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Review

Rheumatic Diseases and Heart

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ABSTRACT

Rheumatic diseases may increase the risk of developing several cardiovascular comorbidities. The increased cardiovascular disease risk in patients with systemic rheumatic diseases is conditioned, partially, by the presence of cardiovascular risk factors such as age, gender, family history, smoking, sedentary lifestyle, and dyslipidemia. However, the inflammatory nature of rheumatic diseases, the shared pathophysiological pathways, and the side effects of antirheumatic therapies have an association with cardiac events. Early diagnosis and treatment are the main key points in preventing future comorbidities.

Keywords: Rheumatoid arthritis, ankylosing spondylitis, cardiac involvement, vasculitis, psoriatic arthritis

INTRODUCTION

Rheumatic diseases are generally examined in three different classes; joint diseases, autoimmune connective tissue diseases, and vasculitides. They progress with significant cardiac involvement in all three groups. Cardiac involvement may present in a spectrum ranging from asymptomatic, mild, or subclinical to serious disease with a risk of mortality and morbidity. Cardiac manifestations in rheumatic diseases are frequently encountered as pericardial, myocardial, and endocardial involvement, atherosclerosis and ischemic heart disease, cardiomyopathy, heart failure, or cardiac conduction system involvement that may cause arrhythmias. This review aims to discuss the impact of main rheumatologic diseases on the heart.

Rheumatic Joint Diseases

Rheumatoid arthritis: The most common chronic inflammatory polyarthritis is rheumatoid arthritis (RA). It mostly occurs between the 4th and 6th decades. Its incidence in the community varies between 0.5-1% and is observed approximately 3 times more frequently in women. Inflammatory involvement of the joints and cardiovascular complications are important causes of morbidity in these patients. Symmetrical involvement of three or more joints (usually hand and foot joints) is a disease characterized by >90% rheumatoid factor positivity and 80-90% anti-citrulline cyclic peptide antibody positivity and an increase in acute phase reactants. Besides heart and vascular involvement, eye, lung, and kidney involvement are also observed (1). Today, ischemic heart diseases and heart failure secondary to coronary atherosclerosis are the most common causes of mortality in this group of patients. The most common form of cardiac involvement is pericarditis. Pericardial effusion is frequently seen on echocardiography (ECHO) and is seen in approximately 35-40% of patients. In addition, nodules in the heart valves, tricuspid regurgitation, aortic stenosis, mitral regurgitation, mitral and aortic valve thickening/calcifications, mitral valve prolapse, atrial fibrillation and prolonged QT interval can be found in the electrocardiogram. While myocarditis and myocardial fibrosis related to RA are less common, cardiac amyloidosis is rare. Changes in the heart valves usually cause an asymptomatic clinic. Patients with a diagnosis of RA present to the cardiology outpatient clinic with symptoms of cardiac pump failure and advanced heart failure. The incidence of heart failure in patients with RA over 80 years of age is 36%, which means that heart failure is twice as high as in individuals of similar age without a diagnosis of RA (2-4). While the cause of heart failure in individuals over 80 years without a diagnosis of RA is 77% of classical cardiovascular risk factors,

this rate is 54% in patients with a diagnosis of RA. This difference may be due to other risk factors associated with RA, such as myocarditis or heart valve disease (4).

The risk of AF is slightly increased in RA patients (3-4%), and it has no effect on mortality. Prolongation in the QT interval, which is a parameter that can be used to predict the risk of cardiovascular mortality, is observed in 48% of patients with RA, and this is more common than in the normal population (5).

Spondyloarthritis (Ankylosing spondylitis, psoriatic arthritis, reactive arthritis): Spondyloarthropathies are a group of diseases that share similar clinical symptoms and findings and similar genetic predispositions to the family of inflammatory rheumatological diseases. This group of diseases is divided into subgroups diseases according to their clinical presentations, and the most common one is ankylosing spondylitis (AS), also known as Bechterew's disease (6). Other subgroup diseases are psoriatic arthritis with a psoriatic picture and reactive arthritis with inflammatory bowel disease or infections. Psoriatic arthritis often progresses with peripheral joint involvement. Other typical organ involvements are the eye (often anterior uveitis) and less commonly the heart.

Typically in ankylosing spondylitis, aortitis, aortic regurgitation, myocardial fibrosis, coronary artery disease, aortic lump formation in the aorta adjacent to the mitral anterior valve, left ventricular dysfunction and heart failure, cardiac conduction system disorders (2nd and 3rd degree atrioventricular [AV] blocks, ventricular involvement such as early beats can be observed) (7). Additionally, the increased risk of mortality in ankylosing spondylitis is primarily associated with cardiovascular involvement. The standardized death rate in these patients is slightly higher in men than in women, and 40% of these deaths are due to cardiovascular causes (8). The pathoanatomical findings of ankylosing spondylitis involve subaortic structures such as ascending aorta and aortic root involvement, membranous part of the interventricular septum, or involvement of mitral anterior valve that may cause mitral regurgitation can be observed (9). Likewise, cardiac conduction system disorders are frequently observed in patients with AS (10). Although aortitis is not observed very frequently nowadays, it can be observed in combination with typical aortic regurgitation due to aortic valve involvement in AS patients. The frequency of aortitis varies between 3-18%, depending on the age and duration of the disease. Therefore, AS patients frequently go to aortic valve surgery as valve surgery (11). Histologically, focal destruction of the media layer of the aortic wall is accompanied by the histopathologically characteristic feature of aortitis, which is a thickening of the intimal and adventitial layers and resulting vascular narrowing. Fibrotic thickening of the aorta and aortic valve may progress under the valve over time and cause a subaortic lump. The frequency of severe cardiac conduction disturbance, especially high-grade AV block, and severe bradyarrhythmias, was observed in AS with a frequency of 5%. This outcome was associated with HLA (Human Leukocyte Antigen) B27 positivity, and in most cases with HLA-B27 positivity, involvement of the AV node was observed and mostly a pacemaker was needed. The risk of AV block may also occur in healthy individuals with HLA-B27 positivity and aortic insufficiency (10). In addition, HLA-B27 positivity was observed at a higher rate in those with pacemakers than in normal individuals (12).

In psoriatic arthritis, unlike AS, the prevalence of cardiac conduction defect or valve involvement did not increase compared to the normal population. While disorders due to HLA-B27-related aortic valve and AV node involvement that develop after streptococcal infection are now defined as reactive arthritis, they were called Reiter's syndrome in the past. Cardiac involvement and acute rheumatic fever in reactive arthritis are less common in developed countries than in developing and underdeveloped countries (13).

There are limited data on cardiovascular, gastrointestinal, or renal risks associated with using non-steroidal anti-inflammatory drugs (NSAIDs) in treating patients <50 years of age with a diagnosis of AS or psoriatic arthritis. These risks have been observed more commonly among elderly individuals. Heart failure, kidney failure, or a history of peptic ulcer are predisposing factors for the development of NSAID-related complications. Except for those mentioned, no increase in risk has been observed with short-term or continuous high-dose NSAID use (14). The results of two independent studies conducted on AS patients, increased mortality was observed with low-dose NSAID intake rather than with those taking high-dose NSAIDs (8,15). These results suggest that NSAID use may be beneficial in patients with chronic inflammatory disease, after considering and evaluating other risk factors.

Autoimmune Connective Tissue Diseases

Idiopathic inflammatory myopathies (IEM) such as systemic lupus erythematosus (SLE), scleroderma (progressive systemic sclerosis (PSS), dermatomyositis and polymyositis, and mixed connective tissue disease are diseases in this group that can involve all layers of the heart. The diagnosis of this group of diseases is made by the presence of autoantibodies (such as antinuclear antibody [ANA], extractable nuclear antigen, and anti-double-stranded DNA) together with the findings of extracardiac involvement such as skin and joint involvement.

The prevalence of myocarditis is 10% in SLE and PSS, and

25% in IEM (16). The earlier echocardiographic finding of myocarditis is usually a regional wall motion defect. The gold standard diagnostic method for myocarditis is an endomyocardial biopsy. Regional edema, late-phase involvement, and wall motion defect detected in cardiac magnetic resonance (MR) imaging (which is a non-invasive method) helps to diagnose myocarditis at an early stage. Cardiac involvement in PSS can progress with myocardial fibrosis together with myocarditis. Poor prognosis can be observed in patients due to the presence of myocardial fibrosis, arrhythmia, and right heart failure secondary to pulmonary hypertension, which is known as 'scleroderma heart disease' (17). A right heart catheterization will be useful in guiding the diagnosis and treatment of pulmonary hypertension in those individuals.

Pericarditis can be observed in any connective tissue disease. It is most frequently observed in SLE, with a frequency of 25-39%. Mitral valve involvement is typically observed as nonbacterial verrucous endocarditis (Libman-Sacks) in SLE. Antiphospholipid antibody levels should be measured to detect these valvular deposits associated with SLE. It has been determined that there is an increased risk of congenital complete AV block in pregnant women with the presence of anti-SS-A/Ro autoantibodies, and this conduction system defect is permanent in a few (2%) cases (18).

Vasculitis

Vasculitic autoimmune diseases are characterized by partial or complete ischemia, necrosis or bleeding of blood vessel walls, in a manner of cellular inflammation. Anti-neutrophil cytoplasmic antibodies (ANCAs) can be found in granulomatous polyangiitis (GPA or Wegener's disease), microscopic polyangiitis, and some eosinophilic granulomatous polyangiitis (EGPA/Churg-Strauss disease). In the cases of giant cell arteritis (Horton's disease) and Takayasu arteritis (TA) ANCAs are absent. Cardiac involvement can be seen with a frequency of 5-25% in systemic vasculitides. Pericarditis, myocarditis, endomyocardial fibrosis, coronary ischemia due to vasculitis, valve insufficiency, and arrhythmias may occur as a result of cardiac involvement.

Malignant hypertension is common in polyarteritis nodosa (PAN), which is more common in chronic hepatitis B (HBV) patients. Compared to giant cell arteritis, cardiac findings such as aortic insufficiency, aortic aneurysm, vasculitis-related ischemia, and pump failure can be seen in TA, often at younger ages (19).

Other Rheumatological Diseases

Still's disease is less frequent and its typical findings are polyserositis and fever, and pericarditis frequently occurs (20-30%). In Behçet's disease, cardiac involvement is between 7-46% and generally causes pericarditis. Constrictive pericarditis, which can sometimes cause hemorrhagic tamponade, is also seen. Again, in more than half of Behçet's patients, intracardiac thrombus formation (often in the right atrium) is the first manifestation (20,21). Coronary vasculitis and aortitis causing aortic aneurysm and aortic regurgitation can be found in Behçet's patients and cardiac surgical aortic valve replacement may be necessary in some cases. Although secondary amyloidosis is seen less frequently in rheumatic diseases due to inadequate treatment or long-term development, AA type amyloid deposits can cause heart failure (22,23).

CARDIOVASCULAR COMORBIDITY IN RHEUMATOLOGICAL DISEASES

All-cause mortality, myocardial infarction rate, heart failure, and ischemia-induced revascularization rate are more prevalent in RA compared to other rheumatologic diseases (24). Additionally, 80% of RA patients have at least one classic cardiovascular risk factor. Arterial hypertension is observed with a frequency of 57% in RA patients (25). The incidence of cardiovascular events has also increased in AS and psoriatic arthritis. The risk of mortality in AS is increased due to the presence of cardiovascular morbidity and multiple risk factors (26).

In patients with connective tissue disease, the atherosclerotic process progresses faster and may cause myocardial infarction at earlier ages. Atherosclerotic vasculopathy is observed more frequently in this group of patients due to innovations in treatment and increased life expectancy due to conditions. Although classical cardiovascular risk factors are responsible for approximately half of the cardiovascular diseases in these patients, the treatment of cardiovascular risk factors plays an important role in reducing mortality and morbidity. Early diagnosis is important in cardiac involvement of some rheumatic diseases such as SLE, and computed tomography is a useful method for detecting calcium deposits. Cardiac MRI is the best method for detecting inflammatory changes (27).

It has been reported that the use of statins in the treatment to reduce CV morbidities reduces mortality in RA patients. It has also been suggested that the use of high-dose statins reduces the risk of developing RA (28).

MANAGEMENT OF CARDIOVASCULAR DISEASES IN RHEUMATOLOGICAL DISEASES

Diagnostic tests should definitely be requested in cardiovascular involvement of rheumatological diseases, especially in the involvement of diseases such as SLE and polymyositis, such as pericarditis and myocarditis. Routine echocardiography should be performed annually to detect early pulmonary hypertension and heart failure in some autoimmune diseases such as scleroderma. In

addition, NT-pro BNP measurement in controls will also help in diagnosing heart failure in these patients (29). Likewise, ECHO should be performed every 1-2 years in the early detection of aortic valve disease that may occur in AS patients. The main treatment in direct inflammatory involvement of rheumatological diseases such as pericarditis, myocarditis, and vasculitis is high-dose glucocorticoid therapy and antirheumatic drugs such as methotrexate, and azathioprine. Methotrexate is one of the rare drugs proven to increase survival by reducing cardiovascular mortality in RA patients. A good response is obtained from new-generation drugs such as tocilizumab and rituximab, which are used in severe cases (30-33). Conventional treatment methods used in cardiology are used in practice for other cardiac conditions and comorbidities in rheumatologic diseases.

CONCLUSION

Cardiac involvement is a consequence of systemic inflammation which occurs in RA, AS, SSc, and SLE with different prevalences and is commonly silent. Inflammatory rheumatic diseases can affect all cardiac structures; the myocardium, cardiac valves, pericardium, conduction system, and arterial vasculature. The increased risk of cardiac mortality, prevention of comorbidities, and surveillance is crucial in patients with rheumatic diseases.

Early diagnosis and effective management of cardiac involvement are essential in inflammatory rheumatic diseases. Electrocardiographic and echocardiographic assessments should also be executed as routine evaluations.

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REFERENCES

1.Agca R, Heslinga SC, van Halm VP, Nurmohamed MT. Atherosclerotic cardiovascular disease in patients with chronic inflammatory joint disorders. *Heart*. 2016;102(10):790-795. doi:10.1136/heartjnl-2015-307838
2.Kobayashi Y, Giles JT, Hirano M, et al. Assessment of myocardial abnormalities in rheumatoid arthritis using a comprehensive cardiac magnetic resonance approach: a pilot study. *Arthritis Res Ther*. 2010;12(5):R171. doi:10.1186/ar3131
3.Myasoedova E, Crowson CS, Nicola PJ, et al. The influence of rheumatoid arthritis disease characteristics on heart failure. *J Rheumatol*. 2011;38(8):1601-1606. doi:10.3899/jrheum.100979
4.Crowson CS, Nicola PJ, Kremers HM, et al. How much of the increased incidence of heart failure in rheumatoid arthritis is attributable to traditional cardiovascular risk factors and ischemic heart disease?. *Arthritis Rheum*. 2005;52(10):3039-3044. doi:10.1002/art.21349
5.Kim SC, Liu J, Solomon DH. The risk of atrial fibrillation in patients with rheumatoid arthritis. *Ann Rheum Dis*. 2014;73(6):1091-1095. doi:10.1136/annrheumdis-2013-203343
6.Braun J, Sieper J. Ankylosing spondylitis. *Lancet*. 2007;369(9570):1379-1390. doi:10.1016/S0140-6736(07)60635-7
7.Lautermann D, Braun J. Ankylosing spondylitis--cardiac manifestations. *Clin Exp Rheumatol*. 2002;20(6 Suppl 28):S11-S15.
8.Bakland G, Gran JT, Nossent JC. Increased mortality in ankylosing spondylitis is related to disease activity. *Ann Rheum Dis*. 2011;70(11):1921-1925. doi:10.1136/ard.2011.151191
9.Roldan CA, Chavez J, Wiest PW, Qualls CR, Crawford MH. Aortic root disease and valve disease associated with ankylosing spondylitis. *J Am Coll Cardiol*. 1998;32(5):1397-1404. doi:10.1016/s0735-1097(98)00393-3
10.Bergfeldt L, Insulander P, Lindblom D, Möller E, Edhag O. HLA-B27: an important genetic risk factor for lone aortic regurgitation and severe conduction system abnormalities. *Am J Med*. 1988;85(1):12-18. doi:10.1016/0002-9343(88)90497-4
11.Bulkley BH, Roberts WC. Ankylosing spondylitis and aortic regurgitation. Description of the characteristic cardiovascular lesion from study of eight necropsy patients. *Circulation*. 1973;48(5):1014-1027. doi:10.1161/01.cir.48.5.1014
12.Bergfeldt L, Edhag O, Vedin L, Vallin H. Ankylosing spondylitis: an important cause of severe disturbances of the cardiac conduction system. Prevalence among 223 pacemaker-treated men. *Am J Med*. 1982;73(2):187-191. doi:10.1016/0002-9343(82)90177-2
13.van der Helm-van Mil AH. Acute rheumatic fever and poststreptococcal reactive arthritis reconsidered. *Curr Opin Rheumatol*. 2010;22(4):437-442. doi:10.1097/BOR.0b013e328337ba26
14.Kroon FP, van der Burg LR, Ramiro S, et al. Non-steroidal anti-inflammatory drugs (NSAIDs) for axial spondyloarthritis (ankylosing spondylitis and non-radiographic axial spondyloarthritis). *Cochrane Database Syst Rev*. 2015;2015(7):CD010952. Published 2015 Jul 17. doi:10.1002/14651858.CD010952.pub2
15.Haroon NN, Paterson JM, Li P, Inman RD, Haroon N. Patients With Ankylosing Spondylitis Have Increased Cardiovascular and Cerebrovascular Mortality: A Population-Based Study. *Ann Intern Med.* 2015;163(6):409-416. doi:10.7326/M14-2470
16.Mavrogeni S, Dimitroulas T, Kitas GD. Multimodality imaging and the emerging role of cardiac magnetic resonance in autoimmune myocarditis. *Autoimmun Rev*. 2012;12(2):305-312. doi:10.1016/j.autrev.2012.05.005
17.Ferri C, Valentini G, Cozzi F, et al. Systemic sclerosis: demographic, clinical, and serologic features and survival in 1,012 Italian patients. *Medicine (Baltimore)*. 2002;81(2):139-153. doi:10.1097/00005792-200203000-00004
18.Crozier IG, Li E, Milne MJ, Nicholls MG. Cardiac involvement in systemic lupus erythematosus detected by echocardiography. *Am J Cardiol*. 1990;65(16):1145-1148. doi:10.1016/0002-9149(90)90329-y
19.Knockaert DC. Cardiac involvement in systemic inflammatory diseases. *Eur Heart J*. 2007;28(15):1797-1804. doi:10.1093/eurheartj/ehm193
20.Gerfaud-Valentin M, Sève P, Iwaz J, et al. Myocarditis in adult-onset still disease. *Medicine (Baltimore)*. 2014;93(17):280-289. doi:10.1097/MD.0000000000000112
21.Geri G, Wechsler B, Thi Huong DL, et al. Spectrum of cardiac lesions in Behçet disease: a series of 52 patients and review of the literature. *Medicine (Baltimore)*. 2012;91(1):25-34. doi:10.1097/MD.0b013e3182428f49
22.Mogulkoc N, Burgess MI, Bishop PW. Intracardiac thrombus in Behçet's disease: a systematic review. *Chest*. 2000;118(2):479-487. doi:10.1378/chest.118.2.479
23.Lachmann HJ, Goodman HJ, Gilbertson JA, et al. Natural history and outcome in systemic AA amyloidosis. *N Engl J Med*. 2007;356(23):2361-2371. doi:10.1056/NEJMoa070265
24.Ogdie A, Yu Y, Haynes K, et al. Risk of major cardiovascular events in patients with psoriatic arthritis, psoriasis and rheumatoid arthritis: a population-based cohort study. *Ann Rheum Dis*. 2015;74(2):326-332. doi:10.1136/annrheumdis-2014-205675
25.Chung CP, Giles JT, Petri M, et al. Prevalence of traditional modifiable cardiovascular risk factors in patients with rheumatoid arthritis: comparison with control subjects from the multi-ethnic study of atherosclerosis. *Semin Arthritis Rheum*. 2012;41(4):535-544. doi:10.1016/j.semarthrit.2011.07.004
26.Szabo SM, Levy AR, Rao SR, et al. Increased risk of cardiovascular and cerebrovascular diseases in individuals with ankylosing spondylitis: a population-based study. *Arthritis Rheum*. 2011;63(11):3294-3304. doi:10.1002/art.30581
27.Lin K, Lloyd-Jones DM, Li D, et al. Imaging of cardiovascular complications in patients with systemic lupus erythematosus. *Lupus*. 2015;24(11):1126-1134. doi:10.1177/0961203315588577
28.Schoenfeld SR, Lu L, Rai SK, Seeger JD, Zhang Y, Choi HK. Statin use and

mortality in rheumatoid arthritis: a general population-based cohort study. *Ann Rheum Dis*. 2016;75(7):1315-1320. doi:10.1136/annrheumdis-2015-207714
29.Thakkar V, Stevens W, Prior D, et al. The inclusion of N-terminal pro-brain natriuretic peptide in a sensitive screening strategy for systemic sclerosis-related pulmonary arterial hypertension: a cohort study. *Arthritis Res Ther*. 2013;15(6):R193. doi:10.1186/ar4383
30.Duru N, van der Goes MC, Jacobs JW, et al. EULAR evidence-based and consensus-based recommendations on the management of medium to high-dose glucocorticoid therapy in rheumatic diseases. *Ann Rheum Dis*. 2013;72(12):1905-1913. doi:10.1136/annrheumdis-2013-203249
31.Krause D, Schleusser B, Herborn G, Rau R. Response to methotrexate treatment is associated with reduced mortality in patients with severe rheumatoid arthritis. *Arthritis Rheum*. 2000;43(1):14-21. doi:10.1002/1529-0131(200001)43:1<14::AID-ANR3>3.0.CO;2-7
32.Lutman C, Finocchiaro G, Abate E, Milo M, Morassi P, Sinagra G. Purulent pericarditis in rheumatoid arthritis treated with rituximab and methotrexate. *J Cardiovasc Med (Hagerstown)*. 2014;15(12):880-882. doi:10.2459/JCM.0000000000000160
33.Yoshida S, Takeuchi T, Sawaki H, Imai T, Makino S, Hanafusa T. Successful treatment with tocilizumab of pericarditis associated with rheumatoid arthritis. *Mod Rheumatol*. 2014;24(4):677-680. doi:10.3109/14397595.2013.874733