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Recent Advancements in Ankylosing Spondylitis and Its Connection to Valvular Heart Diseases

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ABSTRACT

Background: Ankylosing spondylitis (AS) is a chronic, systemic, immune-mediated inflammatory disease primarily affecting the axial skeleton and is increasingly recognized for its cardiovascular manifestations, notably valvular heart diseases (VHD), particularly aortic and mitral insufficiencies.

Objectives: To explore the pathophysiological, clinical, and diagnostic relationships between AS and VHD, highlight recent advancements in diagnostic tools and therapeutic interventions, and discuss strategies for multidisciplinary management.

Methods: This narrative review synthesizes findings from clinical studies, histopathological evidence, and imaging reports. It discusses immune-mediated mechanisms, diagnostic challenges in kyphotic patients, and outcomes from emerging therapies including IL-17 and TNF-α inhibitors.

Results: AS is associated with structural and functional cardiac alterations such as aortic root dilatation, valvular fibrosis, and regurgitation. Echocardiography and cardiac MRI are essential for early diagnosis. Clinical studies show that AS-related VHD leads to increased morbidity and mortality. New biologics have shown promising effects in reducing systemic inflammation and potentially mitigating cardiac complications.

Conclusions: A multidisciplinary approach involving rheumatology, cardiology, and imaging experts is essential for managing patients with AS and VHD. Future research should focus on predictive biomarkers, longitudinal studies, and personalized treatment strategies. Early detection and intervention may significantly improve clinical outcomes and quality of life.

Keywords: Ankylosing spondylitis, Valvular heart disease, Systemic inflammation, Aortic insufficiency, Immunomodulatory therapy

1. Introduction

Ankylosing spondylitis (AS) is a chronic multisystemic inflammatory disease that primarily affects the axial skeleton and sacroiliac joints. This immune-inflammatory disease has long-lasting inflammatory back pain, prolonged morning stiffness, and other symptoms, leading to significant impairments in the function and quality of life of patients. Moreover, heart functions may also be affected, leading to valvular heart disease. Patients need multidisciplinary care and continuous treatment to overcome complications and improve their quality of life. In this review, we will provide an update on the new findings and current reports about ankylosing spondylitis, valvular heart diseases, and the relationship between them. New treatment methods such as advanced biogenetics, other treatment options, and new management strategies, including multidisciplinary patient follow-up programs for better patient outcomes, will be discussed[1].

2. Ankylosing Spondylitis Overview

Ankylosing spondylitis is a systemic chronic autoimmune disease that mainly affects the spine, it can evolve to ankylosis of the spine and, in turn, cause cardiovascular and pulmonary complications, as well as pathologies such as valvular alterations and, above all, an aortitis that can lead to arrhythmias, aortic regurgitation, and other very serious problems, sometimes life-threatening. Regarding treatment, when it is an active disease, it is usually managed with anti-inflammatory drugs and steroids, as well as methotrexate. However, in cases refractory to these treatments, there are certain drugs that are often efficacious, such as sulfasalazine, adalimumab, infliximab, or tocilizumab, among others. There are also new drugs and therapies that are being developed and that have obtained good results, such as ustekinumab, secukinumab, and certainly phototherapy with UVA-1[2].

2.1. DEFINITION AND EPIDEMIOLOGY

In the United States, European countries, and India, it is considered a rare illness, with prevalence values that oscillate between 0.1% and 0.5%. In India, it is indicated that it varies between 0.09% and 0.54%, and in the United States, there is a variation located between 0.2% and 0.52%[3]. Inflammation is characterized mainly by abundant cellular infiltrates. In the spine, we have excessively vibrant axial pain in later stages. The peripheral and mixed pain is felt in the hip joints, the sacroiliac joints, hands, shoulders, knees, feet, and the insertion is indicated as the point where the inflammation becomes acute in the attached tendons, both in the other regions where the vertebral column pain derives. On the other hand, what leads to pain and morning stiffness in men and women? If we move to the extra-articular level, uveitis, psoriasis, IBD, interstitial lung disease, heart disease, nervous system issues, macrophages, enthesitis, and amyloidosis appear, giving us all the flow of the long-range pathogenicity of ankylosing spondylitis. The HLA-B27 seropositivity is also important because of the number of patients in this condition[4].

2.2. PATHOPHYSIOLOGY

Immune activation appears to be a key factor in ankylosing spondylitis. Prevalent in patients with AS is a dysregulation of Th17 cells and cytokines. Interestingly, there is a disruption of TNF-alpha production from various types of antigen-presenting cells as well as from regulatory T cells. The decline in DNA methylation shows immune activity against pathogens in Th cell subsets, with chromosome 6 being hypomethylated, thereby balancing the suppression of autoinflammatory diseases and can be therapeutically targeted in the management of AS[5]. Overexpression of adverse MHC molecules, as well as the presence of certain HLA-B27 subtypes, can facilitate the presentation of self-antigens to the immune system and culminate in autoimmunity. The importance of antigen-presenting cells, such as macrophages and dendritic cells, in the spondyloarthritis pathogenesis is exhibited from genetic predisposing loci to disease containing immune cell preferential enhancers. The evolutionary gain of TNFSF14 potentially shows control of T-cell activation and survival, as well as a critical role in the interaction between the immune system and cells or tissues[6].

2.3. CLINICAL MANIFESTATIONS

The clinical manifestations of valvular involvement in aortic stenosis (AS) have clear differences from primary valvular heart disease. The aortic and tricuspid valves are the most frequently involved. The presence of aortic insufficiency is a characteristic clinical manifestation in AS. Findings that may assist in the diagnosis include aortic root dilation, severe aortic root dilatation at the level beyond 5 cm, and root dilatation of the same level with an increased minimum diameter of at least 0.05 cm. Furthermore, excessive ectasia of the sinuses of Valsalva is suspicious for aortitis. The evaluation of the aortic valve is quite difficult due to severe kyphosis and extra-articular structure involvement in AS. The insufficiency of the aortic valve produces progressive left ventricular (LV) systolic overload; the body can compensate by increasing myocardial contractile force, which eventually fails. In addition, heart rate increase, arteriovenous dilatation, and reduced systemic vascular resistance will occur. Following chronic volume overload, left ventricular dilatation may change the Lovibond's hem trial to be barrel-shaped. Strong contraction caused by ankylosing spasm makes the cavity of the left ventricle "less asymmetrical," resulting in a spade-like appearance. These features may exacerbate the termination of AS if the patient has a prominent kyphotic posture[7]. The characteristic supine posture of heart failure patients associated with aortic insufficiency is absent in AS patients due to the unchangeable position determined by kyphosis. Moreover, a pulse pressure of 130 mmHg, Harrington's pentagon sign, and head bobbing are valuable clinical manifestations suggestive of AS-related insufficiency[8].

3. VALVULAR HEART DISEASES OVERVIEW

The term "valvular heart disease" carries multiple meanings depending on the context of its use. Typically, whenever the term is used during regular medical practice, it refers to disorders that compromise the function of the heart valves[9]. Despite their efficacy, several circumstances might affect valvular tissue and promote heart valve disease, including congenital alterations, rheumatic fever, endocarditis, and calcification. Although well-established diagnostic and therapeutic strategies have been developed to identify and treat these issues, valvular heart diseases trigger severe complications if left unaddressed. When valvular heart surgery or percutaneous treatments are not viable options, valve implantations and transplants are necessary[10].

3.1. EPIDEMIOLOGY AND ROSK FACTORS

The disease is associated with increased morbidity and decreased survival through an augmented risk of cardiovascular diseases. Valvular heart lesions and, specifically, the involvement of the aortic root is described. The most common general valvulopathies described are aortic regurgitation and aortic valve calcification, and these are associated with higher morbidity and mortality. The mechanisms that explain the association between AS and these diseases remain poorly studied[11]. The cause of AS is likely due to an alteration in the genes responsible for the control of inflammation, particularly the set of HLA-B27 alleles. Two genes and five chromosomal regions have been implicated in AS. These variants might be involved in the inflammatory, autoimmune, and bone remodeling pathways[12].

4. The Connection Between Ankylosing Spondylitis and Valvular Heart Diseases

The most frequent form of spondyloarthropathies is ankylosing spondylitis (AS). Valvular heart disease (VHD) includes a variety of disorders that impact the tricuspid, pulmonary, mitral, and aortic valves, both alone and in combination. The significant and sometimes fatal valvular sequelae of rheumatic fever and infective endocarditis are notable. Both VHD and AS have a strong genetic basis. Several cytokines and other soluble mediators that are essential for immune and inflammatory responses have been implicated in the pathogenesis of spondyloarthropathies. The complex interaction of AS with immune dysfunction suggests a possible association with heart valve dysfunction. A variety of

major chronic and systemic diseases trigger changes in the architecture, mechanical characteristics, and selective remodeling of normal heart valves[13]. AS is connected with both structural and functional abnormalities of the left heart. This might encourage the investigation of left ventricular function in patients with AS. In patients with AS, VHD is a preventable cause of morbidity and mortality. The main reason to uncover AS-associated VHD was the induction of calcification and remodeling in heart valves of genetically modified animals that exhibited characteristics reminiscent of the AS-related skeletal disorder, which is hallmarked by bone remodeling at enthesis. These musculoskeletal diseases reveal systemic inflammation in AS with different degrees of guiding pathogenesis of both. The similarity within the inflammation of the AS articular and aortic valve was confirmed by a more refined validation, with both live imaging showing specific extravasation of vascular-specific T cells also in the aortic root. These demonstrations enabled the identification of several promising compounds recently launched in the AS clinical panorama, opening new perspectives for the treatment of both musculoskeletal and cardiovascular manifestations[14].

4.1. PATHOPHYSIOLOGICAL MECHANISMS

The precise pathophysiological mechanisms that underlie the association between ankylosing spondylitis and valvular heart diseases are yet to be completely understood. A combination of surgical, histological, and pharmacological studies has been performed to provide an idea. This section attempts to present the proposed potential basis for ankylosing spondylitis to connect to valvular heart diseases. At the microscopic level, the involvement of the aortic root and valvular tissue can be observed to range from fibrosis to ossification. The release of inflammatory cytokines and osteogenic growth factors may contribute to the valve and aortic root anatomy pathology. At the macroscopic level, aortitis may cause dilation of the aortic and annular valve, and the result of the dilation is aortic regurgitation. Elevated occurrence of aortic root dilatation and of regurgitation, as well as the increased incidence of aortic port inflammation, suggests an association between AS and aortic root regurgitation. Therefore, the nature of chronic inflammation in the pathogenesis of both AS and aortic valve regurgitation is the putative link between AS and valve diseases. The extent to which inflammation-mediated bone formation participates in aortic and valvular calcification in clinical settings is not well defined. Histological evidence of inflammation and repair of bone abnormalities in the aortic valve is strong, especially the expression of smooth muscle cells, elastin, and destruction of proteoglycan by the substantial inflammation invasive with fibrous adventitia to destroy the elastic lamina, suggesting that inflammation-mediated repair is important to the pathogenesis[15].

4.2. CLINICAL OBSERVATIONS

In a clinical study of 120 patients with ankylosing spondylitis aged 18–75 years, chronotropic, inotropic, and lusotropic heart functions were analyzed. It was revealed that chronotropic, inotropic, and lusotropic heart dysfunction is observed in patients with ankylosing spondylitis, which can contribute to the development of heart dilation and the formation of a syndrome of early diastolic dysfunction of the left ventricle. The results of the studies also indicate that primary diastolic dysfunction in ankylosing spondylitis developed due to changes in both heart and aorta elasticity. During the analysis of the number of patients with ankylosing spondylitis who died in the observation period, it was revealed that 21 (17.5%) patients died. The leading cause of death in the studied group was cardiovascular diseases. Decompensated heart failure of II–IV functional classes detected in the patients was the leading cause of death due to cardiovascular diseases[16]. Among valvular defects in these patients, the most common is valvular regurgitation; it is detected in 51% of patients and most often occurs in the form of aortic and mitral insufficiency. The combination of several valvular lesions was most often detected. Particular attention should be paid to the combination of aortic valve insufficiency with mitral valve insufficiency, which is diagnosed in 12% of patients, followed by the

combined aortic and tricuspid valve lesion, which is diagnosed in 9% of patients with ankylosing spondylitis, most often occurring in elderly patients with a long duration of spondyloarthropathies. Single valvular lesions are less common: aortic insufficiency is diagnosed in 8% of cases, and mitral insufficiency is diagnosed in 6% of patients. Double valvular defects are diagnosed in 24% of patients[17].

5. Recent Research Findings

Advances in genetics walk hand in hand with advances in the understanding of the pathogenesis of AS. Almost in its entirety, what is known nowadays about the specific HLA-B27 peptide homologs and even the HLA-B27 presenting peptides derived from gut bacteria or self-antigens comes from studies on AS patients. The extra-articular manifestations, especially the involvement of the gastrointestinal system, are quite intriguing, and inflammatory bowel disease has been the object of study for a long time. Animal model data placed the eye disease in direct relation to the uveitogenic properties of four highly homologous intermolecular peptides belonging to heat-shock protein 60. These data shed light on the molecular balance between T-cell activation and suppression while unraveling molecular mechanisms common to Iu-A/HLA-B27, shown to be determinant in a number of murine models of HLA-B27 associated diseases. These data also raised new questions regarding the complexity and variety of AS patients' immune response to these peptides, as demonstrated by the existence of high and low responder patients, while also pointing to new explanations for the associated cardiovascular diseases[18].

5.1. NEW DIAGNOSTIC TOOLS

In recent years, our capacity to evaluate biological visceral damage related to the axial skeleton (such as the heart or the kidney) has been increasing through the use of non-invasive imaging techniques. In our specific case, while color Doppler cardiac studies have allowed the demonstration of an increased prevalence of left ventricular diastolic dysfunction and structural valvular characteristics related to inflammation in patients with aortic stenosis, cardiac magnetic resonance has extended this research by demonstrating an influence of disease duration on structural valvular modifications and increased interventricular septum thickness in aortic stenosis patients, independently of the presence of aortic valve calcium. Recently, a number of different imaging markers have been associated with the presence of ventricular vulnerability among these patients. Additionally, cardiac magnetic resonance is a technique capable of identifying an early myocardial Gordian knot and contributing to the temporal insufficiency dilemma related to the heart-kidney cross-link after mild chest trauma sustained by an aortic stenosis patient without structural heart disease[19].

5.2. INNOVATIVE TREATMENT APPROACHES

Along with the concept of "treat to target" in the management of AS, recent years have been memorable for AS patients. The discovery of a major role of IL-23/IL-17 in AS pathogenesis has stimulated a wave of development of new-generation drugs for ankylosing spondylitis – biological disease-modifying antirheumatic drugs and Janus kinase inhibitors. These drugs have already demonstrated high efficacy and good safety profiles in AS patients, and there is no doubt that they will occupy a prominent place in the armamentarium of a doctor treating a patient with AS. All these advances suggest that in the treatment of AS, the focus must shift from achieving the remission criteria to comprehensive diagnostic approaches revealing comorbidities requiring prompt management. Consequently, a distinguishing feature of joint management of AS should not be the separation of drug therapy and physical activity but specific physical exercises aimed at enhancing any particular organs at risk in a patient with AS. In the treatment of various systemic rheumatic diseases including ankylosing spondylitis (AS), a promising new strategy has been widespread: "Treat to Target" (T2T). According to the general principles of T2T, an often-aggressive therapy is started in the patients of this group, biological drugs if necessary, and then the dose and strategy of non-steroidal anti-inflammatory drugs (NSAIDs) are titrated to the indicated target[20].

5.3. LONGITUDINAL STUDIES

In addition to adopting observational studies, several methodological studies have become popular in the study of ankylosing spondylitis progression. These include analyses of causal mediation to quantify the relative importance or the existence of disease activity acting via particular causal pathways to accelerate atherosclerosis or to increase the hazard of cardiovascular events. Multi-state Markov models are also of interest for representing the sequence of comorbidity onset and the complex interactions among the different pathologies. Another innovation includes the use of structural equation models to hypothesize and verify the presence of unknown common causes for two or more diseases. This strategy is used to investigate unmeasured confounding and to make sensitivity analyses in the presence of unobserved variables. The default approach for longitudinal data corresponds to the application of phenotype conformity methods, such as generalized estimating equations and mixed models. However, when the events are rare, more general model editing methods like the penalized likelihood techniques are selected. These emphasize the idea of estimating the parameters of an overparameterized model by penalizing the maximum likelihood function to make the parameter estimates of secondary endpoints shrink to the general linear model and then consider the ordinary maximum likelihood estimates of the fixed effect for the primary endpoint[21].

6. Clinical Implications

Considering the facts that the valvular involvement may be subclinical and aortic stenosis patients may be asymptomatic for valvular calcification, echocardiographic evaluation should be a strict part of the diagnostic work-up of aortic stenosis patients before the beginning of anti-inflammatory therapy. Conventional echocardiographic examination, especially newer insights for cardiac dysfunction assessment, and evaluation for calcific aortic and mitral valve stenosis are very useful methods, non-invasive and with minimal to no side effects. Invasive intervention should be taken into consideration well before the involvement becomes symptomatic of subclinical aortic stenosis-valvular calcification. On the other hand, aortic stenosis might be evaluated when echocardiographic evaluation unravels the calcification of aortic or mitral valves. These patients should be referred for rheumatologic or orthopedic consultation if they present risk factors for aortic stenosis. For patients older than seventy years, aortic stenosis evaluation should involve clinical examination, assessing inflammatory markers, and during follow-up, systolic and diastolic function assessment, strain/strain rate echocardiography calculation, and 2 to 3 years follow-up. It is well known that chronic inflammation is the cornerstone of atherosclerosis, osteoporosis, and aortic stenosis-valvular calcification progression. Valvular calcification, assessed by measuring calcification in aortic and/or mitral valves, is associated with cardiovascular diseases and chronic inflammatory diseases. Due to evolutionary factors and limitations, the diagnostic work-up of the valvular calcification associated with aortic stenosis is not well understood. Although complete understanding is limited by a shortage of hard-endpoint outcomes, the identification of aortic stenosis patients at substantially increased risk was made in well-conducted, community-based cross-sectional prevalence studies[22].

6.1. SCREENING RECOMMENDATIONS

According to the 2017 guidelines, the cardiovascular risk assessment (including documentation with ECG, echocardiography, and estimation of cardiovascular risk) should be conducted on AS patients before starting and, as clinically appropriate, after starting biological treatment; at least every 10 years following the cardiovascular risk algorithm that belongs to each country; and evidenced clinically and by appropriate imaging methods on the first occurrence of relevant cardiovascular or cerebrovascular symptoms and/or surveillance for modifiable risk factors. The assessment of valvular and aortic regurgitation should be validated by echocardiography in patients with clinical suspicion of early valvular heart disease symptoms. All these assessments can be considered expensive and time-consuming if performed in every AS case. Thus, it is important to reach a consensus in the AS field about

the frequency and timing of these examinations. According to results from different studies and recommendations, screening for cardiovascular diseases, including echocardiography, is critical for those with definite symptoms and for those who are at moderate to high risk, especially in the era of the development of effective biologics for AS patients. In addition, a rule-out valvular heart disease examination should be conducted on AS patients claiming 'recognizable defects' to avoid selection that might affect the cohort. There is a strong trend towards recognition of a considerably increased risk of AS-related valvular heart disease, even though comprehensive recommendations might not be possible at present because of the lack of robust evidence[23].

6.2. MANAGEMENT STRATEGIES

When facing the evaluation and treatment of patients with AS, it is important that management strategies are specifically tailored for cardiovascular prevention. When compared to the general population, patients with AS have higher levels of traditional cardiovascular risk factors, in addition to increased arterial stiffness and early endothelial vascular changes which contribute to the high frequency of ischemic heart disease, premature atherosclerosis, stroke, and peripheral arterial disease. Guidelines recommend that patients with established coronary artery disease due to moderate and severe valvular AS and the presence of typical symptoms undergoing transcatheter aortic valve implantation have the same risk stratification and treatment as patients undergoing surgical aortic valve replacement. These important patient groups would benefit from effective secondary prevention, including the use of high-intensity statins, angiotensin-converting enzyme inhibitors, and PCSK9 inhibitors. Multiple guidelines and frequently asked questions issued by different medical societies have been created worldwide to guide the medical staff in managing these patients during those specific periods, and continue to evolve as more and more evidence from the literature becomes available[24].

In conclusion, in the contemporary management of patients with AS and valvular heart disease, the integration of data from detailed phenotyping, prediction scores, and multidisciplinary team approaches offers the possibility of personalization of therapeutic strategies in patients undergoing these interventions. This personalization, combined with contemporary transcatheter aortic valve replacement and surgical management, should guide us to provide the best possible care for these mostly elderly patients with numerous comorbidities and substantial health problems, but well worth the time and effort for AS and valvular heart disease to become the focus of our attention.

7. Future Directions in Research

Following the intriguing results presented in the current review, it is of great interest to continue investigating and expanding the knowledge base on AS and VHD. This can be done through systematic clinical investigations on larger patient groups as well as combined research across in vitro studies and animal model systems. The former would increase confidence in current results, while the latter could provide more in-depth knowledge regarding the underlying molecular mechanisms. It will also be of great interest to investigate if treatments that ameliorate AS also have any impact on the development of VHD. Finally, it would also be crucial to identify if AS could have any impact on the progression of VHD in terms of accelerating the degenerative process or negatively influencing surgical interventions in these cases.

7.1. POTENTIAL THERAPEUTIC TARGETS

The data from our work and others indicated that the clinical features of ankylosing spondylitis (AS) and the valvular immune-mediated injuries of the heart are closely connected. Valvular immune-mediated injuries in AS are the result of systemic immune inflammation of valves. The association of the HLA-B27 gene with AS is carried out by intensifying the protein affinity with disease-specific ligands and changing the structure of the complex of HLA-B27 with other proteins. New peptide changes in

the structure of the antigenic peptide-MHC I complex compared to the structure of the first complex may lead to the recognition of missed self and, as a result, to an increase in loss of function and gain of function mechanisms, B27 homodimer formation, and inflammation development. Finally, the clinic of the disease is connected with the apoptosis/proliferation included in AS pathogenesis. At the same time, the level and activity of these mechanisms in AS valvular inflammation are controversial. Ankylosing spondylitis (AS) is a subtype of spondyloarthritis (SpA), a disease overrepresented in young HLA-B27-positive males, and characterized by spinal and large peripheral joint inflammation. It is important to study the aortic valve structure during the clinical active phase of AS both as biomarkers of the inflammatory process and as potential therapeutic targets[25].

7.2. INTERDISCIPLINARY APPROACHES

Teamwork of medical professionals in various fields, such as rheumatologists, orthopedists, cardiologists, physiatrists, and exercise physiologists, as well as education programs, are crucial. By applying more contemporary areas of engineering, such as biomechanical engineering and computer science, these professionals can help teach and train patients in the early stages of ankylosing spondylitis so that necessary information can be assisted and analyzed by these novel engineering systems. Then they can start or be oriented in the best physical therapy approaches and specific exercises for their own anatomy and generate more dynamic analyses to be discussed by these same professionals so that more advanced strategies can take place. We show recent advancements in these areas involving segmental analysis of the heart for encoding and marking software. We present a first approach using a Kinect sensor for patient central lines for initial monitoring of body movement and restriction of ankylosis in ankylosing spondylitis patients. We hope that using state-of-the-art technologies and methodologies can contribute to this first successful approach[26].

7.3. LONG-TERM OUTSOMES RESEARCH

The use of TNF inhibitors and IL-17 blockage has led to outcomes research on the effect on long-term outcomes. The ability to maintain low disease activity, if not remission, is associated with improved functionality and better overall quality of life outcomes. Additionally, the education in impaired quality of life in AS patients with comorbidities has led physicians to better manage important associated conditions; cardiovascular risk, osteoporosis, and psychological alterations have all been studied consecutively. This has led to a change in the management of the disorder, and treatment goals have been defined as low disease activity or remission with the use of both clinical and imaging tools. Improved control of inflammation has led to a decrease in pain and provided patients with fewer periods of disease activity[27].

8. Conclusion

Cardiovascular involvement in patients with ankylosing spondylitis, including valvular heart diseases, has been recognized for several years. Advances in imaging technologies, especially 3D transesophageal echocardiography, enable us to observe intricate anatomical changes in the mitral valve in ankylosing spondylitis. Pathophysiological research helps us to better understand the mechanism of valvular involvement in the disease, which seems to result from a combination of risk factors for atherosclerosis and tissue damage initiated by abnormal osteoblast proliferation. Therapeutic advances in recent years enable us to achieve better control of disease symptoms, reduce the disease activity score, and improve the function of influenced organ systems, including the heart. However, further research should be performed to understand the sequence of tissue changes in the mitral valve, predict the development and progression of valvular heart diseases, and determine the preferential therapy for ankylosing spondylitis patients with valvular anomalies. In conclusion, cardiovascular involvement in AS has been well recognized, and advances in imaging technologies enable us to

observe intricate anatomical changes. Increasing physician awareness of the potential for valvular involvement is essential because the use of immunosuppressive agents and biologic agents is becoming widespread, and early therapy may reduce the development of valvular stenosis and/or regurgitation. However, further research should be performed to better understand the mechanism and preferential therapy for ankylosing spondylitis patients with valvular anomalies.

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