leads to stiffness of the spine joints, which limits mobility, and as the disease progresses, respiratory problems such as reduced lung volume and impaired ventilation may also occur. For this reason, in the treatment of patients with AS, in addition to pharmacological treatment, the use of physical exercises is an extremely important element, which helps maintain respiratory efficiency and improve the overall quality of life.[24]

The Official Journal of the Portuguese Society of Rheumatology describes a study conducted in a group of patients with AS. It assessed the effect of physical exercise, both aquatic and terrestrial, on pulmonary function and the overall health of the patients. The study included 57 patients meeting the diagnostic criteria for AS who were randomly assigned to one of three treatment groups: aquatic exercise (AG), terrestrial exercise (LG), and home exercise (HG). The aim of the study was to determine how different types of exercise would improve disease symptoms, including respiratory function, as well as disease activity indicators such as pain, spinal mobility, and general function. After eight weeks of regular exercise, patients in the aquatic exercise group (AG) showed significant improvements in pulmonary function, including increases in peak expiratory flow, vital capacity, maximal voluntary ventilation, and maximal inspiratory pressure. In contrast, the land exercise group (LG) showed an improvement in indicators related to ventilatory function, such as the ratio of expiratory volume in the first second to vital capacity and an increase in peak expiratory flow and maximal voluntary ventilation. In contrast, the home exercise group (HG) did not show significant changes in pulmonary function scores or any improvement in other aspects of health. [25] The results of this study emphasize the importance of regular physical exercise, both in water and on land, in the treatment of AS, especially in the context of improving

pulmonary function and the general condition of patients. Physical exercise not only supports joint mobility and improves respiratory function, but also helps reduce pain, improves quality of life and reduces disease symptoms.

A study by Baris Gurpinar assessed the effect of mobility exercises performed in two different environments on pulmonary function and disease-related measures in ankylosing spondylitis (AS). None of the participants reported negative side effects. All patients had normal lung function tests. Multidimensional exercises improved pulmonary function such as PEF and MVV, but did not significantly affect the FEV1/FVC ratio. Exercise performed in water (AG) showed greater improvement in respiratory muscle strength and lung volume (VC) compared to land-based exercise (LG). This difference may be due to the resistance of water to respiratory muscles and the reduced effect of gravity. Exercise had a positive effect on pain, spinal mobility, and function. In the AG and LG groups, significant improvements were observed in BASMI, BASDAI and pain scores, whereas in the HG group (home exercises) no significant changes were observed. The study showed that multidimensional exercises can improve pulmonary function and disease symptoms in AS. Aquatic exercise may offer additional benefits, such as increased respiratory muscle strength and function. Future studies should investigate the long-term effects of this exercise and its effect on other parameters, such as quality of life and sleep. [25]

In the study described by Jong Mi Lim and Ok-Hee Cho, “Effects of Home-and-Workplace Combined Exercise for Patients with Ankylosing Spondylitis,” patients with ankylosing spondylitis (AS) were recruited from the rheumatology clinic of a university hospital in South Korea. Inclusion criteria included individuals over 18 years of age, employed full-time, with a diagnosis of AS no older than 15 years, no progression of bamboo spine on radiographs, stable disease symptoms (BASDAI score ≤ 4.0), no regular exercise for the past 6 months, and taking medication during that period. Participants also had to demonstrate an inability to exercise more than 5 days per week at work or at home. Patients with unstable chronic diseases and psychiatric history were excluded. The exercise program based on the combination of home and work exercises (HWE) was developed in three stages: literature review, patient needs assessment, and exercise program design. After literature review and patient interviews, the main barriers to exercise were identified as lack of time, lack of confidence in the effectiveness of exercise, and lack of knowledge about its impact.

Patients expressed the need for individually tailored exercises that could be performed in their free time and that alleviate physical discomfort at work.

The developed program consisted of stretching, muscle strengthening, walking and breathing exercises. The HWE group exercised 5 days a week at home (70 minutes per day) and at work (20 minutes per day), and the control group attended routine treatment and health consultations. Educational materials, videos and exercise notebooks were prepared to increase adherence to the recommendations. The program was reviewed and evaluated by specialists, including a rheumatologist, rehabilitation specialist and therapists, which ensured the high quality and safety of the intervention. After an 8-week home and work exercise program, patients with ankylosing spondylitis (AS) showed improvement in spinal mobility, pulmonary function and work capacity. The HWE group improved the range of lumbar flexion and cervical rotation, and both the HWE and HE groups improved the intermalleolar distance. The program proved effective in improving some aspects of spinal mobility, especially in patients who performed the exercises regularly, which affected the flexibility of the lumbar and cervical vertebrae. However, due to the short duration of the study (8 weeks), long-term effects could not be observed. Long-term studies are necessary. Exercise also improved lung function, especially in the HWE and HE groups, which showed better results in chest expansion and peak expiratory flow (PEF) than the control group. Breathing exercises combined with regular exercise may have helped improve lung function.

After the intervention, patients in the HWE and HE groups had lower levels of depression than the control group, although the differences were not statistically significant. Studies indicate that exercise can improve the psychological well-being of AS patients.

Exercise combining activity at work and at home significantly reduced the work disability of patients. The HWE group showed greater improvement compared to the control group in absenteeism and work impact. The program also had a positive effect on work performance. Despite the high dropout rate (22.7% in the HWE group), mainly due to difficulties in following the exercise plan, it is necessary to introduce more flexible methods tailored to the individual needs of patients. [2]

Conclusions

Ankylosing spondylitis is a chronic, inflammatory rheumatic disease that includes both radiographic (r-axSpA) and non-radiographic (nr-axSpA) forms. Studies show that both forms belong to the same disease spectrum and show similar disease burden and response to

treatment, although they differ in some clinical aspects, such as more frequent peripheral changes in nr-axSpA and more impaired mobility in r-axSpA. The ASDAS index is crucial in the diagnosis and monitoring of the disease, which, compared to BASDAI, takes into account both the subjective feelings of the patient and objective inflammatory markers, making it a more precise tool for assessing disease activity. Furthermore, the role of gut microbiota in the pathogenesis of axSpA is becoming an increasingly important research direction, suggesting potential therapeutic options.

Pharmacological treatment of AS primarily includes nonsteroidal anti-inflammatory drugs (NSAIDs) as the first line of therapy. If they are ineffective, biological treatment is used, including TNF-α inhibitors (e.g. adalimumab, infliximab) and IL-17 inhibitors (e.g. secukinumab, ixekizumab), which effectively reduce inflammation and improve patient functioning. Another new therapeutic option are JAK inhibitors (e.g. tofacitinib, upadacitinib), which may be effective in patients who are insensitive to TNFi and IL-17i.

Physical activity plays a key role in the treatment of axSpA, both in terms of maintaining spinal mobility and improving pulmonary function. Studies confirm that combining pharmacotherapy with individually tailored exercise programs, both aquatic and land-based, provides significant benefits in terms of reducing pain, improving quality of life and functioning of patients. Workplace and home exercise programs can also support work capacity and reduce occupational disability in patients with axSpA. In summary, axial spondyloarthritis is a complex disease that requires a multidisciplinary approach, combining pharmacotherapy, biological therapy, physical activity and potential interventions related to the gut microbiota. The optimal treatment strategy should be individualized, taking into account both disease activity and patient needs.

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Author's Contribution:

Conceptualization: KK, AB; methodology: JA, JM, MB; software: AM, KZ; check: JA, AŚ and WŚ; formal analysis: WŚ, AS, AB; investigation: KK, KS; resources: AM, JA, MB, AB; data curation: KK, KZ, AŚ, AS; writing - rough preparation: AB, AS, AM; writing - review and editing: KK, MB, JA, AB; visualization: JM, KZ, AŚ; supervision: KK, AB, AM; project administration: KK, AB, JA, AM, MA, AS;

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Informed Consent Statement

Not applicable.

Data Availability Statement

The data supporting this study is available within the article's bibliography.

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Conflict of Interest Statement

The authors declare no conflict of interest.

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